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ANNOTATED BIBLIOGRAPHY IN RADIOBIOLOGY

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I

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FOREWORD

Biological scientists, in considerable numbers, continue to be drawn into the field of radiobiology, either as a full-time vocation or as an adjunct to other biological activities. And more and more graduate students are preparing for careers in which knowledge of the biological effects of radiation is of the utmost importance.

This annotated bibliography was initially conceived as a reading guide for those seeking orientation in a complex and rapidly growing field of scientific interest. It still will serve this original purpose, but its scope has been broadened to increase its usefulness as a work of reference, so that it may find a place on the shelves of those who are already established in the field which it represents.

It will be noted that the volume omits consideration of tracer studies on topics not directly concerned with the biological effects of radiation. In the opinion of the editors, this is a desirable limitation, but opinion to the contrary will be given due consideration.

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III

REFERENCES

I GENERAL INFORMATION

1

Behrens, C. F. ed. **ATOMIC MEDICINE**. Thomas Nelson and Sons, New York. 1949.

This collection of 21 articles includes a few general discussions of nuclear theory, but most of the material relates to biological and medical application of nuclear research. Thus, among the topics treated are radiobiology and pathology, the hematology of irradiation, radiation illness, the detection and measurement of radiations, atomic disaster planning, tracer methods in biology, radio-phosphorus and radioiodine, radioisotopes of medical interest, radiation effects in dentistry, and research in atomic medicine. Symbols, units, and definitions pertaining to the subject are given in a three-page appendix. A 21-page table of isotopes and their half-lives and emissions is also given. (NSA)

2

Bliss, R. W. **WHAT YOU SHOULD KNOW ABOUT THE ATOMIC BOMB. A MESSAGE FROM THE SURGEON GENERAL**. Army Medical Department, Washington, D. C. Revised 1950.

This pamphlet contains the following series of articles based on lectures delivered during a course in atomic medicine sponsored by the Armed Forces Special Weapons Project: I. Introduction to Nuclear Physics; II. Biologic Effects of Nuclear Radiation from an Atomic Explosion; III. Medical Effects of Atomic Explosion; IV. The Doctor's Problem in Atomic Warfare; V. The Atomic Explosion; VI. Fundamentals of Radiation Pathology; VII. Pathologic Anatomy of Radiation Effects of Atomic Explosion; VIII. Detection of Overexposure to Ionizing Radiation; IX. Public Health Aspects of Atomic Explosion; X. Psychological Factors in Atomic Warfare; XI. Essentials of Instrumentation; XII. Protection Against Atomic Bombs. (NSA)

3

Bloom, William, ed. **HISTOPATHOLOGY OF IRRADIATION FROM EXTERNAL AND INTERNAL SOURCES**. National Nuclear Energy Series, Division IV, Volume 22H, McGraw-Hill Book Company, Inc., New York. 1948.

This volume was prepared by the Histological Group of the Health Division at the University of Chicago. It covers a wide variety of experiments and gives detailed information on techniques and materials. Among the radioactive agents used in these experiments were β and γ rays, fast and slow neutrons, and x-rays to establish a base line for comparison. The effects of sodium 24, carbon 14, yttrium 91, radium and many others were studied. The isotopes were administered intramuscularly, intravenously, intracardially, or intraperitoneally. The volume describes the histopathological and cytological effect of radioactive agents in the cells, skin, bone, bone marrow, spleen, lymph node and intestinal lymphatic tissue, the thymus, gastrointestinal tract, testis, ovary, kidney, lung, vascular system, adrenal, nervous system, etc. (NSA)

4

British Mission to Japan. **THE EFFECTS OF THE ATOMIC BOMBS AT HIROSHIMA AND NAGASAKI**. [nd] 34p. (NP-1156)

Report by the British Mission to Japan on Hiroshima and Nagasaki three months after the bombing of these two cities. Includes sections on the two cities before the attack; the two cities after the attack; the action of the atomic bomb; blast effects; heat effects; radio-active effects; casualties; conclusions. (S.V.S.)

5

Brues, Austin M. **ISOTOPES: RADIOACTIVE; TOXICITY**, Volume 2, p.465-71 of **MEDICAL PHYSICS**, O. Glasser, ed. The Year Book Publishers, Inc., Chicago. 1950.

Discussion nature of the hazards, chronic radiation toxicity, changes induced by isotopes, dosimetry and clinical use of isotopes. (R.D.B.)

6

Clark, George L. **A SURVEY OF THE BIOLOGICAL EFFECTS OF X-RADIATION**. *Radiology* 26, 295-312(1936).

A summary of the biological effects of radiation, to date, under the following headings: Bactericidal and general lethal effects; Biologic dosimeters; Effects on the hereditary material; Effects on normal cells; Radiosensitiveness of cells; Recovery and the time factor; X-ray effects on human tissues; Stimulating effect of X-rays; Photochemical experiments with a possible bearing on biologic effects; Medical implications of cell radiosensitivity and reactions to radiation with special reference to cancer; and a new X-ray method of pathologic diagnosis. (S.V.S.)

7

Clark, Janet Howell. **THE BIOLOGICAL EFFECTS OF RADIATION**. *Ann. Rev. Physiol.* 1, 21-40(1939).

A review, chiefly of work published between January 1936 and July 1938. 94 references. (V.E.)

8

Copp, D. Harold. **RESEARCH AND TRAINING FACILITIES FOR RADIOBIOLOGY AND FOR USE OF ISOTOPES IN BIOLOGY AND MEDICINE IN THE UNITED STATES AND CANADA**. National Research Council, Washington, D. C. 1950.

The book lists personnel and facilities for research, clinical use, training and health protection and lists isotopes employed in various projects. 151 pages. (R.D.B.)

9

Cronkite, Eugene P. **THE DIAGNOSIS OF IONIZING RADIATION INJURY BY PHYSICAL EXAMINATION AND CLINICAL LABORATORY PROCEDURES**. Naval Medical Research Institute. Apr. 8, 1948. 15p. (NP-573; Report No. 8; NM-007-039)

The symptomatology and diagnosis of acute and chronic radiation illness is discussed. Characteristic symptoms of the acute illness are nausea, vomiting, diarrhea, hemorrhagic manifestations, agranulocytosis followed by non-purulent necrotizing infections, and epilation. The blood picture is the most sensitive biologic index of exposure to ionizing radiation. Lymphocytopenia appears promptly after the single intense exposure. The symptomatology and blood picture of chronic exposure is protean. In order to evaluate the blood changes of chronic exposure, rigid control data must be established. The most significant blood change following chronic exposure is a depression of the

mean leukocyte count of the exposed groups below the control groups. Dosimetry, the measurement of radiation intensities, must remain the basis of all protective measures. (Author Summary)

- 10 Cronkite, Eugene P. and George Brecher. **RADIOLOGY AND RADIOACTIVITY EFFECTS OF WHOLE BODY IRRADIATION.** Nov. 15, 1951. 25p. (Lecture and Review Series 51-11; NP-3796; R-6317)
Biological effects of whole-body irradiation are reviewed. Topics covered include dose measurements and lethal dose, survival time and clinical syndromes, intestinal injury, bone marrow injury, anemia, hemorrhage, infection, late effects, modification of response, and mechanics of protective action. A brief discussion of the medical aspects of atomic warfare is included. 165 references. (NSA)
- 11 Cronkite, Eugene P. and William H. Chapman. **A CRITICAL ANALYSIS OF THE SYNDROME OF ACUTE TOTAL BODY RADIATION ILLNESS, ITS ROLE IN ATOMIC WARFARE AND ITS INFLUENCE ON THE FUTURE PRACTICE OF MILITARY MEDICINE.** *Military Surgeon* **104**, 7-21(1949).
This analysis includes the following material: There is a clinical description of acute total body radiation illness based on bombing experiences at Hiroshima and Nagasaki and on accumulated experimental laboratory data. The pathogenesis of radiation illness is discussed primarily from the standpoint of the initial injury of sensitive cellular systems. The possible presence and influence of circulating toxins from injured tissues and the bowel is discussed. A program for the study and care of human radiation casualties under ideal conditions is outlined, and a general analysis of the therapeutic challenge that atomic warfare presents to military medicine is presented. It is concluded that investigation is urgently needed along many avenues to improve our understanding of this illness: such as (a) Information on the influence of diet and environmental factors on survival after exposure to doses in the lethal range is needed; (b) Information concerning the relationship of the adaptation syndrome and the pituitary-adrenocortical mechanism to radiation illness is desirable; (c) The role of autosensitization and anaphylactoid phenomena in radiation illness must be clarified. And in regard to defensive measures in the event of an atomic war, the most critical and practical needs today are these: (a) The development of an easily read dosimeter; (b) The continuation of basic and applied research along the lines discussed in this paper. (NSA)
- 12 Crowther, J. A. **THE BIOLOGICAL ACTION OF X-RAYS.** *Brit. J. Radiol.* **11**, 132-45(1938).
The author deals with the possible modes of action of X-rays on single cells and unicellular organisms, assuming that the effect is due to some specific reaction in the nucleus. Explanations fall into two classes, which he calls the "poison" hypothesis and the "target" hypothesis, the first assuming the formation by photochemical action of some toxic substance within the cell; the second postulating that something happens to the cell whenever it is "hit" by a photon. Application of the two theories to known biological reactions are discussed. (BA)
- 13 Curtis, Howard J. **THE BIOLOGICAL EFFECTS OF RADIATION.** *Ann. Rev. Physiol.* **13**, 41-56(1951).
Review with 142 references. (V.E.)
- 14 Curtis, Howard J. **THE BIOLOGICAL EFFECTS OF RADIATIONS**, Volume 2, p. 1-51 of **ADVANCES IN BIOLOGICAL AND MEDICAL PHYSICS**, John H. Lawrence and Joseph G. Hamilton, eds. Academic Press, Inc., New York. 1951.
This review is a survey of the problems encountered on the wartime Metallurgical Project, the experimental methods developed, and the chief results attained. It includes sections on (1) the physical properties of radiations; (2) methods of measurement; (3) comparative effectiveness of radiations; (4) and physiological effects. No attempt has been made to review the vast literature of the biological effects of radiations and only such references are made as seems necessary for a coherent account of the general problem. 38 references. (S.V.S.)
- 15 Dobson, R. Lowry and John H. Lawrence. **PHYSIOLOGICAL EFFECTS OF RADIANT ENERGY.** *Ann. Rev. Physiol.* **10**, 479-500(1948).
This review covers the period from August 1946 to August 1947. An attempt has been made to bring out the highlights of recent developments in the field of radiation and to mention pertinent work which has been brought out in this period. Included are sections on the mechanism of action of radiations, neutrons, slow neutrons and fission fragments, protons, β rays, γ rays and x-rays; effects on blood and hematopoietic tissue; immunity; carcinogenic effects; and effects of the atomic bomb. (S.V.S.)
- 16 Dowdy, Andrew H. **MEDICAL AND BIOLOGICAL ASPECTS OF NUCLEAR ENERGY.** Univ. of Rochester. Aug. 13, 1947. (RAD-202)
In this review paper University of Rochester experiments and results are described for the effects of chronic and acute x-radiation and chronic neutron irradiation upon peripheral blood changes (red blood cell count, lymphocyte count, polymorphonuclear count and platelet count), incidence of leukemia, mortality, body weight changes, sterility in the male (aspermia, sperm reduction, sperm motility, and abnormal sperm form), genetic changes (mutations) and histogenetic changes (chromosome abnormalities). Dogs, rabbits, monkeys, rats, and fruit flies were the subject of experimentation. It was concluded that genetic changes are the most sensitive indicators of x-radiation, that chromosome damage is directly proportional to total number of roentgens received, and that alteration in sperm could be detected in cases of chronic radiation down to dosage levels as low as 0.1 r/day. Lymphocytes are the most sensitive to radiation, followed closely by polymorphonuclears and platelets; red blood cells are more resistant. Chronic x- and neutron irradiation increases the incidence of leukemia; the life span of small animals is reduced in proportion to the number of roentgens of x-radiation received. It appears that any amount of penetrating radiation is detrimental and that many of the responses studied fall into the non-threshold group. (NSA)
- 17 Dowdy, Andrew H. **TABULATION OF AVAILABLE DATA RELATIVE TO RADIATION BIOLOGY.** Feb. 1, 1949. 48p. (AECU-353; UCLA-22)
The report tabulates data on the following subjects for several species including humans, rats, mice, guinea pigs, dogs, fruit flies, and grasshoppers: histogenetic and genetic effect of radiations; effect of irradiation upon gonads; incidence of leukemia; hematological effects other than leukemia; acute total body irradiation of rats with 250 kvp x-rays; embryological effects of irradiation; neutron-

roentgen ratios; mortality table for x-radiation; mortality-chronic x-radiation from 3 r to 10 r/day; longevity table for x- and γ -radiation; effect of radiation—human cases; effect of total body irradiation—human cases; comparison of radiation effect by total dose, 26 cases; techniques employed for total irradiation; summary—polycythemic and leukemic patients living one year or more; chemical aspects of x-radiation. The data tabulated in the several tables listed above is summarized. The estimated results to humans exposed to filtered 200-1,000 kvp x-rays are listed. The appendix includes discussions of the general background material concerning the effects of radiation on chromosomes, genetic changes in human sperm and eggs caused by single exposures of 300 r or less, and induced mutation rates. (NSA)

18

Draeger, R. H. and S. Warren. **MEDICINE AT THE CROSSROADS. A REPORT BY THE MEDICAL CORPS OF THE NAVY ON THE STUDY OF ANIMALS USED IN THE BIKINI TESTS.** U. S. Naval Med. Bull. 47, 219-25(1947).

The biological experiments conducted during Operations Crossroads are outlined and their results summarized. Twenty-two scientists, 200 goats, 200 pigs, 5,000 rats, 120 mice, and 60 guinea pigs were transported to Bikini on U.S.S. Burleson, which served as the laboratory. In addition to the mammals, other biological material—insects, bacteria, seeds, sera, hormones, etc.—and inorganic substances such as soil and drugs were included. Most of the animals were used in Test Able, where the atomic bomb was exploded above the ground. All were retrieved within two days. It was found that the majority of early deaths were due to blast injury, radiation effects being a lesser cause of death at this time and flash burns being minimal because of the furry coats of the animals. The animals which were exposed to appreciable amounts of radiation developed the same signs and symptoms as were noted in the human survivors of Hiroshima and Nagasaki. The first sign was atrophy of lymphoid tissue; then appeared a hemorrhagic diathesis and severe enteritis, often with necrosis of mucosa and submucosa. Marked changes in the blood picture occurred and, some weeks later, partial depilation. The sequence of the pathologic changes is being studied by means of sections from the tissues of animals sacrificed at intervals after the exposure. Information obtained by placing swatches of different cloths on fir plywood confirmed the impression gained in Japan that white material protects against flash burns better than dark cloth. After Test Baker, in which the bomb was exploded under water, the test subjects could not be recovered for several days because of the intense residual radioactivity resulting from the flooding of the target ships with radioactive "rain". The animals thus received not only a more intense radiation but also a much longer exposure than those at Test Able. The surviving animals and the inert materials are now being studied at the Naval Medical Research Institute. (BA)

19

Duggar, Benjamin M., ed. **BIOLOGICAL EFFECTS OF RADIATION.** McGraw-Hill Book Company, Inc., New York, 1936.

This book constitutes a collective contribution from representatives of the fields of physics, zoology, botany, etc. The material is carefully selected so that an adequate comprehensive view of the whole field may be obtained. Chapters included are: Measurement of X-Rays and Radium, by Lauriston S. Taylor; Ionization and its Bearing on the Biological Effects of Radiation, by G. Failla; Statistical Treatment of Biological Problems in Irradiation, by Lowell J. Reed; The Effect of Radiation on Proteins, by

Janet Howell Clark; Radiation and the Vitamins, by Charles E. Bills; The Effects of Irradiation on Venoms, Toxins, Antibodies, and Related Substances, by S. C. Brooks; The Effects of Radium and X-Rays on Embryonic Development, by Elmer G. Butler; Effects of X-Rays and Radium Upon Regeneration, by W. C. Curtis; The Biological Effectiveness of X-Ray Wave-Lengths, by Charles Packard; The Physiological Effects of Radiation upon Organ and Body Systems, by Stafford L. Warren; Biological Effects of Alpha Particles, by R. E. Zirkle; The Action of Radiations on Living Protoplasm, by L. V. Heilbrunn and Daniel Mazia; The Effects of Radiation on Fungi, by Elizabeth C. Smith; Effects of X-Rays Upon Green Plants, by Edna L. Johnson; The Effects of Radium Rays on Plants, by C. Stuart Gager; The Influence of Radiation on Plant Respiration and Fermentation, by Charles J. Lyon; Growth Movements in Relation to Radiation, by Earl S. Johnston; Chlorophyll and Chlorophyll Development in Relation to Radiation, by O. L. Inman, Paul Rothemund and C. F. Kettering; Radiation and Anthocyanin Pigments, by John M. Arthur; Effects of Radiation on Bacteria, by B. M. Duggar; The Effects of Radiation on Enzymes, by Harold A. Schomer; Radiation and the Study of Mutation in Animals, by Jack Schultz; Induced Chromosomal Alterations in Maize, by E. G. Anderson; and Biological Aspects of the Quantum Theory of Radiation Absorption in Tissues, by John W. Gowen. (S.V.S.)

20

Edelmann, Abraham. **RADIANT ENERGY.** Ann. Rev. Physiol. 12, 27-46(1950).

The review deals chiefly with physiological effects of ionizing radiations. 172 references. (CA)

21

Edelmann, Abraham. **AAAS SYMPOSIUM ON RADIOBIOLOGY.** Nucleonics 8, 28-36(1951). Apr.

A summary is presented of 22 papers offered at the 117th meeting of the American Association for the Advancement of Science. The subject matter covered in these papers includes the effects of ionizing radiation on plant growth and development, radiation-induced mutations, neutron irradiation of compounds, action of x rays on cells and rodent testicles, effect of I^{131} on thyroid tissue spleen shielding, C^{14} metabolism, and radiation-sickness therapy. (NSA)

22

Ellinger, Fredrick. **THE BIOLOGIC FUNDAMENTALS OF RADIATION THERAPY.** Elsevier Pub. Co., New York, 1941.

Included are effects of roentgen rays and the gamma radiation of radium on various parts of the body, i.e., skin, central nervous system, eye, endocrine glands; direct and indirect effects of ultraviolet light; effects of corpuscular rays; action of visible light and infra-red rays. (M.F.)

23

Evans, Robley D. **HEALTH PHYSICS: INSTRUMENTATION AND HAZARD EVALUATION, Volume II, Chapter 16, p.249-74 OF THE SCIENCE AND ENGINEERING OF NUCLEAR POWER,** Clark Goodman, ed. Addison-Wesley Press, Inc., Cambridge, Mass. 1949.

The author presents a brief review of the function of the health physicist. A brief discussion of the biological effects of radiation follows. Included in the discussion are sections on blood changes due to irradiation, leukemia in radiologists, chronic radium poisoning, lung cancer and radon inhalation, genetic effects, occupational exposure to radiation, and maximum permissible dosage-rate. A brief description is given of instruments for the measurement of gamma-ray ionization intensities in mr/hr, for very small gamma-ray ionization intensities, and for personnel moni-

toring (film-badge and pocket, condenser-type ionization chamber). Included is an evaluation of some of the commercially available instruments. (S.V.S.)

24

Failla, G. IONIZATION AND ITS BEARING ON THE BIOLOGICAL EFFECTS OF RADIATION, Volume 1, p.87-122 of BIOLOGICAL EFFECTS OF RADIATION, B. M. Duggar, ed. McGraw-Hill Book Company, Inc., New York. 1936.

A discussion of the fundamental character of ionization and its bearing on the biological effects of radiation. Includes sections on (1) the distribution of ions in an ionized medium, (2) interaction of radiation and matter, (3) influence of the quality of radiation on the distribution of ions in living matter; (4) intensity of radiation and inverse square law; (5) influence of matter on the intensity of radiation; (6) secondary phenomena; (7) filtration; (8) essential factors for the correlation of ionization and biological effects; (9) effective intensity of radiation; (10) significance of ionization measurements; (11) knowledge of ionization produced in irradiated organism all important; and (12) effective quantity of radiation. (S.V.S.)

25

Fink, Robert M., ed. BIOLOGICAL STUDIES WITH POLONIUM, RADIUM, AND PLUTONIUM. McGraw-Hill Book Company, Inc., New York. 1950. (National Nuclear Energy Series, Division VI, Volume 3)

The general problem undertaken is a comparison of the biological effects of the three α particle emitters, polonium, plutonium, and radium. Part I deals with the distribution and excretion of polonium, Part II discusses the distribution and excretion of radium, and Part III deals with the comparative toxicities of polonium, plutonium, and radium. The book includes a critical survey of available literature concerning these elements. It also describes carefully controlled rat experiments designed to determine accurately the relative toxicity of single injections of radium, polonium, and plutonium over a very wide range of doses, and discusses further the probable correlations between the toxicity results and retention and distribution data. (NSA)

26

Forssberg, Arne. SOME RECENT FINDINGS IN RADIO-BIOLOGY. *Strahlentherapie* 81, 161-72(1950).

This is a review of some of the experimental work done recently on the fundamental phenomena of radiobiology. The dependence of mutation frequencies on the dose in the small-dose region, the chemical changes produced by radiations in the chromosomes, the part played by the solvent in a radio-reaction, the effects of very small doses, are some of the subjects discussed. 18 references. (NSA)

27

Glasser, O., E. H. Quimby, L. S. Taylor, and J. L. Weatherwax, eds. PHYSICAL FOUNDATIONS OF RADIOLOGY. Paul B. Hoeber, Inc., New York and London. 1950.

The first chapters cover the basic concepts of radiation (fundamental concepts of matter, fundamentals of electricity and magnetism etc.), while the later chapters deal with principles of x-ray diagnostic procedure, measurement of x-ray and γ doses, measurement of x-ray and γ ray quality, and dosage in x-ray and γ ray therapy. (M.F.)

28

Glasstone, Samuel, ed. THE EFFECTS OF ATOMIC WEAPONS. U. S. Government Printing Office, Washington, D. C. June 1950.

This book was prepared for the Department of Defense and the AEC by a board of editors under the direction of the Los Alamos Scientific Laboratory. It presents a technical summary of the results to be expected from the deto-

nation of atomic weapons, with chapter describing an atomic explosion, the shock from air, underwater, and underground bursts; blast, radiation, and fire effects; methods of protecting personnel and decontamination methods. One chapter is devoted to the effects on personnel and discusses the types of injuries, nuclear radiation effects, clinical syndrome of radiation sickness (acute radiation syndrome), the pathology of radiation sickness, residual radiation hazards, and genetic effects of radiation. (S.V.S.)

29

Goldsmith, H. H. BIBLIOGRAPHY ON RADIATION PROTECTION. *Nucleonics* 4, 62-9(1949)

This bibliography includes several hundred references under the following general headings: (1) reviews, (2) general biological effects of radiations, (3) blood changes due to radiation, (4) radiation sickness, (5) atomic bomb effects, (6) tolerances doses and dosage measurements, (7) radiation exposure monitoring, (8) health protection measures, (9) dust monitoring and hazards, and (10) laboratory designs. (To appear as part of a report from the Committee on Nuclear Science of the National Research Council.) A more comprehensive bibliography on this subject is being compiled by the author for the United Nations as "An International Bibliography on Atomic Energy. Vol. II-Scientific Aspects". (NSA)

30

Gray, L. H. ELECTRONS, NEUTRONS, AND ALPHA PARTICLES, Chapter XV, p.491-560 of BIOPHYSICAL RESEARCH METHODS, F. M. Uber, ed. Interscience Publishers, New York. 1950.

Ionizing radiations are discussed with regard to: effects on living cells; health hazards; effects as mutagenic and carcinogenic agents. Other subjects are physical characteristics of different ionizing radiations, sources, and measurement. (M.F.)

31

Gray, L. H. BIOLOGICAL ACTIONS OF IONIZING RADIATIONS, Volume 2, Chapter 8, p.240-305 of PROGRESS IN BIOPHYSICS AND BIOPHYSICAL CHEMISTRY, J. A. V. Butler and J. T. Randall, eds. Academic Press, New York. 1951.

Whole body exposure to radiation damages the haemopoietic and lymphoid tissues. Anoxia reduces the sensitivity of the skin whereas increased oxygen during irradiation increases damage. Protection is also afforded by cysteine and cyanide. Tissues most easily damaged by radiation have in common constant proliferation of germinal daughter cells. Probably metabolism plays an essential role in injury to structural components of the nucleus; damage may result from diffusion of toxic products of an irradiated cytoplasm into the nucleus. Inhibition of mitosis is an immediate effect of even low levels of radiation. The visible physical changes may be related to changes in the DNA molecule. Reduction is the rate of synthesis of the purines of DNA has been established. Radiobiology has been greatly influenced by the progress made in the study of reactions induced in aqueous solutions by ionizing radiations, which the author has summarized. (M.F.)

32

Henshaw, Paul S. RADIATION AND THE CELL. *J. Nat. Cancer Inst.* 1, 277-90(1940).

This paper deals briefly with the nature of matter in general and how radiation acts to modify it. The author discusses the action of high energy radiation on living matter and the kinds of radiobiologic responses. The following types of responses are postulated: Type I. Single-Event Action; Type II. Multiple-Event Action; Effect Mani-

fest in Holistic Fashion; Type III. Multiple-Event Action; Effect Manifest by Degree (S.V.S.)

- 33 Hueper, W. C. **OCCUPATIONAL TUMORS AND ALLIED DISEASES**. Charles C. Thomas, Springfield, Illinois, 1942.
- This section is devoted to a general review of occupational roentgen and radium-cancers of the skin. Included are discussions on the geographical distribution and incidence, age distribution, multiplicity, occupational distribution, sex distribution, exposure time, symptomatology, histology, susceptibility, prognosis, experimental roentgen and radium cancer, causative mechanism, therapy, preventive, protective, and sanitary aspects, and medico-legal aspects. A representative bibliography is appended. (S.V.S.)
- 34 Jacobson, Leon O., R. S. Stone, and J. Garrott Allen. **PHYSICIANS IN AN ATOMIC WAR**. J. Am. Med. Assoc. 139, 138-40(1949).
- Authors discuss the role of the physicians in the event of an atomic war and Cite facts which permit formulation of certain broad principles to be followed if large cities are bombed; also discuss research work in progress on biologic effects of radiation. (S.V.S.)
- 35 Kamen, M. D. **RADIOACTIVE TRACERS IN BIOLOGY**. 2nd Ed. 429p. Academic Press, Inc., New York, 1951.
- The second edition as the first (1948) was written to serve as an introduction to tracer methodology in general and as a guide book for those, particularly in biological fields, employing such technics. The first chapters provide an introduction to the properties of atomic nuclei and nuclear reactions, the nature of tracer radiation, methods of measurement of radioactivity, and tracer methodology in biochemistry, physiology, and medicine. Subsequent chapters deal with particular radioactive isotopes such as H^3 , C^{11} , C^{14} , P^{32} , S^{35} , etc. The general plan of the first edition has been retained, although important revisions and enlargements have been made, chief among which is the addition of a chapter on radiation hazards. New appendices have been included, these being, a description of radioactivity units, a listing of working laboratory rules when using tracers, a listing of useful radioactive nuclides, and a pertinent bibliography. (BA)
- 36 Lavedan, Jacques. **THE EFFECT OF RADIATIONS ON THE NORMAL CELL**. Gauthier-Villars, Paris, 1945.
- The book gives a quick survey of the influence of radiation on the normal cell. The main emphasis is on the effect of ionizing radiation (x-rays, α , β and γ rays) rather than on the effect of ultraviolet radiation. A short introduction gives the physical aspects and the following chapters discuss the biological effects under the titles: Action of radiation on the cytological structure of the cell; the radiosensitivity of the cell and the factors which modify it; effects of radiation on the biological function of the cell. The physical interpretation of the radiation sensitivity is given under the chapter headings: The inactivation curve and its interpretation; the influence of different factors like wave-length, time, latent periods, etc.; radiomutations, the primary physical effect, etc. An addendum discusses recent concept of the mechanism of radiation action. Very little of the literature which appeared during the last 10 years is discussed. (BA)
- 37 Lawrence, John H. **THE NEW NUCLEAR PHYSICS AND MEDICINE (THE CALDWELL LECTURE OF THE AMER-**

ICAN ROENTGEN RAY SOCIETY). Am. J. Roentgenol. Radium Therapy 48, 283-301(1942).

This paper presents no new material but is an excellent summary of the subject to date. After a historical introduction Lawrence explains in detail the use of radioactive tracers and radioassay of biological material, amply illustrated by accounts of various experiments. Possibilities of clinical usage of the radioisotopes and of neutrons are emphasized by statements of results already obtained in certain types of disease. A well-selected bibliography is appended. (BA)

- 38 Lawrence, John H. and Joseph G. Hamilton. **ADVANCES IN BIOLOGICAL AND MEDICAL PHYSICS**. Academic Press, Inc., New York. 1948.
- The topics discussed are as follows: heavy and radioactive isotopes in clinical and experimental medicine; nitrogen and carbon isotopes, their application in vivo to the study of the animal organism; the nature and production of artificial radioactivity; fundamentals of radioactivity and its instrumentation; health physics instrumentation and radiation protection; the use of radioactive isotopes in the study of iron and hemoglobin metabolism and the physiology of the erythrocyte; radioactive phosphorus, its application to the study of phospholipid metabolism; iodine metabolism; the effects of the atomic bomb irradiation on the Japanese; and nucleic acid metabolism. (NSA)
- 39 Lea, D. E. **ACTIONS OF RADIATIONS ON LIVING CELLS**. The Macmillan Company, New York. 1947.
- Data on biologic effects which have been produced by X-rays, γ -rays, electrons, neutrons and, to a much lesser extent, by u.-v. rays, and which have been investigated quantitatively, are assembled and correlated in an important effort to achieve an acceptable mechanism for their production. About $\frac{1}{3}$ of the volume is devoted to a presentation of physical and chemical factors, including extensive tabular and graphical data concerning the dissipation of energy by high speed particles and X-rays. Much of this information was previously lacking or inaccessible. Organisms which have been studied quantitatively are limited so that the discussion centers primarily around effects on *Drosophila*, maize, *Tradescantia*, viruses, bacteria, and *Arbacia*. Genetic and lethal studies on *Drosophila*, and chromosomal alterations in *Drosophila* and *Tradescantia* are exhaustively treated, and occupy nearly half of the book. There is also a chapter each on viruses, delayed cell division (mostly in *Arbacia* eggs), lethal effects (in bacteria, *Drosophila*, *Tradescantia*), and on the "target" hypothesis or "hit" theory of radiation effects. The "target" hypothesis is considered valid for explaining various genic and chromosomal effects of high energy particles and quanta. (BA)
- 40 Martin, J. R. **RADIATION--ITS BIOLOGICAL EFFECTS AND PROBLEMS**. Mech. Eng. 71, 893-98(1949).
- The biological effects of radiation are reviewed. Tolerance concentrations of radioactive isotopes in air to produce an average tolerance dose to the affected organ at the end of 1 year are in the order of a millionth of a γ per cc of inspired air for certain α emitters. For β -emitters of long half-life, the amounts which must be detected are minute, ranging from a thousandth to a hundred thousandth of a γ . Ionization chambers and Geiger-Muller tubes are capable of measuring these very minute quantities. The protective measures for safe handling are similar to those used in industries handling toxic chemicals. (CA)

- 41 McDonnell, G. M. **MEDICAL ASPECTS OF THE ATOMIC BOMB.** Ordnance 34, 308-10(1950).
Atomic casualties, which are produced as a result of blast, heat, and ionizing radiation, are discussed. The relative value of these agents determined by a scale of biological significance will vary primarily with the type of detonation, namely, in the air, on or near the ground, and under water. With an air detonation, the ranges of the blast and thermal effects are distributed over the greatest possible area. In the ground detonation the ranges of blast, heat, and ionizing radiation are less than the air-detonation values. The heat and initial ionizing radiation produced as a result of an underwater detonation are largely contained within the surrounding water. It is stated that the danger from radiation has been highly overrated. (NSA)
- 42 Mitchell, J. S. **APPLICATIONS OF RECENT ADVANCES IN NUCLEAR PHYSICS TO CANCER RESEARCH.** Brit. J. Cancer 1, 1-14(1947).
This review summarizes information on the following subjects: (1) Properties and production of isotopes of interest, mainly radioactive, with Tables. (2) Isotopic tracer research, with precautions necessary, including avoidance of risk of carcinogenesis in possible clinical applications. (3) Artificial radioactive sources for use in radiotherapy made by means of the pile. The most promising substitute for radium appears to be radio-cobalt, Co^{60} , of half-life 5.3 years. Unseparated fission products should be investigated as an alternative. (4) Therapeutic possibilities of selectively concentrated radioactive agents, including the present position with regard to therapeutic applications of radio-phosphorus and the radio-iodines. (5) Therapeutic application of high energy (30 Mev) γ radiation and the development of the synchrotron. (Authors' Summary)
- 43 Morgan, K. Z. **MAXIMUM PERMISSIBLE LEVELS OF EXPOSURE AGREED ON AT CHALK RIVER CONFERENCE.** Am. Ind. Hyg. Assoc. Quart. 11, 116(1950).
In September, 1949, representatives of the U. S., Great Britain, and Canada proposed maximum permissible tissue dose limits for ionizing radiation at any point within the body of 0.3 roentgen equivalents physical/week for x- and γ -rays, 0.3 for β -, 0.03 for protons, 0.015 for α -particles, 0.03 for fast neutrons, and 0.06 for thermal neutrons. Data for exposure of the entire body and of hand only are also cited. (CA)
- 44 National Security Resources Board. **MEDICAL ASPECTS OF ATOMIC WEAPONS.** U. S. Government Printing Office, Washington, D. C. 1950.
This is one of a series of reports which assess, in general terms, what is known about the results of an atomic explosion, what damage and injuries a bomb can cause, and what can feasibly be done to protect people and structures. This first report deals particularly with the effects of an atomic bomb explosion upon people within its range, the medical and biological aspects of injuries and their treatment. A general discussion is given of (a) the type of injuries caused by an atomic explosion, and the extent to which they occurred in Japan at various distances from ground zero, (b) the nature of the radiation hazard, the effects of exposure, and some of the treatments for acute radiation sickness, and (c) the nature of the hazard from radiological contamination—not encountered in Japan—and some of the precautions that can be taken against it. (S.V.S.)
- 45 Nims, Leslie F. **RADIATION.** Ann. Rev. Physiol. 11, 527-44(1949).
This review covers the period from July 1947 to July 1948. The author covers the fields of (1) the mechanism of action of ionizing radiation on living cells and materials; (2) whole-body radiation; (3) blood and hemopoiesis; (4) skin; (5) other tissues; (6) internal radiations. No attempt has been made to cover the whole field of radiobiology in this review—genetic effects are not included. Bibliography of 156 references appended. (S.V.S.)
- 46 Rajewsky, B., A. Schraub, G. Kahlau, W. Dreblow, A. Krebs, and H. Schaefer. **DAMAGES BY RADIATION,** in FIAT Review of German Science, 1939-1946: Biophysics, Part I, p. 123-75. Office of Military Government for Germany, Field Information Agencies Technical, 1948.
Radiation injuries are discussed under the following headings: (1) Lethal Dosage Curves; (2) Production of Cancer by Radiation, Especially as Observed in the Radium Mines at Schneeberg; (3) Changes in Blood Produced by Radiation; (4) Radium Poisoning and Its Physical Diagnosis; (5) Measurement of the Content and of the Distribution of Radioactive Substances in the Body; (6) Radiography and the Counting of Single Particle Tracks as Used in Radiobiology. 90 references. (NSA)
- 47 Robinson, Radcliffe F., Michael D. Phillips, and Margaret G. Nagelsen. **A BIBLIOGRAPHY ON "THE EFFECTS OF X-RAY ON BACTERIA"** (1896 - August 1951). Battelle Memorial Inst. Aug. 20, 1951. 18p. (NP-3610)
A list of 178 titles on the effects of x-radiation on bacteria was compiled from abstract journals and indexes. Published articles from 1896 through August 1951 are included. (NSA)
- 48 Rossi, Harald H. **THE BIOLOGICAL SIGNIFICANCE OF THE TISSUE DOSE OF IONIZING RADIATIONS.** Trans. New York Acad. Sci. 2, 270-5(1949).
A general discussion of ionizing radiations is given, with special reference to the problem of a quantitative measurement of radiation and the question as to how far the result of such measurements serves to define the conditions under which a radiobiological experiment is performed. Spatial and temporal considerations of dosimetry in connection with ionization and induced electromagnetic fields are qualitatively discussed; the author suggests the further collaboration of physicists with biologists for more exact dosimetry measurements and for discussion of the complex theoretical problems which arise in treatment of biological material. (NSA)
- 49 Smyth, Henry De Wolf. **ATOMIC ENERGY FOR MILITARY PURPOSES.** U. S. Government Printing Office, Washington, D. C. 1945.
The purpose of this report is to describe the scientific and technical development in this country since 1940 directed toward the military uses of energy from atomic nuclei. It includes a statement of the chain-reaction problem; administrative history of the uranium project beginning with the initial approaches of a group of scientists to the government and including the administrative history to 1945; the Metallurgical Project at Chicago in 1942; the plutonium production problem; a general discussion of the separation of isotopes; gaseous diffusion and electromagnetic separation of uranium isotopes. The author states in his preface that this book is neither a documental official

history nor a technical treatise for experts but rather is a matter-of-fact, general account of work in the United States since 1939 aimed at the production of atomic bombs. As such it represents the official report on the development of the atomic bomb under the auspices of the United States Government, 1940-1945. (S.V.S.)

50

Sparrow, A. H. and B. A. Rubin. **EFFECTS OF RADIATIONS ON BIOLOGICAL SYSTEMS.** Feb. 15, 1951. 94p. (AECU-1207)

An extensive review covering types of radiation, radiation dosage units, radiation energy transfer mechanisms, the target theory, relation between chemical and biological effects of radiations, effects of radiation on microorganisms, cytological and genetic effects, carcinogenesis, physiological and embryological effects, and factors determining radiation sensitivity is presented. The selected bibliography favors recent publications, especially reviews. (NSA)

51

Spear, F. G., ed. **RADIOBIOLOGY: EXPERIMENTAL AND APPLIED.** Brit. Med. Bull. 4, No. 1 (1946).

A comprehensive survey of the field of radiology by F. G. Spear, covers the following subjects: (1) Background theory; (2) Physical dose and biological response; (3) Radio-chemistry; (4) Biological indicators; (5) Genetic effects of radiation; (6) Lethal and injurious actions of radiations; (7) Summary of effects on normal tissues; (8) Radiations and malignancy. In a comparative study of biological effects of ionizing radiations L. H. Gray discusses: (1) Linear ion density, the distinguishing feature of an ionizing radiation, from the biological standpoint. (2) Ion density produced by different ionizing particles. (3) The influence of ion density on radiochemical yield. (4) Ion density in relation to the inactivations of elementary biologic units. (5) The structural changes induced in chromosomes by different types of ionizing radiation. (6) Comparative studies with other biologic material (*Drosophila* eggs, root-tips, of *Vicia faba*, animal embryonic tissue, tumor tissue. (7) Neutron therapy. The topics of genetic effects of radiation discussed by D.G. Catcheside are: (1) Stability of chromosomes and genes. (2) Radiation induced mutation in *Drosophila melanogaster*. (3) Induced chromosome aberrations. Inactivation and other effects of radiation on viruses and bacteria are discussed by D. E. Lea. G. J. Mary discussed the "ionization method" of radiation measurement and other forms of measurement. (TIS)

52

Spear, F. G., ed. **CERTAIN ASPECTS OF THE ACTION OF RADIATION ON LIVING CELLS.** Brit. J. Radiol., Suppl. No. 1, 1947.

This is a report of the London Conference held May 13-14, 1946 on certain aspects of the action of radiation on living cells. The following papers are included: (1) The Distribution of the Ions Resulting from the Irradiation of Living Cells, by L. H. Gray; (2) The Nature of Viruses and the Irradiation of Plant Viruses, by Roy Markham; (3) The Irradiation of Viruses, by P. Bonet-Maury; (4) The Effect of Radiation on Vaccinia Virus, and on Bacteriophages, by M. H. Salaman; (5) The Inactivation of Viruses, in Relation to the Mechanism of Biological Actions of Radiation, by D. E. Lea; (6) Introductory Survey of Experimental Data, by C. B. Allsopp; (7) Action of Radiation on Aqueous Solutions: Experimental Work with Enzymes in Solution, by Walter M. Dale; (8) The Radiochemistry of Aqueous Solutions: A Survey of Recent French Research, by M. Frilley; (9) Some Aspects of the Action of Radiations on Aqueous Solutions, by Joseph Weiss; (10) The Action of

Radiations on Dilute Aqueous Solutions: The Spatial Distribution of H and OH, by D. E. Lea; (11) Survey of Effects of Radiation on Chromosomes, by D. G. Catcheside; (12) The Induction of Chromosome Structural Changes by Radiation: Detailed Quantitative Interpretation, by D. E. Lea; (13) The Effect of Radiation on the Normal and Malignant Cell in Man, by P. C. Koller; (14) The Effects of Radiation on Reproductive Organs, by A. Glucksmann; (15) Genetic Effects of Radiations, by D. G. Catcheside; (16) Effects on Early Embryonic Development of Irradiation of Spermatzoa; (17) Effects of Radiation on Germ Cells: Dominant Lethals and Hereditary Partial Sterility, by D. E. Lea. (S.V.S.)

53

Stone, Robert S. **RADIATION INJURY.** Radiology 46: 59-62(1946).

This paper is one of a combined report of the Standardization Committees of the American Roentgen Ray Society and the Radiological Society of North America. The purpose of these reports is to acquaint recent users of x-rays and radium with the actual hazards involved. This report is necessarily a very generalized one. It describes the types of injuries which may result from overexposure to "radiation": injuries from acute local overexposure; injuries caused by repeated or chronic local overexposure; injuries from local irradiation of hair-bearing areas; injurious effects on the testicles and ovaries; radiation effects from radiation to the entire body or large portions of the body—effects on the blood, lymphatic tissues, bone, general symptoms such as nausea, vomiting, etc. In conclusion the author points out that all of the above conditions are preventable. (S.V.S.)

54

Stone, Robert S., ed. **INDUSTRIAL MEDICINE ON THE PLUTONIUM PROJECT.** McGraw-Hill Book Company, Inc., New York. 1951. (National Nuclear Energy Series, Division IV, Volume 20)

This book is a comprehensive survey of the medical activities of the Manhattan Project. Included are chapters on the medical services of the Plutonium Project, biological bases for permissible exposures, laboratory examination of project personnel, hematological effect of ionizing radiations, biochemical studies, uranium excretion studies, distribution and excretion of plutonium, management and treatment of exposed personnel, industrial medical program at the Hanford Engineer Works, blood changes in human beings following total-body irradiation, hematological studies on patients treated by total-body exposure to X-rays, biometric analysis of blood variability, determination of radium in excreta, health protection at Hanford, tolerance to whole-body irradiation of patients with advanced cancer. (S.V.S.)

55

Uber, F. M., ed. **BIOPHYSICAL RESEARCH METHODS.** Interscience Publications, Inc., New York. 1950.

This book contains chapters on various topics in biophysics by experts in the field, including the following: X-rays and X-irradiation, J. W. Gowen; Electrons, Neutrons, and α Particles, L. H. Gray; Stable Isotopes as Tracers, F. M. Uber; and Radioactive Tracers, A. F. Voigt. (NSA)

56

United Nations Atomic Energy Commission Group. **ISOTOPES IN BIOLOGY AND MEDICINE, PART IV, of the BIOLOGICAL AND MEDICAL EFFECTS OF HIGH ENERGY RADIATION in AN INTERNATIONAL BIBLIOGRAPHY ON ATOMIC ENERGY, VOLUME 2, SCIENTIFIC ASPECTS.** New York. 1951.

This document comprises Parts III and IV of "An International Bibliography on Atomic Energy." References are

listed under the following headings in Part III: Effects of high energy radiations on chemical compounds, on micro-organisms, on cells, on genetics and mutations, on the growth and development of organisms, on organ systems, on physiology, and on botany and agriculture; medical aspects of high energy radiations; radiation protection and dosage measurement; and technical aspects. Part IV includes introductory essays on stable isotopic tracers and on the uses of radioactive isotopes, and references are listed under the following headings: General articles on tracers; agriculture and ecology; physiological chemistry; physiology; medicine and toxicology; technique. (NSA)

57

United States Atomic Energy Commission. **ATOMIC ENERGY AND THE LIFE SCIENCES.** U. S. Government Printing Office, Washington, D. C. July 1949.

This Sixth Semiannual report of the Atomic Energy Commission sums up briefly the major developments in the national atomic energy program and further gives a comprehensive review of one of its major phases—the biological and medical activities. This report outlines the AEC program in all phases of medicine and biology. There is a section describing research on the chemistry of living things, the effects of radiation on living cells and tissue, organs of the body, and the body as a whole. Another section describes research into the effects of radiation upon the mechanism of heredity in living things and upon the precesses involved in heredity. The results of analysis of bomb effects at Hiroshima and Nagasaki and biological surveys at Bikini and Alamogordo two and three years after atomic bomb tests there are discussed in this report. One section of the report is devoted to protective measures for personnel and includes a discussion of the handling of radioactive wastes from atomic energy plants and other sources. Included also are sections on the use of radioactive tracers for chemical studies; the use of radioisotope to diagnose and treat disease, outline of the AEC cancer program, and radiation and agriculture. (S.V.S.)

58

United States Atomic Energy Commission. **CONTROL OF RADIATION HAZARDS IN THE ATOMIC ENERGY PROGRAM.** U. S. Government Printing Office, Washington, D. C. July 1950.

This Eighth Semiannual Report of the Atomic Energy Commission reviews in some detail the control of radiation hazards in the atomic energy program. The report includes sections on radiation safety, the problems, the progress, and the record (hazards of radiation, methods of radiation control, permissible limits on exposure, the record of radiological safety); radiation safety in production operations (processing raw and feed materials; protection in pile buildings, protection in chemical separation plants, protection in plutonium metal work, radiation control at Los Alamos, etc.); safe handling of radioisotopes; control of radiation in research and development (protection in laboratories, choice of building materials, protection against gamma rays, remote control engineering, etc.); environmental safeguards (handling liquid wastes, controlling gaseous wastes, etc.); control of hazards at weapons test; the AEC program for radiation control; and detection instruments for radiation protection. (S.V.S.)

59

United States Atomic Energy Commission. **ISOTOPES--A FIVE YEAR SUMMARY OF DISTRIBUTION WITH BIBLIOGRAPHY.** U. S. Government Printing Office, Washington, D. C. 1951.

An account of the isotope distribution program. Tables show what isotopes have been distributed, to which investigators, where, for what purpose, and where the results are published. 451 pp. 1402 references. (R.D.B.)

60

U. S. Army Medical Department. **WHAT EVERY MEDICAL OFFICER SHOULD KNOW ABOUT THE ATOMIC BOMB.** Bull. U. S. Army Med. Dept. 8, 350-6; 357-62; 422-8; 428-31(1948).

Lethal effects will be produced by air-burst atomic bombs over an area of 2 square miles and measurable effect over an area of 7 square miles as a result of the γ radiation emitted at the time of detonation. There is little importance in the residual radioactivity except in the area close to the center of a low-altitude explosion. In an under-water detonation, radioactive fission products and unfissioned material will be spread by the cloud and base surge over a large area. The γ radiation from these materials will be lethal to exposed personnel more than 2 miles downwind, and serious contamination will result at much greater distance. A serious hazard will be provided by this detonation for an indefinite period. At the time of the detonation prompt evasive action will permit the reduction of casualties. The pathologic effects of radiation are presented by outlining the early and late changes in tissue cells, organ systems, total body irradiation, and internal radiation by radioactive materials introduced into the body either accidentally or therapeutically. The sensitivity of various body tissues has been established and has been expressed largely as the relation of one tissue to another. A table is given which shows the relative radiosensitivities of various body tissues listed in decreasing order. The effects of overexposure may be acute or chronic. The exposures may result from any type of radiation applied externally or internally. The clinical picture will depend on the amount, rate of delivery and depth of the dose. The signs and symptoms such as thermal burns, diarrhea, nausea, vomiting, headache, anuria, purpura, blood changes, fingernail brittleness, pigmentation, etc., are discussed. A procedure to be followed in studying a person suspected of being overexposed is given. (NSA)

61

University of Rochester. **VALIDITY AND USEFULNESS OF CURRENTLY ACCEPTED "TOLERANCE DOSE" FOR X- and γ -Radiation.** Industrial Tolerance Conference. AECD-2832, 98p. 1945.

The main purpose of this conference was to consider the validity and usefulness of the currently accepted human tolerance dosages for x- and γ -radiation, namely, 0.1 r/day for an unlimited length of exposure. Papers were presented on the following subjects: chronic experiments correlating near-tolerance dosages with survival, blood changes, aging, genetic mutations, and skin changes; the mechanism of radiation effects; and the human tolerance dose. (NSA)

62

Warren, Shields. **EFFECTS OF RADIATION ON NORMAL TISSUES.** Arch. Pathol. 34, 443, 562, 749, 917, 1070, and 35, 121, 305, 323, 340(1942).

This review is limited to the effects on normal animal and human tissues of therapeutic radiation from the more important sources—roentgen rays (produced at low as well as high voltages), radium, radon, neutrons, and certain of the temporarily radioactive isotopes. Bibliographies are given at the end of each part. (S.V.S.)

63

Warren, Shields. **THE HISTOPATHOLOGY OF RADIATION LESIONS.** Physiol. Revs. 24, 225-38(1944).

This simple of informative review, citing only 35 references, deals first with the therapeutic types of radiation, electro-magnetic, corpuscular (including the recently used radioactive isotopes), and neutrons. By way of introduction, it tells briefly how these radiation methods can be equated with respect to biological effect, are not specific in their results, are never directly stimulating but only destructive, fail to reach all of the cells of a tissue, always reach some cells of adjacent tissues; how cells differ from one another in susceptibility to damage by irradiation, and differ within themselves from one stage of a life history or a mitosis to another. Then it describes for normal tissues the apparent and real latent periods of injury, the types of visible change (mitotic, cytoplasmic, functional, vascular, intra-cellular); the order of sensitivity of different cells, with special mention of the germ plasma; the role of infection and trauma in radiation damage. It discusses radiation injury as a cause of neoplasms. Finally it gives separate descriptions of the radiation changes in examples of the radio-sensitive, the radio-responsive, and the radio-resistant tumor; and comments on curability in relation to radio-sensitivity. (BA)

64

Warren, Shields. **PHYSIOLOGIC EFFECTS OF NUCLEAR ENERGY.** *Occupational Med.* 2, 447-51(1946).

This is a general review of the physiological effect of nuclear energy. The author states that the white blood cell count, and particularly lymphocyte count is the most sensitive index for possible injury. He discusses briefly other tissues which are affected and touches on the use of radioactive isotopes as therapeutic agents; brief discussion on use of radioactive phosphorus as a radiotherapeutic agent. (S.V.S.)

65

Warren, Shields. **THE PATHOGENESIS OF IRRADIATION SICKNESS.** *Chicago Med. Soc. Bull.* 51: 957-9(1949).

The syndrome of radiation sickness is discussed as it applies to mass radiation by atomic weapons. The cells of the body which have a short life-span are more affected by the radiation than those with long life-spans, and rapidly dividing cells, or those in mitosis, are more affected than cells in the resting phase. A dose of 400 r is usually fatal to about $\frac{1}{2}$ of the human population present. There is great variability in the sensitivity of different cells and organisms in general. It is believed that the heaviest types of doses cause disruption in the enzyme systems and vital functions of most of the body cells and death occurs promptly without much evidence of morphological change. Slides are presented which indicate specific and individual reactions to the radiation doses. These include multiple leukopenic abscesses and cellulitis of the neck. The different stages of development of the symptoms are pointed out. If the radiation dose is more than 500-600 r, the chances of survival are small. Future problems connected with mass effective medical care of radiation victims are discussed. Prevention rather than cure is suggested as the most promising method of handling the radiation sickness problem. Lecture with slides. (NSA)

66

Warren, Shields and Austin M. Brues. **PROTECTION AGAINST RADIATION HAZARDS.** *Nucleonics* 7: 70-6 (1950). Oct.

A general review of the principles on which are based present ideas of radiation safety with special reference to the peculiarities arising from radioactive isotopes in the body. (BA)

67

Warren, Stafford L., Fred A. Bryan, and Robert J. Buettner. **THE ATOM BOMB: HAZARDS INCIDENT TO ITS USE.** *Ind. Med.* 16: 276-8(1947).

This paper was presented at a joint meeting of the American Association of Industrial Physicians and Surgeons and the American Industrial Hygiene Association, Buffalo, New York, April 30, 1947. The authors discuss the physical aspects of the atomic bomb and projected control measures. A general discussion of the physiological aspects is presented. The four major causative factors under which all the pathological results may be classified—blast effects, thermal effects, effects of radiation, and psychological effects—are reviewed. The authors conclude that the physician, and especially the industrial physician, had had a whole new set of problems placed before him with the use of atomic energy and its by-products of radio-isotopes. (S.V.S.)

68

Van der Werff, J. T. **BIOLOGICAL REACTIONS CAUSED BY ELECTRIC CURRENTS AND BY X-RAYS.** Elsevier Publishing Company, Amsterdam and London.

The main thesis of this book, which concerns itself with the experimental data accumulated by both radiologists and physiologists, is that in all living organisms parts are continuously being destroyed and then regenerated. A beam of radiation is thought to change the dissimilation coefficient and thereby the assimilation process. This premise is the basis of mathematical derivations which correlate the data from the two sources. The derived curves often fit the actual observations. (NSA)

69

Zirkle, Raymond E., et al. **PLUTONIUM PROJECT SYMPOSIUM.** *Radiology* 49, 269-365(1947).

A study of the acute lethal action of slow neutrons established the LD_{50} as 4.2×10^{12} slow neutrons per cm^2 of mouse. Results of chronic radiation on mice, guinea pigs, and rabbits are reported. Carcinogenic action and sterility effect dominate the picture of radiation injury. As far as genetic changes are concerned, the data indicate that the present permissible dose (0.1 r/day) gives a sufficiently wide range of safety that a detectable increase in rate of gene mutation and translocations will not occur. The data also suggest that an intensity factor exists. No hematological change is detected in mice, rabbits, or guinea pigs with a daily whole-body exposure to 0.1r of γ radiation extending over 3 years. Changes may be observed for doses above 1.1 r per day with guinea pigs most sensitive, followed by mice and rabbits. Human beings subjected to whole-body x-ray exposure totaling 300 r given in divided daily doses of 5 to 20 r showed a degree of sensitivity of the hemopoietic system roughly compatible to that of the guinea pig and the dog. The clinical sequence of physiological effects of ionizing radiations is briefly reviewed. The effects of total surface β -irradiation in doses below the acute lethal range are shown to result in greater gross and superficial damage than that following irradiation with the more penetrating x and γ -rays. The metabolism of fission products and the heaviest elements are reviewed. Histological changes following a great variety of radiation exposure are discussed. Experiments are reported that have been carried out with mice to determine the late effects of periodic and single exposures of fast neutrons, slow neutrons, γ -rays, and β -rays (limited to the skin, from pile radiation). A general report is given on "Carcinogenic Properties of Radioactive Fission Products and of Plutonium". (TIS)

II EFFECTS OF EXTERNAL RADIATION

Time-Intensity Studies

70

Abele, Adolph. EXPERIMENTS ON RHYTHMIC IRRADIATION OF THE EGGS OF *DROSOPHILA MELANOGASTER* MEIG. *Strahlentherapie* 67: 293-306(1940).

A study was made of the rate of injury to eggs of *Drosophila* produced by irradiation with the same total dose of x-rays when administered at different intensities (95, 47.6, and 23.7 r per min) and with both continuous and rhythmically interrupted irradiation (intervals of $\frac{1}{13}$ to $\frac{1}{200}$ sec). (CA)

70a

Bless, A. A. THE BIOLOGICAL EFFECTS OF X-RAYS AS A FUNCTION OF INTENSITY. *Proc. Nat. Acad. Sci. Wash.* 30, 118-21(1944).

The seeds (wheat) were soaked in water for three hours, and then spread in trays over moist filter paper. After 12 hours the seeds were placed on plates and exposed to x-rays. After 48 hours of sprouting, the length of the stems was measured; this was used as the biological indicator. Graphs of results show that different intensities do not produce any marked differences. (PA)

70b

Brasch, Arno and Wolfgang Huber. ULTRASHORT APPLICATION TIME OF PENETRATING ELECTRONS. *Science* 105: 112-17(1947).

Many drugs, foodstuffs, and cultures of microorganisms were exposed to penetrating electrons which were released during a time period of about 10^{-8} sec. The electronic intensity was about 30,000 - 50,000 amps. To determine the over-all extent of side reactions, distilled and tap water were irradiated, and it was found that with dosages comparable to those causing complete sterilization, the H_2O_2 formation was less than 0.005%.

The experiments were done at room temperature. At $-100^\circ C$, the final $H_2O_2\%$ was only about $\frac{1}{10}$ that formed at room temperature. This method in combination with ultrashort exposure times provided a means to preserve many raw foodstuffs, without changes in appearance, taste, or odor. Not only oxidation but also all other processes, except for very rapid reactions were suppressed. An apparatus called the "Capacitron," based on these principles, which has a high sterilizing capacity is discussed. This device carries sufficient intensities into the targets in such short times that most chemical reactions can be eliminated while the effective biologic impact is maintained. (BA)

70c

Brunst, V. V. and E. A. Sheremetieva-Brunst. THE TIME FACTOR IN LETHAL EFFECTS OF TOTAL ROENTGEN IRRADIATION IN TRITON. *Am. J. Roentgenol. Radium Therapy* 62, 550-4(1949).

The results of an investigation to determine variations in the effect on adult tritons (*Triton cristatus*, Amphibia, Urodels) with variations in the length of time used to distribute a definite total dosage of radiations are presented. The radiations were delivered by a 120-kv source with a filtration of 3 mm Al, and at variable target distance; in the first series of experiments, all groups were given 3,000 r total body irradiation, fractionated in daily doses of 150-3,000 r; in the second series all animals received a total of 2,000 r, delivered in daily doses of 100-2,000 r. The results indicate that the lethal effect of total body irradiation on the adult animals is not dependent on the distribution of the dosage in time; the triton apparently accumulates even small doses during a long period of protracted or fractionated treatments. 21 references. (NSA)

71

Casarett, George W. PILOT EXPERIMENTS ON INDICATIONS OF RADIATION SICKNESS AND COMPARISON OF LETHAL DOSES OF X-RAYS FOR RATS AND DOGS AT INTENSITIES OF 160r PER HOUR AND WHEN DELIVERED IN 24 HOURS. University of Rochester. Apr. 17, 1950. 88p. (UR-113)

Pilot experiments were carried out to investigate correlations among factors including radiation sickness and mortality, and dose and intensity of x-radiation (total-body-exposure). The source of radiation was a 1000-kv peak generator, equipped with a lead parabolic filter, and having a half value layer equivalent to 5.12 mm of lead. In a study of radiation sickness, single doses of 75, 150, 300, and 550 r were administered to groups of 12 rats each; and single doses of 40, 80, 120, and 200 r were administered to groups of 4 dogs each, at an approximate rate of 160 r/hr. Body weight determinations, food consumption measurement, and superficial physical examinations were made daily. There were no deaths among these animals. In rats, a dose of 500 r produced a transient radiation sickness of moderate degree, and a dose of 300 r produced a mild, transient radiation sickness. The effects of doses of 150 r and 75 r were slight and transient. In dogs, a dose of 200 r produced only a mild, very transient reduction in food consumption, and lower doses resulted in no significant change with regard to measurements made. In a comparison of lethal effects of x-rays for rats and dogs, with intensities of 160 r/hr. and when the dose was delivered in 24 hours, single doses of 600, 750, 900, and 1050 r were administered to groups of 20 rats each at a rate of about 160 r/hr., and single doses of 600, 750, 900, 1050, 1300, and 1500 r were administered to groups of 20 rats each at rates such that each dose was delivered in 24 hours. Single doses of 250, 310, 370, and 430 r were administered to groups of 6 dogs each at a rate of about 160 r/hr. Single doses of 300, 400, 500, 600, 750, and 1000 r were administered to groups of 6 dogs each at rates such that each dose was delivered in 24 hours. The data obtained, together with data from other sources, suggest that up to a certain point, decrease in intensity of a single dose of x-radiation may result in decreased mortality to some extent. The data suggest, also, that a dose high enough to produce severe signs of radiation sickness will also have associated with it considerable mortality. Survival times, weights, clinical observations, and gross pathology observed at autopsy are described for these animals, as well as mortality. (NSA)

72

Forssberg, A. THE TIME FACTOR IN BIOLOGICAL EFFECTS OF X-RAYS. II. INVESTIGATIONS OF ALGAE AND *DROSOPHILA*-PUPAE. *Acta Radiol.* 14, 399-407(1933).

In experiments on unicellular algae, 5,000 and 10,000 r x rays at a rate of 22 to 3,235 r/min were used, on *Drosophila chrysallides* 2,000 r at a rate of 5 to 3,235 r/min. The radiation effects on mortality and cell division retardation of the algae increased at first rapidly with increasing intensity until a maximum was reached at 1,620 r/min. In *Drosophila chrysallides*, the limit of effect was reached with about 20 r/min. The amount of effect produced by irradiations of from 22 to 3,235 r/min was more or less the same. (TIS)

73

Furth, F. W., M. P. Coulter, and J. W. Howland. EFFECTS OF A SECOND LARGE DOSE OF X-RADIATION ON DOGS SURVIVING ONE DOSE OF X-RADIATION, p.47-53 of QUARTERLY TECHNICAL REPORT; OCTOBER 1, 1950 THROUGH DECEMBER 31, 1950. University of Rochester. Feb. 1, 1951. 7p. (UR-152 (p.47-53))

Nineteen dogs were given two dosages of 450 r of x radiation with intervals of 5 to 12 months between them. Following the first dose of radiation, only 30% of the dogs showed any signs of radiation toxicity, and all dogs appeared normal at the time of the second radiation dose. The erythrocyte and platelet counts after the first dose of radiation returned to normal within 60 to 90 days, but the leukocyte counts returned to only 70% of normal preradiation value. After the second dose of radiation, all the dogs showed signs of severe radiation illness, and only one animal survived. The weight loss was greater after the second dosage of radiation. The rate of fall of erythrocyte, leukocyte, and platelet counts after the second irradiation was essentially the same as after the first. (NSA)

74

Gershon-Cohen, J., Harry Shay, and S. S. Fels. EXPERIMENTAL STUDIES WITH "CONTACT" ROENTGEN RAYS: THE TIME-INTENSITY FACTOR OF THE "TUMOR DOSE" FOR RAT SARCOMA 39 IN SITU. *Am. J. Roentgenol. Radium Therapy* **45**, 600-4(1941).

Using a Chaoul contact x-ray apparatus operating at 60 kv with 0.12 mm Cu filter, 3 cm focal-skin distance, 450 r per min., the lethal dose for rat sarcoma 39 in situ was 10,000 r administered in a single dose, if the tumor was about 10-15 mm in diameter. This condition usually existed about 15-19 days after transplantation. Under these circumstances the tumor disappeared with survival of the animal. With divided doses the effect was less, and the decrease in effect was more marked as the total irradiation period became greater. (BA)

75

Glucksmann, A., K. Tansley, and C. W. Wilson. THE EFFECT OF VARIATIONS IN THE DOSE-RATE OF GAMMA RADIATION ON CELL DEGENERATION IN THE FROG TADPOLE. *Brit. J. Radiol.* **18**, 158-64(1945).

Tadpoles were exposed to a dose of 336 r of gamma radiation, given at 5 different dose-rates varying from 5 to 20 r/min. The effects, measured by the number of mitotic and degenerate cells present at different intervals after exposure in the brain and the eye, varied with the dose-rate as follows: (a) The maximal degeneration count increased with the dose rate. (b) The interval between irradiation and the time at which degeneration reached its maximum increased with the dose rate. (c) The total amount of degeneration was highest for a dose-rate of 15 r/min. The results show that under the conditions of these experiments there is an optimal dose-rate. The experimental results are discussed in terms of the interaction of the various biological processes involved. (auth)

76

Goldfeder, A. FURTHER STUDIES ON THE EFFECTS OF IRRADIATION ON PROLIFERATION AND METABOLIC PROCESSES OF NORMAL AND MALIGNANT TISSUES. IV. EFFECTS PRODUCED BY DIFFERENT DOSAGE RATES OF X-RAY RADIATION ON THE PROLIFERATION OF VARIOUS TISSUES GROWN IN VITRO. *Radiology* **35**, 210-28(1940).

The tissues studied were kidneys and spleens of $\frac{1}{2}$ day old rats, mouse sarcoma 180 of 8-10-day growing tumours in the animal body, and 8-day-old chick embryo hearts. Freshly excised tissue fragments of 2-5 mg were placed in a thin layer of nutritive medium, irradiated, washed in Tyrode solution, placed in a freshly prepared medium, and incubated. The dosage rates employed were 234 and 936 r per min. produced at 200 kv, 20 ma, 0.5 mm Cu plus 1 mm Al filter with a half-value layer of 0.85 mm of Cu, the tissue target distance being 25 and 12.5 cm, respectively, and 10,000 r per min. produced by a contact therapy tube

(cf. Braestrup, A., 1941, III, 46). The critical doses preventing proliferation rose from 80,000 to 140,000 r for rat kidneys and the three dosage rates, from 130,000 to 260,000 r for chick embryo heart using the two higher dosage rates, from 50,000 to 90,000 for sarcoma 180 at the same rates, and lay at 60,000 r for rat spleen at 936 r per min. whilst the first growth-inhibiting effects were seen at 50,000-90,000, 90,000-100,000, 30,000-50,000, and 40,000 r, respectively, representing a drop of 15-25% of proliferating explants against the controls. In addition to the decrease in per cent of growing explants within the range of critical dosage, a decrease in size of the new growth, a latent period of 48-72 hr, and liquefaction of the nutritive medium were also observed. (BCPA)

77

Heeren, I. G. THE EFFECT OF DISCONTINUOUS X-IRRADIATION ON RETICULOCYTE COUNTS IN THE MOUSE. *Strahlentherapie* **77**, 383-6(1948).

The course of the reticulocyte count in male white mice was used to compare the effects of continuous and discontinuous irradiation. In both cases the dose was 100 r in nine minutes. The lowering of the reticulocyte value was less after discontinuous irradiation. The reticulocyte count fell from an average of 5.5 to 2.5% two to three days after continuous irradiation. It had risen to 10.6 to 18.5% six days after and subsequently moved rhythmically between these values. However, after discontinuous irradiation, produced by a rotating lead shutter with an irradiation-interval relation of 1 to 9, the fall was less than three days after, namely 3.6 to 4%, and subsequent variations lay between 12.3 and 15.4%. With 16 intervals per second the figures were 3.6 and 16.5 to 31.2%. The author concludes that it is possible through rhythmical interruption of irradiation to regulate the irradiation reactions of tissue. (NSA)

78

Lamarque, Paul. STUDY OF RECOVERY AFTER IRRADIATION WITH X RAYS. *J. chim. phys.* **48**, 252-5 (1951).

Hatching-rate curves of repeatedly x-irradiated eggs of the common silkworm (*Bombyx mori*) point to the existence of a recovery effects; the total dose of two irradiations, separated by a time interval, is larger than the dose of a single irradiation producing the same damaging effect. For a 7-hr interval the optimal recovery is observed when the ratio between the first partial dose and the total dose is equal to $\frac{2}{3}$. Recovery processes are ascribed to metabolic activities of the cell. (NSA)

79

Lorenz, Egon, Allen B. Eschenbrenner, M. Derringer, and W. E. Heston. BIOLOGICAL ACTION OF GAMMA AND X-RAYS. I. EXPOSURE OF MICE TO DAILY DOSES OF GAMMA RADIATION AT TWO RATES: 5.5 r/HR. AND 0.11 r/8 HR. *J. Natl. Cancer Inst.* **6**, 349-53(1946). (MDDC-907; CH-2576)

Haematology: Female LAF-1 mice were exposed to daily doses of 5.5 r in one hour (I_1) and 5.5 r in one hour, plus 0.11 r in eight hours. Biweekly blood counts were taken on these animals. They came to autopsy after having received total doses ranging from 600 to 1,600 r. The blood picture of these animals is comparable to that of controls of the same age with the exception that the neutrophil count was higher than normal for most of the experimental animals. This increase in neutrophils was probably due to a low grade pneumonia and not due to the irradiation. Radiation effects were observed only in lymph nodes, spleen and ovaries while all other organs were within normal limits histologically. An exposure of mice to 5.5 r/hr/day up to total doses of approximately 1,600 r produces radiation

effects on the ovaries similar to and not more pronounced than those observed when similar doses are given at the rates of 4.4 r/day, 8.8 r/day and 8.8 r/8 hr/day. The discrepancy between a single sterilization dose of 300 r and a dose of approximately 900 r given daily at the above rate seems to indicate that a certain amount of recovery of the ovary is possible when doses are subdivided. Whether the subdivision of the dose or the rate of administration of the dose is more important in producing sterility has to be decided by further experiments. (ADD)

80

MacKee, G., A. Mutscheller, and A. C. Cipollaro. **TIME FACTOR IN IRRADIATION.** Arch. Dermatol. and Syphilol. 47, 490-7(1943).

Two series of experiments were performed on a total of 29 persons: in the first series two adjacent skin areas of the inner surfaces of the forearm or the thigh were exposed to non-filtered X-ray radiation of 52 kV and 10 mA, in the second series 100 kV and 5 mA were used. The half-value layer of the first experimental series amounted to 0.5 mm of aluminum, the second series to 0.8 mm of aluminum. The variable factors were represented by distance and time of exposure. The experiments confirmed the general validity of Holthusen's radiation intensity curve and suggested the logarithmic formula for the definition of radiation quantity of $\log r/m = K (\log [r_t - r_1])$, in which formula r/m represents roentgens per minute, r_t the total exposure time, and r_1 , the value of latent radiation. The generally observed decreases in the effectiveness of radiation with lower intensities is explained as being due in reality to the healing or recovery of the tissues during the course of irradiation. (EM)

81

Noonan, T., F. Van Slyke, and J. Hursh. **EFFECT OF SINGLE DOSES OF X-RAY ON THE SURVIVAL OF RATS.** University of Rochester. Apr. 20, 1951. 12p. (UR-161)

Parallel groups of male and female 5-month-old Wistar albino rats were used. Three groups, each of 24 rats, received respectively 150, 300, and 600 r in single doses of 250-kvp x irradiation delivered at 18.5 r/min. Twenty-four male and 24 female rats served as controls. The mean survival times appear to be reduced by an amount proportional to the dose in both the male and female series. The spread of the data does not permit the exclusion of a possible threshold effect on survival as tested for the 150-r groups vs. the controls. Tumors which were grossly visible occurred in a larger number of 150- and 300-r female rats than in the control group. (NSA)

82

Paterson, Edith. **THE TIME-INTENSITY FACTOR IN X-RAY IRRADIATION.** Brit. J. Radiol. 17, 26-30(1944).

Studies of experiments are recorded on the effect of varying the over-all time, dose and dosage-rate per session being kept constant. Culture of chick fibroblasts, maintained by the hanging drop method as described previously by Paterson (1942) were divided into two or more groups and were x irradiated. The dosage levels chosen were those found by experience to give, on a short term basis, a moderate proportion of surviving cultures. The dosage rate per session of irradiation was the same for the short-term and long-term parts of any one experiment. Three variations of short-term irradiation were employed: (a) short continuous irradiation which was completed in a matter of hours; (b) short-term intermittent irradiation in which the total dose was given in two sessions over a period of three days; and (c) short-term irradiation in which the total dose was given in three sessions covering

a period of 4 days. In all cases the long-term irradiation covered a period of 21 days. The criteria of effect employed was the survival rate and survival time of the cultures. An increase of the over-all time of radiation to 21 days increased the lethal effect when the dose was split into 11 sessions. This increased effect was seen as a decreased proportion of survivors and a decreased survival time if the latter was calculated for long-term experiments from any point subsequent to the beginning of radiation. A qualitative difference was also shown by a lessened variation from the median point of death and a failure of cultures to show the recovery phenomena after long-term radiation. The degree of splitting of long-term radiation was of importance in influencing the effects. Some of the implications of these findings are discussed. (S.V.S)

83

Paterson, Edith and M. V. Thompson. **TIME-INTENSITY FACTORS IN X-IRRADIATION. PART II. THE INFLUENCE OF THE DOSAGE RATE.** Brit. J. Radiology 21, 414-19(1948).

Four groups of experiments were made on chick fibroblasts grown in vitro with the purpose of determining the lethal influence of dosage-rate uncomplicated by other factors. The over-all time was kept constant for all the sections of any one experiment. Dose levels of 10,000 r to 12,000 r were given by 250 kv continuously evacuated X-ray tubes. Dose-rates of 4 r/min. to 5 r/min. were contrasted with rates of over 100 r/min. The lethal effect of irradiation by a high dosage-rate, highly fractionated, was found to be the same as that of low dosage continuous irradiation. The effect of highly fractionated high dosage-rate irradiation, however, was less than that of irradiation given at the same dosage-rate in fewer fractions but with an interval of over 40 hours. Therefore, dosage-rate as such is of less importance than the dose per fraction or the intervals between fractions, and it may be concluded that, in comparisons between high dosage-rate irradiation given over a short time and that at low dosage-rate continued over a longer period, the operative factor is the over-all time. (NSA)

84

Paterson, Edith. **TIME-INTENSITY FACTORS IN TOTAL BODY IRRADIATION,** p.161 of INTERNATIONAL CONGRESS OF RADIOLOGY, 6th Congress, London. 1950.

The effect of prolonging the over-all time of irradiation has been studied in two pure-bred strains of mice, using 250 kv. X-radiation. Various biological criteria have been adopted, including the L.D.50/30 days, the Mean Survival time and the Variance. Over-all times of about 10 minutes are compared with those of 24 and 48 hours, and also with periods of 5, 10 and 21 days. For any given time factor the probits of mortality percentages plotted against dose give a straight line. As the over-all time of irradiation is extended by fractionation of the dose into daily sessions, the L.D.50 rises; with an over-all time of 21 days the L.D.50 dose is nearly double that for single session radiation given in both cases at the same dosage rate. Another approach has been made by finding the L.D.50 when irradiation is given in two sessions at varying intervals.

85

Poulsen, B. R. **INVESTIGATION INTO THE TIME FACTOR IN THE ROENTGEN IRRADIATION OF CANCER CELLS. PROTRACTION EXPERIMENTS WITH A TRANSPLANTABLE MOUSE CARCINOMA.** Acta radiol. 26, 463-83(1945).

Protraction experiments have been made with two mouse-transplantation tumours: a rapidly growing, sensitive

round-cell sarcoma, and a slowly-growing, resistance carcinoma. The criterion of the effect was the percentage of takes and the latent period for the development of the tumours. The investigations were carried out with a new experimental method which gives great statistic reliability. The objects were irradiated with the middle dose at the intensities of 58-13.3-3.3- and 1 r/min. In the case of carcinoma there was found (expressed both by the percentage of takes and by the latent period) a steadily decreasing effect with increasing protraction. The percentage of takes falls about 20% when the intensity is varied from 58 r/min to 1 r/min. The latent period for the development of the tumours was decreased at 1 r/min. to about half of what it was at 58 r/min. The round-cell sarcoma shows unchanged effect when the intensity is varied from 58 r/min. to 3.3 r/min. but at 1 r/min. there is a distinctly increased effect, the percentage of takes in the two experiments being lowered by at least 25%. This increased effect is also observable in the latent period for the development of the tumours. The decreasing effect on the carcinoma with increasing protraction is easily explained as an incomplete cumulation as a result of regeneration during irradiation. The increased effect of a low intensity on the round-cell sarcoma must be assumed to express that at this intensity (round about 1 r/min.) a critical intensity has been demonstrated, as with steadily increasing protraction the effect must again decrease at some low intensity or other. Two hypothesis are advanced in explanation of the critical intensity. (auth)

86

Russ, S. and G. M. Scott. **BIOLOGICAL EFFECTS OF GAMMA IRRADIATION (SERIES II).** Brit. J. Radiol. **12**, 440-1(1939).

In a previous paper (Brit. J. Radiology **10**, 1937) the authors reported biological effects of continuous exposure of rats to γ rays. In the present experiments the same daily dose and the same total dose were administered, but on two days no irradiation was given, the lost days being made up by extending the time over which the treatment series lasted. The biological effects were just as marked as when daily irradiation was performed. There was a considerably greater death rate among the irradiated rats during the period of irradiation (45.8% to 14.8%); more rapid aging with persistence of the higher death rate; and great damage to breeding powers. (BA)

87

Sacher, George A. **A NEW PROCEDURE FOR THE INVESTIGATION OF X-RAY INJURY AND RECOVERY, AND SOME PRELIMINARY RESULTS**, p.83-5 of **BIOLOGICAL AND MEDICAL DIVISIONS; QUARTERLY REPORT, FEBRUARY, MARCH, APRIL, 1948.** Argonne National Lab. May 1, 1948. 3p. (ANL-4163(p.83-5))

Author describes preliminary experiments carried out on mice and rabbits in which the animals were given single "conditioning" X-ray doses in the fractionally lethal range. After a period of time sufficient for the initial phase response to subside, the surviving animals were subjected to daily X-ray exposures at a relatively high dose rate for the duration of life. The results to date are summarized in a table. (S.V.S)

88

Sacher, George A. **THE SURVIVAL OF MICE UNDER DURATION-OF-LIFE EXPOSURE TO X RAYS AT VARIOUS DOSE RATES.** Univ. of Chicago Metallurgical Lab. Apr. 1950. 43p. (CH-3900)

The survival of two strains of mice is reported for dose rates extending from 20 to 1000 r/day. The relations between mean survival time, mean accumulated dose, and dose

rate are exhibited. The relation of repeated-dose lethality to single-dose lethality is investigated and the quantitative consistency is discussed. The hypothesis of a lethality process is introduced. On this hypothesis a lethality function is deduced, and its characteristics discussed. The deduction of the lethality function required certain mediating assumptions about linearity and about the properties of a defined lethal bound of injury. These assumptions are discussed. Applications of the conceptions developed are considered briefly. 18 references. (NSA)

89

Schottelndreyer, H. **STUDIES OF THE EFFECT OF THE PROTRACTION OF X-RADIATION BY 12 FRACTIONATIONS ON THE ERYTHEMA REACTIONS.** Brit. J. Radiol. **22**, 386-92(1949).

Three experiments were carried out on women patients in order to study the effects of the protraction of x-radiations on the erythema reactions. Two of the patients were under treatment for gynecological carcinomas and the third was being treated for an inflammation of the adnexa; all had normal skin conditions at the time of treatment. Each experiment is described in detail. The results show that the biological effect of a single irradiation with 631 r on the skin is equivalent to that of 2064 r when given in 12 fractions irrespective of whether an effective dose rate of 5.25 r/min. or a rate of 112 r/min. is used, confirming the observation of Kepp (Strahlentherapie **72**, 195 (1942)) that, when using 12 fractionating doses, protraction of the delivery time has practically no effect on the biological erythema dose. Similarly, it was found that a similar protraction does not have any detectable influence on the erythema effect using 12 fractions when the above doses are increased or decreased by 20%. The sensitivity of the reaction lies between ± 10 to $\pm 20\%$ of the normal dose. (NSA)

90

Sievert, R. M. and A. Forssberg. **THE TIME FACTOR IN THE BIOLOGICAL ACTION OF ROENTGEN RAYS. III. INVESTIGATIONS AT VERY SHORT IRRADIATION TIMES.** Acta Radiol. **17**, 290-8(1936).

The authors describe investigations of the death rate of *Drosophila* eggs after irradiation with about 165 r in very short periods, varying from 0.39 to 1.16 seconds. This corresponds to radiation intensities of 24,000-7,800 r/min. They compare the results with those previously obtained with the same dose given in from 2.1 seconds-30 minutes. A critical study of the possible sources of error indicates the probability that the irradiation effect diminishes at very short radiation times. The experiments show that the death rate is reduced at 0.39 seconds by more than 20%. The authors are of the opinion, however, that experiments with still greater intensities are advisable in order to confirm the results. (AR)

91

Stearner, S. Phyllis. **THE EFFECT OF VARIATION IN DOSAGE RATE OF ROENTGEN RAYS ON SURVIVAL IN YOUNG BIRDS.** Am. J. Roentgenol. Radium Therapy **65**, 265-71(1951).

Survival following roentgen irradiation of young birds depends on total dose, dose rate at which the exposure is made, and age at time of exposure. Exposure of 2- to 3-day chicks to 1000 r at a rate of 15 r/min or more resulted in a 75% mortality within 24 hr. Exposure to the same dose at 6 r/min resulted in only 1% mortality within 24 hr, and 46% between 5 and 10 days after irradiation. The mechanisms leading to the early deaths are not clearly understood. It is suggested that the biological effects of variation in dose rate indicates that recovery is taking place during an exposure at the low rate so that the total

effect of the dose is less than if it were given at a high rate. (NSA)

92

Stearner, S. Phyllis and Emily J. B. Christian. PROGRESS REPORT; INFLUENCE OF DOSAGE RATE ON X-RAY EFFECTS IN YOUNG CHICKS AND RATS, p.125-9 of BIOLOGICAL AND MEDICAL DIVISIONS; QUARTERLY REPORT, NOVEMBER, DECEMBER, JANUARY, 1949-50. Argonne National Lab. [nd] 5p. (ANL-4401(p.125-9))

Mortality of 2- to 3-day chicks within 24 hours after x-irradiation (1,000 r at 43 r per minute) has been described earlier. Administration of vitamin P substances had no effect on survival or hemorrhagic tendencies. Histamine is probably not an important factor in the reactions leading to the early deaths, for the chick shows a relatively low sensitivity to histamine shock. Although the speed with which death follows irradiation suggests that some part of the effect might be mediated through the autonomic nervous system, prophylactic and therapeutic treatment with atropine and physostigmine was without effect. Adrenaline was effective in increasing survival and in decreasing the severity and number of hemorrhages when its time of administration was close to that of x-irradiation. Further experiments are under way to determine more precisely its time of action. Hematocrit determinations indicated that a hemoconcentration was present at 3 and 5 hours after exposure at the high dosage rate. Exposure of 1- to 5-hour rats to 600 r at 80 r per minute resulted in 48% mortality within four days, but no deaths occurred during this period if the exposure rate was 6 r per minute. In all animals, cerebral hemorrhages developed within a few hours after irradiation, but the hemorrhages were greater (more diffuse) and more numerous after high rate exposure. Histopathological studies are planned following exposure of newborn rats. Experiments are in progress to determine effects of other dosages and intermediate dosage rates. (auth)

93

Stearner, S. Phyllis and Emily J. B. Christian. THE EFFECT OF OVER-ALL TIME OF EXPOSURE UPON SURVIVAL OF YOUNG CHICKS FOLLOWING ROENTGEN IRRADIATION. Am. J. Roentgenol. Radium Therapy 65, 272-6(1951).

Survival following exposure to fractionated roentgen-ray dosages indicates that over-all time is of greater importance than dosage rate in determining the lethality of a given dosage for newly hatched chicks. Survival is increased as the over-all time of exposure is increased, but not at a proportional rate. (NSA)

94

Van Roojen, J. INTENSITY OF RADIATION AND SELECTIVE ACTION. Brit. J. Radiol. 12, 547-53(1939).

It is now generally agreed that the action of radiation is independent of the wave length. If there is a difference between the action of the gamma and X-rays, it must be due to some other factor. The only other possible variation is intensity. Experiments have indicated that variation in effect might be due to variation in the periodicity of sensitivity of cells or to a process of recovery taking place while the destructive process is going on. The shape of dose-intensity curves indicates that the latter takes place. With high intensities the dose is independent of the intensity. With low intensity the dose must be increased. These facts are confirmed by clinical experience. Equations are derived showing these effects mathematically, disregarding recovery effects, making use of several reasonable assumptions. The concept of a specific sensitivity of cells so that they can be arranged in an order of susceptibility does not hold for low intensities. Selectivity of action appears

when the intensity is so low that the factor of recovery comes in. It is possible that we may be able to improve results by further decreasing the intensity but we do not yet know if this is so, nor how much reduction is best. Lowering of the intensity cannot be pushed beyond a certain point if the desired result is to be obtained. The destruction must be greater than the normal rate of growth. Reducing the intensity may allow us to continue the radiation until the tumor has vanished, thus relieving us of the uncertainty about the total dose required. Geometrical homogeneity of distribution is important. Successive application of beams from various ports is not equivalent to continuous action in a homogeneous field. (R)

95

Warren, S. L. and G. H. Whipple. THE CUMULATIVE EFFECT OR SUMMATION OF X-RAY EXPOSURES GIVEN AT VARYING INTERVALS. J. Exptl. Med. 38, 725(1923).

It is generally accepted that X-ray exposures repeated at short intervals give a summation effect, but the observations are largely concerned with skin injury. Accurate measurements have been made on the dose necessary for destruction of the mucosa of the small intestines in dogs. From experiments performed by dividing the maximum sublethal dose in dogs, it was found that the ordinary cumulative effect noted in skin reactions does not apply to depth reactions. A single large dose of X-rays over the abdomen will cause a definite injury of the mucosa of the small intestine and the severity of the clinical intoxication seems to parallel this recognizable epithelial injury. This clinical intoxication lasts 4 to 6 days, if the X-ray dose is sublethal. Subsequent doses of radiation given with this period of clinical intoxication give recognizable evidence of summation or a cumulative effect. Small but repeated doses of radiation given within a 5 or 6-day period will cause practically the same cell injury and clinical intoxication as will a single dose representing the sum of small doses expressed in milliamperes minutes. Doses of radiation given at 6-day or longer intervals show no evidence of summation. The reaction of this relatively sensitive intestinal epithelium to radiation may be similar to the reaction of certain deep-lying tumor tissues to X-ray therapy, and our experiments may give information of value to physicians concerned with X-ray or Ra therapy. (R)

Lethal Dose Studies

96

Altland, Paul D., Benjamin Highman, and Betty Wood. SOME EFFECTS OF X-IRRADIATION ON TURTLES. J. Exptl. Zool. 118, 4-14(1951).

Box turtles were given whole-body x irradiation with doses ranging from 500 to 10,000 r. In general the effects of x irradiation on turtles appeared to be similar to those on mammals, but they occurred at a much slower rate. Turtles survived for 270 days (alive at writing) with doses of 500 r; 4 of 6 survived longer than 4 months after 1000 r; 2 of 6 turtles receiving 1500 r survived 4 months; higher doses up to 10,000 r caused death in from 18 to 48 days. The carapace and plastron reduced the tissue dose by approximately 10%. Effects on circulatory and general systems are noted. (NSA)

97

Betz, H. THE IMPORTANCE OF THE RESISTANCE PHASE OF THE ORGANISM AT THE TIME OF APPLICATION OF A LETHAL DOSE OF X RADIATION. Compt. rend. soc. biol. 144, 1439-42(1950).

In order to determine whether a radiation-resistance phase could be produced, three lots of C57 mice were irradiated with a nonlethal dose of 500 r of x rays followed at 7, 10, and 15 days, respectively, with a 700-r dose. In contrast to a 700-r-irradiated control lot, all of which succumbed by 10 days, the lots receiving the 7-, 10-, and 15-day fractionated exposures showed decreased rates of mortality and 20, 26.5, and 36% survival, respectively. The protective action of the nonlethal exposure is discussed inconclusively. (NSA)

98

Boche, R. D. and F. W. Bishop. STUDIES ON THE EFFECTS OF MASSIVE DOSES OF ROENTGEN RADIATION ON MORTALITY IN LABORATORY ANIMALS. Univ. of Chicago Metallurgical Lab. [nd] 13p. (MDDC-250)

The object of these experiments was to supplement the existing literature on the effects of single acute exposures of animals with a view of forming an estimate of what variations exist among different mammalian species. The applicability to man is uncertain but one may assume as a first approximation that his sensitivity lies within the range of other species. Systematic studies have been made on the behavior of peripheral blood elements in the rat, dog, and monkey following single exposures. Tissue studies on animals sacrificed serially have been carried out for the rat and fairly complete histology has been done on animals at death. It is now well established that curves relating mortality to dose are of the sigmoid type for most organisms studied and the mammals are no exception in this respect. Such sigmoid curves may be conveniently transformed to straight lines by the method of Bliss which is based on the assumption (a) of normally distributed susceptibility of the individuals radiated and usually (b) geometric increase in effect with increasing dose. Such straight lines proved the simplest method of estimating the median lethal dose for a given set of conditions and variations in LD-50's constitute a convenient basis for comparison of species or other factors. Mortalities and average survival times are tabulated and plotted for various animals given varying doses of roentgen radiation. (ADD)

99

Bonet-Maury, P. and F. Patti. LETHAL IRRADIATION OF MICE BY X-RAYS AND GAMMA-RAYS. THERAPEUTIC TRIALS. J. radiol. et electrol. 31, 286-9(1950).

A study on the effects of X-rays administered in doses varying between 400 and 100,000 r, on the survival of mice (heterogeneous groups). For 100% of the mice the lethal dose is attained at 600 r. At 800 to 13,000 r the mean time of survival remains constant (80 hr). From 13,000 r onwards a new rapid fall in the survival time develops according to the dose. The first deaths during irradiation appear at doses of 60,000 r (output: 470 r/min). At 100,000 r the mean survival time is 2 hours and 30 min. The variations due to age, weight, and sex proved negligible. Attempts to protect mice exposed to 1,000 r by using various substances (DOCA, horse serum) and certain methods of physical therapy (short waves, UV rays, grenz rays, darkness, illumination) did not meet with success. The effects of gamma radiation were submitted to similar investigations. The gamma X-ray ratio of effectiveness varied between 2.1 and 3.6. (EM)

100

Bonham, Kelshaw, Allyn H. Seymour, Lauren R. Donaldson, and Arthur D. Welander. LETHAL EFFECT OF X-RAYS ON MARINE MICROPLANKTON ORGANISMS. Science 106, 245-6(1947). (MDDC-1158)

Literature on the effect of x-rays on bacteria, yeasts, and Protista is summarized in a table showing that the average immediately lethal dose is 595,000 roentgens

(20,800-1,250,000) and that the average dose capable of stopping growth or cell division of these micro-organisms is 93,000 r (12,000-400,000). In this experiment vialled samples of *Chlorella* sp., *Nitzschia clostrarium*, a carteriid, and another mastigophoran (unidentified, brown) were each subjected to five exposures from 1,000 r to 100,000 r. Numbers of organisms per unit volume of culture were counted using ruled blood counting chambers. Immediate immobilization of the brown mastigophoran was 50% effective at 50,000 r, and 100% at 100,000 r. Counts for an organism were comparable only with other counts for different irradiation samples of the same organism on the same date. Counts over a period of four months were most nearly as might be expected in the case of *Chlorella* where the concentration of individuals remained inversely proportional to the amount of irradiation for practically the entire time, except in the case of the 1,000 r sample which exceeded one of the two controls. *Nitzschia* counts in the higher irradiations decreased earlier and more drastically than did those of *Chlorella*, but later these more heavily irradiated samples gave higher counts than the lower dosages. Counts of the two *Mastigophora* were arranged erratically with only a general tendency for count to be inversely related to exposure. In no case did a sample count drop to and remain at zero. (auth)

101

Clark, W. G. and R. P. Uncapher. DOSAGE-MORTALITY IN RATS GIVEN TOTAL BODY ROENTGEN IRRADIATION. Proc. Soc. Exptl. Biol. Med. 71, 214-6(1949).

Over 500 young male rats were used in studies to determine the dosage-mortality ratio for total body roentgen irradiation. The doses were delivered at different lengths of time by a 200-kv machine, at 52.5 cm target distance, and through $\frac{1}{2}$ mm Cu and 1 mm Al filters; the dose-rate was 30.4 r/min. in air. The mortality data represent indefinite survival of the rats (past 30-60 days) and are included in three graphs. The results show that the maximum dosage for rats in this series is 640 ± 5 r with a 30-day end-point. Because of the steep mortality curves in the rat groups, and the consequent errors in calculation, dosages in the lethal range should not be used. (NSA)

102

Cronkite, Eugene P., Clyde R. Sipe, Dean Eltzholtz, William H. Chapman, and F. W. Chambers. THE INCREASED TOLERANCE OF MICE TO A LETHAL DOSE OF X-RAY RADIATION AS A RESULT OF PREVIOUS SUBLETHAL DOSES. Naval Medical Research Inst. Report Number 15. Aug. 17, 1948. 6p. (NP-589)

It has been demonstrated with a fair degree of certainty (probability that results are due to chance, calculated by a pooled Chi square found to be between 0.02 and 0.05) that three weekly exposures of 144 r followed by a 30-day rest period increases the resistance of mice to a subsequent lethal dose of x-radiation. It is concluded that no adequate explanation for this phenomenon of increased tolerance to X-ray radiation is available at the present time. (NSA)

103

Ellinger, Friedrich. LETHAL DOSE STUDIES WITH X-RAYS. Radiology 44, 125-41(1945).

The applicability of a method for the determination of lethal doses of X-rays derived from the study of mice has been demonstrated for a larger animal, the guinea pig. With increasing doses of X-rays, an increase in the percentage mortality was found up to 500 r in air. This dose represents the absolute lethal dose (ALD) for guinea pigs under the conditions of the exposure used. As in mice and goldfish, the relationship between dose of X-rays and percentage mortality is expressed by an S-shaped curve. Comparison of the mortality curves of mice and guinea

pigs shows a steeper slope of the curve for guinea pigs. In connection with some observations concerning the latent period, this is considered to be an expression of species specificity. (R)

104

Ellinger, Friedrich. INFLUENCE OF DOSE FRACTIONATION ON THE LETHAL X-RAY EFFECT PRODUCED BY TOTAL BODY IRRADIATION IN MICE; A PRELIMINARY NOTE. *Radiology* 49, 238-41(1947).

Data are presented on the lethal effect upon mice of total body irradiation by a single dose, and a comparison is made with the effect of the same dose fractionated, 252 white male mice having been irradiated with 1,000, 500, and 400 r in air. Fractionation consisted in giving a dose of 100 r on successive days. The results are given in graphs, and show that there was in every case a reduced mortality rate after the fractionated dose, as compared with the mortality rate after the same dose given as a single exposure. The effect was found to be most pronounced for that dose which, when given unfractionated, resulted in the lowest mortality rate—in this case the 400 r dose. The author considers the result significant from the point of view of the physician, since there is here some suggestion that the living organism may tolerate as general radiation, multiple applications of a dose which is high enough to have an effect upon neoplastic tissue. (NSA)

105

Ellinger, Friedrich and James C. Barnett. FURTHER STUDIES ON THE INFLUENCE OF DOSE FRACTIONATION ON THE LETHAL X-RAY EFFECT PRODUCED BY TOTAL BODY IRRADIATION IN MICE. *Radiology* 54, 90-2(1950).

The influence of the size of the single exposure and overall exposure time on the lethal effect of total body irradiation of mice with x-rays was studied. A total of 220 white male Swiss mice were used in this experiment, 20 of which served as unirradiated controls. The irradiation was delivered by a 200 kv source through 0.25 mm Cu and 1.0 mm Al total filtration at a target distance of 50 cm and a dosage rate of 23.4 r/min. The effect of 1,000 r in air in one exposure (LD-100) was compared with that of the administration of the same dose when given in single fractions of 100-50 r in air within 10-20 days. It was found that the effect of dose fractionation in total body irradiation depends on the size of the single fraction as well as on the over-all exposure time; of these two factors, the size of the fraction appears as the more important. It also appears that, as with observations on tumor destruction, there exists a certain optimum for dose fractionation in total body irradiation. (NSA)

106

Ellinger, Friedrich, Jasper E. Morgan, Francis W. Chambers, Jr., C. R. Biles, and J. T. Istock. THE USE OF SMALL LABORATORY ANIMALS IN MEDICAL RADIATION BIOLOGY. I. APPLICATION OF A 200 KVP X-RAY THERAPY UNIT TO LETHAL DOSE STUDIES. Naval Medical Research Inst. Bethesda. Apr. 30, 1952. 35p. (NP-4120; U23980; NM-006-012.04.43)

A critical study of irradiation techniques and apparatus has been undertaken, with particular reference to the effective application of conventional X-ray therapy equipment. Major emphasis has been assigned to details of accurate physical dosimetry, with the goal of consistently reproducible interlaboratory comparison of experimental data. By automatic regulation of input line voltage fluctuations to less than 1.0%, plus maximum care in manual control and timing, individual calibration readings are reproduced by the same Victoreen chamber to the order of

+0.5%. Approximately uniform simultaneous exposures are obtained in animal containers designed for twelve mice, and for two guinea pigs. The radiation quality is variable from H.V.L. of 2.3 mm Al to 1.8 mm Cu. The incident backscatter becomes constant in each case after approximately a 10 cm thickness of Masonite, while the harder radiations approach an H.V.L. near 0.25 mm Cu after traversing large thicknesses of Masonite. (auth)

107

Engelhard, Hermann and Thea Houtermans. ACTION OF ALPHA RAYS AND OF ULTRAVIOLET LIGHT ON *BACTERIUM COLI*. *Z. Naturforsch.* 5b, 264-9(1950).

By combining phase-contrast microscopic observations with a counter technique, the killing effect of ultraviolet light and α radiations on *Bacterium coli* was determined as a function of the absolute dose. It was found that, at equal doses, the effect is independent of the radiation intensity. The survival versus dose curve falls off exponentially at small and medium doses and becomes steeper at higher doses. In the case of ultraviolet light the curve terminates in a horizontal tail possible reflecting the presence of bacteria resistant to ultraviolet radiations. Morphological pictures point to a many-hit radiobiological process, while the shape of the curves indicates the presence of two separate mechanisms, one of the one-hit and another of the many-hit nature. (NSA)

108

Fram, Harvey, Bernard E. Proctor, and Cecil G. Dunn. EFFECTS OF X-RAYS PRODUCED AT 50 KILOVOLTS ON DIFFERENT SPECIES OF BACTERIA. *J. Bacteriol.* 60, 263-7(1950).

The effects of irradiation with x-rays produced at 50 kv were studied with six bacteria, *Escherichia coli*, *Aerobacter aerogenes*, *Staphylococcus aureus*, *Serratia marcescens*, *Pseudomonas aeruginosa*, and *Pseudomonas fluorescens*. The rate of destruction followed a first-order reaction. The "37% dose" for each species of bacteria was calculated. *S. aureus* was found to be the most radioreistant of those studied. The percentage of bacteria of a given species killed by a specific total dosage of x-rays was the same regardless of the initial concentration of bacteria in the suspension irradiated. These results indicate that the bacteria were destroyed by soft x-rays according to the "direct hit" theory of radiation. (NSA)

109

Gray, L. H. and John Read. THE EFFECT OF IONIZING RADIATIONS ON THE BROAD BEAN ROOT. I. GENERAL CONSIDERATIONS. II. THE LETHAL ACTION OF GAMMA RADIATION. III. THE LETHAL ACTION OF NEUTRON RADIATION. *Brit. J. Radiol.* 15, 11-17, 39-43, 72-7(1942).

The technique of growing and measuring the roots, and the statistical method of handling the mortality data are given in detail. For gamma radiation, data on 50 beans give the mean lethal dose; for neutron radiation data on 146 beans give a lethal dose about $\frac{1}{2}$ as great as for gamma rays. Statistical considerations of these data and of the mortality curves drawn from them indicate that the difference in shape of mortality curves for gamma and neutron rays, previously published is not real. (BA)

110

Gray, L. H., John Read, and M. Paynter. THE EFFECT OF IONIZING RADIATIONS ON THE BROAD BEAN ROOT. V THE LETHAL ACTION OF RADIATIONS. *Brit. J. Radiol.* 16, 125-8(1943).

Roots of *Vicia faba* were exposed to X rays having a mean wavelength of about 0.16 Å. The duration of exposure ranged from 52 to 230 minutes for X-ray, with a

mean time of 145 minutes for doses in the neighborhood of the mean lethal dose. Corresponding average durations of exposure for gamma rays, neutrons, and alpha particle experiments were 131 minutes, 133 minutes, and 81 minutes, respectively. Relative efficiencies of the different radiations (reciprocal of mean lethal dose relative to that for gamma rays) are (gamma rays 1.0), X rays 1.5 ± 0.1 , neutrons 8.7 ± 1.6 , alpha particles 8.9 ± 0.8 . Relationship of the findings to radiology and radiation injury is discussed. (V.E.)

111

Gray, L. H. and John Read. THE EFFECT OF IONIZING RADIATION ON THE BROAD BEAN ROOT. IV. SUMMATION OF THE EFFECTS OF RADIATION OF DIFFERENT ION DENSITY. A. NEUTRON PLUS GAMMA RADIATION. B. ALPHA PLUS X-RADIATION. *Brit. J. Radiol.* **17**, 265-71(1944).

Bean roots were exposed in succession to two ionizing radiations of different types, either gamma + neutron, or x-rays + alpha. Data on the first pair of radiations are inconclusive. For the combination x-rays + alpha, to kill $\frac{1}{2}$ the roots it was necessary to administer slightly more than half a mean lethal dose of each. The primary cell injury responsible for the death of the root is apparently the same, whichever radiation is used, so that large differences among mean lethal doses for various types of radiation must be ascribed to a difference in the efficiency of the radiations in bringing about the primary injury. (BA)

112

Gray, L. H. and J. Read. IONIZING RADIATION ON THE BROAD BEAN ROOT. VI. SUMMATION OF THE EFFECTS OF RADIATION OF DIFFERENT ION INTENSITY. A. NEUTRON AND GAMMA RADIATION. B. ALPHA AND X-RADIATION. *Brit. J. Radiol.* **17**, 271-3(1944).

The authors' earlier work showed that in killing the bean root densely ionizing radiations (neutrons, x-rays) were more effective, per ionization, than less densely ionizing radiation (γ -rays, x-rays). It is now shown that the effects of successive exposures of bean roots to partial doses of x-rays and α rays, or to partial doses of neutrons and γ -rays, are additive. It is considered that the lethal effect of all four radiation is due to the same type of primary injury, and that differences in the efficiency of different radiations arise from differences in the amount of ionization needed to produce this particular injury, due to the spatial distribution of the ions. (EM)

113

Hagen, C. W. Jr., L. O. Jacobson, R. Murray, and P. Lear. EFFECTS OF SINGLE DOSES OF X-RAYS ON RABBITS. Univ. of Chicago Metallurgical Lab. Sept. 9, 1944. Decl. June 4, 1947. 47p. (MDDC-999)

Rabbits were exposed to 200 kvp x rays. The median lethal dose (based on survival for 30 days) was $790 \text{ r} \pm 20 \text{ r}$. Heavy (older?) rabbits were more resistant to the lethal effects of x rays than were light rabbits. Deaths occurred most frequently at 1 day, at 5 to 15 days, and at 35 to 60 days after exposure. Clinical effects were also most severe on the first day, at 5 to 15 days and between 35 and 60 days after irradiation. The most conspicuous changes observed were listlessness, diarrhea, excessive salivation and lachrymation during the first day, epilation, paleness, edema, diarrhea, occasional paralysis of the hind legs, and bloody discharge from the mouth at 5 to 15 days; and emaciation and diarrhea at 35 to 60 days. After 800 r and sometimes after 400 r, rabbits lost weight for the first 2 days. This loss of weight was associated with a decrease in food intake. The weight changes after the first 2 days varied with the individual rabbit but in general consisted of

one or more consecutive periods of gain and loss. The period of weight minima corresponded roughly with the periods at which deaths were most frequent. Following single doses of 400 r and 800 r on rabbits the blood forming tissues showed the most severe damage. Histological changes of various tissues and of the blood picture are described to some detail. (TIS)

114

Hagen, C. W., Jr. and George A. Sacher. EFFECTS OF X-RAYS ON RABBITS. PART I. MORTALITY AFTER SINGLE AND PAIRED DOSES. Argonne National Lab. Dec. 9, 1946. Decl. Aug. 29, 1947. 38p. (MDDC-1252; CH-3754)

Mortality statistics were collected on 227 young adult rabbits treated with single doses of x rays. The distributions of times of death for males and females show that there are 3 distinct modal times of death in the first days after exposure. The first peak of deaths occurred in the 1st day after treatment, and males were more sensitive than females at this time. The second peak appeared between the 4th and 8th days, and was shown only in the females. The main peak of mortality occurred at 10 days and showed little difference between the sexes. The LD_{50} for the entire population, based upon all deaths in the first 20 days, was 800 r. When animals which died during the first 3 days were excluded from the population, the LD_{50} for the remaining group was 810 r, and the standard deviation of the survival curve was 145 r. The effects of dose and of weight and sex of the rabbits on the LD_{50} at various intervals is discussed to some detail. (TIS)

115

Hagen, C. W. Jr., and George A. Sacher. THE ACUTE LETHAL ACTION OF SINGLE DOSES OF X-RAYS ON GUINEA PIGS. Univ. of Chicago Metallurgical Lab. Aug. 1951. 12p. (CH-3907)

Groups of guinea pigs were exposed to x-ray doses ranging from 0 to 800 r and their survival followed for 90 days thereafter. The guinea pig dosage survival curve is very broad, almost exponential in form. The LD_{50} is about 200 r. The relation of mean survival time to dose was determined and it was found that the mean survival time of guinea pigs exposed to lethal doses are quantitatively similar to those of the other experimental animals. The relation of mean survival time of 30-day decedents to proportion killed in cage groups was also exhibited. An unusual phenomenon was noted in that the survival time of decedents is on the average longer in cages which sustained about 50% 30-day killing than in cages in which the 30-day mortality was either higher or lower. (auth)

116

Hagen, C. W. Jr., and E. L. Simmons. EFFECTS OF TOTAL BODY X-IRRADIATION ON RATS. PART I. LETHAL ACTION OF SINGLE, PAIRED, AND PERIODIC DOSES. Univ. of Chicago Metallurgical Lab. May 1947. 47p. (MDDC-1210; CH-3815)

Exposures of Sprague-Dawley white rats to single doses of 200 kvp X-radiation demonstrated a median lethal dose of 600 r which was not markedly dependent upon sex, weight, or, in the case of females, stage of the estrous cycle at the time of irradiation. Deaths within 30 days were most frequent between the fourth and eighth, and between the tenth and fifteenth post-irradiation days, indicating the existence of at least two processes leading to death in the "acute" period. Male rats exposed to 300 r were less resistant to X-rays than unexposed animals for at least six weeks. During the first three weeks after the initial exposure, recovery was exponential at a rate of 8.2% per day. Beyond three weeks, the rate of recovery apparently decreased. Deaths that occurred after

daily exposure to doses greater than 50 r per day occurred in less than 30 days; whereas with lower daily doses, the period of survival was greatly extended. These results are compatible with the recovery rate of 8.2% per day determined by paired-dose studies and indicate that after high daily doses, the lethal mechanisms are the same as those after single doses. With low daily doses, other mechanisms may operate. A bibliography of 19 references is appended. (ADD)

117

Halberstaedter, L. and A. Back. THE EFFECT OF X-RAYS ON SINGLE COLONIES OF PANDORINA. *Brit. J. Radiol.* **15**, 124-8(1942).

In the green alga *Pandorina*, death is produced within 45 minutes after irradiation with 300,000-600,000 roentgens of 35 kv x-rays. All daughter cells of the same clan are killed by approximately the same dose, while in wild cultures the lethal dose varies over the above range, indicating that different colonies have varying degrees of radio-sensitivity. With doses of 3,000-300,000 r, the cells behave normally until the time for division, then become immobile, and undergo cytolysis. Doses <3,000-4,000 r do not produce demonstrable effects. No recovery was observed. (BA)

118

Jacquez, John A. and David A. Karnofsky. THE TOCICITY AND PATHOLOGICAL EFFECTS OF ROENTGEN RAYS IN THE CHICKEN. *Am. J. Roentgenol. Radium Therapy* **64**, 289-97(1950).

Acute deaths are produced by roentgen rays in young chicks at dose rates above 10 r/min. and total doses of 1,000 r or higher. The delayed LD-50 dose, in those chicks surviving the acute effects of high dose rates, is about 800 r, and a low dose rates it is about 1,100 to 1,200 r. Adult chickens of both sexes may die acutely at total doses of 1,250 to 3,000 r, but they have often survived a dose of 5,000 r for several days. Chickens surviving the acute effects succumb within 3 to 10 days, and the LD-50 is in the range 600 to 800 r. The chickens dying acutely following irradiation show, within two hours after irradiation, necrotic foci in their livers, and pyknosis and fragmentation of their lymphatic cells. The delayed deaths are not associated with liver injury, but the lymphatic tissues, including the thymus and spleen, involute, the bone marrow becomes aplastic, erosions and degenerative changes occur in the intestinal tract, and there is frequent evidence of bacterial infections. These observations on the delayed effects of roentgen rays parallel those reported for mammals. (NSA)

119

Lambert, G., J. Maisin, M. Mandart, F. Meersseman, G. Podio, and E. Pluygers. INFLUENCE OF CERTAIN METALLIC IONS ON THE SURVIVAL OF RATS RECEIVING A LETHAL DOSE OF X-RAYS. *Compt. rend. soc. biol.* **144**, 444-8(1950).

Bi and Li ions injected in non-lethal doses into rats receiving a lethal dose of X-rays hasten their death. The mercuric ions tend to delay death and decrease the percentage of deaths. (BA)

120

Lorenz, Egon, Delta Uphoff, Harriet Sutton, and R. Schweisthal. PROGRESS REPORT: THE 30-DAY LD₅₀ FOR HYBRID GUINEA PIGS, p.50-2 of BIOLOGICAL AND MEDICAL DIVISIONS; QUARTERLY REPORT, FEBRUARY, MARCH, APRIL, 1950. Argonne National Lab. [nd] 3p. (ANL-4451(p.50-2))

In previous experiments designed to determine the 30-day LD-50 for hybrid guinea pigs groups of animals were given single total-body exposures to 220 r, 260 r,

and 310 r x-radiation. This study has been concluded with two additional exposure groups of 360 r and 420 r. In the first three groups there was no sex difference in survival but in the last two groups, the female seemed more radio-sensitive than the males. However, this finding is probably due to chance since the experiments were spread over a year and hybrid stock was used. The 30-day LD-50 is calculated to be 409 r with 2σ limits of 307 r and 543 r. This value is at variance with previously published data of other investigators and it is suggested that the low figures reported by these investigators may have been caused by irradiating diseased guinea pigs. (auth)

121

Lorenz, Egon, Delta Uphoff, and Harriet Sutton. PRELIMINARY REPORT: THE 30-DAY LD₅₀ AND ACCOMPANYING BLOOD PICTURE OF HYBRID GUINEA PIGS, p.57-65 of BIOLOGICAL AND MEDICAL DIVISIONS; QUARTERLY REPORT, MAY, JUNE, JULY 1950. Argonne National Lab. July 1950. 9p. (ANL-4333(p.57-65))

For the determination of the 30-day LD₅₀ dose, two groups of animals, each consisting of 30 males and 30 females, approximately 3 months of age, was given 220 r and 260 r, respectively, of 186 kv. x-irradiation. To obtain as uniform distribution of energy within the animal as possible, a double tube setup, irradiating the animal from above and below simultaneously, was used. Irradiation was delivered at the rate of 63 r per minute. The exposure to 220 r killed 27% of the animals within 30 days, and the 260 r dose killed 38%. It can be stated from these two experiments that the 30-day LD₅₀ will lie between 250 r and 300 r for the hybrid guinea pigs used. Mortality in the two groups reached a peak between the 10th and 12th days, corresponding with the lowest values in blood counts, except for a second peak in the 260 r group on the 20th day, after blood values had almost returned to normal. Clotting time was not materially affected. The decrease in blood cells started shortly after exposure and reached a maximum on the 12th day, the abrupt fall resembling that seen in chronic exposures when the dose approaches lethal levels. However, recoveries here were much more rapid than those seen in chronic exposures. The acute 30-day LD₅₀ is comparable with the mean survival time and mean accumulated dose causing death from pancytopenia in chronic exposures (at 8.8 r dose level, 187 days, and 1700 r, at 4.4 r dose level, 653 days and 2900 r, and at 2.2 r dose level, 987 days and 2200 r, respectively). (V.E.)

122

Lorenz, K. P. and Paul S. Henshaw. RADIOBIOLOGIC ACTION AND THE KILLING EFFECTS OF X-RAYS ON *ACHROMOBACTER FISCHERI*. *Radiology* **36**, 471-81 (1941).

A short historical review has been presented of the prevailing ideas and experimental studies on the biological action of radiation. Experiments are recorded in which the survival curve for *Achromobacter fischeri* after treatment with 200 kv x-rays was found to be of the exponential type. (auth)

123

Packard, C. THE BIOLOGICAL MEASUREMENT OF RADIATIONS. *Am. J. Roentgenol. Radium Therapy* **41**, 441-3(1939).

Arguments are presented in favor of the use of the biological method of measurement of radiations. Survival data obtained from experiments with the fruit fly, *Drosophila*, are cited as proof of the constancy of response of biological material. The biological method of measurement can be used to determine surface and depth doses and is

the only method that can be employed effectively to measure the effectiveness of different wave lengths. It is concluded that this method of measurement is logical, it is accurate, and it can be put to practical use. (S.V.S)

124

Powers, E. L., Carlene M. Allen, Charles F. Ehret, Sylvia D. Mayer, Richard Sato, and D. Shefner. LETHAL CHANGES INDUCED BY X-RAYS IN *PARAMECIUM AURELIA*, p.159-64 of BIOLOGICAL AND MEDICAL DIVISIONS; QUARTERLY REPORT, FEBRUARY, MARCH, APRIL, 1949. Argonne National Lab. [nd] 6p. ANL-4291(p.159-64))

Paramecium aurelia, variety 4, was exposed to increasing amounts of 250 kv x-rays, ranging from 500 r to 25,000 r. No untoward physiological effects such as depression of fission rate or delay of entrance into autogamy were observed in the animals isolated after irradiation. When the clones arising from these isolations were allowed to go into autogamy the proportion surviving autogamy decreased regularly with increasing dosage of x-ray. Comparison of this dose response with that determined by $Sr^{89,90}$ Y^{90} in solution reveals no significant difference between the types of radiation even though the dosage rates differed greatly. (auth)

125

Powers, E. L. and Deborah Shefner. EFFECTS OF HIGH DOSAGES OF X-RAYS IN *PARAMECIUM AURELIA*. Genetics 35, 131(1950).

Stock 51 Paramecium aurelia was given in culture solution dosages of unfiltered 50 kv X-rays up to 1,000,000 r at 62,200 r per minute. Fifty per cent of the cells died after 650,000 r, and fission rate of survivors was 50% of control rate at the same level. Death after autogamy increased to 98% at 50,000 r, followed by a decrease to about 80% at 250,000 r and a subsequent slow rise at higher doses. These responses are like those observed following mustard treatment. However, in contrast, the peak in the autogamy curve induced by X-rays is higher, and it occurs at doses below those causing physiological effects of any magnitude. (G)

126

Quastler, Henry. STUDIES ON ROENTGEN DEATH IN MICE. I. SURVIVAL TIME AND DOSAGE. Am. J. Roentgenol. Radium Therapy 54, 449-56(1945).

Mice of 20 gm. weight were irradiated with roentgen rays. The doses ranged from 500 to 25,000 r. The tissue doses were about homogeneous throughout the whole body. The reactions produced are classified as subacute, acute, and hyperacute reactions. The survival time (between irradiation and death) is used as a quantitative measure of the irradiation effect. To characterize the reaction of a whole class of mice, we use the mean logarithmic survival time, or the almost identical median survival time, i.e., the time after which one-half of all fatalities have occurred. The relation between survival time and dose administered shows four zones with distinctive dose-response characteristics. There are two zones where the survival time decreases with increasing dose, and two plateaus where the survival time remains constant over considerable dosage ranges. Simple mathematical formulae for the survival time-dosage relations are given. (auth)

127

Ralston, H. J. THE IMMEDIATE AND DELAYED ACTION OF X-RAYS UPON THE PROTOZOAN *DUNALIELLA SALINA*. Am. J. Cancer 37, 288-97(1939).

The survival curves of Dunaliella populations were determined after x-irradiation. The experimental curve changes in form with time after irradiation. The sugges-

tion is advanced, and quantitatively supported, that two separate processes are involved, one causing immediate death and affecting the cytoplasm of the cell, and the other acting indirectly by way of the nucleus, inhibiting reproduction and thus representing death after some time has elapsed. The analysis of survival curves as exemplified by the work of previous investigators is discussed and criticized. (BA)

128

Rekers, Paul E. THE EFFECT OF X-IRRADIATION ON RATS WITH AND WITHOUT *BARTONELLA MURIS*. J. Infectious Diseases 88, 224-9(1951).

Rats free of a common laboratory infection such as Bartonella muris, showed a mortality rate of 90% when exposed to single dose, total-body X-irradiation. When these rats had become infected with B. muris for 10 days or longer and then irradiated, there was not only prolongation of the survival period but a reduction in the mortality rate to 50%. It seems that the infection not only conferred a resistance to the infection but an increased tolerance to the physical agent X irradiation. (BA)

129

Sacher, George A. THE ACTUARIAL CALCULUS OF CHRONIC RADIATION LETHALITY, p.82-3 of BIOLOGICAL AND MEDICAL DIVISIONS; QUARTERLY REPORT, FEBRUARY, MARCH, APRIL, 1950. Argonne National Lab. [nd] 2p. (ANL-4451(p.82-3))

The logarithm of the rate of mortality (Gompertz function) is (except for a short period after birth) approximately a linearly increasing function of age for all species of mammals investigated and for many other metazoan forms. If the Gompertz function is a linear function of age, all the commonly used actuarial functions can be evaluated explicitly. A simplified picture of the effect of exposure to radiations on the Gompertz function is presented. The effect of single exposure may be described as consisting primarily of a displacement upward of the Gompertz function without change in slope, while the effect of duration of-life exposure is to increase the slope of the Gompertz function subsequent to exposure. These effects have been confirmed in investigations on populations of mice and drosophila images. Various consequences of this schema with respect to effects of a single dose at a given age, continuous exposure, and specie difference are presented. (NSA)

130

Sacher, George A., John Sackis, and Austin M. Brues. ANALYTIC STUDY OF EFFECTS OF VARIOUS PATTERNS OF X-IRRADIATION ON SURVIVAL. Federation Proc. 8, 136(1949). (AECU-488)

This document is in abstract form; it is reproduced here in its entirety. Sixteen-hundred female CF-1 mice were treated with 250 kv total-body x-radiation according to the following dosage patterns: 400 r in a single dosage, or in 10 or 40 daily treatments; 800 r in 10 or 40 treatments; 1200 r in 40 treatments, 5 r daily throughout life; 800 r in 40 treatments superimposed upon 5 r daily throughout life. There were 1400 control mice. Gross mortality rates have been computed as a function of time, in addition to rates associated with certain prominent types of pathologic change. As a general rule, all patterns of treatment increase the incidence of all types of pathology at all ages. The effect of radiation on rates of mortality is best expressed by means of the Gompertzian diagram (logarithm of rate of mortality against time). In this form, all categories of pathology in control animals show a linear increase with age, as is well known in the case of many human diseases. A dosage administered to young adult

mice within a short interval (weeks) displaces these lines upward by a constant amount. The incidence of lymphoid tumors is phasic and constitutes an exception to this rule. The effect of daily small exposures throughout life combined with a heavy exposure early in life is discussed in terms of gross mortality excluding lymphoid tumors. To a first approximation, the results are additive on the Gompertzian diagram. The results indicate lines along which a calculus of radiation mortality may be developed for arbitrary time patterns of exposure. (auth)

131

Sacher, George and Sylvanus A. Tyler. **SOME BIOLOGICAL PHENOMENA UNDERLYING RADIATION MORTALITY.** Argonne National Lab. Aug. 1, 1947. 25p. (AECD-2024-F)

In recent years much progress has been made in the application of modern statistical methods to the evaluation and comparison of dosage-mortality curves based on small samples. In this paper an extensive body of dosage-mortality data is analyzed. Records on some thousands of mice which received single doses of X-rays were available. These mice were irradiated in groups which were kept together throughout the period of observation. On each group of mice, information was obtained on (1) the X-ray dose given, (2) age, (3) the proportion of the group which died within 20 days after treatment, and (4) the mean survival time of the nonsurvivors. The analysis was directed toward exhibiting the relations between these variables as clearly and completely as possible. The aim was to determine whether mortality could be investigated as a physiological variable, i.e., whether degree of killing and mean time to death could reveal anything about the functional nature of the mechanisms of radiation injury and mortality. There are several observations which can be made. First, the existence of successive orders of injury can be postulated. A given order of injury can appear only when injury of the previous order has reached a certain degree of severity. Second, if successive orders of injury exist, and if the appearance or non-appearance of a certain order of injury depends on external factors other than the administered dose, then multiple-valued relations between dose and mortality can exist. Present evidence indicates that the rate of mortality at a given time after irradiation is dependent on the instantaneous intensity of injury existing at that time, and further that rate of mortality is a rapidly increasing function of intensity of injury. The results so far reported are sufficient to justify the further investigation of the process of radiation injury and mortality, by methods which could be developed for use with data from properly designed experiments. (NSA)

132

Stearner, S. Phyllis. **THE EFFECTS OF X IRRADIATION ON RANA PIPIENS (LEOPARD FROG), WITH SPECIAL REFERENCE TO SURVIVAL AND TO THE RESPONSE OF THE PERIPHERAL BLOOD.** J. Exptl. Zool. 115, 251-62(1950).

Survival of the frog, *Rana pipiens*, was observed following x-ray dosages ranging from 600 to 2000 r. The greatest number of deaths occurred between 2 and 5 weeks after exposure to dosages below 1200 r, and deaths reached a minimum after 6 weeks. Exposure to 700 r results in 50% mortality at 6 weeks. Comparison with survival studies on irradiated mammals indicates that in the frog there is a wider range of dosages producing less than 100% mortality and that the slope of the survival curve is not as great. The cells of the circulating blood of the frog include the types characteristic of higher vertebrates. Peripheral blood counts following exposure to 600 and 900 r indicate

that the relative sensitivities of the leukocytes to radiation injury were similar to those of most mammals; however, the response following irradiation occurred more slowly than in most mammals and indicates that the lower metabolic rate of the frog may increase the duration of the so-called latent period. No significant effect was seen on the number of thrombocytes or erythrocytes, or on the hemoglobin concentration. It is suggested that the relatively long life span of the erythrocytes would mask any but a prolonged decrease in erythropoiesis. (NSA)

133

Tobias, Cornelius A., Hal Anger, P. P. Weymouth, and R. Lowry Dobson. **THE RADIOLOGICAL USE OF HIGH ENERGY DEUTERON BEAMS.** Radiation Lab., Univ. of Calif. May 28, 1948. Decl. July 9, 1948. 19p. (AECD-2099-A)

The suitability of the 190 Mev deuteron beam as a source of radiation for producing biological effects was investigated. There is a good indication that fast particle beams will become precision tools in the study of the biological effects of radiation and in experimental tumor therapy. The lethal effect of the high energy deuteron beam on Bagg Albino mice was measured. The LD 50 was 150 rep when the length of exposure was 15 seconds. The LD 50 appeared to change approximately proportionately to the fourth root of the length of exposure time. (NSA)

134

Tullis, John L., Carl F. Tessmer, Eugene P. Cronkite, and F. W. Chambers, Jr. **THE LETHAL DOSE OF TOTAL-BODY X-RAY IRRADIATION IN SWINE.** Radiology 52, 396-400(1949).

Adult, healthy, hybrid swine were exposed in groups of eight (four males and four females) to predetermined amounts of total-body radiation delivered in succession to each lateral aspect of the body one meter from a 1,000 kv, 3-ma, X-ray source. Within a 30-day period following exposure, animals died from the effects of irradiation in the proportions of 1 of 8 (12.5%) that received 200 r, 5 of 8 (62.5%) that received 300 r, 7 of 8 (87.5%) that received 400 r, and 8 of 8 (100%) that received 600 r. The 30-day percent mortality plotted as a function of the bilaterally administered dose gave an "S"-shaped curve, the LD 50/30 of which was taken by interpolation to be 275 r. (NSA)

135

Tyler, Sylvanus A. **PROGRESS REPORT (BIOMETRICS) p.61-9 of BIOLOGICAL AND MEDICAL DIVISIONS; QUARTERLY REPORT, NOVEMBER, DECEMBER, JANUARY, 1948-1949.** Argonne National Lab. Feb. 1, 1949. 9p. (ANL-4253(p.61-9))

Statistical investigation of survival at varying single dosages of X-rays, observed for 9.5 young mice by shipment groups, disclosed a non-significant difference between group survival patterns. By the methods of probit analysis, the 20-day LD-50 and associated standard error for the total group were computed. The problem of determining the mean length of the totality of rays emanating from a point to the bounding surfaces of regular configurations is underway. The required mathematical expressions are set down and the mean radial lengths for a circle with point of emanation (1) at the center of the circle and (2) on the boundary (circumference) of the circle are computed. The excretion time relationship, $E = E_0 t^b$ (b < 0), for animals injected with a selected class of radioisotopes is considered. A modification and extension of this excretion function that ensures, over the time continuum, (1) a finite mean retention time and (2) a total excretion equal to the injected dose is proposed. (ACD)

Wavelength Studies

136

Chase, H. B., Henry Quastler, and L. S. Skaggs. BIOLOGICAL EVALUATION OF 20 MILLION VOLT ROENTGEN RAYS. II. DECOLORATION OF HAIR IN MICE. *Am. J. Roentgenol. Radium Therapy* **57**, 359-61(1947).

Graying of the coat in mice is produced by appropriate doses of roentgen rays. It occurs with high and low energy rays (20 million volt and 200 kilovolt, respectively). Quantitatively, the two radiations are not equally effective. If the effectiveness of high and low energy rays with regard to the Victoreen r-meter is considered identical, then the effectiveness of high energy rays with regard to graying of the coat is 70% of the effectiveness of low energy rays. (auth)

137

Crabtree, Herbert G. and L. H. Gray. THE INFLUENCE OF WAVE LENGTH ON THE BIOLOGICAL EFFECTIVENESS OF RADIATION. *Brit. J. Radiol.* **12**, 39-53(1939).

The rate of an aerobic glycolysis in normal and irradiated rat retinas was studied at temperatures of 3-8°C, for beta, gamma, and X-irradiation. This material is radiosensitive, a dose of 1000 r producing easily measured effects in a few min. Considerations due to mitosis do not enter, since the tissue consists of non-dividing cells. Details are given of the physical measurements made to ensure the equality of dose for the different qualities of radiation. The results of the expts. show no significant variation between the effects of the various qualities of radiation on the rate of glycolysis. (BA)

138

THE RELATIVE EFFECTS PRODUCED BY 200 KV ROENTGEN RAYS, 700 KV ROENTGEN RAYS, AND GAMMA RAYS, SYMPOSIUM HELD ON THE 33rd ANNUAL MEETING OF THE ANNUAL ROENTGEN RAY SOCIETY, DETROIT, MICH. SEPT. 27 - 30th 1932. *Am. J. Roentgenol. Radium Therapy* **29**, (3), 293-367(1933).

The work reported in this symposium was undertaken to determine whether the effects of these types of radiation were due to quantity of energy measured only, or whether there was a differential effect due to wave length, especial attention being paid to the possible bearing of the results on the radiation therapy of cancer. I. The material of the ionization chamber influences greatly the measurements of depth doses in a water phantom. The variation from one type of radiation to another is different for different chambers. II. The chemical effects studied show some differential action among themselves and lack of agreement with the small celluloid ("air-wall") ionization chamber which has been taken as standard. III and IV. The various biological effects agree fairly well among themselves and with the small celluloid chamber. V. The production of erythema on the human skin does not at all agree with the other biological effects or with the standard ionization chamber. It indicates that the skin is more resistant to shorter wave length (higher voltage) radiation. VI. The clinical impression is that, whereas the skin is more resistant to shorter wave length radiation, malignant tissue is not. Therefore a selective action of radiation between the two types of tissue is more marked for the higher voltage. VII. The fact that two or three biological effects taken by themselves, or even with ionization measurement show no differential action of radiation with respect to wave length, is not sufficient to warrant the generalization that such action does not exist. Experiments with skin erythema show that there is a very marked differential action in some cases. Explanations are offered for this phenomenon. It is concluded that better clinical results may be expected from the use of high voltage X-rays and γ -rays. (BA)

139

Gall, E. A., J. R. Lingley, and J. A. Hilcken. COMPARATIVE EXPERIMENTAL STUDIES OF 200 KV AND 1000 KV ROENTGEN RAYS. I. THE BIOLOGIC EFFECTS ON THE EPIPHYSIS OF THE ALBINO RAT. *Am. J. Pathol.* **16**, 605-18(1940).

Ninety-five albino rats, 50 to 54 days old, were treated with single dosages of roentgen rays ranging from 600 r to 3000 r. The rays were directed at the thighs and knees of one hind extremity. The animals were divided into two groups, one of which received treatment from a 200 kv machine, and the other from an apparatus operated at 1,000 kv. Growth was impeded by all doses utilized and completely inhibited with the higher dosages. Major damage was inflicted upon the epiphyseal cartilage in the zone of chondroblastic proliferation. Despite the extent of injury to the epiphyseal cartilage neither the articular cartilage nor osteoblastic function was significantly affected. There were no detectable differences in the degree of histological modification produced by equal doses from either the 200 kv or 1,000 kv generators. The ultimate effects and the entire sequence of events were exactly similar regardless of the type of rays employed. (BA)

140

Gall, E. A., J. R. Lingley, and J. A. Hilcken. COMPARATIVE EXPERIMENTAL STUDIES OF 200 KV AND 1000 KV ROENTGEN RAYS. III. THE BIOLOGICAL EFFECT ON THE SKIN OF THE ALBINO RAT. *Am. J. Pathol.* **17**, 319-40(1943).

Equal amounts of roentgen rays, as measured with the Victoreen dosimeter were obtained from a 200 kv and a 1000 kv generator. Two large groups of albino rats were given graded amounts of irradiation to the skin of the thigh from either of these sources. The character of the histologic changes produced at periods of 1 to 19 weeks after irradiation are described. It was noted that high dosages of 200 kv rays (1800 to 3000 r) caused severe and permanent injury to the skin and its appendages. Equal doses of supervoltage rays, however, caused only mild transient morphologic changes. The differences apparent in the lesions produced by the two types of rays are far greater than the amount of error attributable to the Victoreen dosimeter. The hypothesis is therefore advanced that the discrepancy must than result from either a specific cutaneous tolerance for supervoltage rays (wave length effect) or an enhanced skin penetrability, inherent upon the physical qualities of the rays themselves, due fundamentally to the difference in the degrees of ionization produced by the two types of rays at the level of the skin. (auth)

141

Hudson, J. C. THE DEPENDENCE OF X-RAY ERYTHEMA ON WAVE LENGTH. *Radiology* **29**, 95-8(1937).

Experimental data are presented showing the variation of erythema dose in roentgens with effective wave length over the region from 200 kv, 0.5 mm copper filter, to 100 kv unfiltered radiation. Calculations indicate that the difference in dose necessary for an erythema at the various wave lengths is due chiefly to the difference in absorption by the tissue. (auth)

142

Lacassagne, A. THE INFLUENCE OF WAVE-LENGTHS ON CERTAIN LESIONS PRODUCED BY THE IRRADIATION OF MICE. *Proc. Roy. Soc. Med.* **39**, 605-12(1946).

Irradiation of a limited area of the dorsal lumbar region in mice was carried out with 3 types of radiation of different wave-lengths: K radiation of molybdenum, L radiation of silver and ultraviolet rays. Naturally deep-seated histological lesions, apart from those of the skin, were observed only in the first case. (1) With a dose of K radiation of molybdenum, 3,000 r on the surface of the skin (correspond-

ing to an incident energy of 760 ergs per square mm) the only effect produced on the skin of the adult mouse is a clearly defined loss of hair, effected by selection, without ulceration of any kind. On the other hand, the ovary and parts of the kidney, situated about 5 mm below the surface, are clearly and seriously affected. There is complete sterilization of the ovary and destruction of the uriniferous tubules, the glomeruli being unaffected. The fact that the intensity of the rays at a depth of 4 mm is only about 25% of that on the surface makes it very clear that the epithelial tissues of the ovary and kidney are far more sensitive to irradiation than those of the epidermis. (2) With L radiation of silver, a dose producing an incident energy of 500 ergs per sq mm applied to the skin of a newborn mouse causes destruction of the epidermis by a histological process of selective radioepidermitis. The effect on the skin is thus much more severe than that caused by a stronger dose of K radiation of molybdenum. This difference is easily explained by the fact that the absorption of the rays by the skin is proportionately much higher in the case of the longer wave-length. (3) Two radiations of different wave-lengths—L radiation of silver and ultraviolet rays—absorbed in depth in considerable proportions—both cause destruction of the skin of the newborn mouse, but the histological process in the two cases is totally different. (auth)

143

Lasnitzki, Ilse and D. E. Lea. VARIATION WITH WAVE-LENGTHS OF THE BIOLOGICAL EFFECT OF RADIATION. *Brit. J. Radiol.* **13**, 149-62(1940).

The effects were compared of radium gamma-rays, and of X-rays of effective wavelengths 0.170, 0.150, 0.363 Å. Dose-rates ranged from 8 to 29 r/min., doses from 20 to 200 r. Chick fibroblasts were grown in tissue culture, irradiated and fixed 80 minutes later. Cells in mitotic prophase, metaphase and telophase were counted in the stained cultures and the mitotic count of an irradiated culture expressed as a percentage of the mitotic count in an unirradiated matched control culture. Usually six pairs of cultures were used for each exposure time. The mitotic percentage diminished with increasing exposure time, the shapes of the curves being similar with the different radiations. The doses in roentgens required for reduction of mitotic percentages to 50 per cent were determined by a least squares method, and were: Gamma-rays (0.014 Å, 26.9 r/min.) 85 ± 7 ; X-rays (0.107 Å, 8.25 r/min.) 46 ± 6 ; X-rays (0.150 Å, 29.0 r/min.) 42 ± 3 ; X-rays (0.363 Å, 9.50 r/min.) 43 ± 5 . It was concluded that the three wavelengths of X-rays do not differ significantly in efficiency, and that gamma-rays are, per roentgen, less effective than X-rays. Data by Spear and other authors are quoted for neutrons on tissue cultures, suggesting that for equal ionization in the tissue cultures, neutrons are about as effective as X-rays. The relation between dosage in roentgens and energy dissipation in the cultures is discussed, with consideration of secondary electrons from the glass coverslips on which the cultures are grown. The precision obtainable in tissue culture experiments is discussed. (GPR)

144

Lea, D. E. THE DEPENDENCE OF THE BIOLOGICAL EFFECT OF RADIATION ON INTENSITY AND WAVE LENGTH, AS MEASURED BY THE DELAYED LETHAL ACTION ON CHICK EMBRYOS. *Am. J. Roentgenol. Radium Therapy* **45**, 605-13(1941).

Chick embryos were irradiated after 6 days' incubation, with γ rays, 160 kv x-rays, or 60 kv x-rays; the criterion of effect was death 2-3 days afterward. The doses of these 3 qualities of radiation necessary to produce the same ef-

fect were in the ratio 1:0:0.6:0.55. When the given dose was delivered in a single exposure at intensity greater than 10 r per min. the effect was practically independent of intensity. For lower intensities, or for divided doses, the effect of a given dose was less. A theory of recovery under such conditions is elaborated. (BA)

145

Lingley, J. R., E. A. Gall, and J. A. Hilcken. COMPARATIVE EXPERIMENTAL STUDIES OF 200 KV AND 1000 KV ROENTGEN RAYS. II. THE BIOLOGICAL EFFECTS ON THE BONE MARROW OF THE ALBINO RAT. *Am. J. Pathol.* **16**, 845-54(1940).

Graded doses (600 r - 300 r) of irradiation derived in one group from a 200 kv machine and in another from a 1,000 kv apparatus were directed at the femoral bone marrow of albino rats. A prompt diminution in cellular content proportional to the dose was noted. This was initially contributed to almost wholly by normoblasts and was invariably followed by a brief period of apparent regeneration which subsequently gave place to a progressive decline in cellularity. The degree of hypocellularity ultimately attained was again proportional to the dose administered. Qualitatively there was a depression of normoblasts, primitive cells, and myelocytes, with a persistent predominance of mature granulocytes. Comparative analyses after irradiation with 200 kv and 1,000 kv roentgen rays demonstrated no essential difference in the effects on the marrow of equal amounts of both types of rays. (BA)

146

Luce, W. M., H. Quastler, and E. F. Lanzl. BIOLOGICAL EVALUATION OF 20 MILLION VOLT ROENTGEN RAYS. V. BAR EFFECT IN DROSOPHILA. *Am. J. Roentgenol. Radium Therapy* **64**, 963-7(1950).

The reduction of eye facet number in *Drosophila melanogaster* after irradiation during the sensitive period was used to compare effects of high- and low-energy roentgen rays. It was found that the efficiency η (20 million volt at 200 kv) ≈ 0.85 , the amounts of both radiations being measured by a certain thimble chamber. The result falls in line with values previously obtained with responses to single doses: 0.79 for acute roentgen death in mice, 0.72 for graying of hair in mice, 0.75 for production of sex-linked lethals in *Drosophila*. (NSA)

147

MacKee, G. M., A. Mutscheller, and A. C. Cipollaro. THE AREA FACTOR IN ROENTGEN IRRADIATION. *Arch Dermatol. and Syphilol.* **47**, 657-64(1943).

Continuing their previous work on the effects of variations in radiation intensity, the authors studied the radiotherapeutic importance of the area factor in a total of 35 persons. Two areas were exposed on the inner surfaces of the forearm or the thigh of both males and females with various complexions and different ages. An area 2.5 cm. squared was used as standard; the size of additional areas was increased or decreased accordingly. Three series of observations were made: one with 52 kilovolts unfiltered; one with 100 kilovolts unfiltered, and one with 120 kilovolts filtered through 3 mm aluminium. The results of the 52 kv and 100 kv experiments coincided so closely that the drawing of a third curve could be dispensed with. For nonfiltered or only slightly filtered radiation the area factor above 2 cm. squared showed no appreciable change; in other words, in order to obtain equal biological reactions in areas larger than 2 cm. in diameter considerably increased quantities of radiation are needed to obtain the same result. For highly filtered radiation of high voltage, the effect of the area variation is slight in areas above 10 cm. squared; in order to achieve comparable results in

areas below 10 cm. squared, increased radiation quantities must be applied. Graphs demonstrate the respective factors indicating, e.g., that identical skin reaction will ensue in areas of 2.5 cm. squared, regardless whether 330 r non-filtered or 540 r filtered through 3 mm of aluminum are administered. Special attention is called to the fact that the tinted area of skin reaction does not exactly correspond to the opening of the lead mask or diaphragm employed. When unfiltered radiation of 52 or 100 kv was used, the area of reaction was 1.5 mm smaller than the mask opening; with 120 kv and 3 mm aluminum filtration of the area of reaction was 3 mm smaller than the mask. With further increase of voltage and filtration the area of skin reaction decreased to a greater degree. In practice it will therefore be necessary to increase the diameters of the exposed fields at least by the same measurements (approximately 1.5 mm for unfiltered radiation and 3 mm for aluminium filtered rays). (GPR)

148

Mitchell, J. S. WAVE-LENGTH EFFECT IN THE RE-ACTION OF HUMAN SKIN TO X- AND GAMMA RADIATION. *Nature* 145, 105-6(1950).

In the production of moist desquamation of normal human skin, 0.7-0.8 r unit of x-radiation of effective wave length 145 x.u. is equivalent to 1 r unit of gamma-radiation of effective wave length 15 xu. Attempted physical and chemical explanations of this fact are not entirely adequate. (CA)

149

Mottram, J. C. and L. H. Gray. THE RELATIVE RESPONSE OF THE SKIN OF MICE TO X-RADIATION AND GAMMA RADIATION. *Brit. J. Radiol.* 13, 31-4(1940).

Equal-sized sections of the tails of mice were irradiated with equal quantities of x-radiation and gamma radiation, measured in roentgens. The time factor was the same for both types. In each instance the effect from x-radiation was the greater. Although the dose applied was the same, it does not follow that the energy affecting the tissues was the same. The calcium in the bones and the S in the skin would give rise to different amounts of photo-electrons with the two applied radiations. As under x-radiation, the photo-electron emission is higher, which may account for the difference in observed effect. (R)

150

Packard, C. THE BIOLOGICAL MEASUREMENT OF HIGH VOLTAGE RADIATIONS. *Radiology* 34, 17-23(1940).

Studies about the biologic effect of roentgen rays on the fruit fly, *Drosophilla*, which previously were made in the range 12 to 220 kilovolts were extended to the range 220 to 900 kilovolt. A Victoreen Dosimeter was calibrated in terms of the biologic dose in such a manner that the % of survival of eggs exposed to the radiations between 220 to 900 kilovolts was compared with the survival rate, which follows the same doses of low voltage radiation. The results were tabulated. With voltages from 400 to 900 kilovolts the biologic dose is about 80% of the physical dose. No explanation for this discrepancy is advanced. Depth dosage measurements indicated that there is but little increase in the biologically measured depth dose when the voltage is increased from 500-900 kilovolts. Depth dosage measurements have been made in 10 cm depth of a water phantom. The eggs were covered by a celluloid sheet, for the measurements on the surface of the phantom, and were used in a bakelite container sealed with cellophane and beeswax, in the depths. The submersion of the eggs for periods up to 15 min. did not produce ill effects, provided the chambers contained not less than 1 cc of air. (BA)

151

Potter, J. Craig. THE BIOLOGICAL EFFECT OF ROENTGEN RAYS OF LONG AND SHORT WAVELENGTH

ON THE TOTALLY IRRADIATED RAT. *Radiology* 37, 724-5(1941).

Experiments were performed in order to determine the comparative lethal effects of total irradiation of the rat by 3 different wavelengths. At the same time the effects on the fertility of rats by irradiation of the ovaries were also investigated. The study was carried out over a period of 8 years and 500 rats were used. (BA)

152

Quastler, Henry. THE BIOLOGIC EFFECTS OF HIGH ENERGY ROENTGEN RAYS. *Acta Unio Intern. contra Cancrum* 6, 825-30(1949).

The results of an investigation to determine the specific effects of high energy roentgen rays, the qualitative efficiency of such rays and whether the efficiency of the rays varies with regard to different reactions are reported. A clinical and histological study of mice irradiated with 20-Mev roentgen rays, and other investigations on many plant seedlings irradiated with high energy indicated that no specific effect of high energy rays could be found. The survival time of irradiated mice, the greying of hair in mice, the stunting of growth in beans and the sex-linked mutations in *Drosophila* were some biologic tests used in reaching the conclusions that the biologic efficiency of high energy photons is roughly three-fourths that of conventional roentgen rays, if both doses are measured and referred to the 25 r thimble chamber of an ionmeter. Biologic investigations undertaken to determine whether the differences found in the factor of equivalence are due to random sampling or to actual differences indicated that the qualitative effectiveness of the high energy rays seems to vary slightly with regard to various biologic reactions. It is concluded that the main advantage of this type of ray will reside in the possibility of administration of optimum tumor doses anywhere within the human body without skin burns and without very severe systemic reactions. (NSA)

153

Quastler, Henry and Robert K. Clark. BIOLOGICAL EVALUATION OF 20 MILLION VOLT ROENTGEN RAYS. I. ACUTE ROENTGEN DEATH IN MICE. *Am. J. Roentgenol. Radium Therapy* 54, 723-7(1945).

It can be predicted, on the basis of established depth dose curves, that the high energy radiation of the betatron will be useful in the treatment of deep-seated cancer. It cannot be predicted how the betatron radiation will act on any element of living tissue. The elementary actions of high energy roentgen rays must be established by biological evaluation, conducted in such a manner that the influence of the depth dose distribution is eliminated. Mice were subject to irradiation of the whole body with a homogeneous dose of 20 million volt roentgen rays. Qualitatively, the clinical and pathological effects observed were the same as those attending the use of conventional roentgen rays. A quantitative evaluation of effectiveness was obtained, using the Victoreen r-meter as a physical measure and the survival time of mice (between irradiation and death) as a biological measure. It was found that, under the conditions stated, 1 r of the 20 million volt rays of the betatron, is equivalent to about 0.65 r of the conventional 200 kv rays. The significance of this conversion factor will be established only by further experimental investigation. (auth)

154

Quastler, Henry and Elisabeth F. Lanzl. BIOLOGICAL EVALUATION OF 20 MILLION VOLT ROENTGEN RAYS. IV. EFFICIENCY AND DOSAGE RANGE. *Am. J. Roentgenol. Radium Therapy* 63, 566-74(1950).

The efficiency of 20 million volt roentgen rays produced by the betatron was compared with that of conventional roentgen rays at different dose levels. The lethal effect of

divided doses on mice was used as test reaction. At a dosage level which causes death after about one week of daily treatments, high-energy rays are about as efficient as in the massive dose test; at a dosage level which causes death after about three weeks of daily treatments, their efficiency is significantly lowered. The lower relative efficiency of high-energy roentgen rays at small doses is compared to the higher relative efficiency of neutrons under similar conditions. (auth)

155

Spiers, F. W. EFFECTIVE ATOMIC NUMBER AND ENERGY ABSORPTION IN TISSUES. *Brit. J. Radiol.* **19**, 52-63(1946).

Measurement of the effective atomic number of excised tissues were made by an absorption method. The results of these studies were used to calculate the linear absorption coefficients and the true energy absorption of the tissues for a wide range of wave lengths. From the results thus obtained, approximations were made for conditions of actual treatment, indicating that there is a significant difference in energy absorption between fat, muscle, and bone. (R)

156

Stone, Robert S. and J. M. Robinson. A COMPARISON OF SKIN REACTIONS PRODUCED BY 200 KV AND 1000 KV RADIATIONS. *Am. J. Roentgenol. Radium Therapy* **44**, 601-9(1940).

Similar skin reactions can be produced by 200 kv and 1,000 kv radiations on opposite sides of the abdomen of the same patient. The similarity includes: (1) time of appearance; (2) degree of erythema; (3) extent of blistering and peeling; (4) degree of pigmentation; (5) subjective symptom. The physical doses as measured by a thimble chamber are not the same. It required approximately 25% more roentgens in "total skin dose" of the 1,000 kv radiations. To produce these similar reactions the fractional doses as well as the total doses must be "biologically equivalent". The distribution of the dose in days, and the total elapsed time must also be the same. The difference in the number of roentgens, as measured by a thimble chamber, required to produce "biologically equivalent" skin reactions with the two qualities of radiation is approximately the same as that found by Packard using *Drosophila* eggs. "Biologically equivalent" doses, merely because they require a greater number of roentgens of higher voltage radiations, should not be described as "larger doses". (auth)

157

Sugira, K. THE BIOLOGICAL MEASUREMENT OF GAMMA RAYS IN "EQUIVALENT ROENTGENS" WITH MOUSE SARCOMA 180 AS THE TEST OBJECT. *Am. J. Cancer* **37**, 445-52(1939).

A quantitative comparison of effectiveness of 200 kv x-rays and γ -rays was made on mouse sarcoma 180. The survival curves obtained for 200 kv x-rays and γ rays showed an almost identical course, indicating that the nature of the effect produced by hard x-rays and γ rays on mouse sarcoma 180 irradiated in vitro is essentially the same. An "equivalent roentgen" value for γ rays of 96 to 114 r/min/g was obtained for the standard conditions of 1 cm distance from an effective point source of γ radiation, with a filtration of 0.5 mm platinum. The corresponding value obtained by Failla and Marinelli with physical measurements was 111 r/min/g. The equivalent roentgen value of 93.2 r/min g was found by Henshaw and Frances for *Drosophila* eggs, and 103 r/min/g by Muller for *Drosophila* pupae. (BA)

Depth Dose Studies

158

Braestrup, Carl B., Gordon H. Cameron, and Patricia McClement. DEPTH DOSE MEASUREMENTS FOR 250 KV ROENTGEN RAYS. *Am. J. Roentgenol. Radium Therapy* **61**, 397-401(1949).

Earlier depth dose measurements made by Braestrup have been extended to include 250 kv roentgen radiation. The measurements were made in a "presdwood" phantom with a density of 0.985 gm./cc. as previously described (*Radiology*, **42**: 258 (1944)). A thimble-type ionization chamber, in conjunction with a projection-type lead-shielded electrometer, was used to measure the radiations. The results obtained are shown graphically in the form of curves of "roentgens per 100 r in air" as a function of the depth in cm for a range of 0 to 20 cm. Tabulated dosage calculations for target skin distances of 50, 70, and 80 cm are given in terms of skin dose to permit direct calculation of the tumor dose in percentage of the radiation received by the skin. Another table is also given in terms of 100 r in air for the convenience of radiologists who calculate in terms of the air dose. The results obtained are in general agreement with those obtained by Exner and Packard (*Radiology*, **44**: 367, 1945), although the depth dose values obtained by the authors (using considerably different equipment) are somewhat higher. This discrepancy is consistent with a similar discrepancy observed at 200 kv. The results obtained indicate a definite improvement in the depth dose as the quality is increased from a half-value layer of 2 to 3.2 mm of Cu, i.e., it is possible to thus increase the tumor dose at a given depth for the same exposure of the skin. (NSA)

159

Ellinger, Friedrich, and R. Gross. DEPTH DOSAGE MEASUREMENTS BY MEANS OF GOLDFISH. *Radiology* **37**, 717-21(1941).

Comparing the mortality curves obtained by lethal doses administered at the surface and those obtained on the basis of the calculated depth dose it was apparent that the anticipated depth effect did not occur. There was a greater lethal effect from the depth dose than was predicted on the basis of the calculated data. It appeared that the depth dose showed a biologic activity which was 20% greater than that calculated for the given surface measurement. (BA)

160

Johns, H. E., E. K. Darby, T. A. Watson, and C. C. Burkell. COMPARISON OF DOSAGE DISTRIBUTIONS OBTAINABLE WITH 400 KVP X RAYS AND 22 MEV X RAYS. *Brit. J. Radiol.* **23**, 290-9(1950).

Isodose curves made in a water phantom with 400 kv X-rays and 22 Mev rays (from a betatron) were compared for single and multiple fields. The depth dose was from 2 to 4 times greater with the higher voltage. The ratio of integral dose to tumor dose is about 4 times as high for 22 mev as for 400 kv. The isodose curves with the higher voltage are flat, making the distribution more homogeneous. The depth dose with X-rays from the betatron are independent of the size of the field, which simplifies clinical applications. (R)

161

Klumpar, J. RELATION BETWEEN THE RADIATION DOSE TOLERATED BY THE SKIN AND THE DISTANCE OF THE RADIANT SOURCE FROM THE SKIN. *Acta Radiol.* **31**, 223-32(1949).

The surface dosage of γ rays required to produce a certain degree of skin reaction by radium therapy depends on the

distance between the radiophore and the surface of the skin; at small distances a five times greater surface dose may be applied than at greater distances. On the basis of empirically determined application times and of graphs showing the dependence of the intensity of radiation on distance, it could be demonstrated that the depth dose 4 mm below the surface was responsible for the reaction of the skin. In all cases, with distances of 0.25 to 0.28 cm, the same degree of reaction was obtained if the dose 4 mm below the surface was 3,500 ± 600 r. It is concluded that dosage figures obtained with ionization chambers of an external diameter of 7 to 8 mm are convenient for all types of surface applicators. (NSA)

162

Koch, H. W., D. W. Kerst, and P. Morrison. EXPERIMENTAL DEPTH DOSE FOR 5,000,000, 10,000,000, 15,000,000, and 20,000,000 VOLT X-RAYS. *Radiology* 40, 120-7(1943).

X-ray specimens from the betatron are used for depth-dose measurements of ionization in a Pressdwood phantom. Data are plotted as percentage of peak ionization with respect to distance of the surface from the phantom. The point of maximum ionization moves into the phantom with increasing energy and the maximum becomes broader. A dose as high as 75% is found at 20,000,000 v with the target-to-surface distance only 45 cm. (CA)

163

Laughlin, J. S. and W. D. Davies. PROCEDURE IN DOSE DISTRIBUTION MEASUREMENT OF 25-MEV X-RAYS. *Science* 111, 514-16(1950).

In preparation of a 25-Mev betatron for human therapy and animal experimentation, extensive measurements of depth-dose and isodose distributions were made under a variety of conditions. Two general techniques were employed, one based on measurements with small ionization chambers and the other on x-ray film density response. The ionization measurements were carried out in a remote-controlled water phantom whose construction and mode of operation are described in detail. A series of measurements of the dose-density relation of industrial x-ray films established a linear relation $r = \text{const} \times D$ for type A and type M films, where D refers to the net density measured with an electronic densitometer employing a photocell and amplifier, and r refers to the dose as recorded by a Victoreen thimble chamber. (NSA)

164

Mayneord, W. V. and L. F. Lamerton. A SURVEY OF DEPTH DOSE DATA. *Brit. J. Radiol.* 14, 255-64(1941).

A survey has been made of published depth dose and backscatter data. The influence of (1) focal-skin distance, (2) quality of radiation expressed as half-value layer in copper, and (3) area of field or percentage depth dose has been investigated. In the light of this analysis, published data have been corrected to standard radiation conditions, and mean values obtained. Tables have been drawn up giving the percentage depth dose for qualities of radiation from 1.0 to 5.0 mm copper half-value layer at depths to 20 cm for field areas up to 400 cm² and focal-skin distances from 40 to 100 cm. A less comprehensive survey has been made of radiations up to 17 mm copper half-value layer, the results of which are embodied in curves and tables. Mean values of percentage surface backscatter have been derived from the literature for field areas up to 400 cm² for qualities up to 14 mm copper half-value layer. Information is also given whereby one may derive half-value layers in copper from the radiation conditions. (BJR)

165

Moos, Walter S. EFFECT OF SLOW CATHODE RAYS ON MICROORGANISMS. *Nucleonics* 8, No. 1, 50-3(1951).

The influence of very slow electrons (1 to 8 kev) on *Pseudomonas aeruginosa* has been studied. Results show a maximum effect of the electrons at a voltage that gives them a penetration in depth corresponding to the cell diameter. (NSA)

166

Skaggs, L. S. DEPTH DOSE OF ELECTRONS FROM THE BETATRON. *Radiology* 53, 868-73(1949).

By means of a water phantom the author measured the depth dosage due to a collimated beam of electrons from a betatron. Depth dose curves, normalized to peak ionization at 100%, are given for electron energies of 16.4, 14.3, and 12.2 Mev. They show a rise of ionization from the surface of the phantom to a point a few cm deep, the effect becoming less pronounced at higher energies. A short distance beyond the point of maximum ionization, the dose falls rapidly to a small value, and finally reaches a value of about 1.2% due to X-ray background. The extrapolated ranges obtained from the experimental depth dose curves agree to within 3% with the theoretical ranges. Finally, isodose curves are given for 16.4-Mev electrons. (NSA)

167

Tullis, John L., Francis W. Chambers, Jr., J. E. Morgan, and John H. Zeller. MORTALITY IN SWINE AND DOSE DISTRIBUTION STUDIES IN PHANTOMS EXPOSED TO SUPERVOLTAGE X RADIATION. *Am. J. Roentgenol. Radium Therapy* 67, 620-7(1952) (NP-1887)

Lethal dose curves established for 110- to 160-pound swine exposed to 2000-kvp total-body x radiation at 2 m indicate that bilateral (one-half the total dose to each lateral aspect) irradiation is more lethal than unilateral (total dose to one lateral aspect) irradiation. The 2000-kvp bilateral x radiation is also more lethal than 1000-kvp bilateral x radiation. The LD_{50/30} values for each technique at 2 m are 350 to 400 r for 2000-kvp bilateral, 500 r for 2000-kvp unilateral, and 510 r for 1000-kvp bilateral exposure. Depth dose values taken throughout a 28-cm phantom show that the internal distribution of incident radiation is more uniform when it is divided and administered bilaterally. In the case of 1000-kvp bilateral exposure, while the per cent air dose at the periphery is comparable with that in 2000-kvp bilateral exposure, the fall off in the mid-portion of the phantom is considerably more. The dependence of dose distribution on method of x radiation and wavelength of the source is demonstrated. The importance of uniform dose distribution and the difficulties in obtaining the same in a subject 28 cm thick are discussed. (NSA)

Effects of Beta Rays

168

Campbell, Berry and Rosalind Novick. EFFECTS OF BETA RAYS ON CENTRAL NERVOUS TISSUES. *Proc. Soc. Exptl. Biol. Med.* 72, 34-8(1949).

The gross morphological changes evoked in the neurons and glial cells of the nervous system of cats by high doses of ionizing β radiations are described here. The use of local irradiation by means of a radon applicator was made in order to study a sharp gradient of tissue reaction in the cerebral cortex. Trephining of the calvarium over the parietal region of the cerebral cortex was performed under anesthesia, and the region was exposed to the radiations for 5-32 minutes, the calculated activity of the applicators being 30-78 mc; the dura was then returned to place, and after the animal was killed, the irradiated region was dissected out fresh or after perfusion with formalin. Restricted lesions were found, complete necrosis being observed in some cases only a few mm. from normal tissue.

Nerve cells showed two types of destruction: lysis of the cytoplasmic structures and degeneration into a small aggregation of basophilic granules; and, chromophilic alteration of the cells, the pyramidal cells of layers 2, 3, and 5 evidencing special susceptibility. The astrocytes were the most susceptible of the cerebral cortex cells, undergoing lysis in the middle of the lesions; the mesogial cells, oligodendroglia, and microglia were highly resistant. (NSA)

- 169 Carvalho, S. de. APPLICATION OF BETA RADIATION FROM RADIOACTIVE SUBSTANCES ON THE CEREBRAL CORTEX IN THE CAT. *Portugaliae acta biol. ser. 1A*, 175-84(1946).

The cerebral cortices of 17 normal cats were exposed to filtered β rays from Radium E. Only the more penetrating β -rays, which passed Al filters of 0.10-0.15 mm gave rise to evident histologic lesions. (BA)

- 170 Cupp, M. N., H. I. Kohn, and G. E. Stapleton. THE EFFECT OF LOCAL BETA IRRADIATION FROM AN EXTERNAL SOURCE UPON THE GROWTH OF THE BONES AND SOME OTHER TISSUES OF RATS. Oak Ridge National Lab. July 22, 1948. Decl. Aug. 16, 1948. 10p. (AECD-2219)

One-day-old rats were subjected to one-half (anterior or posterior) body irradiation by the beta rays of P^{32} . The skin exposure on the body was about 1,700-2,000 rep. The skin exposure on the tail, hands, feet, forearm, and leg was somewhat less than twice this. The animals were sacrificed at 200 days of age. No cutaneous tumors occurred. The irradiated animals weighed 5-10% less than the controls. Males and females reacted alike. Changes were observed only in the part directly irradiated. The "anterior" animals had significantly smaller ears, skulls, and forelimbs; the "posterior" animals had smaller tails, hindlimbs, and testes. Skeletal measurements are given. No effect was observed on the stomach, kidneys, liver, or heart. (NSA)

- 171 Douglas, D. M., W. R. Ghent, and S. Rowlands. ATROPHY OF THE GASTRIC GLANDS PRODUCED BY BETA RAYS. HISTOLOGICAL FINDINGS IN ANIMALS. *Lancet* 258, 1035-8(1950).

The stomachs of dogs were exposed to β -rays from an intragastric balloon having a layer of latex containing P^{32} . Biopsy specimens taken from 39 to 74 days after irradiation showed atrophy of the gastric glands. The gastric muscularis and submucosa appeared histologically normal. (CA)

- 172 Forse, R. Armour, J. B. R. McKendry, and D. R. Webster. THE EFFECT OF RADIATION FROM RADIOACTIVE IODINE ON GASTRIC SECRETION. *Surgical Forum American College of Surgeons* 54-8(1951).

A limited but carefully controlled study of the effect of radiation from radioactive iodine on gastric secretion indicated that it is possible to reduce gastric secretion by radiating the gastric mucosa with radioactive iodine. The reduction in gastric secretion produced in one dog by radiating a gastric pouch with 30 mc of I^{131} for 5 hours has persisted for 6 months. The reduction in gastric secretion produced in another dog by radiating a gastric pouch with 30 mc of I^{131} for 9.5 hours has started to return to normal 40 days after radiation. This may indicate an individual resistance or susceptibility of the gastric mucosa to radiation from I^{131} . If radiation from radioactive iodine is to become of value in the treatment of peptic ulcer, larger doses than 30 mc for 9.5 hours will be required and the short period of hypersecretion due to stimulation of the gastric mucosa will have to be controlled. This was done using subcutaneous banthine on the first dog. This dog weighed

approximately 12 kg and it was possible to reduce his post-radiation daily secretion from over 100 cc to less than 10 cc with 15 mg of subcutaneous banthine. This parenteral means of administration is extremely effective and may be of value during this period. (NSA)

- 173 Hedin, Raymond F., Winston R. Miller, and Demetrius G. Jelatis. EFFECTS OF BETA IRRADIATION ON GASTRIC ACIDITY. *Arch. Surg.* 61, 748-57(1950).

The stomachs of 10 dogs were exposed to various doses of β -irradiation from P^{32} to determine the effect on gastric acidity. The capacity of the dog stomach was determined and a balloon filled with radioactive P solution allowed to come in contact with the ironed out gastric mucosa for various times. There was a striking correlation between the changes in gastric acidity and histologic changes in the gastric mucosa after various doses of P^{32} . A dosage in the order of 10,000 rep produces marked reduction in acidity for a prolonged time without complete achlorhydria. (CA)

- 174 Henshaw, Paul S., R. S. Snider, and E. F. Riley. ABERRANT TISSUE DEVELOPMENTS IN RATS EXPOSED TO BETA RAYS. THE LATE EFFECTS OF P^{32} BETA RAYS. *Radiology* 52, 401-15(1949).

Phosphorus 32 β rays coming from P-impregnated plastic were applied to Sprague-Dawley rats single massive doses obtained with an enclosure-type treatment device or by repeated small daily doses (6x/week) obtained by passing the animals on a conveyer belt through a tunnel lined with the radioactive plastic. Tumors of practically every type that can arise from skin and connective tissue appeared at 10 months to 1 yr after treatment. Tumors arose in animals irrespective of whether they were receiving single or repeated treatments. Epithelial tumors were almost absent in control animals, both males and females, but were present in large numbers in certain experimental groups. Subcutaneous tumors occurred in more than half the female controls but in control males only rarely. Treatment increased the incidence in females by only a few per cent, but in males many fold. The optimal single dose treatment for tumor induction appeared to be in the range of 4,000 to 6,000 rep. In the case of repeated treatments, the 50 rep/day treatments were most effective, however, since the dosage levels were widely separated, this cannot necessarily be regarded as optimal. The tumors in many instances showed a high degree of differentiation, with a tendency for the epithelium to form squamous-cell and basal-cell carcinomas, as well as adenomas, and for connective tissue to form tendon, cartilage, and even bone. Nonmalignant abnormalities were also seen. (auth)

- 175 Hughes, W. F. Jr. and C. E. Iliff. THE EFFECTS OF BETA IRRADIATION ON THE RABBIT'S EYE. *Am. J. Roentgenol. Radium Therapy* 56, 502-12(1946).

The effects of β irradiation from Rn on the normal rabbit's eye are described. A contact glass holder for the β applicator is described. Low doses of β irradiation affect primarily the epithelium. Larger doses can affect all layers of the conjunctiva and cornea, but the iris and lens are not damaged. Strong exposures to β rays are followed by a latent period free of clinical or histologic changes, the length of this period varying inversely with the dosage. Changes thereafter include disorganization of the corneal epithelium, especially loss of cytoplasm, variation in size and shape of the cells, and alteration in the chromatin; loss of stromal cells; desquamation of corneal endothelium with edema of the stroma; relatively little inflammatory cell reaction; secondary iritis; and late regenerative changes. The cumulative effects of repeated doses of beta radiation is described. (auth)

176

Hughes, W. F., Jr. and C. E. Iliff. BETA IRRADIATION OF THE EYE. *Am. J. Ophthalmol.* **32**, 351-60(1949).

Beta particles of radon represent a concentrated source of irradiation which is largely absorbed within the first 2 mm of tissue and is therefore useful in the treatment of superficial conditions of the lid, the conjunctiva, cornea, and sclera. The effective use of β -irradiation in ophthalmology depends upon and exact knowledge of the differential between the sensitivity of normal tissues and the pathologic tissues to be destroyed. In general, lymphoid tissues (the follicles in vernal conjunctivitis) epithelial growths (papillomas), and vascular endothelium (in corneal vascularization) form the most sensitive tissues which can be destroyed by beta-irradiation without undue injury to the normal ocular structures. Because of the great sensitivity of the corneal epithelium and stoma cells, direct irradiation over the cornea should be used with caution. Corneal vascularization is best obliterated by irradiation over the scleral portion of the limbus. An ocular condition associated with great cellular destruction or pyogenic infection may respond poorly to beta-irradiation. (NSA)

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This abstract has been intentionally omitted.

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Knowlton, Norman P., Jr., Edgar Leifer, John R. Hogness, Louis H. Hempelmann, Loren F. Blaney, Dan C. Gill, William R. Oakes, and Charles L. Shafer. BETA RAY BURNS OF HUMAN SKIN. *J. Am. Med. Assoc.* **141**, 239-46 (1949).

Four cases of β -ray burns of the hands are reported, and the methods of treatment are presented. Estimates indicate that the men received 3,000-16,000 rep (roentgen equivalent physical) to the outer surface of the skin. The β -ray dosages were approximately 300-1,600 rep at 3 mm below the surface and 30-160 rep at a depth of 6 mm. Since there was little evidence that whole body irradiation exceeded 15 r of γ rays in any case, it is assumed that the whole body exposure had little effect on the radiation effects on the hands. The clinical response to the irradiation consisted of four phases: a tingling and itching at the time of exposure, followed closely by a slight erythema and edema, lasting two to three days; a latent, asymptomatic period of three to five days; a secondary erythema, soon followed by vesicle and bulla formation, the vesicles drying and desquamating within three weeks, leaving a new layer of epithelium; and, a chronic phase characterized by atrophic epithelium and loss of secondary epidermal structure. The only significant hematologic findings were a neutrophilia, an increased sedimentation rate, and increase in the number of refractive granules in the cytoplasm and a low grade of reticulocytosis. The treatment was local and consisted of routine burn therapy with accessory chilling, surgical debridement and skin grafting. Rutin, a high protein diet, multiple vitamins and parenteral penicillin were also given. The results are incomplete at this time (NSA)

179

Lasnitzki, Ilse. THE EFFECT OF BETA RAYS ON CELLS CULTIVATED IN VITRO. *Brit. J. Radiol.* **21**, 265-9(1948).

Tissue cultures of avian fibroblasts were exposed to a dose of 1000 r of pure β -rays from uranium UX-1. Alteration in mitosis and the production of abnormal mitotic and degenerate cells were examined quantitatively for a period of 24 hours following irradiation. A steep fall in mitosis, the appearance of abnormal mitotic figures, and degenerate cells were observed shortly after exposure. This was followed by a return of mitotic activity accompanied by more

abnormal mitosis and cell degeneration. Mitotic recovery was half the normal value at the end of the observation period. A comparison with changes seen in tissue cultures treated with the same dose of X-rays shows that the effect is qualitatively similar, and that the total damage produced is of the same order in both cases, but the time relation differs markedly in the two experiments. β -irradiated cultures show the greatest effect shortly after exposure and an early recovery, while after X-rays the radiation effect is delayed and recovery is slow. (NSA)

180

McKendry, J. B. R. INTRACAVITY VISCERAL RADIATION: EFFECT ON GASTRIC ACID SECRETION. *Proc. Soc. Exptl. Biol. Med.* **75**, 25-7(1950).

A double-walled balloon apparatus is described suitable for intracavity irradiation of hollow organs accessible to intubation. A solution of a radioactive substance is introduced into the space between the two walls of the balloon after it is in place. In preliminary experiments achlorhydria was induced in dog stomachs by the radiation from I^{131} . (CA)

181

Parker, H. M. SOME PHYSICAL ASPECTS OF THE EFFECTS OF BETA RADIATION ON TISSUE. [Univ. of Chicago Metallurgical Lab.] Sept. 10, 1943. Decl. June 20, 1950. 55p. (AEC-2859)

This report is concerned with the determination of the depth in tissue at which damage by beta radiation can occur, and the calculation and measurement of beta radiation doses in the superficial tissue arising from exposure to various distributions of beta emitter. Part I is devoted to the calculation of dosages and Part II deals with the experimental methods and techniques used in beta radiation dosage determinations. (NSA)

182

Tahmisian, Theodore N. and Jeanne Gasvoda. THE EFFECT OF BETA IRRADIATION ON THE RESPIRATION AND MORPHOLOGY OF MELANOPLUS DIFFERENTIAL-IS EMBRYOS, p.154-80 of BIOLOGICAL AND MEDICAL DIVISION; QUARTERLY REPORT, AUGUST, SEPTEMBER, OCTOBER, 1948. Argonne National Lab. Nov. 1, 1948. 27p. (ANL-4227(p.154-80))

Low dosages of β radiation produced extensive damage in the embryonic cells of grasshoppers. The respiration of grasshopper embryos was increased during irradiation; immediately after irradiation there was inhibition. By the use of Fleming's triple stain it was shown that β irradiation caused pyknotic chromatin to remain as if it were in the metaphase condition. There is evidence that injury sustained by the chromosomes may be direct and indirect. β irradiation caused the appearance of some osmophilic material associated with the chromosomes. The nature of this material is as yet unknown. (auth)

183

Warren, S. and O. K. Scott. PHYSARUM AS A RADIATION TEST OBJECT. *Proc. Soc. Exptl. Biol. Med.* **52**, 149-51 (1943).

P. polycephalum is a moderately sensitive object for β radiation reacting by cessation of growth in the field of radiation and sometimes reversal of protoplasmic streaming. (BA)

184

Zirkel, Raymond E., ed. BIOLOGICAL EFFECTS OF EXTERNAL BETA RADIATION. New York, McGraw-Hill Book Co., Inc. 1951. 259p. (National Nuclear Energy Series, Division IV - Plutonium Project Record, Volume 22E)

The volume presents in book form the first studies of pure β irradiation of considerable tissue areas and of the whole body of laboratory animals. Explanations, with suitable diagrams, are provided for the methods employed using radio-P plaques and impregnated plastic exposure chambers. The first experiments described are on restricted areas of skin exposed to β dose of 1000-30,000 r. Damage at lower doses is not greatly different from thermal effects, but at 15,000 r and above, failure of healing may occur and there may be separation of the outer layers of skin. Acute lethal effects caused by total-surface irradiation were studied. MLD-values were found for baby rats at 2200 r; mice, 4700 r; rats, 7500 r; guinea pigs 7750 r; rabbits, about 17,500 r. Gross responses and the histopathological changes are described. Of the several species of laboratory animals treated, mice and rats showed significant tumor induction. The optimum dose range for production of tumors was 4000-5000 r of total body-surface radiation, and practically every type of epithelial tumor was produced. Periodic total-surface β radiation at 625 r/day gave an expanded time-scale as compared with single exposures, so that 50% mortality occurred in mice at 89 days with a total dose of 43,750 r and in rats at 90 days with an accumulation of 46,250 r. Mice and rats exposed to 50 r/day for one year yielded tumor production in the rats and occasional ulceration and some precancerous changes in the mice. Lower daily doses of 5 r were essentially ineffective. In rate exposures of 4000-5000 r or 50 r/day appeared to be optimal for production of malignancies. The book closes with a review of the effects of agents which can produce skin abnormalities. (TIS)

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This abstract has been intentionally omitted.

Effects of Neutrons

186

Abelson, Philip H. CONFERENCE ON RADIATION CATARACTS AND NEUTRON EFFECTS. Division of Medical Sciences, NRC. Feb. 17, 1950. 100p. (NP-1826)

A report is given of the above conference, which comprised two parts, (1) a discussion of the production and detection of neutrons and of experimental neutron-irradiation of animals and (2) a discussion of various studies made on the lens of the eye and the effects of radiation thereon. 181 references. (NSA)

187

Abelson, Phillip H. and P. G. Kruger. CYCLOTRON-INDUCED RADIATION CATARACTS. *Science* **110**, 655-7 (1949).

This is a preliminary report of a survey, carried out under the auspices of the Division of Medical Sciences of the National Research Council, concerning cyclotron-induced radiation cataracts. A summary is given of the results of an examination carried out at the Wilmer Ophthalmological Institute, Johns Hopkins School of Medicine, by Drs. Alan Woods, Jonas Friedenber, and Algernon Reese, on 10 scientists, who in connection with their work on high energy machines had been exposed to harmful radiation. Furthermore, information is given as to the probable dates of exposure, the estimated total exposure to neutrons, and the duration of the exposure, for all 10 men. It seems probable that the cataracts were caused by chronic exposure to neutrons in the energy range from 0-20 Mev. (NSA)

188

Aebersold, P. C. and G. A. Anslow. FAST NEUTRON ABSORPTION IN GASES, WALLS, AND TISSUE. *Phys. Rev.* **69**, 1-21(1946).

The ionization produced by a collimated beam of fast neutrons, filtered for γ rays, resulting from neutron collisions in various hydrogenous and nonhydrogenous gases at pressures ranging from 3 mm to 3 atm or resulting from collisions with various hydrogenous and nonhydrogenous wall materials has been measured in ionization chambers of various types. In large wire-defined gas-walled chambers the ionizing particles are the recoiling gas nuclei. The long-range protons of hydrogenous gases expend part of their energy in the walls of the container at ordinary pressures, hence their ionization-pressure curves are quasiparabolic and become linear at higher pressures in accordance with theoretical predictions. The ionization-pressure curves for nonhydrogenous gases are linear except at low pressures. The limiting pressures at which linearity sets in lead to max. values of the range and energy of the recoiling nuclei and indicate that in the beam of the 37-in. Berkeley cyclotron 5-Mev neutrons predominate. The slopes of the linear portions of the i-p curves permit the calculation of the rate, E_i , at which energy is transferred from the neutron beam to nuclear constituents of the gas. The component of the ionization resulting from γ -rays, produced in the target and in the walls of the collimator and chamber, was found less than 1% in hydrogenous gases and only 2-6% in other gases. In thimble chambers with 1-cm, and in cylindrical chambers with 2-mm, wall separations, the ionization results in large part from the recoiling wall nuclei. Ranges and energies of the heavier recoiling wall nuclei are indicated by the limiting pressures revealed in i-p curves. The γ -ray percentage is greater than in large-vol. chambers. Neutron responses from most nonhydrogenous walls is proportional to proton content. From the E_i values measured in large chambers the energies absorbed per g of various biological substances and of hydrogenous and nonhydrogenous wall materials have been calculated, and (1) predict the respective responses measured in thimble chambers and (2) indicate that the energy absorption per g of tissue must be similar to that for a wall material like amber. Finally analyses of the relative x-ray and neutron energy absorptions in such materials yields a factor k_n greater than 2, which must be applied to reduce neutron exposures measured in certain hydrogenous-walled chambers to tissue doses. (CA)

189

Aebersold, P. C. and J. H. Lawrence. THE PHYSIOLOGICAL EFFECTS OF NEUTRON RAYS. *Ann. Rev. Physiol.* **4**, 25-48(1942).

A review covering production, properties, and measurement of neutron rays as well as their biological effects and possible therapeutic uses. Thirty-one references appended. (CA)

190

Biram, M. B. THE CALCULATION OF THE ENERGY DEPOSITION IN SOFT TISSUE BY FAST NEUTRONS EMERGING FROM A NON-CAPTURING MEDIUM. Atomic Energy Research Establishment, Harwell, Berks. (England). Nov. 21, 1949. 10p. (AERE-T/R-443)

The dose in rep is calculated at interior points of a half space of soft tissue, for the case of monochromatic fast neutrons entering the tissue from a noncapturing isotropically scattering medium. The variation of mean free path with energy is neglected, and, with this approximation, the biological effects can be shown to be proportional to the energy flux. This is then expressed as a function of depth of tissue, using the Spherical Harmonics P_1 approximation (MDDC-236). (NSA)

191

Catsch, A., K. G. Zimmer, and O. Peter. RADIO-BIOLOGICAL RESEARCH WITH FAST NEUTRONS. *Z. Naturforsch.* 2, 1-5(1947).

Radiation effects of fast neutrons are characterized by damage to the leukocytes whereas the erythrocytes are to a large extent resistant to radiation damage. The effect of radiation on the blood forming organs damages cells in the process of dividing as well as immature cells. As a result of the damage to the blood forming organs, secondary changes in the blood appear long after the irradiation. The importance of these results in determining the tolerance dose lies in the fact that with neutrons, changes in the blood picture are apparent even with very small doses. This is quite different from X-rays. Apparently too in the case of neutrons there is no correlation with radiation intensity nor is there a quick recovery as with X-rays. It is important therefore to study the effects of neutrons, especially the correlation between radiation intensity and damage. It is important too to study the effect on other organs in order to properly protect personnel engaged in nuclear research. (NSA)

192

Cogan, David G., John L. Goff, and Elizabeth Graves. EXPERIMENTAL RADIATION CATARACTS: II. CATARACTS IN THE RABBIT FOLLOWING SINGLE EXPOSURE TO FAST NEUTRONS. [Los Alamos Scientific Lab.] [nd] 23p. (AECU-1743)

The production of radiation cataracts and other ocular effects in rabbits has been studied using single exposures to relatively pure neutron sources of 14 Mev and fission energy. The course of events following neutron radiation is basically similar to that following x-ray exposures, and comparable effectivity as regards cataracts is obtained with 5×10^{10} neutrons/cm² (14 Mev) or with 9×10^{10} neutrons/cm² (fission energy) as was obtained with 500 r (1.2 Mev). While the morphologic changes in the lenses with neutrons and x rays showed the same differences when heavy and light doses were used, neutron radiation with 14 Mev produced more of the transient vacuoles than did the x-ray radiation or the fission neutron radiation. The threshold dose for cataract production by neutrons is less than 2×10^9 neutrons/cm² incident on the lens. (NSA)

193

Curtis, H. J. and J. D. Teresi. ACTIVITY IN TISSUES INDUCED BY SLOW NEUTRON BOMBARDMENT. [Clinton Labs.] Feb. 25, 1946. 21p. (AECU-2872)

When tissue is exposed to slow neutrons, a nuclear reaction takes place between the neutrons and the various atoms of the tissue which will produce radioactive isotopes. It can be shown theoretically that phosphorus and sodium are the most dangerous elements in this regard, and this prediction has been borne out in experiments on mice. However, it is shown that this radiation produced only about 1% of the biological effect produced by a slow neutron exposure; the rest being due to radiations emitted at the time of the exposure. From an analysis of the urine for radioactive elements it is possible to estimate the magnitude of a slow neutron exposure. Either phosphorus or sodium analysis should be used depending upon the circumstances of the exposure and the analysis; but in general it may be said that sodium analysis should be used for short exposures and phosphorus for chronic exposures. A tolerance dose of slow neutrons has been computed as an 8-hour exposure in a flux of 9×10^3 n/cm²/sec. Using this value it can be shown that under most circumstances it would be possible to detect an over-exposure by a urine analysis, but this is not recommended as a routine procedure. (NSA)

194

Davison, B. PRELIMINARY ESTIMATE OF THE ENERGY DEPOSITION IN SOFT TISSUE DUE TO A FAST NEUTRON FLUX. Atomic Energy Research Establishment, Harwell, Berks. (England). [nd] 34p. (AERE-T/M-13; H.S. 1467)

The energy deposition in soft tissue due to a fast-neutron flux is examined for the following three extreme models: Model A assumes that after a hydrogen collision the mean free path of a neutron reduces to zero, i.e., all the further collisions take place at the same spot as the first collision with hydrogen. Model B assumes that the mean free path for all energies is the same as for the initial energy, and in all collisions neutrons are scattered isotropically. Model C assumes that on a collision with hydrogen a neutron either loses all its energy or continues to move with the same energy and in the same direction as before the collision. It is shown that the correct answer should be between the limits set by these three models. For each model the spatial distribution of energy deposition is determined for the case when the human body is replaced by a half-space consisting of soft tissue with neutrons from outside either falling at right angles to the exposed surface, or coming from an isotropic plane source. The total amount of energy deposition in the body, the density of energy deposition at the exposed surface, and the mean depth of energy penetration are tabulated for the three models mentioned above for the initial neutron energy range from 0.5 to 5.0 Mev. (NSA)

195

Eschenbrenner, A. B., T. Wang, and Eliza Miller. PRELIMINARY REPORT; THE VALUE OF MOUSE TESTES FOR BIOLOGICAL DOSIMETRY OF IONIZING RADIATIONS, p.39-41 of BIOLOGICAL AND MEDICAL DIVISIONS QUARTERLY REPORT FEBRUARY, MARCH, APRIL, 1950. Argonne National Lab. [nd] 3p. (ANL-4451(p.39-41))

Some preliminary observations have been made on the pattern of damage and recovery of the testes of mice exposed to neutron irradiation, and the data have been compared with x-irradiation damage and recovery findings from earlier studies. Mice, confined in plastic cages, were exposed to neutrons of an average energy of 4 to 5 Mev. The cages were located about 60 cm from the target and the maximum γ background of the cyclotron at this distance from the cages was estimated to be about 30% of the total dose. The animals received a total of 29N at about 3N/min. Irradiated and nonirradiated mice were sacrificed and the testes removed at week intervals after exposure. The close similarity of the x-ray and neutron data strongly suggested the same biologic response. This is also true for mice exposed to x rays from a 50-Mev betatron. It appears that the response of the mouse testis to irradiation may prove to be a valuable tool for future studies on the relation between biologic effect and physical dose. (NSA)

196

Evans, Titus C. EFFECTS OF SMALL DAILY DOSES OF FAST NEUTRONS ON MICE. *Radiology* 50, 811-34(1948).

Daily doses of 0.014 "N" of fast neutrons (0.07 "N" per week) equivalent to 0.1 r per day of X-rays (on the basis of relative effects of single exposures), had no definite effect on mice treated for approximately 87 weeks. Some effects (though still not pronounced) were observed in animals exposed daily to 0.07 "N" with a total dose of approximately 30 "N". Daily exposures of 0.14 "N" (total of 60 "N") definitely reduced survival time slightly, reduced growth activity of hemopoietic organs and gonads, and slightly increased the frequency of cataracts. Doses of 1.4 "N" per day resulted in death of over 50% of the animals by about the 29th week (total "N" - approximately 200). This irradi-

ation caused pronounced changes within a few weeks in blood counts, activity of hemopoietic organs and gonads. In addition, extreme damage to the lens was evident by the time half of the original number of animals had died. Daily exposures of 1.4 "N" were more effective than those of 11 r (equivalents on the basis of relative effects of single exposures). Some effects, based on total dose at time of appearance, indicated a ratio of 12-13 r = 1 "N". The effects of 1.4 "N" per day on gonads and lens were more pronounced than even this ratio, 12 r = 1 "N" would indicate. Considering the results generally, the most important finding was that the lens was especially sensitive to the neutron radiation. (NSA)

197

Evans, Titus C. THE FAST NEUTRON HAZARD. *Nucleonics* 4, 2-8(1949) Mar.

Recent experiments have been made to obtain information on the biological effects of fast neutrons (1-4 Mev) using mice as test objects. The chief purpose of the investigations was to determine whether distribution of the exposure in time would alter the relative effectiveness of neutrons (ca. 4 Mev) as compared to X-rays (185 kv). The effects of the two types of radiations were determined under three conditions of exposure: (1) single acute, (2) multiple subacute, and (3) multiple very small or chronic. Data on the number of survivors and mean survival time are shown in a number of curves. An equivalence of 1 n = 10 r has been accepted as a temporary working basis for permissible exposures; however, the difficulty in converting data of the type obtained into data applicable to humans, is noted. (NSA)

198

Gray, L. H., J. C. Mottram, John Read, and F. G. Spear. SOME EXPERIMENTS UPON THE BIOLOGICAL EFFECTS OF FAST NEUTRONS. *Brit. J. Radio.* 13, 371-88(1940).

Methods of measuring neutron dosage in biological experiments are not well standardized. Details of a measuring method based on ionization and of one based upon the radio-activation of P were discussed. The relation of dose to inhibition of mitosis in tissue cultures of chick embryo fibroblasts and in roots of broad beans was determined and compared quantitatively with corresponding data obtained with γ rays. In both cases the neutron effect curve was exponential, while the γ ray curve was sigmoidal. No intensity dependence was observed in the neutron experiments. The data indicate that the "sensitive volume" must, if spherical, have a radius of about 2 μ for the chick fibroblasts and 3 μ for the bean roots. In each case, the same number of ions have to be produced. The differences in the shapes and magnitudes of the mitosis-dose curves indicate that with γ rays the ionization is produced by several hundred recoil electrons, and in the neutron case by a single recoil proton. The literature of quantitative effects of fast neutrons is reviewed. A hypothesis is advanced to account for the large relative efficiency of neutrons as compared with γ rays. (BA)

199

Henshaw, P. S. EFFECTS OF PERIODIC DOSES OF SLOW NEUTRONS. *Clinton Labs.* Aug. 27, 1946. Decl. Feb. 28, 1947. 12p. (MDDC-754; MonH-118)

Periodic doses of a radiation designated as "slow neutron" were given to two groups of 100 CF-1 female mice. Each arbitrary unit of dose, expressed in a, was composed of slow neutrons considerably contaminated with fast neutrons. The mice were exposed in a manner similar to that used for fast neutron exposures, but in the cart designed specifically for "slow neutron" irradiation. The results are very similar to those observed as a consequence of periodic fast neutron treatments. A comparison of the shortening of life induced by each radiation indicates that 1 n is as effective

as 7.5 a, a ratio roughly equivalent to that observed after single doses. A dose of 10 a per day depressed the leukocyte level to a range between 2000 and 3000 cells cu mm more pronounced blood changes probably would have been noted had other strains been used. The terminal pathological condition of the experimental mice was essentially like that observed after periodic fast neutron or gamma ray irradiation. (ADD)

200

Hoffman, Joseph G. ESTIMATION OF SLOW NEUTRON DOSAGE IN WHOLE BODY IRRADIATION. *Los Alamos Scientific Lab.* May 24, 1948. Decl. July 17, 1948. 22p. (AECD-2114; LADC-527)

Approximation formulae are used to compute theoretically the integral doses arising from capture gammas from the reaction $H^1(n,\gamma)H^2$ in the human body. For an integrated slow neutron density of $4 \cdot 10^{10}$ neutrons gm. tissue the whole body dose is 0.95 megm-R. This includes the $N^{14}(n,p)C^{14}$ contribution to the dose. Experiments on a mock-up of the human body filled with Na^{24} dissolved in water, are described which indicate the validity of the reciprocity theorem between source and absorber. The physical parameters and data from Mayneord's tables on integral doses are shown to apply in the case of the Na^{24} gamma rays. The data are used to approximate the H^1 capture gamma dose which is found to agree with the theoretically computed dose. The use of induced activities in Na^{24} and Cl^{38} is discussed with reference to the assessment of tolerance doses of slow neutrons. The gamma activities permit the measurement of slow neutron doses which are 35 to 100 times above tolerance levels. (NSA)

201

Larkin, J. C. SOME PHYSIOLOGICAL CHANGES IN THE SKIN PRODUCED BY NEUTRONS. *Am. J. Roentgenol. Radium Therapy* 47, 733-9(1942).

Vasodilation and vasoconstriction of the capillaries, changes in their sensitivity produced by irradiation with neutrons, changes produced by injecting chemical substances into the skin itself, and skin temperatures were studied with the aid of the 60-in. Berkeley cyclotron. In skin showing an erythematous reaction to the irradiation, a scratch test shows a persistent white reaction, indicating increased sensitivity of the endothelial tubules. No wheal formation is observed, indicating that the erythematous skin is refractory to histamine action. There is no elevation in skin temperature during the latent period of several days between the irradiation and the appearance of the erythema, but a marked rise (as much as 3°C.) after it appears, indicating vasodilation. Even in these areas, the injection of adrenalin, a vasoconstrictant, produces blanching. The nervous mechanism controlling flare formation following the scratch test is not influenced by irradiation. (BA)

202

Lawrence, John H. and Ernest O. Lawrence. THE BIOLOGICAL ACTION OF NEUTRON RAYS. *Proc. Natl. Acad. Sci. U. S.* 22, 124-33(1936).

By bombarding beryllium with neutrons in the cyclotron or magnetic resonance accelerator, an intense source of neutrons, adequate for biological investigation, is obtained. After whole body neutron irradiation of white rats, there results a leukopenia, the lymphocytes being more affected than the polymorphonuclears. Per unit of ionization, neutrons are much more effective biologically than are X-rays in producing a lymphopenia in white rats. The ionization produced in tissue by neutrons is many times more dense than that produced by X-rays or gamma rays, so these greater biological effects after neutron irradiation are not surprising. (BA)

203

Leitch, James L., Douglas M. Gay, and George A. Neville. **EFFECTS OF REPEATED LOW DOSES OF NEUTRONS ON THE ESTROUS CYCLE OF THE WHITE RAT.** *Am. J. Roentgenol. Radium Therapy* 61, 530-3(1949).

Further investigations of the effects of neutrons on white rats with particular reference to the relationships between tumor production and the possible appearance of an irregular estrous cycle are presented. Investigations of the effects of low neutron doses on the estrous cycle of the white rat as determined by vaginal smears are presented. A daily dose of 3 n was given to 23 rats six days a week until 111 n had been delivered. Hematological studies indicated a lowering of the white blood cell count to a minimum of 6,000-7,000 cu mm after 16 doses, followed by recovery. A slight loss of weight as well as a retardation of the growth occurred. The main effect was a disruption of the estrous cycle. Swellings appeared in the mammary glands, and are under investigation. (NSA)

204

McDonald, E., ed. **NEUTRON EFFECTS ON ANIMALS.** Staff of the Biochemical Research Foundation. Baltimore. Williams and Wilkins Company. 1947.

When atomic energy is applied industrially, one of the problems is the protection of workers against the chief by-product "neutron bombardment". The various types of electro-magnetic and subatomic-particulate radiation are reviewed and the techniques involved in the production of neutrons and the exposure of animals to these are described. The specific effects of neutrons on rats, rabbits, dogs, and various bacteria and other micro-organisms are described. The method of measuring the dosages is somewhat similar to that for measurement of X-rays in that Victoreen ionization chambers are used to measure radiation intensity. The units are expressed, however, as neutron radiation intensity, abbreviated as "n" to distinguish this unit from the roentgen. In these and other studies the biological effect of an n-unit of neutrons is different from that of an r-unit of X-rays even though both give the same reading when measured with a Victoreen 100-r chamber. In rats the medium lethal dose for neutrons lay between 60-n and 120-n. Neutron doses above 180-n caused death of rats in from six to eight days accompanied by extreme loss of weight and maximum leukopenia. A high percentage of the rats surviving for more than 150 days developed malignant tumors of various types. Attention was called to the fact that no ovarian tumors were observed in the neutron treated rats whereas Furth has reported a consistent induction of ovarian tumors in mice with 50-r of x-radiation. The authors raise the question of whether or not this indicates a difference between the action of X-rays and neutrons. Furth's animals developed ovarian tumors approximately one year after radiation. The data given for the rats in this book do not appear to extend over more than 150 days. Numerous other specific effects of neutrons are described and in general, testicular changes, blood changes, and other physiological effects were similar to those which follow treatment with X-rays and gamma radiation. Since the γ radiation was screened out by three inches of lead, these effects could not have been due to radiation of this type. The authors seem to have been impressed, however, by the fact that neutrons have a greater biological effect than γ and x-radiation. (GPR)

205

Mitchell, J. S. **PROVISIONAL CALCULATION OF THE TOLERANCE FLUX OF THERMAL NEUTRONS.** *Brit. J. Radiol.* 20, 79-82(1947).

This paper deals with the derivation of a theoretical tolerance of neutrons in the absence of the availability of

any experimental determinations on the subject. Doses are considered in relation to (1) the surface of soft tissues, (2) the n- γ reaction in H¹, (3) total surface dose, (4) dose in bone, (5) diffusion reflection of thermal neutrons at the surface of the body, and (6) safety factors. Assuming the value of 0.1 r per day recommended by the National Bureau of Standards, Washington (1938), for the tolerance dose rate for total body γ irradiation, the author concludes that the tolerance flux of thermal neutrons should not exceed 1250 thermal neutrons per cm² per second during a period of eight hours in any one day. (E. G.)

206

Mitchell, J. S. **PROVISIONAL CALCULATION OF THE TOLERANCE FLUX OF FAST NEUTRONS.** *Brit. J. Radiol.* 20, 177-80(1947).

The flux of fast neutrons of energy E, which will give the same energy absorption in an element of volume near the surface of the body as the gamma ray tolerance dose rate of 0.1 r in eight hours, is calculated with the aid of Placzek's expression for the mean energy loss per elastic collision in the slowing down of fast neutrons without capture. If E₀ is the energy of a neutron before elastic collision with a nucleus of atomic mass M, and E its energy after collision, then the average value of

$$\left(\log \frac{E_0}{E} \right)_{Av} = 1 - \frac{(M-1)^2}{2M} \log \left(\frac{M+1}{M-1} \right)$$

A useful table is given of the collision cross sections for elements of importance in human tissue and a range of neutron energies, the number of atoms of each element per cc of tissue, the average energy loss of a neutron per collision, and other data used in the calculation. The biological efficiency of ionization due to recoil protons relative to that produced by γ rays is discussed and the most likely value for each energy is tabulated. About 80 neutrons per cm²/sec, having energies in the range 2 to 20 Mev, produce energy absorption biologically equivalent to the gamma ray tolerance dose rate, but this number rises to 120 neutrons of 1 Mev and 165 of 0.5 Mev. In view of the uncertainty in the values chosen for the relative biological efficiencies, and of proposals to reduce the tolerance dose to 0.05 r per eight-hour day, it is finally suggested that a flux of 20 neutrons per cm²/sec be taken as the provisional tolerance flux of neutrons of energy in the range 2 to 20 Mev, which can be doubled for neutrons of 0.5 Mev energy. (EM)

207

Mitchell, J. S. **EXPERIMENTS ON THE MECHANISM OF THE BIOLOGICAL ACTION OF FAST NEUTRONS USING THE SUMMATION METHOD FOR LETHAL EFFECTS IN MICE (WITH A SECTION OF DOSIMETRY OF FAST NEUTRONS).** *Brit. J. of Radiol.* 20, 368-80(1947).

Adult male mice were individually exposed either to γ radiation from radium or to a beryllium-polonium neutron source which gave in tissue a dose due to fast neutrons 21 times as great as that due to the associated γ rays. It is concluded that the "mixed" radiations applied consecutively are less lethal than comparable doses of either radiation alone, and that this indicates a difference in the mechanism of the biological action of fast neutrons and gamma rays. When the overall time of exposure is 48 hours the relative biological efficiency of neutrons compared with γ rays, is 32.0 ± 8.6 . It is suggested that the lethal effects of γ radiations on normal cells are produced, at least in part, by certain types of chromosome interchanges resulting from an intensity-dependent "two hit" process. Possibly, whereas proliferating cells are more sensitive to γ radiation during a short interval in the prophase stage of mitosis, cells exhibit a much more uniform sensitivity to neutrons through-

out both the resting stage and mitosis, because of the greater efficiency of the neutron radiation. A section deals with the measurement of neutron dose by comparison of the ionization produced in a graphite ionization chamber and a carbon-polystyrene chamber, and the deduction of the corresponding tissue dose. Tables give values of the collision cross sections of H, C, N, and O for neutrons of energy 2.0 to 6.0 Mev and of the fractional energy absorption per unit volume in different media, including water and tissue. (NSA)

208

Nishina, Y., Y. Sinoto, and O. Sato. EFFECTS OF FAST NEUTRONS UPON PLANTS. III. CYTOPLASMIC CHANGES IN SPIROGYRA. *Cytologia* **11**, 311-18(1940).

The elasticity of cytoplasm in *Spirogyra*, measured by means of the centrifuge method, decreased when exposed to neutron rays. Change of the elasticity induced by the neutron bombardment may be attributed chiefly to alteration in the condition of the peripheral cytoplasm especially of Rinnen-plasma which connects chloroplasts to the cell membrane. The methods of plasmolysis was also employed, but the results were inconclusive. (Authors' Summary)

209

Robinson, John N. and Earl T. Engle. EFFECT OF NEUTRON RADIATION ON THE HUMAN TESTES: A CASE REPORT. *J. Urol.* **61**, 781-4(1949).

A case showing the radiation injury effects from a neutron bombardment involving the human testes is presented. The accurate radiation dosage is not known, but the exposure time to the bombardment was only a fraction of a second. Three weeks after injury there was no evidence of spermatozoa, and loss of facial and head hair had occurred. The results of two bilateral testes biopsies are summarized. The first biopsy revealed normal tissue with no tubular fibrosis, but few spermatogonia were present. The second biopsy showed some residual damage to one testis, and marked improvement in the amounts and stages of spermatogenesis in the other testis. The spermatogenesis had begun to return between the 12th and 15th month following injury. (NSA)

210

Sato, Keiji and Yoshio Nishina. EFFECTS OF FAST NEUTRONS UPON FOREST TREE SEEDS. II. RELATIONS BETWEEN THE INTENSITIES OF IRRADIATIONS AND THE GERMINATIONS OF SEEDS, THE GROWTH OF SEEDLINGS OF *PINUS DENSIFLORA*. *Sci. Bull. Faculty Agr. Kyushu Univ.* **13**, 238-42(1951).

Seeds of *Pinus densiflora* were exposed for 5 to 120 min to neutrons produced by bombarding Be with 2.8- to 3-Mev deuterons from the Institute of Physical and Chemical Research cyclotron (this work was carried out in 1943). Neutron intensities are expressed in arbitrary units. The percentages of germinations, the survival rates, and the growth of seedlings were found to be better in the classes exposed at certain doses than in the controls. Exceeding these limits, the percentages of germinations, the survival rates, and the growth of seedlings were inversely proportional to the doses of radiations. Pine seeds soaked in tap water for 1 to 3 days were more susceptible to neutron-irradiation damage than were dry seeds. (NSA)

211

Snell, G. D. and P. C. Aerbersold. THE PRODUCTION OF STERILITY IN MALE MICE BY IRRADIATION WITH NEUTRONS. *Proc. Natl. Acad. Sci. U. S.* **23**, 374-8 (1937).

Twelve male mice were irradiated with doses ranging from 110 to 215 r of neutrons and mated to untreated females. Males receiving the larger doses failed to give fertile matings. The other males gave fertile matings for about three weeks, after which there followed a sterile

period of about nine weeks. Production of sperm probably ceases within a few days following treatment. The initial fertile period lasts only until the mature spermatozoa already in the sperm tract at the time of treatment have become too inactive to effect fertilization. Litter size during the initial fertile period was 3.1 ± 0.5 . For a control group, the litter size was 8.4 ± 0.6 . Neutron rays, as measured by the amount of ionization produced in a Bakelite-walled thimble chamber are about 5-6 times as potent as X-rays in producing dominant lethal changes in the mature sperm of mice. (BA)

212

Snider, R. S. HISTOPATHOLOGICAL STUDIES OF MICE EXPOSED TO FAST NEUTRON RADIATIONS. *Univ. of Chicago Metallurgical Lab. Dec. 5, 1946. Decl. Sept. 8, 1947. 34p. (MDDC-1278; CH-3730)*

Histological observations were made on the following structures of CF-1 male and female mice after exposure to 65n, and 117n units of fast neutrons: spleen, liver, pancreas, thymus, bone, cartilage, mesenteric lymph node, heart, lung, kidney, bone marrow, adrenal, testis, ovary, stomach, duodenum, ileum, colon, peripheral nerve, autonomic ganglia, and skeletal muscle. The bone marrow, thymus, lymph node, and spleen suffered severe damage, and the intestinal epithelium was damaged to a lesser extent. All these organs had completely recovered by 30 days after the two lower doses. The testis, which was also badly damaged, showed a few signs of repair 30 days after 65n and 96n. All other organs were resistant to irradiation by fast neutrons at these doses. Damage was more severe after the larger doses, but no alterations were characteristic of one dose and not of another. In general, the changes observed following fast neutron irradiation were similar to those described by all workers as following irradiation. A bibliography is appended. (ADD)

213

Snider, R. S. ACUTE HISTOPATHOLOGICAL EFFECTS OF SINGLE DOSES OF SLOW NEUTRONS ON MICE. *Univ. of Chicago Metallurgical Lab. Feb. 5, 1947. Decl. Sept. 15, 1948. 17p. (AECD-2326; CH-3766)*

Histological observations were made on the following structures of CF-1 female mice (after exposure to 400 arbitrary units of slow neutrons): spleen, liver, pancreas, thymus, bone, cartilage, mesenteric lymph node, heart, lung, kidney, bone marrow, adrenal, ovary, fallopian tube, stomach, duodenum, ileum, colon, peripheral nerve, autonomic ganglia, and skeletal muscle. The spleen, lymph node, bone marrow and thymus were the organs most severely damaged by the treatment. All of these organs had returned to the appearance of those in the control animals by 30 days post-treatment time. No damage was noted in the bone, cartilage, skeletal muscle, peripheral nerve, autonomic ganglia, liver, kidney, pancreas, heart, lung, adrenal, stomach, fallopian tube, or colon. There was minor damage in the ovary and duodenum. It is pointed out that the tissue response following slow neutron irradiation is similar to that following X-ray treatment, as reported in the literature. (NSA)

214

Spear, F. G. THE ACTION OF NEUTRONS ON BACTERIA. *Brit. J. Radiol.* **17**, 348-51(1944).

Experiments are described which were made to determine the lethal action of a neutron beam on colon bacilli and on spores of *Bacillus mesentericus* when they were exposed to gradually increasing doses of radiation and to compare the results with those obtained with other types of radiation. The work was done with Lawrence's 37-inch cyclotron at the Radiation Laboratory, Berkeley, California. A diagram is given showing the position of the bacterial suspensions 7.0

cm. from the target of the cyclotron and two tables, the first showing the complete details of a single experiment and the second a summary of all the experimental results. An n-unit was used for measuring the neutron radiation; it is the neutron dose given when the Victoreen dose meter, calibrated for x-rays records roentgen. Survival curves are given for the cultures of bacteria which are exponential in form. A tentative comparison between the effects of roentgen, γ and neutron irradiation may be obtained by determining the dose required to produce a 5% lethal action and expressing the result as a r n ratio, r being the measurement of x or γ radiation in roentgens and n that of the neutron dose in the author's unit. The r n ratio for colon bacilli is 3.2 and that for *Bacillus mesentericus* 5.3. The r n ratio shows wide variation according to the material irradiated. It varies from 1 to 10 with a value of 5 to 6 in most experiments. Until the dosimetry of neutrons has been studied more completely, however, the values of the ratio must be considered provisional. It must not be assumed, however, that for equal energy absorption neutrons produce a greater effect than roentgen or γ irradiation. It seems probable that the energy absorbed per unit volume of tissue exposed to 1 n of neutrons is about the same as that from 2.5 r of γ irradiation. (AJR)

215

Spear, F. G., L. H. Gray, and John Read. **BIOLOGICAL EFFECTS OF FAST NEUTRONS.** *Nature* **142**, 1074-5 (1938).

Chick fibroblasts were irradiated in vitro by 2.4 Mev neutrons produced by bombarding "heavy wax" with a ~ 700 microamp. of 300 kv. deuterium ions. Doses averaged 3.75 E.S.U. cc for 49 minutes in one experiment and 10.5 E.S.U. cc for 42 minutes in another. The biological effect was measured by counting the mitotic cells in the culture and calculating the percentage of the corresponding control counts. Results averaged 81% and 54% respectively, in the two experiments. The relation between dose and effect is more nearly exponentially than the sigmoid relation found for γ -radiation. The exponential relation is that to be expected from a situation in which inhibition of mitosis results from the production of about 1500 ion pairs in a volume of about 3μ in diameter. (V.E.)

216

Spear, F. G. and Katharine Tansley. **THE ACTION OF NEUTRONS ON THE DEVELOPING RAT RETINA.** *Brit. J. Radiol.* **17**, 374-9(1944).

It has been found that degeneration in tissues irradiated with roentgen and radium rays depends on mitotic activity. The experiments here described were made to determine whether neutron irradiation of doses which permit ultimate recovery of the tissues has the same biological effect. The irradiations were given with the cyclotron on immature rat retinas. The technique is described. A table is given showing the mitotic phase and degenerate cell counts after each dose of neutron and a similar table is given for radium irradiation. Degenerate cells appeared after one to three hours. In all the experiments this initial decrease was followed by a renewal of mitosis and with doses above 5 n this return of mitosis was characterized by a marked distortion of the phase ratio. (Doses from 2.5 n to 60 n were used.) As the dose is increased to 60 n the initial decrease of mitosis increases and recovery is more delayed. Some recovery follows the initial fall of mitotic rate caused by neutron irradiation but the increase to a supernormal level seen with roentgen and radium irradiation does not occur after a dose of more than 2.5 n. Up to 1.5 n there is an increase in the prophase count but not in the metaphase and telophase counts. It seems that the mitotic curves after neutron irradiation do not differ materially from those after

roentgen and radium irradiation but the effect on cell degeneration is much more marked. The degenerate cell count on neutron irradiation is made up partly of cells that are injured and die later when they attempt mitosis. The curve of cell degeneration which accompanies increased dosage occurs much sooner and is markedly steeper than with radium. The curves given show that roughly neutrons are 2.6 times as effective as radium rays per unit energy and 6.5 times as active per n unit. (R)

217

Stapleton, G. E. and H. J. Curtis. **THE EFFECTS OF FAST NEUTRONS ON THE ABILITY OF MICE TO TAKE FORCED EXERCISE.** *Oak Ridge National Lab.* Aug. 22, 1946. Decl. Feb. 26, 1948. 18p. (MDDC-696)

In an attempt to gain some insight into the physiological condition of mice surviving massive doses of radiation, a study of their vitality was undertaken. It was assumed that the ability of these animals to do forced work would be a measure of their vitality. Stimulating exposed animals to run in exercise wheels to their fullest capacity, has resulted in a demonstration of a striking vitality loss during a post-irradiative period, when no other effects are demonstrable by gross examination. Mice subjected to a median-lethal dose of fast neutrons show a continuous vitality loss over a 300 day period following exposure. Control animals show no appreciable loss of vitality up to about eight months of age, after which a gradual loss can be noted, probably due to a normal gerontologic process. (ADD)

218

Tait, J. H. **THE CALCULATION OF THE TOLERANCE FLUX OF FAST NEUTRONS.** *Atomic Energy Research Establishment, Harwell, Berks (England).* Feb. 4, 1949. 13p. (AERE-T/R-273)

The dose in roentgen is calculated at interior points of a semi infinite space consisting of human tissue, for the case when a monochromatic collimated beam of neutrons falls perpendicularly upon the free surface. The variation of the mean free path with energy is neglected, and with this approximation the biological effects can be shown to be proportional to the energy flux. This latter quantity is then determined as a function of the distance into the tissue using the Spherical Harmonics method P_1 approximation (AERE-T/R-231). (NSA)

219

Tait, J. H. **THE CALCULATION OF THE ENERGY DEPOSITION IN SOFT TISSUE BY THERMAL NEUTRONS.** *Atomic Energy Research Establishment, Harwell, Berks (England).* Oct. 1949. 20p. (AERE-T/R-416)

The amount of energy is calculated, which would have to be deposited by γ rays in a semi-infinite medium containing tissue, to obtain the same biological effect as a unit flux of neutrons entering normally to the free surface. Two alternative values for the tolerance flux of thermal neutrons are obtained. One is obtained by comparing the dose received in the epidermis, from a given neutron flux over an 8-hour period, with the maximum permissible dose from β rays, and the dose received in the connecting tissue with the maximum permissible dose from γ rays. This gives a tolerance flux of $1800 \text{ n/cm}^2/\text{sec}$. If, however, it is specified that the maximum dose in the tissue is not to exceed the maximum permissible dose from γ rays in an 8-hour period, the tolerance flux is $1200 \text{ n/cm}^2/\text{sec}$. (NSA)

220

Tait, J. H. **CALCULATION OF THE ENERGY DEPOSITION BY FAST NEUTRONS IN SOFT TISSUE.** *Brit. J. Radiol.* **23**, 282-6(1950).

The dose in roentgens (rep) is calculated at interior points of a semi-infinite space consisting of human tissue for the case when a broad monochromatic collimated beam

of neutrons falls perpendicularly upon the free surface. The variation of the mean free path with energy is neglected, and with this approximation the physical effects can be shown to be proportional to the neutron energy flux. This latter quantity is then determined as a function of the distance into the tissue, using the spherical harmonics P_1 approximation. (NSA)

221

Wilson, H. A. BODY TISSUE IONIZATION DUE TO NEUTRONS. Univ. of Chicago Metallurgical Lab. July 26, 1943. Decl. May 29, 1947. 8p. (MDDC-1025; CH-821)

A calculation is outlined for determining ionization due to slow neutrons. It appears that the number of γ rays per cm^2 per second at the surface of tissue is approximately equal to the number of slow neutrons entering the tissue per cm^2 per second. The ionization in body tissue due to neutrons from an aperture in a pile shield is also calculated. (ADD)

222

Zahl, P. A. and F. S. Cooper. LOCALIZATION OF LITHIUM IN TUMOR TISSUE AS A BASIS FOR SLOW NEUTRON THERAPY. Science **93**, 64(1941).

By injection of the Li salts of dyes into tumor bearing mice, an increase of about 43% in the radiation dosage of the tumor over that of other tissues was obtained. (BA)

223

Zahl, P. A., F. S. Cooper, and J. R. Dunning. SOME IN VIVO EFFECTS OF LOCALIZED NUCLEAR DISINTEGRATION PRODUCTS ON A TRANSPLANTABLE MOUSE SARCOMA. Proc. Natl. Acad. Sci. U. S. **26**, 589-98(1940).

Transplantable mouse sarcomas were injected with various forms of slow-neutron-capturing materials. When the injected tumor-animal was irradiated with slow neutrons, a significant increase in tumor regression was observed. The increase is attributed to the localized ionization resulting from the nuclear disintegration products of the capture process. (BA)

Effects of Pile and Fission Radiations

224

Henshaw, Paul S. and George E. Stapleton. THE BIOLOGIC EFFECTS OF PILE RADIATIONS. Radiology **49**, 349-60 (1947).

Experiments have been carried out with mice to determine the late effects of periodic and single exposures of fast neutrons, slow neutrons, γ -rays, and β -rays (limited to the skin). With penetrating radiations these effects are generalized atrophy and neoplasia of hemopoietic organs, attended by shortened life, loss of weight, increase in tumor incidence, etc. No fundamental differences are found in responses of different sexes. The degree of acute damage varies with dose and intensity. The accumulated evidence indicates that the degree of biological effect thus varies with dose and density of ionization produced. (CA)

225

Tobias, C. A., P. P. Weymouth, L. R. Wasserman, and G. E. Stapleton. SOME BIOLOGICAL EFFECTS DUE TO NUCLEAR FISSION. Science **107**, 115-18(1948).

Colloidal uranium oxide, enriched with radioactive U^{235} , was injected into mice. Three days later the mice were bombarded with a sublethal dose of slow neutrons. All the bombarded mice died within three weeks; some within eight days. Fur was ruffled, backs were arched, and diarrhea occurred in most of the mice from 2 to 14 days after the bombardment. Neutron bombardment without U killed no control mice. Neither did U that had not been subjected to fission by neutron bombardment. The mice lived even when

roentgen rays were substituted for neutrons. Li and B also undergo nuclear disintegration. Whenever any fissionable substance is bombarded with slow neutrons, the action of the fission products and of induced radioactivity is superimposed on that of the neutrons. The specific effectiveness of fission products may be important in understanding the mechanism of radiation effects. Fission has possible application in radiation therapy, if fissionable element can be put into compounds that localize at specific areas. This knowledge is also of interest from the standpoint of radiation health protection in atomic energy plants. (BA)

Chronic Whole-Body Irradiation

226

Boche, R. D. OBSERVATIONS ON POPULATIONS OF ANIMALS EXPOSED TO CHRONIC ROENTGEN RADIATION. [Univ. of Rochester] [nd] Decl. Aug. 17, 1946. 56p. (MDDC-204)

This report discusses the effects of chronic roentgen radiation on the basis of survival of animals, and the effects on their reproductive systems. Dogs, rabbits, mice, rats, and monkeys were used as the experimental animals in this study. (ADD)

227

Brues, A. M., G. Sacher, and H. O. France. EFFECT OF TOTAL BODY X-RAY ON WEIGHTS OF ORGANS IN THE RAT. Univ. of Chicago Metallurgical Lab. June 1946. Decl. Aug. 7, 1947. 15p. (MDDC-1197; CH-3835)

Weights and water content of organs were investigated in a group of growing male rats that had received 1498 r at 13.82 r/day average. The weights of the majority of the visceral organs were affected less than body weight as a whole; weights of muscle and femur were affected in the same ratio as body weight; and spleen, thymus, gonads, and gonadal fat were reduced out of proportion to body weight. Adrenal weights were normal. Water content per gram of tissue in muscle and bone of irradiated animals was 4.3% greater than in the control animals. Thus the retardation in growth is similar to that seen in inanition except for the relatively greater effect on organs known to be radio-sensitive. Organ weights and total body weights of rats that had received single doses of X-ray up to 100 r several months previously, showed no deviations from the normal. (ADD)

228

Dowdy, A. H., R. D. Boche, and F. W. Bishop. OBSERVATIONS ON ANIMALS EXPOSED TO WHOLE BODY ROENTGEN RADIATION IN DIVIDED DOSES OVER LONG PERIODS. Univ. of Rochester. [nd] Decl. Aug. 21, 1946. 22p. (MDDC-254)

This report discusses only the routine and the techniques that were used in radiating laboratory animals over a long period of time in order to determine whether the accepted tolerance levels for exposure of persons to roentgen and γ radiation are adequate to insure a reasonable degree of safety. The general objective of the experiments described was to determine whether there exists any exposure level to which animals may be subjected without the manifestation of any deleterious effects, and if so what this level of radiation exposure is, and which organ system is the most sensitive to chronic radiation injury. Actual results are reported elsewhere. (ADD)

229

Eschenbrenner, Allen B. BIOLOGIC EFFECTS OF LONG-CONTINUED WHOLE BODY IRRADIATION WITH GAMMA RAYS ON MICE, GUINEA PIGS, AND RABBITS. Argonne National Lab. Sept. 17, 1946. Decl. Jan. 24, 1947. 46p. (MDDC-642)

Histologic observations in animals exposed to long continued irradiation with γ rays were the following. Mice: The lymphoid tissue was only affected in the 2.2 r, 4.4 r, and 8.8 r levels but changes observed initially did not progress with increasing total dose. Malignant lymphoma (leukemia), which was associated in only a small number of cases with a lymphomatosis in the circulating blood, involved all lymphoid tissues frequently with local invasiveness and metastases to many organs. The interstitial tissue of the testes appeared unaffected for the highest accumulated doses (approx. 5000 r). Damage to the testes was restricted to the tubules and the various spermatogenic elements, but even at the highest total doses occasional spermatogonia or spermatocytes, but no spermatozoa, were found. Damage to testes is dependent upon dose rate rather than total dose. Damage to the ovaries is dependent upon total dose and is irreversible. It consists of diminution in the number of follicles and final disappearance of these structures followed by tubular downgrowth of the germinal epithelium, and finally the development of several types of ovarian tumors. In a few cases a sarcoma at the site of the mammary gland was associated with the ovarian tumors. Guinea pigs: The most important changes were observed in the blood forming organs. All animals of the 8.8 r and most of the animals of the 4.4 r and 2.2 r levels died of anemia and thrombocytopenia. Bone marrow in these animals was aplastic to a varying degree. The testes were as radio-sensitive as those of mice and showed a similar picture of damage. Ovaries were not affected and showed numerous developing follicles even for total doses as high as 4000 r. Lung tumors were observed in two animals that were exposed to total doses of 4000 r. These tumors were of alveolar origin. (ADD)

230

Furth, J. and D. H. Kabakjian. STUDIES ON THE EFFECT OF CONTINUOUS EXPOSURE OF MICE TO GAMMA RAYS OF RADIUM. *Am. J. Roentgenol. Radium Therapy* **32**, 227-34(1934).

Mice were exposed continuously to γ rays emanating from 0.003 to 5 mg. of Ra. Rays from 1 to 5 mg. of Ra shortened the life of the animals, the average length of life after exposure being 66 and 106 days. The leukocyte count of mice exposed continuously to 5 mg. of Ra dropped much below normal within a week, yet the mice lived for 2-3 months in spite of the uninterrupted exposure to the same quantity of rays. Continuous exposure to 0.3 mg. and to smaller amounts of Ra did not prevent the development of spontaneous neoplasm (lymphoid and myeloid leukemia, tumors of the lung, heart, and ovary). Continuous exposure of mice with transmitted lymphomatosis to 1-5 mg. of Ra did not prevent the fatal termination of the disease but often prolonged life. These rays increased susceptibility to transmitted lymphomatosis. (BA)

231

Lorenz, Egon. BIOLOGIC EFFECTS OF LONG-CONTINUED WHOLE BODY IRRADIATION WITH GAMMA RAYS ON MICE, GUINEA PIGS, AND RABBITS, PART II. Argonne National Lab. Oct. 29, 1946. 16p. (MDDC-654; CH-3653)

Experimental arrangements are described for the simultaneous irradiation of considerable numbers of animals with γ rays. Three experimental setups were available. In the first a source of approximately 1 g. of radium element was used, with four sets of shelves forming part of a sphere surrounding the source. Daily doses at the different shelves were 8.8 r, 4.4 r, 2.2 r, and 1.1 r in eight hours. In the second setup a source of 1000 mg. radium element in a lead box with a hinged lid was employed to irradiate one set of shelves. The daily dose at this set of shelves was 0.11

r in eight hours. In the third setup a source of 250 mg. element, also housed in a lead box, was used with six sets of shelves. Here the exposure was continuous, the daily doses amounting to 8.8 r, 4.4 r, 2.2 r, 1.1 r, 0.55 r, and 0.11 r in 24 hours. Dose measurements with calibrated 0.25 r, Victoreen ionization chambers, were made in every one of the animal cages which were placed on the different shelves. Errors are discussed which arise mainly from the dimensions of the cages. They are for mouse and guinea pig cages approximately $\pm 15\%$, and for rabbit cages $\pm 25\%$. The precautions taken to reduce the residual dose to a minimum are described. (ADD)

232

Lorenz, Egon. BIOLOGIC EFFECTS OF LONG-CONTINUED WHOLE BODY IRRADIATION WITH GAMMA RAYS ON MICE, GUINEA PIGS, AND RABBITS, PART III. Argonne National Lab. Nov. 14, 1946. Dec. Feb. 5, 1947. 118p. (MDDC-655; CH-3698)

Experimental arrangements and amounts of radiation used are given in the previous abstract. On all daily dose levels, including the 0.11 r level, there was a decrease in the life span of mice. The decrease in life span was pronounced in guinea pigs exposed to 8.8 r, 4.4 r, and 2.2 r per day. The life span of rabbits was decreased in the animals exposed to 8.8 r and 4.4 r. An increase in weight was found in irradiated animals on the lower exposure levels mounting, in male mice exposed to 1.1 r, to 50% of that of the control animals. The hemopoietic system of rabbits is extremely radio resistant, and changes in the blood picture were found only in the animals exposed to 8.8 r per day. The hemopoietic system of mice is also radio-resistant; the main effect of irradiation consisting in a depression of the lymphocyte count. No damage to bone marrow was observed (max. accumulated dose 5800 r). The hemopoietic system of guinea pigs is very radiosensitive. Anemia and thrombocytopenia, were observed in all animals exposed to 8.8 r and in most animals exposed to 4.4 r and 2.2 r per day. Bone marrow damage of moderate to severe degree was associated with the anemia. The carcinogenic action of irradiation was mainly observed in mice, but some irradiated guinea pigs and rabbits also developed tumors after 3 years of irradiation. The observed tumors are described in detail. (ADD)

233

Lorenz, Egon. SOME BIOLOGICAL EFFECTS OF LONG-CONTINUED IRRADIATION. *Am. J. Roentgenol. Radium Therapy* **63**, 176-85(1950).

The data presented permit the following conclusions: Chronic irradiation will reduce the life span of experimental animals. This effect is a function of many factors some of which are unknown. The effects of irradiation are seen relative to a certain degree. Our experiments do not give a clear-cut answer to the question whether or not a 0.1 roentgen (the so-called permissible dose for man) also will cause a reduction in life span. Data on higher dosage rates make such a result likely but in any case the reduction at this dose level will be small. The determination of the extent of the reduction of life span for this important dose level requires the collection of experimental data on a large group of animals. Carcinogenesis plays the most important role in the reduction of the life span in mice. The carcinogenic action of chronic irradiation has been observed in three species, one of which, the guinea pig is considered one of the least susceptible animals to spontaneous tumor formation. It seems that we are justified in assuming that this carcinogenic action of chronic irradiation will hold for other species as well as man. (Author's Summary)

234

Lorenz, Egon, Allen B. Eschenbrenner, Walter E. Heston, and Delta Uphoff. MAMMARY-TUMOR INCIDENCE IN FEMALE C₃Hb MICE FOLLOWING LONG CONTINUED GAMMA IRRADIATION. *J. Natl. Cancer Inst.* **11**, 947-61 (1951).

Virgin C₃Hb mice were chronically irradiated over total body with 8.8 r daily (8 hr) of γ radiation from a RaSO₄ source beginning at 1 month of age and continuing throughout their entire life span. Mean survival time of irradiated animals was shortened by 36% in comparison to nonirradiated controls. The injurious action of the irradiation was evidenced by a considerable reduction in weight after 1 yr of age. Of the animals 47% developed tumors of the mammary gland, 88% ovarian tumors, and 36% lymphoid tumors. Pulmonary tumor and hepatoma incidences were also increased in experimental animals in comparison to nonirradiated controls. Physiological and hormonal factors involved are discussed. (NSA)

235

Lorenz, Egon and W. E. Heston. BIOLOGIC EFFECTS OF LONG-CONTINUED WHOLE BODY IRRADIATION WITH GAMMA RAYS ON MICE, GUINEA PIGS, AND RABBITS, PART I. Argonne National Lab. Oct. 29, 1946. Dec. Feb. 6, 1947. (MDDC-653)

Male and female mice of the C3H strain were continuously irradiated with 4.4 r, 1.1 r, 0.11 r, and 0.044 r per day. No significant damage to the hematopoietic system as evidenced by blood counts was found although the highest total dose was over 2000 r. Mammary tumor incidence was not changed significantly in the animals exposed on the different dose levels. Histologically only the gonad showed radiation damage and mainly in the animals exposed to 4.4 r per day. The damage consisted in the testes in diminished spermatogenesis and was reversible. Irradiation damage to the ovaries was irreversible and progressive and resulted in some cases in tubular downgrowths of the germinal epithelium which progressed to early tumor formation. Breeding experiments indicated that C3H females were permanently sterilized with total doses of 465 r given at the rate of 4.4 r per day. Subsequent generations reared and maintained in exposure fields of 1.1 r and 0.11 r per day showed no damage to chromosomes as evidenced by raising of 5 to 6 generations with normal litter size and apparently normal life span. (ADD)

236

Lorenz, Egon, Leon O. Jacobson and Harriet Sutton. SUMMARY OF FINISHED EXPERIMENTS; PART I. SURVIVAL AND BLOOD PICTURE OF HYBRID GUINEA PIGS EXPOSED TO LONG-CONTINUED TOTAL-BODY GAMMA RADIATION, p.38-52 of BIOLOGICAL AND MEDICAL DIVISIONS; QUARTERLY REPORT, NOVEMBER, DECEMBER, JANUARY, 1949-50. Argonne National Lab. [nd] 15p. (ANL-4401(p.38-52))

Groups of hybrid guinea pigs were chronically exposed to γ radiation at 8.8, 4.4, 2.2, 1.1, or 0.11 r, 8 hr/day, 7 days/week, beginning in February 1943. The last survivor died in May 1949. In the animals exposed to 2.2, 4.4, and 8.8 r there was a pronounced increase in mortality. All the animals in the 8.8 r group died of pancytopenia, which also caused most of the deaths at the other two levels. There were no deaths from pancytopenia in the 1.1 r group. In guinea pigs it appears that death from radiation-induced pancytopenia is a function of dose rate rather than total dose, and there is no linear relationship between mean survival time and mean lethal total dose. (NSA)

237

Lorenz, Egon, Leon O. Jacobson, Harriet Sutton, and R. Schweisthal. SUMMARY OF FINISHED EXPERIMENTS; PART II. RECOVERY FROM ANEMIA INDUCED IN

GUINEA PIGS BY A LIMITED EXPOSURE TO CHRONIC TOTAL-BODY GAMMA RADIATION, p.53-71 of BIOLOGICAL AND MEDICAL DIVISIONS; QUARTERLY REPORT, NOVEMBER, DECEMBER, JANUARY, 1949-50. Argonne National Lab. [nd] 19p. (ANL-4401(p.53-71))

Inbred guinea pigs were given limited chronic exposure to γ radiation. The smallest accumulated dosage was 757 r (86 days) and the largest, 1804 r (205 days). The animals were removed from the field when the red blood counts reached about 2.5 millions. Three different responses followed removal from exposure: (1) some animals died within a few weeks; (2) some showed partial recovery lasting about 25 weeks at which time there was a lethal recurrent anemia; and (3) in some there was complete recovery. Blood data are given for each of these groupings. Pancytopenia was the cause of death in guinea pigs exposed to 8.8 r (8 hr/day, 7 days/week). There was such an abrupt onset of anemia that a hemolytic factor was suggested. (NSA)

238

Lorenz, Egon, Delta Uphoff, Harriet Sutton, and R. Schweisthal. PROGRESS REPORT; THE 30-DAY LD₅₀ FOR HYBRID GUINEA PIGS, p.50-2 of BIOLOGICAL AND MEDICAL DIVISIONS, QUARTERLY REPORT FEBRUARY, MARCH, APRIL, 1950. Argonne National Lab. [nd] 3p. (ANL-4451(p.50-2))

In previous experiments designed to determine the 30-day LD₅₀ for hybrid guinea pigs, groups of animals were given single total-body exposures to 220, 260, and 310 r of x radiation. This study has been concluded with two additional exposure groups of 360 and 420 r. In the first three groups there was no sex difference in survival, but in the last two groups, the females seemed more radiosensitive than the males. However, this finding is probably due to chance since the experiments were spread over a year and hybrid stock was used. The 30-day LD₅₀ is calculated to be 409 r with 2 limits of 307 and 543 r. This value is at variance with previously published data of other investigators, and it is suggested that the low figures reported by these investigators may have been caused by irradiating diseased guinea pigs. (NSA)

239

Metcalfe, Roger G. and Frank A. Inda. PATHOLOGY IN ANIMALS SUBJECTED TO REPEATED DAILY EXPOSURE TO ROENTGEN RAYS. Atomic Energy Project, Univ. of Rochester. July 5, 1951. 59p. (UR-88)

Detailed observations and conclusions are presented on tissue injuries observed in rats exposed to 0.1, 0.5, 1.0, or 10 r/day of x irradiation for 2 yr, in rabbits exposed to the same daily doses for 1 yr, and in dogs exposed to 0.1, 0.5, 1.0, 3.0, 6.0, and 10.0 r for either 500 or 622 days. In rats, the testes are severely injured with administration of 10 r/day, but not specifically injured at 0.1, 0.5, or 1.0 r/day. There is evidence to suggest that the incidence of leukemia in all treated rats and mammary fibroadenomata in females is increased by chronic x radiation. There is no histologic evidence of x-radiation injury in other organs. The histologic changes are not influenced by the voltage used in this experiment. In rabbits, the only consistent lesion attributable to x radiation is testicular injury in the 10-r/day groups. Injury to testes, appearance of bone marrow hypoplasia, decrease of megakaryocytes, focal bowel hemorrhages, and lymph node hemorrhage in the dogs are related to the chronic x irradiation. 19 figures. (NSA)

240

Pape, Rudolph. BIOLOGICAL EFFECTS OF VERY SMALL X-RAY DOSES ADMINISTERED DAILY FOR ONE YEAR. *Strahlentherapie* **84**, 245-54(1951).

It is possible to stimulate blood-forming tissues by means of microdoses. One rat was irradiated for 3 months and two rats for 1 yr with daily doses of 0.25 r. Reactions

were noted in the reticulo-endothelium of the spleen and liver, the resistance of the spleen follicles was found to be increased, and a considerable lymphocytosis was observed. (NSA)

241

Prosser, C. L. and M. C. Moore. **THE CLINICAL PHYSIOLOGY OF DOGS EXPOSED TO DAILY TOTAL-BODY DOSES OF X-RAYS.** Univ. of Chicago Metallurgical Lab. Feb. 6, 1947. Decl. Sept. 9, 1947. 109p. (MDDC-1271; CH-3658)

Dogs that received 50 r and 40 r and one dog that received 25 r daily, died after accumulating an average of 880 r. Clinically, these animals resembled dogs that received single, acute, lethal doses of x-radiation. They developed a severe leucopenia, showed terminal reversal of heterophil lymphocyte ratio, and had a mild anemia accompanied by increased plasma volume. They differed from single dose dogs in showing earlier diminutions in food and water intake and earlier weight loss. Dogs that received 12.5 r, and a young dog that received 25 r daily, accumulated an average of 1262 r and clinically showed a subacute picture in which aplastic anemia was prominent. During the first two months of treatment, leucopenia and anemia developed slowly. There was no change in food and water balance or in body weight until 65-80% of the total dose had been accumulated. The destruction of red cells was accelerated during the last month of life, terminal hemoglobins averaged 3.4 as compared with 7.8 g/100 ml. at the higher doses, and mean corpuscular volumes increased. (ADD)

242

Sacher, George A. **PRELIMINARY REPORT: DAILY DOSE LETHALITY DATA FOR RABBITS,** p. 128-35 of **BIOLOGICAL AND MEDICAL DIVISIONS, QUARTERLY REPORT, AUGUST, SEPTEMBER, OCTOBER 1950.** Argonne National Lab. Oct. 1950. 7p. (ANL-4531(p.128-35))

Forty-eight rabbits of the Swift strain were exposed to daily doses of 200 kv. x-rays at rates ranging from 40 to 325 r per day, for 6 days per week. Six animals were irradiated at 11 r per minute, and the remainder at 3.5 r per minute. The derived impulse lethality function of the rabbit shows peaks at 12, 25, and 70 days; rabbits exposed to single doses show maximum rate of mortality at 10 days, with a secondary peak at 6 days. It was concluded that the cumulant lethality function of the rabbit must consist of a succession of waves. The mouse shows a somewhat similar behavior in that its impulse lethality function shows peaks of injury at certain times. However, it barely reaches normality or slightly exceeds it in recovery, while the rabbit shows transient states of marked supernormality. (V.E.)

243

Vogel, Howard H., Jr. **THE EFFECT OF X IRRADIATION ON FIGHTING BEHAVIOR IN MALE MICE.** *Anat. Record* **108**, 547(1950).

This paper is one abstract and is reproduced here in its entirety.

These experiments were carried out to test the effects of chronic x irradiation upon fighting behavior. Male mice (5 weeks old) of three strains, C-57 black, C-3H agouti, and CF-1, were kept in isolated cages and were trained to fight in a multiple-escape pen. Six males were trained to become aggressive, whereas, under the conditions of the experiment, fighting was inhibited in their daily opponents. After the trained fighters had defeated a dozen other males of their strain, they were irradiated daily with 50 r of x radiation, 5 days a week, and fighting was continued daily. The body weights of the irradiated

fighting mice were compared with those of nonirradiated controls over a period of approximately 15 weeks. The accumulated x-ray dosage given to each of the 6 experimental mice at the time all fighting ceased and at the time of death are given. The effects of x irradiation upon fighting behavior in male mice were cumulative. Each fighting mouse retained its characteristic method of attack up to the day when all fighting ceased. There was a definite threshold after which no fighting occurred, but before this threshold the irradiated fighters defeated their daily opponents. The aggressiveness of the attacks decreased as the cumulative x-ray dose increased. The conditioning that the mice had received was strong, and it took a large dosage (1200 to more than 2000 r) to eliminate it completely. All signs of fighting were not suppressed until shortly before the death of the irradiated animal.

X- and Gamma Regional Irradiation

244

Abrams, Herbert L. and Henry S. Kaplan. **THE EFFECT OF SHIELDING ON MORTALITY FOLLOWING IRRADIATION.** *Stanford Med. Bull.* **9**, 185-6(1951).

Lead shields placed over the head, chest, abdomen, or thighs during irradiation conferred a significant degree of protection on mice of all four groups as compared with unshielded controls. Protection was most striking when the abdomen was shielded. (NSA)

245

Ariel, Irving M. **THE EFFECT OF SINGLE MASSIVE DOSES OF ROENTGEN RADIATION UPON THE LIVER.** *Radiology* **57**, 561-75(1951).

The acute morphological changes in the rabbit's liver following single massive doses of x radiation to that organ were studied. Single doses of 300 to 100,000 r at 90 kv were given and the animals were sacrificed or succumbed at various intervals thereafter. Edema, hyperemia, and leukocytic infiltration were produced in the vascular system. Edema appeared to be most marked in the central portion of the lobule and polymorphonuclear leukocytic infiltration in the portal areas. Liver cells were damaged or destroyed in proportion to the dosage, very high doses causing complete necrosis, while the lower dosages produced only slight swelling of the cells. In the lower dosage range, focal destruction of the liver cells was produced, indicating apparently a variable sensitivity to radiation. Repair was rapid when possible; otherwise death occurred, depending upon the dosage and extent of the damage. (NSA)

246

Arkin, Alvin, Norman Simon, and Robert Siffert. **ASYMMETRIC SUPPRESSION OF VERTEBRAL EPIPHYSEAL GROWTH WITH IONIZING RADIATION.** *Proc. Soc. Exptl. Biol. Med.* **69**, 171-3(1948).

The lumbar spines of 30 young rabbits were unilaterally irradiated with radon seeds and X-rays. Twenty-one animals died of gastrointestinal disturbances unrelated to radiation. Five of the nine survivors showed wedging of the vertebral bodies with the narrowing of the bodies on the more heavily irradiated side. Dosage estimates indicate the growth of the epiphyses of the vertebral bodies of baby rabbits may be suppressed with 700 to 1000 r to the epiphysis. Doses of 350 r or less have no apparent effect on the growth. (NSA)

247

Bacq, Z. M., J. Lecomte, and A. Herve. **THE ACTION OF IONIZING RADIATIONS ON STRIATED FROG MUSCLE.** *Arch. intern. physiol.* **57**, 142-53(1949).

Experiments are reported on the rectus abdominus muscle of *Rana temporaria* suspended in oxygenated Ringer

solution and excited at regular intervals by 5% KCl. The β rays from P^{32} were employed as one test of ionizing radiation effects; the P^{32} was added in increasing amounts to a bath containing the frog muscle. The X-ray experiments were of several types: x-radiation at 190 kv with a 5 mm Al filter and at a target distance of 40 cm. was employed to deliver doses at the rate of 200 r/min. to previously dried muscle; contact X-ray therapy at 50 kv and with no filtration was also used on the dried muscle; x-irradiation of the frog muscle in Ringer's solution was used; and, irradiation of the Ringer's solution itself with 4,000-8,000 r was also attempted and the H_2O_2 content determined. It was found that both the X-rays and β radiations determined the appearance of the Lundsgaard effect (contraction of striated muscle after work). This is considered proof by the authors of muscular glucidic metabolism; the irradiations are enzyme poisons. The calculations of the amounts of peroxides formed in the solution during different stages of the irradiations made possible accurate observations. (NSA)

248

Baidins, A., L. Claesson, and A. Westman. THE EFFECT OF X-RAY IRRADIATION ON THE PITUITARY BODY OF INFANTILE RATS TREATED WITH ALPHA-ESTRADIOL MONOBENZOATE. *Acta Endocrinol.* **1**, 133-40(1948).

Fourteen female rats were treated with a total of 160 μ g of α -estradiol benzoate subcutaneously, over a period of eight days and then irradiated with 40 r in a single exposure over the pituitary region with the rest of the body shielded with lead; seven rats were similarly treated with estradiol and four others served as untreated controls; all the animals were observed for 50 days after treatment. It is concluded that under the influence of estrogen, the pituitary of the infantile rat is sensitive to radiation doses (1 to 1,000 r) which fail to affect normal infantile rats. (NSA)

249

Bender, A. E. EXPERIMENTAL X-IRRADIATION OF THE RAT THYROID. *Brit. J. Radiol.* **21**, 244-8(1948).

Treatment of the thyroid of rats with doses of x-rays ranging from 50-5000 r produces no change in their oxygen consumption, nor in the histological appearance of the glands in (a) mature male rats; (b) young growing rats, (c) mature animals in which the gland had been rendered hyperplastic by oral administration of thiouracil. Doses greater than 5000 r invariably resulted in death of the animals, 9-10 days later, which could be delayed or prevented by the subcutaneous administration of glucose-saline. Although death was apparently due to insufficient intake of fluid, no cause for this was found. (NSA)

250

Billings, Marta S., A. H. Dowdy, Louise Burlingame, and Juanita Lampert. SYSTEMIC EFFECTS OF IRRADIATION OF THE EXTERIORIZED SMALL INTESTINE IN RABBITS. Atomic Energy Project, University of California at Los Angeles. Oct. 26, 1951. 30p. (UCLA-152)

The object of this work was to study the systemic effects of intestinal irradiation in rabbits. In order to eliminate irradiation of other intra-abdominal organs and structures, as well as side scatter effects to bone marrow, the irradiation was given directly to the small intestine after surgical exteriorization. Doses up to 1800 r did not cause any significant morbidity. Doses from 1800 to 6000 r causes illness after a latent period of 5 days terminating with 100% lethality in the fourth week. At no time did the animals exhibit diarrhea. Irradiation of the exteriorized small intestine had no immediate specific effect on the circulating blood cells. The eventually developing granulocytopenia and increase in red blood cells after intestinal exposure to dose of 2000 r or more appear to be the result

of inanition and dehydration which follow local intestinal radiation injury. Leukopenia and anemia developing after total-body irradiation were not modified by lead shielding of the exteriorized small bowel. Lead protection of the exteriorized small intestine prevented initial shock and early death of rabbits after total-body irradiation. Lethal doses were slightly higher in the shielded group. (NSA)

251

Bischoff, F., H. J. Ullmann, and L. P. Ingraham. THE INFLUENCE OF IRRADIATION OF THE OVARIES UPON ESTRUS AND NEOPLASTIC DEVELOPMENT IN MARCH-BUFFALO MICE. *Radiology* **43**, 55-8(1944).

Respective groups of 40 Marsh-Buffalo mice each received doses of 200 and 400 r of roentgen rays (HVL 1.15 mm Cu) over the ovaries following the establishment of vaginal canalisation. Equal numbers of litter mates served as controls. Immediately after irradiation, the lower dose reduced estrus entirely. For the higher dose, the extent of estrus established for the controls was never attained throughout a 13 month period. The lower dose produced an increase in estrus the 4th month followed by a 6-month period in which the mean estrus did not deviate markedly from that of the controls. The irradiation of the ovaries with 200 r increased the incidence of adenocarcinoma of the breast significantly, but did not increase the incidence of lymphoid tumors. Irradiation with 400 r, while reducing estrus markedly, was without influence upon the cumulative incidence of cancer of the breast, but increased the incidence of lymphoid tumors. (BA)

252

Bond, V. P., Marguerite N. Swift, A. C. Allen, and M. C. Fishler. SENSITIVITY OF ABDOMEN OF RAT TO X-IRRADIATION. *Am. J. Physiol.* **161**, 323-30(1950).

Rats were irradiated either with the abdomen shielded or with only the abdomen exposed. The shields were designed to permit equal gram-roentgen exposures with both types, at any given dose level. A comparison of mortality, survival time, body weight change, and gross symptomatology between the 2 groups revealed distinct differences, suggesting different mechanisms of death referable to the region irradiated. (CA)

253

Braasch, Nancy K. and Margaret J. Nicholson. A STUDY OF THE HANDS OF RADIOLOGISTS. *Radiology* **51**, 719-27(1948).

A group of radiologists was studied for evidences of radiation damage to the skin of their hands. The technique used consisted of (1) examination of wax impressions of the finger ridges, and (2) examination of photographs of the vessels and papillae in the nail fold. Of the 323 radiologists examined by the first method 48% were found to have ridge abnormalities. The incidence of abnormality increased with years of exposure to radiation up to 100% after 35 years. The irregular use of lead gloves does not give adequate protection against damage of the ridges by radiations. Photographs of the nail fold of 152 radiologists were studied and compared to similar photographs of 101 laboratory workers and of 41 persons over 63 years of age. Some of the abnormalities occurred in all three groups. All of the changes which were found among the radiologists were found also in the aged. The incidence of abnormality among the radiologists increased with years of exposure to radiation and exceeded the incidence of abnormality in the aged. No radiologist had normal findings after 30 years of exposure. It is concluded that abnormalities of the vessels and of the papillae in the nail fold are induced earlier in radiologists than in persons not exposed to radiation. (ADD)

254

Burstone, M. S. THE EFFECT OF X-RAY IRRADIATION

ON THE TEETH AND SUPPORTING STRUCTURES OF THE MOUSE. J. Dental Research 29, 220-31(1950).

Forty-four Swiss and C-57 black mice, 2 to 28 days of age, were irradiated in the area of the mandibular joint and the molar teeth; littermates and littermate controls were used whenever possible. The X-rays were delivered by a Philips Metalix contact X-ray machine operating at 50 kv with no filtration, at a target distance of 20 mm and at the output rate of 5,000 r/minute; the three dosages which were used were 1,500, 3,000, and 5,000 r. Following the irradiation, 32 of the mice which survived were sacrificed at intervals from 5 to 37 days; control animals were also sacrificed, and the weights and sex were recorded; the heads of the mice were examined by serial sectioning for changes in the dental structures. It was found that the degree of radiation damage to the teeth and jaws of mice is dependent upon the age at which the animals are irradiated and the stage of histogenesis of the individual teeth. (NSA)

255

Cogan, David G. and David D. Donaldson. EXPERIMENTAL RADIATION CATARACTS. Arch. Ophthalmol. (Chicago) 45, 508-22(1951).

The eyes of rabbits of ages ranging from 3 weeks to 3 years exposed to 200 and 1200 kv x rays showed epilation occurring in 15 to 35 days with doses of 1500 r or greater. Epilation was increased the larger the dose and the less the energy of the x rays. Little variation in susceptibility was found with age. The same generalizations held for kerato conjunctivitis. Cataracts occurred with a latent period that was on inverse function of the dose; the threshold dose for 10-week old rabbits was 250 r or less, and the latent period for the development of radiation cataracts was much less the younger the animal. With x-ray doses (1200 kv) of less than 1000 r, cataracts were the only abnormality produced. Gross and cytological changes due to x-irradiation of the eye are discussed in detail. (NSA)

256

Davidoff, L. M., C. G. Dyke, C. A. Elsberg, and I. M. Tarlov. THE EFFECT OF RADIATION APPLIED DIRECTLY TO THE BRAIN AND SPINAL CORD. I. EXPERIMENTAL INVESTIGATIONS ON MACACUS RHESUS MONKEYS. Radiology 31, 451-63(1938).

Exposed brain and spinal cord of *Macacus rhesus* monkeys were given single doses of 1,000 to 5,000 r. Three were given two doses totalling 4,800, 5,400, and 7,200 r. Four-thousand r to the cerebrum is followed almost immediately by paralysis of the contralateral limbs. Two-thousand to 3,000 r results in hemiparesis after several months. Cerebellar disturbances do not appear until 3 to 5 months after irradiation of the cerebrum. Five-thousand r to the mid-thoracic spinal cord produces immediate paraplegia, and after 4,000 r paraplegia develops after 5-1/2 months. There are marked histological changes in the central nervous system after treatment. The contralateral as well as the homolateral hemisphere may be involved after irradiation of one cerebral hemisphere. Similar histological changes are observed in the cerebrum, and the spinal cord. Chromatolysis of ganglion cells of the cerebellum was found after irradiation of the cerebrum and vice versa. There are marked changes in the glia and nerve tissues and only slight vascular alterations. Myelin sheaths appear to be affected more than axis cylinders. (BA)

257

Dobbs, W. H. H. A STATISTICAL STUDY OF THE EFFECT OF ROENTGEN RAYS ON WOUND HEALING. Am. J. Roentgenol. Radium Therapy 41, 625-32(1939).

In this study, the determination of the tensile strength of tissue is used as a measurement of the effect of roentgen

irradiation on wound healing. In addition, histological sections of control and irradiated wounds were taken at intervals of 4, 5, 6, 8, 10, 20, and 50 days after operation. The results of the effect of exposure of wounds to 300 r, 1020 r, and 1800 r immediately after operation; effect of exposure of wounds to 1800 r 24 hours after operation; effect of exposure of skin to 1800 r 1 and 3 weeks before operation are described. Adult, male, albino rats were used. (S.V.S.)

258

Dobbs, W. H. H. A STATISTICAL STUDY OF THE LATE EFFECTS OF HEAVY ROENTGEN IRRADIATION ON HEALING OF SKIN WOUNDS. Am. J. Roentgenol. Radium Therapy 45, 107-8(1941).

Thirty-nine adult, male albino rats were given roentgen irradiation to a 4 x 1 cm ventral skin field to a total dosage of 4,500 r in weekly fractions of 1,500 r each. Roentgen rays were produced by a full wave, mechanically rectified generator, operated at 95 kv with a Coolidge tube using 4 ma at 25 cm distance, the output being 152 r per min. Sixty days following irradiation, a 4 cm linear incision was made in the treated skin and a similar incision in normal skin and the wounds were closed with black silk sutures. At intervals of 10, 20, 30, and 50 days following operation, the expl. wounds were excised and tested for tensile strength. The wounds receiving irradiation showed a considerable decrease in tensile strength as compared to normal wounds, confirming the feeling of surgeons and roentgenologists generally that wounds in heavily irradiated skin heal but that the process is slow and the scar is not so strong as normal scar tissue. (BA)

259

Eck-Vermande, van G. J. and J. Freud. STRUCTURE AND FUNCTION OF MOUSE OVARIES AFTER X-RAYING. Arch. intern. pharmacodynamie 78, 49-62(1949).

A total of 230 mice (in groups of 3 to 5 animals) under light ether anesthesia were x-rayed from the back without filter, at a focal distance of 78 mm, in 100 or 200 sec, with total doses of 333 or 666 r; ovaries were serially cut; tubes, uteri, and vaginas were extensively investigated at intervals ranging from one day to 3, 7, and 14 weeks after irradiation. The histological findings are reported in detail; one hour after irradiation, marked destructive changes were found in the ovaries, followed by hyperemia and violent follicular atresia with destruction of granulosa cells and fragmentation of the ovocyte during the first days; other results are discussed. (NSA)

260

Engelstad, R. B. THE EFFECT OF ROENTGEN RAYS ON THE STOMACH IN RABBITS. Am. J. Roentgenol. Radium Therapy 40, 243-63(1938).

Irradiation of the stomach with roentgen rays was carried out on 59 rabbits, with doses ranging from 125 r to 4,500 r. After the heavy doses of 2,000 r or more the mortality was very high; but even after smaller doses (1,500 r) a number of the animals died. After irradiation there was a mild initial reaction during the first 24 hours with degeneration of the lymph follicles and hyperemia; thereafter a period of latency, followed by the onset of the main reaction about seven days after irradiation, with degenerative and inflammatory changes. (Author's Summary)

261

Essenberg, J. M. THE RESPONSE OF GERM CELLS TO GONADOTROPIC HORMONES IN X-RAY INJURED OVARIES OF YOUNG WHITE MICE. Western J. Surg. Obstet. Gynecol. 57, 61-6(1949).

Most of the ovaries in 34 young mice, 3 to 4 weeks of age, X-rayed with 244 to 300 r remained sterile from 3 to

6 months, the length of the experimental period. Most of the X-rayed ovaries, treated with gonadotropic hormones, either in the form of injection of gonadophysins or the implantation of the pituitary gland, regenerated germ cells and follicles of all sizes except fully formed or graafian follicles. Degeneration of germ cells and follicles occurs simultaneously with germ cells and follicle formation. The cells of degenerated follicles are segregated by connective tissue into alveoli-like structures, which are found in the medulla of hormone-treated ovaries and the entire ovary of X-ray controls. The germinal epithelium was very active in hormone treated ovaries; germ cells were proliferated and passed through developmental stages before the fully formed stage was reached. Undifferentiated germ cells of germinal epithelium origin may become ova, follicle cells, and probably, interstitial cells. There is great variability; a few X-ray controls may proliferate germ cells spontaneously and some gonadotropin treated ovaries may fail to form germ cells. This study supports the conclusion that in the white mouse, germ cells originate from the germinal epithelium. (NSA)

262

Farr, Richard S. and Peter P. H. DeBruyn. **THE EFFECT OF SELECTIVE SHIELDING OF RABBIT INTESTINE DURING TOTAL BODY IRRADIATION.** Argonne National Lab. Oct. 1951. 11p. (AECU-1820; UAC-459)

Rabbits have been exposed to irradiation with x rays while most of the colon or small intestine was surgically exteriorized into a lead chamber. The results indicate that the selective shielding of the rabbit intestine during otherwise total-body irradiation does not decrease the lethal effects of x rays. It is suggested that the protection conferred on animals when the entire abdomen is shielded during otherwise total-body irradiation can best be attributed to a summation of several "organ effects" rather than to one specific organ. (NSA)

263

Friedman, N. B. and S. Warren. **THE EVOLUTION OF EXPERIMENTAL RADIATION ULCERS OF THE INTESTINE.** Arch. Pathol. 33, 326-33(1942).

Evolution of intestinal radiation ulcers in rabbits was produced by roentgen ray treatment and observations made up to a period of six months following treatment. Irradiation of the intestine resulted in an altered and damaged mucous membrane which was especially susceptible to ulceration. Ulceration, though focal, was not localized by vascular occlusion. It seemed rather the chance effect of mechanical trauma and subsequent infection acting on a mucosa and bowel wall structurally and functionally damaged by radiation and imperfectly regenerated. (BA)

264

Friedman, W. B. **CELLULAR DYNAMICS IN THE INTESTINAL MUCOSA: THE EFFECT OF IRRADIATION ON EPITHELIAL MATURATION AND MIGRATION.** J. Exptl. Med. 81, 553-8(1945).

Rats were irradiated in groups of 6 with 1,000 r given in 30 min. at 140 kv, or with 1,000 r given in 8 to 20 min. at 186 kv. All but a 5 cm band across the middle of the abdomen was shielded with Pb. The rats were killed at regular intervals during a 96 hr interval after irradiation and the so-called "post irradiation mucous change" in relation to atrophy and regeneration of the intestinal epithelium were studied. Detailed description of these changes is given. It is concluded that although irradiation of the duodenum of rats inhibits mitosis in the crypts and halts the normal passage of cells up the villi, the maturation of goblet cells is not affected. The ripening of mucous elements while arrested in the crypts, where they form, instead of during their migration along the villi, results in

the so-called mucus change, which has hitherto been considered a form of degeneration. During the phase of recovery, the reestablishment of normal migration and desquamation is marked by the appearance of strata of fully formed goblet cells at successive levels out along the villi. It is suggested that some gastrointestinal disturbances known to occur in spontaneous and experimental vitamin deficiency might be explained in terms of aberrations in the cellular replacement of the intestinal mucosa. (TIS)

265

Gastaldi, Gildo. **MORPHOLOGICAL ASPECTS OF THE REGENERATION OF NERVES SECTIONED AND SUBJECTED TO THE ACTION OF X-RAYS.** Riv. sper. freniat. 73, 5-41(1949).

The repeated irradiation of the peripheral nerves by x-rays offered in the present studies an approach to the general problem of the action of x-radiation on traumatic lesions of the nerves. The research was conducted on 30 rabbits and on 6 guinea pigs, half of each group serving as controls. The local irradiation (80 r/session, for a total dose of 160-720 r, with a filtration of 0.5 mm Cu plus 2 mm Al, and 170 kv and 30 cm target distance) began immediately after the hemisection of the sciatic nerve and continued on the following days; the animals were sacrificed in pairs in stages from the second to the 19th day after the nerve sectioning. In 14 of the 30 rabbits, a vital coloration state (by successive injections of a 5% solution of trypan blue intravenously) was produced; the animals were treated each day before the sectioning and continued to receive injections of the dye for variable periods afterwards. Several observations are reported: an initial state of active hyperemia with capillary dilatation and a focal miliary diapedesis occurred on the second or third day after sectioning; a slight proliferation of blood vessel walls occurred on the sixth day; other phenomena such as accentuated fibrotic metamorphosis of granulosa tissue, traumatic degeneration, accentuated leucocyte migration, accentuated phagocytic activity, and prolonged disorientation of young nerve fibers also occurred; there was, however, no appreciable difference in the contents of the cells of Schwann. 12 references. (NSA)

266

Gershon-Cohen, J., M. B. Hermel, and J. Q. Griffith, Jr. **THE VALUE OF SMALL LEAD SHIELDS AGAINST THE INJURIOUS EFFECT OF TOTAL-BODY IRRADIATION.** Science 114, 157-8(1951).

The effect of shielding of the liver, right lung, or right lower abdomen of young white rats during whole-body irradiation has been investigated. The survival rates of all the partially shielded rats were higher than those exposed to whole-body irradiation. Of 20 rats which received whole-body irradiation, 8 survived. There were 10 survivals of the 12 rats protected over the liver, 7 survivals of 9 rats protected over the right lung, and 6 survivals of 9 rats protected over the right lower abdomen. Survival times, weights, and blood counts are recorded in 7 tables. (NSA)

267

Glucksmann, A. and Katherine Tansley. **SOME EFFECTS OF GAMMA RADIATION ON THE DEVELOPING RAT RETINA.** Brit. J. Ophthalmol. 20, 497-509(1936).

A method of exposing the eyes of young rats to γ radiation is given. With such radiation the undifferentiated cells of the retina degenerate, the amount depending on the dosage and the age of the rat. The size of the eye is reduced, and a new fiber layer is formed dividing the inner nuclear layer into two under certain conditions. Rosettes may also be produced. The formation of the new fiber

layer and the rosettes is secondary to the degeneration and not a direct effect of radiation. (BA)

268

Harvey, R. A. EFFECT OF ACUTE AND CHRONIC DOSES OF ROENTGEN RAYS ON MONKEY FINGER RIDGE DETAIL. [Univ. of Rochester] [nd] Decl. Aug. 12, 1946. 16p. (MDDC-215)

Acute roentgen exposures up to 800 r cause no detectable gross changes in finger ridge details of monkeys. Acute doses of 800 r to 1,100 r result in temporary atrophy of ridges. Acute doses above the level cause more severe atrophy, slower regeneration, less complete regeneration and some tendency to secondary weakening of detail. Chronic roentgen exposures of 10 r per day for 50 treatments cause no change in ridge detail. Chronic exposures of 20 r or more per exposure for 50 exposures cause detectable weakening which like that following acute exposures is more severe with increasing dosage, shows a slower tendency to regenerate, less complete regeneration and more secondary weakening. (ADD)

269

Harvey, R. A. THE EFFECT OF SHORT WAVELENGTH RADIATIONS ON HUMAN FINGER RIDGE DETAIL. [Univ. of Rochester] [nd] Decl. Aug. 17, 1946. 33p. (MDDC-216)

Atrophy of ridges of the finger point area were detected in 68% of radiologists, 55% of orthopedists who use a fluoroscope, 40% of dentists who hold films during exposure to x-rays and 1.8% of the controls. The findings in professional groups were subclinical in a high percentage of cases, and they should not cause alarm if present standards of protection are appreciated. Personnel of the Manhattan Project were surveyed in this respect, and steps to be taken for employee safety are proposed. (ADD)

270

Heald, A. H., C. Beard, and W. R. Lyons. THE EFFECTS OF ROENTGEN RADIATION AND PROLAN UPON THE TESTES OF IMMATURE RATS. *Am. J. Roentgenol. Radium Therapy* **41**, 448-52(1939).

Direct irradiation (1,152 to 4,608 r) of immature rats' testes caused degeneration of the seminiferous epithelium, but left the Leydig tissue capable of responding to gonad-stimulating hormone (prolan). Judging by the weights and histologic appearance of the prostates, the stimulated Leydig tissue formed male sex hormone. For the duration of the experiment (12 days) the harmful action of the roentgen rays upon the semi-irradiated testes was sharply limited to the irradiated halves. (Authors' Summary)

271

Hinkel, C. L. THE EFFECT OF IRRADIATION UPON THE COMPOSITION AND VASCULARITY OF GROWING RAT BONES. *Am. J. Roentgenol. Radium Therapy* **50**, 516-26(1943).

Roentgen irradiation of the femora of young growing rats is followed by an almost immediate increase in bone ash and fat content, associated with a drop in matrix and water. The mechanism of augmented mineral deposition is not clear. It is associated with a compensatory decrease in matrix. Several days after irradiation there follows a diminution in the number and caliber of the metaphyseal blood vessels. The resultant relative avascularity may well be a basic factor in the production of the high ash and low water contents observed. In the months after irradiation of the intensity used in these experiments there is a gradual return toward normal content of ash matrix and fat. Although there is considerable regeneration of vessels some degree of hypovascularity persists throughout the period of observation. (BA)

272

Hueper, W. C. and J. de Carvajal-Forero. THE EFFECTS OF REPEATED IRRADIATION OF THE GASTRIC REGION WITH SMALL DOSES OF ROENTGEN RAYS UPON THE STOMACH AND BLOOD OF DOGS. *Am. J. Roentgenol. Radium Therapy* **52**, 529-34(1944).

This study was undertaken to determine the possible action of roentgen therapy upon the erythropoietic activity of the bone marrow and upon the blood through a possible effect upon the production of the so-called "intrinsic factor" of Castle. It was found that roentgen rays given in doses of 15 to 120 r up to a total of 4,875 r within 25 weeks over the gastric region of dogs caused only minor anatomic changes in the gastric mucosa and a transitory and moderate anemia of the secondary type followed by an erythrocytic phase after the cessation of the actinic treatment. Roentgen rays administered in doses of 300 r, up to a total of 6,000 r within four weeks, produced a considerable loss in body weight, a moderate to severe secondary anemia, and perforating gastric ulcers at the end of this period. In neither instance was there evidence of anemia of the pernicious variety, which would have resulted if the treatment given had interfered with the production of the "intrinsic factor" generated by the gastric mucosa, according to Castle. The chief cells of the gastric mucosa are, according to the observations made, definitely more sensitive to the action of the roentgen rays than any other cellular element of the gastric mucosa. The histologic changes found in the organs of the dogs which were treated with larger doses over a shorter period of time are described in detail. (R)

273

Hursh, John B., Priscilla A. Van Valkenburg, and John B. Moheny. EFFECT OF ROENTGEN RADIATION ON THYROID FUNCTION IN RATS. *Radiology* **56**, 411-18 (1951).

Rats were irradiated by x rays applied locally to the thyroid area at total dose levels of 3000, 4500, and 6000 r. Thyroid function was tested by injecting I^{131} at various intervals after irradiation, sacrificing the animals four hours after injection, and analyzing the excised thyroid gland for uptake of I^{131} , as well as the percentage of I^{131} bound in an undialyzable complex. Histologic sections of the thyroids were prepared and examined. In the rats receiving 3000 r and 6000 r the iodine uptake was greater than in the control rats, and the increase was greater the higher the x-ray dose and the longer the post-irradiation interval within the limits investigated. In spite of the increased iodine uptake, no morphological changes of the thyroids could be found at these dose levels on the basis of examination of random sections. The increased uptake is tentatively regarded as an indirect consequence of a systemic response to radiation. The level of local X irradiation necessary to produce destruction of thyroid tissue is greater than the highest dose (about 5000 r delivered as a single dose) which can be administered to a rat without causing its death. (NSA)

274

Jacobson, Leon O., Edna K. Marks, Melba Robson, and R. E. Zirkle. THE EFFECT OF SPLEEN PROTECTION ON MORTALITY FOLLOWING X-IRRADIATION. *J. Lab. Clin. Med.* **34**, 1538-43(1949) (AECU-535)

Survival data on groups of mice exposed to single dosages of 600, 700, 800, 975, 1050, and 1200 r of total-body x-radiation (250 kv) with or without lead protection of the surgically mobilized spleen are presented in this paper. These data show that the LD-50 for total-body x-irradiation, exclusive of the lead protected spleen, is nearly twice as great as the LD-50 for total-body x-irradiation

inclusive of the spleen. The mechanism whereby lead protection of the spleen so significantly increases survival from irradiation is yet to be determined. (NSA)

- 275 Janzen, A. H. and S. Warren. EFFECT OF ROENTGEN RAYS ON THE PERIPHERAL NERVE OF THE RAT. *Radiology* **38**, 333-7(1942).
- Exposure of the peripheral nerves of the rat to roentgen rays in doses of 4,000, 8,000, and 10,000 r generated at 200 kv produced no demonstrable histological or physiological changes. Complete degeneration of nerve and some evidence of degeneration of the sensory neurones resulted from exposure to 1,200-1,600 millicurie hours of γ radiation. Nerve tissue is extremely resistant to radiation. (Authors' Summary)
- 276 Jolles, Benjamin. X-RAY SKIN REACTIONS AND THE PROTECTIVE ROLE OF NORMAL TISSUES. *Brit. J. Radiol.* **14**, 110-12(1941).
- The skin of the rat has been irradiated under constant physical conditions, but with fields of various sizes. The size of the field was found to influence quite profoundly the degree of reaction of the skin; the bigger the area irradiated, the more severe the damage done, even though the dose of x-rays given per unit area was kept constant. More experiments have shown that the reaction becomes a minimum when the normal tissues can exert their maximum protective role; this has been arranged experimentally by surrounding the x-rayed area by as much normal tissue as possible. (Author's Summary)
- 277 Jolles, Benjamin. THE RECIPROCAL VICINITY EFFECT OF IRRADIATED TISSUES ON A DIFFUSIBLE SUBSTANCE IN IRRADIATED TISSUES. *Brit. J. Radiol.* **23**, 18-23 (1950).
- A dose of X-rays was given to two small areas of human skin separated by protected skin, and the reaction produced was significantly more marked than that over a single area of skin at a symmetrical site exposed to the same dose of radiation. When the separation between the two paired areas was greater than a certain minimum value, the reaction was equal to that on a single area. A diffusible substance is tentatively suggested, and the protective role of normal surrounding tissues is discussed. (CA)
- 278 Jolles, B. and R. G. Mitchell. OPTIMAL SKIN TOLERANCE DOSE LEVELS. *Brit. J. Radiol.* **20**, 405-9(1947).
- The problem of optimal skin tolerance dose levels is approached on novel lines and a tolerance dose formula postulated, taking into consideration the perimeter treated area ratio. Figures are given for treatment under stated conditions for treatment periods of 1-6 weeks. (Authors' Summary)
- 279 Leach, J. E. and K. Sugitara. LATE EFFECTS OF HIGH VOLTAGE ROENTGEN RAYS ON THE HEART OF ADULT RATS. *Am. J. Roentgenol. Radium Therapy* **48**, 81-7 (1942).
- Late effects of roentgen irradiation on skin; subcutaneous tissue, muscle, and bone are well known. Similar effects were looked for in heart muscle, some months after direct heavy irradiation to the organ. There was no demonstrable effect 2-14 months after irradiation with single doses up to and including 7,500 roentgens. (BA)
- 280 Lecomte, J., A. Herve, and Z. M. Bacq. ACTION OF X RAYS AND CYANIDES ON FROG STRIATED MUSCLES. *Compt. rend. soc. biol.* **144**, 708-9(1950).
- The authors have observed (Herve et al., *Compt. rend. soc. biol.* **143**, 881(1949)) that an injection of NaCN or of cysteine immediately before a total x irradiation of mice reduces considerably the lethality rate due to the radiation. The question arose whether or not these substances would protect isolated striated muscles of frog against a peculiar contraction called the Lundsgaard effect, that follows an irradiation and is related to the organ's respiration disturbances; it was thought that the reducing effect of the cyanide or cysteine might inhibit the oxidizing action of x rays on enzymes. Experimental results did not confirm the hypothesis. (NSA)
- 281 Lindenbaum, B. THE RADIOSENSITIVITY OF THE PERIPHERAL NERVOUS SYSTEM. *Fortschr. Gebiete Röntgenstrahlen* **71**, 988-93(1949).
- After several treatments with deep x-rays, sensitivity changes occurred; applications of the rays to the tongue disturbed taste. These changes were mostly reversible, but only after long periods of time (months). (NSA)
- 282 Ma, W. C. and C.-L. Hsu. THE EFFECT OF ROENTGEN RADIATION ON SPINAL GANGLIA OF ALBINO RATS. *Am. J. Cancer* **40**, 335-42(1940).
- In a parallel cytological study of direct and indirect effects of roentgen radiation on the spinal ganglia of rats, using special stains, it was found that the extent of cellular change varied directly with the dosage. Effects were: shrinkage and irregularity of cell-outlines, decrease in size and staining quality of nuclei, decrease or increase in mitochondria, which were granular and stained poorly, loss of Nissl substance, and reduction of Golgi apparatus. (BA)
- 283 MacComb, W. S. and E. H. Quimby. THE RATE OF RECOVERY OF HUMAN SKIN FROM THE EFFECTS OF HARD OR SOFT ROENTGEN RAYS OR GAMMA RAYS. *Radiology* **27**, 196-207(1936).
- Following the technique of Duffy, Arneson and Voke (*Radiology*, **23**: 486, 1934) the amount of 200 kv X radiation necessary to produce the threshold effect, when given in two equal doses, at intervals of from 6 to 96 hr, has been found, also the amount for 3 daily and 5 daily doses. From these data have been calculated the recuperation from the first dose after any of the above intervals. Recovery is found to set in promptly, for even after 6 hr, 36% of the effect has been lost, and after 12 hr, 50%. It proceeds more and more slowly with larger intervals. For soft X rays and for γ rays, the factor for the 24-hr recovery has been found when radiation is administered in 2 equal doses. For the soft X rays, recuperation is greater than for hard; for γ rays, it is definitely less. (Authors' Summary)
- 284 Miyakawa, Tadahiro. EXPERIMENTAL STUDIES CONCERNING THE INTERRUPTION OF FUNCTION OF THE KIDNEYS BY MEANS OF X-RADIATION. *Tohoku J. Exptl. Med.* **40**, 169-88(1941).
- The kidneys of 66 2-kg healthy male rabbits were radiated. Group A received a total dose of 3000 r; group B, 6000 r; group C, 9000 r; and group D, 6000 r in divided dosage. Urine, blood, and P.S.P. studies were made periodically from 24 hr to 39 wk, following radiation. Macroscopic and microscopic studies of the kidneys were made. In the first 24 hr. the urine output decreased and a trace of protein, a few erythrocytes and leukocytes, and some epithelial cells were present in the urine. There were slight changes in the hemoglobin and erythrocyte count of the blood, and abrupt decrease of the leucocyte blood level occurred which returned only slowly to normal. A definite

eosinophilia and lymphopenia were noted, which returned to normal incompletely. Petechial hemorrhages were noted on the kidney surface. Collapse of renal parenchyma with a relative increase of the interstitial supporting tissue with a round-cell infiltration was noted. Considerable destruction of tubular epithelium was noted. Regeneration in group A occurred in 20 wk; in group B, in 9 wk; in group C, in 24 hr; and in group D, in 9 wk. The glomeruli were quite unchanged with but slight capillary atrophy. Cortical lesions were slight. The P.S.P. excretion was not delayed. The earliest changes were noted in the tubules, and only repeated dosages of radiation caused atrophy of the glomerular vessels, and these effects were slight. (BA)

285

Neumayr, Anton and Bruno Thurnher. EFFECT OF LOCAL ROENTGEN IRRADIATIONS ON THE PERMEABILITY OF CAPILLARIES IN MAN. *Strahlentherapie* **84**, 297-305 (1951).

Increased permeability of the capillaries after x-ray treatments was observed in man, with a threshold effect varying from 3 to 100 r, depending on the individual sensitivity of the capillaries, which also determined the duration of the morbid state; above the threshold no proportionality between the increase of the protein loss and the dose was observed. These facts prove both the inadequacy of permeability measurements as a way of establishing biological dose units and their utility in the study of the comparative sensitivity of capillary membranes. Twelve-day observations showed that after the healing no changes in the permeability reappeared; therefore, in all probability, the reaction is a one-phase process. (NSA)

286

Nickson, M. REPORT OF HAND STUDY. Argonne National Lab. Aug. 1, 1945. Decl. Aug. 29, 1947. 37p. (MDDC-1270; CH-3368)

Observations have been made of the hands of 973 laboratory and office personnel. Deviations from normal have been noted and photographs taken. Finger ridge impressions have been made of 1,287 individuals of whom 15% showed some abnormality. Capillary counts have been done on 838 individuals. The number of capillaries in a given area of nail fold shows some correlation with possible exposure to radioactive materials. Capillary photographs have been taken of 93 individuals. There is a rough correlation between the morphology of the capillaries and the exposure of the hands of young individuals. Normal aging tends to produce the same or similar changes. Further capillary studies are necessary to confirm or deny the apparent relationship between hand exposure and increased or prematurely aged terminal capillaries. Photographs and a bibliography of 119 references are included. (ADD)

287

Nickson, M. EFFECT OF SINGLE DOSE X-RAY TO THE NAIL FOLD AREA OF HUMAN SUBJECTS. Argonne National Lab. June 20, 1947. Decl. Sept. 11, 1947. 6p. (MDDC-1269; CH-3833)

The nail fold area of the left fourth finger of 15 subjects was observed before and after a single radiation exposure. The total dose ranged from 200 r to 600 r. From this brief and incomplete study it appears that radiation exposures of 600 r or less when given as a single dose under the conditions described, produce no constant microscopic or macroscopic reaction. The transitory effects were most often microscopic and consisted of hyperemia of the small terminal vessels and dilation of vessels visible in this area before and after radiation. (ADD)

288

Nickson, M. and L. Warner. SECOND REPORT OF HAND STUDY PROGRAM. Argonne National Lab. Jan. 1, 1947. Decl. Aug. 26, 1947. 23p. (MDDC-1217; CH-3753)

Methods to determine early radiation damage or damage which has occurred without the individuals' being conscious of any change fall into two categories, macroscopic and microscopic. Two methods were used in the laboratory for determining macroscopic changes: (1) direct inspection of the hands. (2) The hands were photographed, the photographs enlarged and the enlarged photographs were studied. There are two macroscopic changes in the skin after acute and chronic radiation, namely erythema following acute radiation, and atrophy after chronic radiation. Unfortunately, both radiation erythema and/or atrophy will also result from stimulation other than radiation. Microscopic examinations of the vessels at the base of the nail were made. Of the 593 individuals studied for radiation damage to finger ridges, 18% had some abnormality. All of these abnormalities were minimal. Reversible changes due to mechanical flattening of the ridges were found among machinists, carpenters, and others doing manual labor. Such findings which may be confusing after a single examination can be excluded by repeated studies after time intervals to allow for regeneration. Capillary counts were found to range between 18 and 22 in over half of the individuals studied and between 18 and 27 in 80%. Persons with dark skin pigment had slightly lower counts whereas persons over 50 years of age had counts in the high portion of the average range. Sex had no effect on the count. Radiation exposure at levels received in the laboratory had no effect on the count during the period of time covered by this study. This report is a continuation of studies described in MDDC-1270. (ADD)

289

Novick, Rosalind. TIME COURSE OF CHANGES IN SENSORY CELLS OF TRIGEMINAL GANGLION OF THE RABBIT FOLLOWING IRRADIATION. *Proc. Soc. Exptl. Biol. Med.* **61**, 355-8(1946).

In a series of rabbits irradiated in the head with a single dose of 3,000 roentgen units, examination of the Nissl-stained trigeminal ganglion cells reveals injury which may be separable, by analysis of the time course, into three phases. Initially in animals killed immediately following irradiation, chromatolysis is short-lived, so that as early as three hours after the end of the irradiation period marked improvement can be noted, and at 18 hours, the ganglion cells appear normal. The normal phase persists until 43 hours at which time there is clearly observable the beginning of 2nd wave of chromatolysis which slowly becomes increasingly widespread in amount and severe in degree (BA).

290

Pendergrass, E. P., P. J. Hodes, and J. Q. Griffith. EFFECT OF ROENTGEN RAYS ON THE MINUTE VESSELS OF THE SKIN IN MAN. *Am. J. Roentgenol. Radium Therapy* **52**, 123-7(1944).

A method of following changes in visible cutaneous capillaries depends on relating the number visible to the total number present. The total number is obtained by counting the area with a capillary microscope after pricking 1:1000 histamine. Changes in relative count following adm. of about 300 r of 200 kv x-rays in $\frac{3}{4}$ min., 7.2 min., and 30.8 min., respectively, were essentially the same, an increase at the end of 6 hours, which was almost or entirely gone after 24 hours. The same dose of 50 kv x-rays resulted in a mild effect at 6 hours, which was much more pronounced at 24. (BA)

291

Raab, W. and A. B. Soule. EFFECT OF ROENTGEN IRRADIATION ON THE HORMONE CONTENT AND SECRETION OF THE ADRENAL MEDULLA. *Radiology* **41**, 56-60(1943).

Rats, anesthetized with nembutal, were irradiated with

roentgen rays generated at 200 kv, 20 ma, filtration: 0.5 mm Cu and 2.0 mm Al. The cone was focused on the back over the adrenal area. Detn. of hormone content was made, using a modification of Shaw's colorimetric detn. of "Adrenalin". No significant change in the medullary hormone content of the glands was found within 68 hours after irradiation. The doses 100 r to 1000 r were given in a single session. After 68 days, however, there was indication of a diminished secretory activity following a dose of 100 r, a similar decrease combined with slightly diminished hormone production was observed after irradiation with 1000 r. (BA)

292

Rigdon, R. H. and H. Curl. EFFECT OF ROENTGEN IRRADIATION ON CAPILLARY PERMEABILITY AND INFLAMMATION IN THE SKIN OF THE RABBIT. *Am. J. Roentgenol. Radium Therapy* 49, 250-7(1943).

Trypan blue injected intravenously localizes and concentrates in areas of inflammation in the skin during a specific interval following irritation. It has been suggested that this is due to a change in the permeability of the cells because of the injury. Irradiation with x-rays results in changes in cell permeability. Small shaven areas on the sides and back of adult rabbits were irradiated with 680-2720 r of 86 kv unfiltered x-rays. Changes in the skin in these areas occurred immediately, as shown by localization and conc. of trypan blue therein, for a brief time after the injection. Areas irradiated 1 hr or less prior to the administration of the dye, become blue. Areas irradiated 3 hours or more before the dye is injected do not show any more color than untreated areas. Polymorphonuclear leukocytes are present in the corium of the irradiated skin after approx. 60 min. Their number increases for several hours. There is no correlation between the time in which trypan blue localizes and concentrates in areas of irradiated skin and the time in which polymorphonuclear leukocytes infiltrate the corium in the same area. It is suggested that both inflammation and irradiation disturb the Ca-K-P balance in cells, and bring about increase in capillary permeability for this reason. (BA)

293

Russell, Dorothy S., C. W. Wilson, and Katharine Tansley. EXPERIMENTAL RADIO-NECROSIS OF THE BRAIN IN RABBITS. *J. Neurol. Neurosurg. Psychiat.* 12, 187-95 (1949).

It was found that a single surface dose of 2,850 r 200 kv X rays will produce delayed irradiation necrosis in the rabbit's brain after a latent period of approximately 100 days. The latent period was lengthened by reducing the dose to 2,440 r. Field size was 3 x 4 cm; surface dose-rate 154.5 r/min; focus-skin distance 25.5 cm. The approximate depth doses were: 1 cm depth, 85%; 2 cm depth, 70%; 3 cm depth, 57%. The initial histologic changes consisted of minute foci of hemorrhage and necrosis which are intimately related to the perforating vessels and, in particular, capillaries. Increase of capillary permeability accompanied the established lesion but was not demonstrated at earlier stages. The lesions, when once initiated, appeared to extend rapidly and to progress to non-irradiated parts of the brain. They were characterized, in later stages, by pronounced glioses, and by progressive degeneration and sclerosis of the adjacent vessels. The neurones were only focally and secondarily affected. The meninges and their blood vessels were unaffected, and the superficial parts of the cerebrum escaped, even though the cerebellar cortex might be extensively damaged. (R)

294

Sallman, Ludwig von. EXPERIMENTAL STUDIES ON EARLY LENS CHANGES AFTER RÖNTGEN IRRADIATION.

I. MORPHOLOGICAL AND CYTOCHEMICAL CHANGES. *Arch. Ophthalmol.* (Chicago) 45, 149-64(1951).

Cataractous changes were observed in 53 of 56 rabbit eyes 4-10 weeks after irradiation with 2,000 r of penetrating X-rays. Histological changes are described. Two weeks after irradiation, individual nuclei in a given area contained less desoxyribonucleic acid of high polymerization than did the nuclei of a comparable area of the control lens. (CA)

295

Sallman, Ludwig von, and Beatrice Locke. EXPERIMENTAL STUDIES ON EARLY LENS CHANGES AFTER RÖNTGEN IRRADIATION: II. EXCHANGE AND PENETRATION OF RADIOACTIVE INDICATORS (Na^{24} , K^{42} , I^{131} , P^{32}) IN NORMAL AND IRRADIATED LENSES OF RABBITS. *Arch. Ophthalmol.* (Chicago) 45, 431-44(1951).

Experiments with Na^{24} showed increased permeability of the blood-aqueous barrier up to 6 weeks after irradiation. This phenomenon did not play an integral part in pathogenesis of radiation cataract. The uptake of Na^{24} and I^{131} by lenses with radiation cataract was greater than the uptake by control lenses and increased with the progress of the cataractous process. In the normal lens P^{32} accumulated principally at the equator and in the surface layers of the cortex due to the high metabolic rate of these parts. This difference between superficial cortical and deeper portions vanished with total radiation cataract. The uptake of K^{42} by normal lenses was very rapid. The uptake of K^{42} was slightly decreased by radiation cataract. (CA)

296

Saxon, K. P. THE EFFECT OF X-RAYS ON THE OVARIES AND OESTROUS CYCLE OF THE GOLDEN HAMSTER (*CRICETUS AURATUS* WATERHOUSE). *J. Tennessee Acad. Sci.* 21, 128-34(1946).

Ovaries of adult virgin female hamsters were subjected to 900 r in two equal doses one week apart and studied at intervals of 1, 7, 15, 30, and 45 days after irradiation. Degeneration of the follicles was not observed the first day after irradiation. Seven days after irradiation, the small follicles were the first to exhibit signs of degeneration. The small follicles appeared to be more susceptible to X-rays than did the large follicles. Groups examined 15 and 30 days after irradiation were characterized by the presence of many small and large degenerating follicles. Hemorrhagic areas occasionally were present and a relatively large number of mitotic figures and multinucleate ova were observed in the large degenerating follicles in contrast to the number found among the controls. Forty-five days after irradiation, primary follicles were absent and only a few large follicles were observed, most of which were in some stage of degeneration. Estrous cycles of normal duration, as determined from vaginal smears, recurred rhythmically after irradiation in 20 to 25 cases. (BA)

297

Sturkie, P. D., J. A. Pino, J. L. Weatherwax, A. J. Donnelly, and G. M. Dorrance. EFFECT OF X-RAYS ON FERTILITY IN WHITE LEGHORN MALE CHICKENS TREATED BEFORE PUBERTY. *Radiology* 52, 112-17 (1949).

Male white Leghorn chicks 4-6 weeks of age were irradiated over an area of the body including gonads, adrenals, and parts of the kidney. Doses: 1200, 1600, 2100, and 2800 r given in equal doses of 4 weekly treatments within 3 weeks. Ten animals were exposed in each group, 2-4 of which were killed about 4 weeks after the last exposure for histologic examination. The rest were mated. All of the animals receiving more than 1600 r were sterile. Irradiation had no effect on comb size or mating habit. The

testis of the irradiated animals were reduced in size, but the histological state of the testes was found not always a reliable criterion of fertility. (BA)

298

Toosy, M. H. HISTOLOGICAL AND CHEMICAL ALTERATIONS PRODUCED IN MOUSE EPIDERMIS BY SOFT X-RADIATIONS. *Cancer Research* 11, 361-5(1951).

Areas of epidermis of the backs of adult, female Swiss Albino mice, approximately 4 to 5 months old, were exposed to soft x-radiation from a Phillips Contact-Cavity therapy machine at a distance of 20 mm, the source of radiation being 50 kv, 2 ma, 100 r per second without a filter. Histological and chemical examinations of the irradiated hyperplastic epidermis were made, and the data so obtained were compared to those relating to normal and methylcholanthrene-treated epidermis.

Histological findings, including the results of cell type determination, revealed only minor difference between irradiated and methylcholanthrene-treated epidermis. However, total calcium of irradiated epidermis was about 30% less than normal, while that of methylcholanthrene-treated epidermis was about 50% less than normal. No difference was noted in the iodine number of lipids of both, as compared to normal epidermis. The total lipids of the irradiated as well as of methylcholanthrene-treated epidermis were nearly the same in both, being significantly less than normal. A polarographic study indicated no difference in a reducible substance from the lipids of irradiated epidermis (between half-wave potentials of unbuffered solution and in buffered solutions at pH 4.40 and at 6.38) compared to those of normal and methylcholanthrene-induced hyperplastic epidermis. (NSA)

299

Viets, H. THE EFFECT OF RADIATIONS ON THE SYMPATHETIC NERVOUS SYSTEM. *Strahlentherapie* 79, 13-58(1949).

The article is a survey of the action of radiations on the sympathetic nervous system and on some biochemical blood data, e.g., sugar, K, and Ca values and eosinophilia. No experiments are reported, but material scattered in 101 papers has been collected and is discussed. The sympathetic nervous system seems quite radio-resistant when histologically investigated; possible ganglia cells are more sensitive than other parts, while functional disturbances appear at therapeutic doses. When irradiation is applied in a state of normal tonus a vagotonia occurs. Irradiation in a state of increased tonus leads to a reversion towards the normal tonus. Ca, K, and sugar values, which in certain pathologic states are too high or too low, become normalized through irradiation. In many instances, such irradiation effects can be shown to take a biphasic or periodic course. Many examples are discussed, e.g., the skin reaction. Maxima and minima and latent period, as well as other details of the curves are discussed. The author concludes with some speculations on the mechanism of the action on the sympathetic nervous system. The primary effect is probably on the synaptic ganglion cell nuclei. He presumes that the action on the cells with a large nucleus is stronger and more rapid than on those with a small nucleus. (EM)

300

Vogel, Howard H. Jr. CATARACT FORMATION AND RETINAL DAMAGE FOLLOWING X IRRADIATION OF THE HEADS OF NEWBORN MICE. *Anat. Record* 111, 497(1951).

Data are presented on the percentage of radiation cataracts developed in newborn mice following x-irradiation of the head, and the approximate latent periods before these opacities of the lenses were observed. (NSA)

301

Wattenwyl, H. von. ACTION OF ROENTGEN RAYS ON RAT TESTICLES. *Schweiz. med. Wochschr.* 72, 765-6 (1942).

The work described here was undertaken with the idea of injuring the testicles of rats and studying the influence of various hormones on their regeneration. Control studies of regeneration without hormone administration are reported in this paper. Doses of from 60-2400 r (factors not given) were administered and the testicles were examined 4 to 50 days later. The findings confirm those previously reported by Regaud and by Schinz and Slotopolsky. (R)

302

Wilde, W. S. and C. W. Sheppard. ELECTROLYTES IN MUSCLE OF RAT FORELIMB AFTER INTENSE LOCAL X IRRADIATION. *Oak Ridge National Lab. [nd]* 1p. (AECU-1796)

Wistar adult male rats under nembutal were secured under a 13-mm lead-plate shield containing a window for exposure of the muscles of one forelimb to x rays (single doses, 250 kvp, 10 to 73 r/min, 30 mm from shutter and filtered through 3 mm Al; scatter to other parts of animal 0.11% of dosage). Companion muscle from the other shielded forelimb served as control against indirect influences which might arise from whole-body effects of scattered radiation. For many hours after exposure, the animal continued to use the limb freely. The rayed muscle, sampled 22 hr after exposure began, showed swelling but no other visible evidence of damage and remained functional. All analyses were expressed per 250 g dry weight of muscle completely cleaned of fat and membranous and tendinous connective tissue. Changes would otherwise be masked by swelling. Total water of the exposed muscle increased with dosage to exceed controls by 25%. Potassium content remained unchanged. Simultaneous inulin and Na²⁴ spaces in a separate group of rats, nephrectomized at 22 hr to prevent urinary loss of inulin, proved that the water gain was entirely interstitial. Gain in total water and gain in Na²⁴ and inulin space were all three equal. Shielded control muscles from all rats collectively showed no changes correlated with total-body irradiation such as might occur from scatter. Thus water, K, and Na were unchanged in exposed muscle fibers, but edema occurred because of local vascular disturbances. (Entire report)

Radiosensitivity

303

Abderhalden, R. CONTRIBUTION TO THE PROBLEM OF BIOLOGICAL EFFECTS OF RADIATION. DETERMINATION OF THE SUSCEPTIBILITY OF ORGANS TO X-RAYS IN VIVO BY MEANS OF A BIOCHEMICAL METHOD. *Strahlentherapie* 68, 17-29(1940).

The author studied the susceptibility of a number of organs to roentgen rays in rabbits. He found certain ferments in the urine which are capable of breaking down the proteins of the irradiated organs but not those of non-irradiated organs. If doses high enough to produce injury were applied to the hypophysis disturbances in the entire endocrine system could be noticed. With this biochemical method, which is described in the article, the author found that the lower limit of radiosensitivity of the liver is around 330 r, for the brain around 247.5 r, and for the hypophysis around 165 r. (R)

304

Abrams, Herbert L. INFLUENCE OF AGE, BODY WEIGHT, AND SEX ON SUSCEPTIBILITY OF MICE TO THE LETHAL EFFECTS OF X-RADIATION. *Proc. Soc. Exptl. Biol. Med.* 76, 729-32(1951).

The age at which mice are irradiated profoundly alters

their resistance to a single exposure of whole-body irradiation. Mortality is low after irradiation at 1 and 15 days of age, very high at 30 days, and decreases rapidly with increasing age thereafter. The possible mechanisms of this effect are discussed. The response of mice to whole-body irradiation is not related to body weight except insofar as weight reflects a particular age range. In general, sex appears to exert no significant influence on the capacity of mice to withstand whole-body irradiation. (NSA)

305

Anderson, Rubert S. and H. Turkowitz. THE EXPERIMENTAL MODIFICATION OF THE SENSITIVITY OF YEAST TO ROENTGEN RAYS. *Am. J. Roentgenol. Radium Therapy* **46**, 537-41(1941).

Cultures of *Torula cremoris* were irradiated in the presence or in the absence of atmospheric O₂, with 190 kv x-rays (unfiltered) at an intensity of 190 r/min. In some cases the air was removed by de-aerating the culture, in others, by allowing the culture to grow until it was so crowded that an O₂-lack was produced. In the latter case the controls were aerated by shaking vigorously. In either case, the cells irradiated in the presence of O₂ were more sensitive to the x-rays than those which lacked it. (BA)

306

Back, A. and L. Halberstaedter. INFLUENCE OF BIOLOGICAL FACTORS ON THE FORM OF ROENTGEN-RAY SURVIVAL CURVES, EXPERIMENTS ON *PARAMECIUM CAUDATUM*. *Am. J. Roentgenol. Radium Therapy* **54**, 290-5(1945).

Experiments were carried out with *P. caudatum* to determine the difference in roentgen-ray response between a group of immediate descendants of a single parent (family) and remote descendants (clone). Using 35 kv, a Cu target, and an Al foil window in the roentgen-ray tube, an intensity of 90,000 r/min, was obtained at the position of the test object. The immediate lethal dose was obtained for specimens irradiated in small drops of water under thin mica cover slips. This is the dose which produces complete cessation of motility within 10-15 minutes after irradiation. For families this dose varied between 200,000 and 700,000 r, but for any particular family, all individuals died of the same dose. For clones the variation was the same, but the individuals within the clone died at different doses. Both mortality curves were sigmoid. The difference in behavior pattern between members of a family and of a clone can only be explained on the basis of biologic variability, the variability being greater between members of a clone than between members of a family. (BA)

307

Bennison, B. E. and G. Robert Coatney. INACTIVATION OF MALARIAL PARASITES BY X-RAYS. *Pub. Health Repts. (U. S.)* **60**, 127-32(1945).

Sporozoite and trophozoite suspensions of *Plasmodium gallinaceum* were exposed to graded doses of x-ray. Infectivity of the irradiated suspensions were tested by inoculation into young chicks (*Gallus domesticus*). Trophozoites were inactivated by 20,000 r but not by 10,000; sporozoites, by 8,000 r but not by 6,000. Trophozoite suspensions exposed to 2,000 to 8,000 r produced infections characterized by lengthened prepatent periods and lengthened survival times. Therapeutic irradiation of infected chicks had no significant effect on the outcome of the infection. A sample of human blood parasitized by *P. malarie* and exposed to 5,000 r failed to produce an infection in a susceptible patient. (BA)

308

Bloom, Margaret A. ACQUIRED RADIORESISTANCE OF THE CRYPT EPITHELIUM OF THE DUODENUM. *Radiology* **55**, 104-15(1950). (AECU-531)

Repeated total-body exposures of mice to 60 r x-radiation day resulted in a lessened sensitivity of the crypt epithelium of the duodenum. Debris in these cells 3 hr after the last irradiation passed on successive days through a maximum and then diminished despite continued treatment. An attempt has been made to measure the degree of this acquired radioresistance in terms of decrease in debris and persistence of mitosis. The duodenal crypt cells showed mild damage after 60 r per day, reaching a peak in mice autopsied 3 hr after 6 to 9 daily exposures. Recovery was complete in mice autopsied 24 hr after the final irradiation. With continued treatment (10 or more exposures) these cells became resistant to this daily dosage (as indicated by negligible amounts of debris and persistence of mitotic activity), even when the total dosage had accumulated to 2,100 r. Mitosis was not interrupted and was rarely diminished in this series of low-dosage repeated irradiations. This acquired radioresistance was not sufficient to prevent degeneration of the basal crypt cells or a cessation of mitosis when 600 r or 1200 r was given subsequently in a single dosage. When the single dosage following the daily exposures was 200 r, and an interval of only one day or one week intervened, there was partial protection against the 200 r exposure: the amount of debris was not diminished, but there were many more mitosis in the crypt cells of mice which has been previously irradiated than in those which had not. The enhanced radioresistance present at one day and one week was lost when the interval between the termination of the small daily dosages and the 200 r dosage was extended to two or four weeks. (NSA)

309

Burnett, W. T., Jr., G. E. Stapleton, M. L. Morse, and Alexander Hollaender. REDUCTION OF X-RAY SENSITIVITY OF *ESCHERICHIA COLI* BY SULFHYDRYL COMPOUNDS, ALCOHOLS, GLYCOLS, AND SODIUM DITHIONITE. *Proc. Soc. Exptl. Biol. Med.* **77**, 636-8(1951).

The x-ray sensitivity of the organisms is reduced if they are irradiated in the presence of low concentrations of 2,3-dimercaptopropanol (BAL), cysteine, mercaptosuccinic acid, mercaptopyruvic acid, 2-(2-mercaptoethoxy) ethanol, Na₂S₂O₄, MeOH, EtOH, iso-Pr-OH, BuOH, 2-methyl-1-propanol, 2-methyl-2 propanol, 1, 2, 3, -propanetriol, and 1,2-propanediol. (CA)

310

Clark, A. M. and E. M. Kelly. DIFFERENTIAL RADIOSENSITIVITY OF HAPLOID AND DIPLOID PREPUPAE AND PUPAE OF *HABROBRACON*. *Cancer Research* **10**, 348-52(1950).

Habrobracon prepupae and pupae were exposed to x-radiation, and the lethal effects of the radiation were studied. Eclosion ratios show that x-rays have a greater lethal effect upon haploid males than upon diploid males or diploid females. Diploid males and diploid females are equally susceptible to the lethal effects of x-radiation. Prepupae are more sensitive than pupae. No significant difference in eclosion ratios was obtained for adults given the same total dose but at different intensities. The response, therefore, seems to be independent of intensity. Comparison of adults developing from irradiated prepupae and pupae shows that a greater number of haploid males show structural malformations than do diploids irrespective of sex and that the haploids show these malformations to a greater degree. Comparison of individuals unable to emerge from cocoons shows that the diploids are in general more advanced in their development than are the haploids. The data show that diploids are more resistant than haploids to the lethal action of x-rays, suggesting that the number of chromosome sets is a factor in determining the radiosensitivity of cells. (NSA)

311

Clark, A. M. and C. J. Mitchell. **RADIOSENSITIVITY OF HAPLOIDS AND DIPLOIDS OF HABROBRACON.** *Genetics* **36**, 547(1951).

Haploids and diploids of *Habrobracon* were exposed to x-rays during various stages of pupal development. The ability to emerge from the cocoon was taken as the criterion of viability. Dosage-eclosion curves show that diploids are more resistant than haploids at all stages of pupal development. During the earlier stages, diploids are about three times as radioresistant as comparable haploids, while during the later stages, the differential radiosensitivity is not as great. For haploid pupae the increase in resistance is exponential with age. Younger diploid pupae increase in resistance at a rate identical to haploids, but older diploid pupae do not increase in resistance as rapidly so that the "survival" curves for haploids and diploids tend to approach each other in older pupae. Investigation of egg and adult stages is being done. These data indicate that a correlation exists between the genome number and radiosensitivity. They suggest that the deleterious action of radiation upon somatic tissues may be due to injury to the genetic mechanism. (RG)

312

Evans, T. C. and H. D. Kerr. **MODIFICATION OF RADIOSENSITIVITY OF THE SKIN. VI. EFFECTS OF COMPRESSION AND LOW TEMPERATURE ON THE ROENTGEN IRRADIATION REACTION OF HUMAN SKIN.** *Am. J. Roentgenol. Radium Therapy* **50**, 629-35(1943).

It was previously shown (Evans, T.C., *Effects of Roentgen Irradiation at Low Temperatures on the Skin of Young Rats*, *Am. J. Roentgenol.*, **45**; 888-894(1941)) that radioresistance of the skin of newborn rats was greatly increased by chilling the animal to or near 0°C during the irradiation. The use of cold and compression during radiotherapy in humans was tested on a series of patients undergoing treatment for cancer of the uterine cervix. Pressure was applied by the cone defining the x-ray beam; circulation of cold water through the tip of this cone provided cooling, but not the drastic chilling applied to the rats. Some decrease in radiation reaction was observed, but it was slight and variable. (BA)

313

Friedewald, W. F. and R. S. Anderson. **FACTORS INFLUENCING THE INACTIVATION OF THE RABBIT PAPILLOMA VIRUS BY X-RAYS.** *Proc. Soc. Exptl. Biol. Med.* **45**, 713-15(1940).

The amount of irradiation required to completely inactivate the rabbit papilloma virus is influenced by the virus concn., as also by the extraneous material present along with it in the irradiated suspensions. Berkefeld filtrates, which contained the virus in large amount, were rendered non-infectious upon exposure to 2-4 million r of irradiation; only 400,000 to 800,000 r was required when the virus had been partially purified by repeated differential centrifugations. Normal rabbit serum or the non-infectious supernatant fluids removed from virus filtrates after centrifugation at 30,000 rpm for 1 hr. protected purified virus suspended therein instead of in saline, these suspensions requiring about half as much irradiation to abolish their infectivity as the original virus filtrates. (BA)

314

Friedewald, W. F. and R. S. Anderson. **INFLUENCE OF EXTRANEEOUS PROTEIN AND VIRUS CONCENTRATION ON THE INACTIVATION OF THE RABBIT PAPILLOMA VIRUS BY X-RAYS.** *J. Exptl. Med.* **74**, 463-87(1941).

2-4 million r were required to inactivate crude papilloma extracts (Shope) prepared for the present work; 100,000 r

or less was enough to inactivate comparable concns. of virus after extraneous matter had been excluded by repeated differential centrifugations. Addition of normal rabbit serum or crystalline egg albumin to purified suspensions of virus was found to increase greatly the amount of irradiation required to inactivate the virus. The % destruction of virus in purified suspensions by a given amount of irradiation increased as the concn. was decreased by dilution. As little as 3000 r will inactivate much of the virus in very dilute suspensions. The factors of concn. and extraneous protein also influence the inactivation of the serum antiviral antibody which specifically fixes complement in mixture with the papilloma virus. Evidently, under certain conditions of purity and concn. most of the radiation does not act by direct hits on virus or antibody particles, but indirectly by ionizing or exciting some other molecules present in the exposed suspension, probably those of water, which then react with the virus or antibody molecule. (BA)

315

Froier, K. and A. Gustafsson. **THE INFLUENCE OF SEED SIZE AND HULLS ON X-RAY SUSCEPTIBILITY IN CEREALS.** *Hereditas* **30**, 583-9(1944).

Examination of seed properties with respect to their possible significance in x-ray induction of mutations indicated (1) that an increase in seed size—and accordingly also of embryo size—causes better germination and more vigorous growth after treatment, except for the highest dose used, when the average leaf length decreased, and (2) that the hull covering in barley and oats makes the seeds less susceptible to irradiation. The latter result was obtained after a comparison of covered and naked vars. in barley, as well as of normal and hull-less seeds in Victory oats. (BA)

316

Halberstaedter, L. and A. Back. **INFLUENCE OF COLCHICINE ALONE AND COMBINED WITH X-RAYS ON PARAMECIUM.** *Nature* **152**, 275-6(1943).

Paramecium caudatum were maintained for 48 hours in solutions of colchicine, transferred to normal culture media, and irradiated. The irradiation was carried out in a hanging drop through a mica cover glass by means of a demountable x-ray tube which was operated at a tension of 18.5 kV and 15mA using a copper anticathode. The X-ray intensity at the distance of the irradiated object was 80,000 r/m. The experiments showed that the immediate lethal dose is considerably smaller—about 50%—for *Paramecia* which received prior treatment with colchicine. (S.V.S.)

317

Haley, T. J. and Harriette Harris. **THE RESPONSE OF THE GUINEA PIG TO 200 r ACUTE WHOLE BODY X-IRRADIATION.** *Science* **111**, 88-90(1950). (AECU-357)

It is concluded that the guinea pig responds similarly to other animals subjected to x-irradiation and that for many purposes is much more suitable for such studies than the mouse or rat. Extremely valid results may be obtained using the guinea pig because its size and general temperament are suitable for studies employing large numbers of animals. However, all hematological studies should be reported in both relative and absolute terms to avoid a misinterpretation of the results observed. (NSA)

318

Hall, B. Vincent. **GROWTH OF TUMOR FRAGMENTS X-IRRADIATED IN VITRO FOLLOWING PRETREATMENT WITH CYSTEINE.** *Argonne National Lab.* Aug. 1951. 24p. (AECU-1866)

The data presented on the survival and growth of mouse tumor fragments following x irradiation in vitro with and without prior treatment with 0.008 M cysteine clearly demonstrate the prevention and alleviation of radiation in-

jury of mammalian tumor cells by cysteine. The radiation dose that damaged untreated implants to the extent that only 50% grew when transplanted into host mice, had to be increased by nearly 20% or 569 r, to effect equivalent injury of cysteine-treated implants. Delay in initiation of growth by tumor fragments following implantation was increased by radiation effects, and the effect was found to bear roughly an exponential relation to the radiation dose. Intra- and intercellular cysteine rather than the cysteine of the ambient medium was found to be the effective agent in reducing the radiosensitivity of tumor fragments. It is suggested that the intracellular cysteine is most effective in preventing and alleviating the cellular response to ionizing radiation. 31 references. (NSA)

319

Hall, B. Vincent. CHANGES IN THE RADIOSENSITIVITY OF TUMOR FRAGMENTS INDUCED BY PRE-TREATMENT IN VITRO WITH CYSTEINE, METHYLENE BLUE, AND SODIUM CYANIDE. *Cancer Research* 11, 254(1951).

Fresh tumor fragments of a vigorously growing, anaplastic mouse carcinoma were pretreated for 20 min. with cysteine, methylene blue, or NaCN solutions, and then irradiated in culture dishes under standard conditions. Solutions of 1.25 mg cysteine per cubic centimeter enabled 58% of the implants to survive 4000 r, whereas none of the control tumor fragments, irradiated in 0.85% NaCl, survived. The growth nonirradiated tumors was not influenced by cysteine at this concentration. Pretreatment of tumor fragments with 0.01 or 0.001 M NaCN or methylene blue, on the other hand, greatly decreased the number of surviving implants. Treatment of nonirradiated tumors with NaCN, or methylene blue solutions of this concentration, had little effect upon the number of subsequent takes, but the more concentrated solutions tended to retard the initial growth of the implants. The decreased tumor radiosensitivity afforded by pretreatment in vitro with cysteine paralleled effects observed in vivo. The other agents, which under certain circumstances were protective in vivo, rendered the tumor more sensitive, suggesting either that they act through different mechanisms or that a summation of injuries is involved. (NSA)

320

Held, Edward E. and Albert W. Bellamy. IRRADIATION RESPONSES IN DAPHNIA MAGNA. I. INCREASED RESISTANCE TO X-IRRADIATION UNDER LOW OXYGEN TENSION. Atomic Energy Project University of California Los Angeles. Apr. 20, 1950. 10p. (UCLA-69)

Daphnia magna exposed to x-rays under conditions of oxygen depletion show a marked increase in resistance to the irradiation. The increased resistance is evident both from survival curves and productivity records. (NSA)

321

Henshaw, Paul S. and D. S. Francis. A CONSIDERATION OF THE BIOLOGICAL FACTORS INFLUENCING THE RADIOSENSITIVITY OF CELLS. *J. Cellular Comp. Physiol.* 7, 173-85(1935).

The inter-relationship of radiosensitivity and a number of different biological conditions in *Triticum vulgare* were investigated. Starting germination of dry seeds by addition of moisture enhanced the radiosensitivity considerably. A quantity of radiation which would barely affect dry seeds would retard growth to about 50% in forms which had undergone 18 hr of germination. Stopping growth in germinated forms by lowering temperature did not increase resistance to radiation appreciably. Stopping growth by drying increased the resistance considerably. Stopping growth by asphyxiation increased resistance somewhat, but not nearly to the same extent as dessication. No quantitative relations were found to exist between radiosensitivity, oxygen con-

sumption, water absorption, and mitosis. In 2 experiments an abundance of water was supplied to dry seeds for germination purposes but development was prevented either by inadequate aeration by low temperature. It was found that although water was absorbed by the organisms, their susceptibility did not increase appreciably as is the case when normal development takes place. (TIS)

322

Hewitt, H. B. and John Read. SEARCH FOR AN EFFECT OF OXYGEN ON THE DIRECT X-RAY INACTIVATION OF BACTERIOPHAGE. *Brit. J. Radiol.* 23, 416-23(1950).

An *E. coli* phage has been irradiated with x-rays in broth which contained sufficient protein to suppress the indirect effect due to ionization in the water. One phage suspension contained 10 to 15 ml./l. of dissolved O₂, and a second zero. The activity of each suspension diminished exponentially with increase in the x-ray dose. If the O₂ did increase the sensitivity of the phage at all it was unlikely to have been by more than 10%. The mean diameter of the phage particle, deduced from the 37% inactivation dose and Lea's theory, was 54 mμ. Other methods have given values of 45 and 75 mμ for the same phage. Broth, without phase, containing the normal amount of dissolved O₂, was given the maximum dose used previously, and then the phage particles were added immediately after the end of the irradiation. No inactivation was detected. (CA)

323

Hollaender, Alexander. PHYSICAL AND CHEMICAL FACTORS MODIFYING THE SENSITIVITY OF CELLS TO HIGH ENERGY AND ULTRAVIOLET RADIATION. Oak Ridge National Lab. Nov. 7, 1950. 22p. (ORNL-884)

The effect on the sensitivity of various organisms (bacteria, fungi, algae, etc.) to radiation death or chromosomal rearrangements, of exposure before or after irradiation to heat or to visible, ultraviolet, or infrared light, of water content, and of oxygen content is discussed. It may be possible to vary the number of "targets" at will, by means of adjustment of growth conditions or physical conditions during irradiation. (NSA)

324

Hollaender, Alexander. PHYSICAL AND CHEMICAL FACTORS MODIFYING THE SENSITIVITY OF CELLS TO HIGH ENERGY AND ULTRAVIOLET RADIATION, p.49 of INTERNATIONAL CONGRESS OF RADIOLOGY, 6th Congress, London. 1950.

This paper deals with changes in the radiosensitivity to X-rays of bacteria, fungi, paramecia and higher organisms at the cellular level by additional treatment with infra-red radiation, heat, light (photoreactivation), and ultrasonics; and by alteration in relative water content, age of cells, oxygen tension and chemical composition. By themselves, these additional treatments produce no recognizable effects but striking modifications in radiosensitivity are observed when they are combined with X-ray exposure. The results of secondary treatment with infra-red radiation and heat will be demonstrated by work done with *Tradescantia* and fungi; photoreactivation, by work with bacteria, fungi and paramecia; ultrasonics, by work on *Tradescantia*. Experiments in alteration in age of cells will be demonstrated by the work on *Escherichia coli*; results of alteration in chemical composition and oxygen tension, by work on bacteria, fungi, cells in tissue culture, and paramecia.

325

Hollaender, Alexander, W. K. Baker, and E. H. Anderson. EFFECT OF OXYGEN TENSION AND CERTAIN CHEMICALS ON THE X-RAY SENSITIVITY OF MUTATION PRODUCTION AND SURVIVAL. Cold Spring Harbor Symposia Quant. Biol. 16, 315-26(1951).

Recent studies of the effect of oxygen tension on x-ray

sensitivity as measured by the lethal effects, chromosome changes, and mutations produced in *E. coli*, *Drosophila*, and *Tradescantia* are reviewed. Results of studies of the effects of chemicals, and the mechanisms which may be involved in the action of these chemicals in regard to x-ray sensitivity, are discussed. Compounds which were found to afford protection against radiation damage included strong reducing compounds, especially $\text{Na}_2\text{S}_2\text{O}_4$; glycerin, propylene glycol, triethylene glycol, and alcohols like methanol, ethanol, and propanol; carboxylic acids, and sulfhydryl-containing compounds. (NSA)

326

Hollaender, Alexander, George E. Stapleton, and W. T. Burnett, Jr. **CHEMICAL ASPECTS OF RADIATION SENSITIVITY ON LIVING CELLS.** Oak Ridge National Lab. [nd] 2p. (AECU-1699)

The report is reproduced here in its entirety.

Remarkable decreases in many x-ray-induced cellular phenomena by reduction of oxygen concentration during irradiation have been reported including alteration of inactivation rates, frequencies of lethal mutations and chromosomal aberrations, as well as the duration of mitotic inhibition. As an extension of these studies an investigation has been made concerning the ability of chemical substances to modify the cell sensitivity to the damaging effect of x rays. The discussion will deal mainly with the results of x-ray lethal effects obtained with bacteria, but will include also studies with other organisms as far as the data are available. The following groups of chemical compounds have been found to reduce significantly the x-ray lethal effect on bacterial cells: sulfhydryl compounds (cysteine, BAL, mercapto succinic acid, and others), reducing compounds (sodium hydrosulfite), respiratory inhibitors (sodium cyanide), alcohols and glycols, carboxylic acids (formic, succinic, etc.), and sugars (glucose). It is interesting that compounds of group one and two will protect at either 2 or 37°C. High concentrations (10 to 20%) of the alcohols are required to give significant protection at low temperature (2°C) while much lower concentrations (<1%) are effective if the cells are incubated with them for a short period (30 min) at 37°C prior to irradiation. The carboxylic acids and glucose are effective only if the bacterial cells are incubated with them prior to x-ray exposure. Several of these compounds have been tested with interesting results for protective action on mice. The interpretation of results on the basis of removal of radiodecomposition products of water will be given. All of the chemical compounds used yield similar curves relating protective action to concentration, indicating a saturation phenomenon, the plateau level being different for the different types of compounds used. If two compounds are used simultaneously at the plateau level, additional protection is obtained, indicating perhaps different protective mechanisms. The possible role of metabolism, reductive capacity as well as synthetic processes, especially nucleic acid synthesis in the protective action of the carboxylic acids, amino acids, and glucose will be indicated. The significance of these findings on the chemistry of radiation damage in general will be discussed. (Paper presented at the American Chemical Society, New York City, Sept. 3-7, 1951).

327

Hollaender, Alexander, G. E. Stapleton, and F. L. Martin. **X-RAY SENSITIVITY OF *E. COLI* AS MODIFIED BY OXYGEN TENSION.** *Nature* **167**, 103-4(1951) (ORNL-832)

The influence of oxygen tension on sensitivity of *E. coli* to x-irradiation damage and the influence of cultural conditions to sensitivity were studied. It was shown that lowering the 0 tension of bacterial suspensions results in a

striking decrease of radiosensitivity of the cells, as compared with oxygenated suspensions. The order as well as the slope of the survival curves is different under low and high 0 tension. To set apart radiation effects produced through the intermediate aqueous suspension and those concerned with the bacterial cells as such, various culture conditions were studied which might alter recognizable effects on the cell. Results emphasize the importance of 0 tension, state of oxidation or reduction inside the organisms during exposure to x irradiation and the possible modifying effect of the type of metabolism carried out by the organism before irradiation. Most of the data are consistent with the idea that radiodecomposition products of water are contributing toxic agents, e.g., H, OH, HO_2 , H_2O_2 , some of which are produced only in the presence of 0 irradiation. However, it is thought that not all the findings in regard to 0 concentration can be explained on this basis. (NSA)

328

Hollcroft, Joanne Weikel, Egon Lorenz, and Marion Matthews. **FACTORS MODIFYING THE EFFECT OF X IRRADIATION ON REGRESSION OF A TRANSPLANTED LYMPHOSARCOMA.** Argonne National Lab. Oct. 25, 1951. 27p. (AECU-1819; UAC-458)

A synergistic effect on regression of a transplanted mouse lymphosarcoma occurred after simultaneous systemic and local tumor irradiation and was absent when the blood supply of the tumor was clamped off during systemic irradiation. The synergistic effect disappeared rapidly when the time interval between systemic and local tumor irradiation was increased from 0 minutes to four hours. Starving the animals for 20 hours before and during local irradiation of the tumor was found to increase tumor regression, while starvation following irradiation had no effect. H_2O_2 administered intravenously to the tumor-bearing animals immediately before tumor irradiation increased the effect on tumor regression in comparison with non-injected, irradiated controls, but hydrogen peroxide administered after irradiation did not. H_2O_2 injected five minutes before irradiation did not significantly increase tumor damage. Irradiation of the tumors of mice kept in a high-oxygen atmosphere produced a greater regression and irradiation of the tumors of mice in a low-oxygen atmosphere produced less regression than irradiation of the tumors of mice breathing air. Clamping off the blood supply to the tumor during local irradiation of the tumor had no effect on tumor regression. (NSA)

329

Jacobson, L. O. **STUDIES OF RADIOSENSITIVITY OF CELLS.** *Science* **107**, 248-50(1948).

It has been commonly believed that the sensitivity of mammalian cells to ionizing radiations is proportional to cell activity in terms of mitotic proliferation—the more active the proliferation, the higher the sensitivity. An increased erythropoiesis can be initiated in the laboratory animal by phlebotomy or by the hemolytic action of acetyl phenylhydrazine on the circulating erythrocytes. The effect of 800 r whole-body x-irradiation upon animals that have a previously induced regenerative anemia was compared with the effect of this same dose on normal animals of comparable age and weight. The normal irradiated animals developed an anemia that reached a maximum at 14 days. The animals in which a regenerative anemia had been produced prior to irradiation with 800 r developed no further anemia. The recovery time in both groups was comparable (23 days). The mean reticulocyte value of the phenylhydrazine-injected, X-rayed animals was reduced below the normal control value on the 6th post-irradiation day only. The phlebotomized group on animals responded to irradiation in a manner comparable to the animals

treated with phenylhydrazine and X-ray. The histologic studies made on appropriately sacrificed animals revealed that erythropoietic tissue in the bone marrow and the spleen was essentially completely destroyed by three days in normal animals that received 800 r. A relatively slow recovery ensued beginning on the 7th to the 9th day. On the other hand, the erythropoietic tissue in the bone marrow and spleen was only partially destroyed in animals that were irradiated with 800 r after a regenerative anemia was produced by phenylhydrazine or phlebotomy. These data would tend to indicate that erythroblast vulnerability to irradiation injury is not enhanced by increased mitotic activity and proliferation. In fact, the hyperplastic erythroid tissue sustained less histologic injury than the normal, and the production of erythrocytes was maintained. (ADD)

330

Jennings, F. Lamont. EFFECT OF PROTEIN DEPLETION UPON SUSCEPTIBILITY OF RATS TO TOTAL BODY IRRADIATION. *Proc. Soc. Exptl. Biol. Med.* **72**, 487-91 (1949).

The results of the first of a series of experiments undertaken to evaluate the role of protein in radiation damage are presented. Male albino rats of Sprague-Dawley strain were kept on a low-protein diet until they lost about 25% of their weight (10 weeks) and then were irradiated with total body x-radiation; the irradiation was delivered by a 200 kv machine through 0.5 mm Cu and 3 mm bakelite filters at a target distance of 71 cm. and a dosage rate of 17-18 r/min.; the depleted rats, the weight controls, and the age controls received 300-800 r doses. During the 30-day observation period following the irradiation, all the animals were maintained on the same diets as before. It was found that the protein depletion materially increase the rat susceptibility to total body irradiation and its effects; the age and weights of the controls, however, had little effect on the susceptibility to radiation. (NSA)

331

Joyet-Lavergne, P. A NEW CONCEPT OF THE RELATION BETWEEN CELL METABOLISM AND SENSITIVITY TO IRRADIATION. *Arch. phys. biol.* **15**, 94-5(1938).

Discussion. Intensity of cell metabolic activity and sensitivity of the cell to irradiation with X-rays and gamma rays are both in some way dependent on the condition of the mitochondria. (CA)

332

Kaplan, Henry S. INFLUENCE OF AGE ON SUSCEPTIBILITY OF MICE TO THE DEVELOPMENT OF LYMPHOID TUMORS AFTER IRRADIATION. *J. Natl. Cancer Inst.* **9**, 55-6(1948).

Black mice, strain C-57, were divided into age groups of two weeks, one, two, three, and four months, and given fractional dosages totalling 1,000 r of x-radiation administered in 12 consecutive daily doses at 125 kv, 5 milliamperes, 30 cm. mouse-to-target distance, 3 mm Al added filtration, output 42 r/minute, and a daily dose of 84 r. However, the dosage for the 2-week group had to be reduced to 750 r because of the high death rate following irradiation at 1,000 r. The animals were autopsied and examined histologically. The tumors were all lymphatic leukemias and lymphosarcomas. The maximum susceptibility was found to be at one month or earlier and it is associated with a shorter mean induction time. (NSA)

333

Kimball, R. F. MODIFICATION OF THE EFFECTS OF X RAYS ON STOCK 90 OF VARIETY 1 OF PARAMECIUM AURELIA. Oak Ridge National Lab. 1p. (AECU-1689)

(The report is reproduced here in its entirety.)

Various conditions have been used to attempt to modify the effect of x rays as measured by death and number of

divisions in the first day after irradiation and by reduced vigor and death after autogamy. The postautogamous effects were less severe when the animals were irradiated under low oxygen tension or in 0.6 M ethyl alcohol. No noticeable effect was exerted by starvation before irradiation, temperature during the day after irradiation (9 to 31°C), or presence of 0.001 M sodium hydrosulfite ($\text{Na}_2\text{S}_2\text{O}_4$), 0.0009 M British anti-Lewisite (BAL), or 0.01 M sodium formate. The last three compounds and alcohol were tried because they had been found by others in this laboratory to protect bacteria against inactivation by x rays. The oxygen effect is well known for a variety of organisms as a result of work in this and other laboratories. The negative results with hydrosulfite and BAL are not too significant since very low concentrations had to be used. Quite different results were obtained in the investigations of death and division delay in the first day. Low oxygen tension, BAL, and formate cause increased death and delay in division. All three treatments have a distinctly injurious effect upon the control animals, and it seems probable that this injurious effect combined with that of the radiation accounts for the results. It is surprising that low oxygen tension which clearly protects against postautogamous effects fails to do so for the immediate effects. Alcohol and hydrosulfite both decrease division delay despite the fact that they are clearly injurious to unirradiated animals. However, in some experiments, there is more death following irradiation in the presence of these agents than in their absence, suggesting again a combination of injurious effects. Finally, both division delay and death are markedly greater when the animals are irradiated in phosphate buffer with 3% of culture fluid added than when irradiated in undiluted culture fluid, suggesting a protective action of one or more of the components of the culture fluid. One can conclude that it is possible to protect paramacia against both the genetic and nongenetic effects of x rays, but it is not necessarily true that an agent which protects against the one will protect against the other. It appears likely that this is due, at least in part, to the independent injurious action of the x rays and of the substance adding together to produce a total effect greater than for either alone. (Paper presented at Paramacia Genetics Symposium, September 1951, Bloomington, Indiana).

334

Kimball, R. F. and Nenita Gaither. MODIFICATION OF THE ACTION OF X RAYS UPON PARAMECIUM AURELIA. *Genetics* **36**, 558(1951).

The following is an abstract and is reproduced here in its entirety.

A number of agents which previously have been shown to modify one or more effects of x irradiation have been tested on Paramecium aurelia. The mutagenic action of x rays in doses of 1 to 6 kr was found to be reduced when the irradiation was performed in an atmosphere of N_2 or in the presence of 0.7 M ethyl alcohol. On the other hand, 0.001 M sodium hydrosulfite, a reducing agent, had no influence on mutagenesis. No effect of the metabolic state was found since irradiation of either fed or starved paramacia, with or without incubation with 0.01 M sodium formate, produced identical amounts of mutation. Likewise, the rapidity of multiplication of the cells after irradiation, as influenced by temperature, was without influence. Two nongenetic actions, division retardation and death with 24 hr., were studied using doses of 100 to 300 kr. Both the amount of division retardation and of death were decreased by 0.7 M ethyl alcohol present during irradiation. Sodium hydrosulfite (0.001 M) clearly protected against the lethal action but had no influence upon division delay or, perhaps, enhanced it. Neither starvation nor incubation with formate was

found to have any effect. Thus there is at least one agent which affects a variety of different kinds of radiation damage in *Paramecium*. It may be suggested that some step which is common to the various effects is involved. However, it is possible that some agents influence the steps leading to certain kinds of damage only or else act more effectively upon one kind than the other.

335

Kimeldorf, D. J., D. C. Jones, and M. C. Fishler. THE EFFECT OF EXERCISE UPON THE LETHALITY OF ROENTGEN RAYS FOR RATS. *Science* 112, 175-6(1950).

As a means of determining the effect of metabolic activity or radiation sensitivity, equal dosages of x-rays (total body irradiation) were given as the test exercise, all animals were subjected to the treatment for 10 trials prior to inactivation and thereafter at daily intervals 5 times per week. It was found that the exercised animals had a higher mortality and a much shorter post-irradiation survival time. (EM)

336

Latarjet, R. CELL CONSTITUENTS IN RELATION TO RADIOSENSITIVITY, p.49-50 of INTERNATIONAL CONGRESS OF RADIOLOGY, 6th Congress, London. 1950.

At the stage of the primary reactions, the following factors are considered and illustrated by the results of various experimental investigations:—Size of the cellular volume involved. Multiplicity of the cellular units (targets) which must be altered in order to produce the lesion, e.g., enzymes. Experimental results obtained by studying the loss of virulence in bacteria infected with 1,2,3...n virus particles. Genetic structure: comparative study of a bacterium and of its "radioresistant mutant" as regards lethal effect and mutations induced by radiations. Structure of the chromosomes: comparative study of a diploid yeast and of its haploid mutant. Chemical factors in the cell increasing its radiosensitivity, e.g., oxygen. Chemical factors in the cell increasing its radioresistance, e.g., peroxydases, oxydation buffers, etc. During the course of the obscure reactions, cell radiosensitivity may be decreased by several processes of recovery. In this connection consideration is given to polyploidy, which seems to favour certain types of spontaneous recovery.

337

Latarjet, R. and E. Epharati. PROTECTIVE ACTION OF CERTAIN SUBSTANCES AGAINST INACTIVATION OF A BACTERIOPHAGE BY X-RAYS. *Compt. rend. soc. biol.* 142, 497-9(1948).

Phage T-2 active on *E. coli*, was used in aqueous suspension. Thioglycolic acid, tryptophan, glutathione, cystine, and cysteine had marked protective action, decreasing in the order named, and glucose, sucrose, ascorbic acid, phenylalanine, alanine, and histidine had somewhat protective action. In all cases the protective effect was less marked if dissolved O was removed from the medium before x-ray irradiation. (CA)

338

Latarjet, R. and B. Ephrussi. SURVIVAL CURVES OF HAPLOID AND DIPLOID YEASTS SUBMITTED TO X-RAYS. *Compt. rend.* 229, 306-8(1949).

Several investigators have noted the sigmoidal shape of the survival curve of yeasts submitted to ionizing radiations. One of the present authors has obtained such a curve and interpreted it as due to a "two-hit" process (*Ann. Inst. Pasteur* 70, 277(1944)); subsequently, by using highly ionizing radiations, he has shown that in these two hits two distinct targets were involved (Frilley and Latarjet, *Compt. rend.* 218, 480(1944)). It seemed probable that these results might be a consequence of a diploid nature of the yeasts employed. To test this hypothesis, haploid and diploid cultures,

derived from the same strain of *Saccharomyces cerevisiae*, received various doses of x-rays, at 33 kv, the intensity at the level of the preparation being 4,000-8,000r/min. The lesions were observed and counted microscopically after 20 hour incubation at 25°C. The lesions of haploid yeasts are all irreversible, while those of the diploids, besides irreversible cases, show frequent cases of restoration and of further reproduction of colonies. The corresponding survival curves, viz., a sigmoid graph for the diploid organisms and a simple exponential curve for the haploids, confirm well the above stated hypothesis. From the slopes of the curves, the targets could be determined as spheres of 33-38 m radius. The real significance of these facts is unknown; death, due to chromosomal lesions, of a diploid cell seems to be related to the appearance wither of two recessive lethal mutations, or of a single dominant one; the sigmoid curve may result as a combination of these two processes. (NSA)

339

Lea, D. E. INACTIVATION OF VIRUS BY RADIATION. *Brit. J. Radiol.* 19, 205-12(1946).

The paper is a brief review of experiments on the inactivation of viruses by radiations. It is claimed that when the virus is irradiated dry or in an aqueous solution of high solid content, the inactivation of the virus is direct and due to a single ionization. There is correlation between the dose and the size of the virus. Departure from the theoretical curve of the inactivation dose indicates that the virus is composed of radio-sensitive and insensitive structures. The size of the sensitive region was calculated for the vaccinia virus. The result which the author arrived at greatly differs from that of Bonét-Maury and Péreault (1941). (EM)

340

Mottram, J. C. ON THE ALTERATION IN THE SENSITIVITY OF CELLS TOWARDS RADIATION PRODUCED BY COLD AND BY ANAEROBIOSIS. *Brit. J. Radiol.* 8, 32 (1935).

Two sets of experiments were carried out: exposures in the cold and exposures in N. In the experiments to test the effect of cold, the roots were exposed under water, 6 roots in ice-water and six in water at 24°C. The experiments showed that the application of cold outside the period of radiation had no effect on the growth and that even with short exposures the cells of the bean root are more sensitive when cold than when warm. Anaerobiosis was obtained by placing the beans in a closed chamber and then displacing the air by passing in commercial nitrogen. Bean roots were exposed to the N and to air, the N exposure from 120 to 200 min, the air from 100 to 170 minutes. The beans under anaerobic conditions were much less sensitive to the γ radiation than when oxygen was present, 100 minutes exposure in air being equivalent to 170 in N. Anaerobiosis greatly decreased the sensitivity of the roots. The conclusion of Crabtree and Cramer that cold renders cells more, and anaerobiosis less, sensitive to radiation is confirmed; and is shown to apply to the plant as well as the animal cell.

341

Patt, H. M., Marguerite N. Swift, and Ella B. Tyree. OXYGEN CONSUMPTION AND WATER BALANCE IN THE X-IRRADIATED FROG. *Federation Proc.* 8, 124(1949). (AECU-507)

(This document is in abstract form and is reproduced here in its entirety.)

As a part of a study of the radiation response of frogs and of factors contributing to their radiosensitivity, we have investigated 1) oxygen consumption after x-irradiation and 2) rate of water uptake in dehydrated irradiated frogs. Oxygen consumed by individual unfed Autumn frogs, sedated

with nembutal, was measured volumetrically at atmospheric pressure and 23°C. Results of a pilot study in which determinations were made during a control period of several days and at frequent intervals after x-irradiation with 300 r (completely lethal, mean survival time 26 days), suggest a slight early decrease in oxygen consumption with maximal depression (34%) 15 days after exposure. This is followed by return to control levels (0.086 ± 0.002 cc/gm/hr) around 25 days after irradiation. Although there is evidence that ionizing radiation accelerates catabolism in mammals, especially terminally, we failed to observe any increase in oxygen consumption in these frogs. Body weight of unfed irradiated frogs also did not change appreciably. Frogs kept in dry individual containers at 23°C for 3 days lose 35-40% of their water. After irradiation with 3000 r and immediate return to water, such partially dehydrated irradiated frogs regain water at the same rate as non-irradiated controls. In both groups, recovery is essentially complete by 4 hours. There is no change in water content of non-dehydrated irradiated frogs over this period. Experiments are in progress to evaluate the influence of water content at the time of exposure on radiosensitivity in the frog.

342

Petrova, J. CONCERNING THE VARIOUS EFFECTS OF ALPHA RAYS ON THE NUCLEUS AND PLASMA OF THE CELLS. *Botan. Centr. Beih. A*, **61**, 399-430(1942).

When agar cultures of the alga *Zygnema* were subjected to Po alpha-rays, the extent of the radiation to various parts of the cells was controlled by use of filters of varying strength. When the entire cell (nucleus plus cytoplasm) was fully irradiated, the injurious effects were the same as after beta and gamma radiation: cessation of cell division for several days, abnormal starch storage, longitudinal growth, occurrence of modifications and death of the cell after several months. If only the cytoplasm was irradiated, the usual dose had no effect, while several hundred times this amount caused cell death within 24 hours, without the other effects mentioned above. The cell nucleus appears 700 times more sensitive than the cytoplasm to radiation, and alpha- seems about 10 times more active than beta-radiation. (CA)

343

Quastler, Henry. STUDIES ON ROENTGEN DEATH IN MICE. II. BODY WEIGHT AND SENSITIVITY. *Am. J. Roentgenol. Radium Therapy* **54**, 457-61(1945).

The survival time, after administration of constant doses, is proportional to the weight, provided the survival time is between 11.25 and 3.3 days. The two plateaus, at 11.25 and 3.3 days, occur in adult mice of all weight classes. The 3 relations, between age and sensitivity, between age and weight, and between weight and sensitivity, are concordant in adult mice. Infant mice survive longer than adult mice after application of the same dose. Simple mathematical formulae for the relations between dosage, weight, and survival time are given. (auth)

344

Read, John. THE INFLUENCE OF OXYGEN TENSION ON RADIOSENSITIVITY, p.50 of INTERNATIONAL CONGRESS OF RADIOLOGY, 6th Congress, London. 1950.

Previous work concerned with the influence of oxygen on the radiosensitivity of normal and tumour tissue is reviewed. Experiments on *Vicia faba* roots are described which support the following conclusions:—X-radiation of roots in the presence of oxygen causes much greater growth reduction than the same dose given in the absence of oxygen. The oxygen augments the effect of all X-ray doses in the same proportion, by a factor which increases with concentration in a sigmoid fashion to a maximum of 3. With alpha-rays the factor is 1.3. The numbers of abnormal

anaphases produced by the two radiations are affected in the same way. The histological picture of root tips irradiated with and without oxygen seem qualitatively similar but in the former case the quantitative change is much greater, particularly when judged by the inhibition of mitosis. Oxygen supplied immediately after X-radiation has no observable effect. When the oxygen concentration in a root is suddenly changed, the radiosensitivity readjusts itself with a lag (if any) not greater than one minute. The X-ray sensitivity is the same whether anaerobiosis is produced by bubbling nitrogen, argon, or hydrogen through the water in which the roots are immersed. Reduction in growth after immersion in nitrogen mustard solution is similar to that after X-rays, but anaerobiosis during, and for 30 minutes after immersion does not diminish the effect. The results suggest that radiosensitivity is altered by a change in the metabolic state, or that oxygen reacts with the immediate products of ionization to increase the yield of some effective toxin, subsequent biological changes being unaffected by the oxygen itself.

345

Reboul, J. and J. M. Maynard. REMARKS ON SEVERAL CASES OF CUTANEOUS HYPER-RADIOSENSITIVITY. *J. radiol. electrol.* **30**, 732-3(1949).

Four cases of reaction to radiotherapy are given in detail: one received six doses of 250 r/dose delivered at 200 kv through a filter of 1 mm Cu and 1 mm Al at a distance of 50 cm. and a rate of 12 r/min., resulting in a radiodermatitis; the second received five doses of 250 r/dose at 200 kv through the same filter and distance at a rate of 14 r/min., resulting in radiodermatitis; the third received the three doses with radiation delivered as in the second case except that the focal distance was 40 cm., resulting in peeling, and, after a second course of irradiation of 15 doses at 200 r/dose delivered at 220 kv through a filter of 1 mm Cu, resulting in dermatitis; the last received three doses of 250 r/dose delivered at 180 kv through 1 mm Cu and 1 mm Al at a distance of 40 cm., resulting in an exudative radiodermatitis four days after the last dose. In these cases all technical imperfections of the therapeutic course were eliminated, and similar courses on other individuals did not cause any reaction. The authors conclude that certain individuals are hypersensitive to these doses and discuss the possibility that percentage plots of the population reacting against the dose may show a sigmoid population distribution for sensitivity. (NSA)

346

Sallmann, Ludwig von. FURTHER EFFORTS TO INFLUENCE X-RAY CATARACT BY CHEMICAL AGENTS. *Trans. Am. Ophthalmol. Soc.* **69**, 391-418(1951).

Intravenously administered cysteine had a markedly protective action against radiation damage to the lens of rabbits when the treatment preceded the exposure of the eye to 1500 r. This protective influence has persisted for at least one year. When cysteine was injected subconjunctivally twice weekly for three weeks following the irradiation of cysteine-pretreated rabbits, the fine cortical opacities were not reduced by the additional therapy. Subconjunctival injection of 1.0 cc of an 8 percent solution of cysteine prior to irradiation was moderately beneficial in preventing the damage to the lens induced by local exposure of the eye to 1500 r. Analysis of microscopically visible changes in the lens, which develop in the first two or three weeks after x-ray irradiation with 1500 r, showed that almost all lesions were less pronounced in the cysteine-pretreated eyes than in the eyes rayed before the use of cysteine. X-ray-induced inhibition of cell division, recovery, and compensatory increase of mitotic activity of the lens epithelium differed very little in cysteine-pretreated animals and nonpremedi-

cated controls. Under the conditions of the experiment, glutathione and thiourea were less effective than cysteine in increasing the radioresistance of sensitive elements of the lens. Sodium thioglycollate and BAL were totally ineffective. Pretreatment with other reducing chemical agents (dihydroxyacetone and tocopherol), with the citrovorum factor, and with cyanide did not reduce the injurious effect of 1500 r applied locally to the rabbit's eye. (auth)

347

Schrek, Robert. **STUDIES IN VITRO ON THE PHYSIOLOGY OF CELLS. FACTORS AFFECTING THE DELAYED CYTOTOXIC ACTION OF X-RAYS.** *J. Cellular Comp. Physiol.* **28**, 277-304(1946).

By the method of unstained cell counts, the number of viable cells were determined in suspensions subjected to irradiation (1000 r) and incubation under varying conditions. Irradiation of suspended thymic cells of the rabbit produced no observable immediate changes, but after 5 hours of incubation at 37°C many of the cells developed irregularity of shape or edema of the cytoplasm. After 17 hours of incubation nearly all of the cells were dead, as indicated by stain ability with eosin. Lymphocytes were susceptible to the delayed cytotoxic action of x-rays in vitro but granulocytes were resistant. Thymic cells of the rabbit and kitten were equally susceptible to radiation although the non-irradiated cells of the kitten survived about twice as long as those of the rabbit. Varying the temperature (0° and 25°C) during the radiation period did not alter the radiosensitivity of thymic cells. Varying the temp. (2-45°C) during incubation showed that the maximum radiosensitivity was at approx. 37°C and the minimum at 17° and 45°. The non-irradiated survived longer at lower temps. with a temp. coefficient of 3. The addition of acid to the suspension after radiation decreased the radiosensitivity of rabbit thymic cells. The survival of non-irradiated cells was not appreciably affected by pH's varying 6.0 to 8.4. The cells were rapidly killed at pH 5.9 and 9.5. (BA)

348

Smith, Falconer, and Marie M. Grenan. **EFFECT OF HIBERNATION UPON SURVIVAL TIME FOLLOWING WHOLE-BODY IRRADIATION IN THE MARMOT (MARMOTA MONAX).** *Science* **113**, 686-8(1951).

Experiments have been performed to find whether sensitivity to radiation is lower in the hibernator than in the non-hibernator. One group of marmots was allowed to hibernate in a constant-temperature room held at 3.5 to $\pm 0.5^\circ\text{C}$ and was irradiated 3 weeks after the onset of deep hibernation. A similar group was maintained at room temperature and served as nonhibernating, irradiated controls. Results indicate that a delay in the rate of development of the lethal processes following irradiation accompanies lowered body temperature and reduced metabolic rate in the marmot. The fact that irradiated marmots died in hibernation after only slightly higher doses (one 650 r, one 800 r) than that found for most nonhibernators (550 r) indicates that no great decrease in sensitivity to radiation is attendant upon the change to the poikilothermic state. (NSA)

349

Smith, L., Lousie R. Sieburth, and Barbara Norby. **THE RELATION OF OXYGEN CONCENTRATION IN BARLEY SEEDS TO THE BIOLOGICAL EFFECTS OF X-RAY.** *Genetics* **35**, 692(1950).

In recent years a number of workers (cf. Hayden and Smith, *Genetics* **34**: 26-43, 1949) have shown that the atmosphere (O_2 , CO_2 , N_2 , vacuum) surrounding tissues has a profound effect on the biological effects of irradiation. Therefore an attempt was made to try to test the effect of increasing and decreasing the oxygen content inside germinating seeds prior to irradiation. This was accomplished by

pre-soaking seeds for 24 hours in: 1) cooled, boiled distilled water (reduced supply of oxygen); 2) untreated distilled water (normal supply of oxygen); 3) distilled water to which oxygen was added (increased supply of oxygen). Preliminary observations indicate that no cell divisions have occurred at the end of the 24-hour period. At the end of pretreatments, the seeds were X-rayed (usually 1,500 r) under identical conditions in air. The seeds which were provided with additional oxygen were injured markedly more than those which had had a normal or reduced amount of oxygen. Seeds with the normal amount of oxygen were injured slightly more than those soaked in boiled water. Injury was measured in terms of survival and rate of growth (height) of seedlings. A summary of four experiments totaling 400 seeds for each treatment gave the following results. For the control, boiled (HOH, untreated HOH, and oxygen-added treatments, the survival values were respectively, 1.9, 1.6, 1.3, and 1, and the heights were 3.4, 2.2, 2, and 1. Cytogenetic data are being obtained to supplement the observations on injury symptoms. (G)

350

Sparrow, A. H. **CHANGES IN SENSITIVITY OF CHROMOSOMES TO X-RAY BREAKAGE DURING MICROSPOROGENESIS.** *Genetics* **32**, 106-7(1947).

It has previously been established that chromosomes of *Trillium* undergo changes in radiosensitivity during meiosis. This investigation has been continued and a fairly complete sensitivity curve, including most stages from early meiotic prophase through pollen grain resting stage, has been constructed. A standard dosage of 50 r was given at all stages. Sensitivity is determined by counting the number of fragments per 100 PMC. Meiotic prophase stages up to and including diplotene were scored at AI. All later stages were scored at microspore metaphase. The data show a gradual increase of sensitivity from early meiotic prophase up to metaphase I. The curve then drops down again to a low at the tetrad (or very early resting) stage and starts up again during the resting stage. The results are interesting in that (1) the range of sensitivities is very large (about 1 to 27), and (2) that high and low sensitivity stages respectively correspond to stages of high and low concentrations of desoxyribose nucleic acid in the chromosomes. (RG)

351

Stapleton, George E., Daniel Billen, and Alexander Hollaender. **PROBABLE MECHANISMS OF PROTECTIVE ACTION OF SOME CHEMICALS AGAINST RADIATION DAMAGE.** Oak Ridge National Lab. 1p. (AECU-1690)

The report is reproduced here in its entirety.

The protective action against x-ray damage of a wide variety of chemical substances on *E. coli* B/r has been reported (Burnett et al., *Federation Proc.* **10**, 22(1951)). Some of these compounds have been further investigated in an attempt to elucidate the mechanism of protection of bacterial cells. At low temperatures some of the commonly metabolized compounds, e.g., formate, succinate, serine, threonine, and -alanine, afford little if any protection. However, if cells were incubated at 37°C in the presence of these compounds, prior to x irradiation, a marked increase in their protective capacity was noted. Parallel studies on respiration, utilizing some of these compounds as substrates, indicate that their protective capacity can be correlated with the rate at which these substances are oxidized by the bacterial cells. This suggests that preincubation of cells with these compounds may result in protection, in part, by removal of oxygen at critical locations within the cell, thereby inhibiting the formation of some oxidizing radiodecomposition products of water. Further confirmation of the suggested mechanism has been obtained

by use of respiratory inhibitors such as sodium cyanide. The inhibition of oxygen uptake by NaCN on several substrates used (amino and carboxylic acids) resulted in loss of protective action by these compounds. Some organic and inorganic sulfur-containing compounds which show protective action have been investigated in a similar manner and the results will be discussed in relation to the proposed mechanism. (Paper presented at Botanical Society of America, Physiological Section, September 1951, Minneapolis.)

352

Stearner, S. Phyllis and Emily J. B. Christian. EFFECTS OF X-IRRADIATION IN NEWBORN RATS. *J. Exptl. Zool.* **118**, 495-508(1951). (AECU-1508; UAC-404)

Newborn rats were x irradiated shortly after birth ($\frac{1}{2}$ to 5 hr) and at 1 or 2 days of age. Radiation doses ranged from 400 to 1000 r, and exposures were made at 6, 40, and 80 r/min. Effects of x irradiation upon survival indicated that the newborn rat was more radiosensitive than the adult; but resistance increased rapidly after birth, and at 2 days the sensitivity was only slightly less than that reported for adults. A higher and earlier death rate followed exposure of $\frac{1}{2}$ - to 5-hr old rats to 600 r at 80 r/min than that observed in groups exposed at 6 r/min. No effect of variation in dose rate was observed after exposure to 400 and 800 r. Exposure to 1000 r, however, produced a shorter mean survival time when delivered at 6 r/min than when delivered at higher rate. Animals exposed at 24 hrs after birth showed no dose-rate effects upon survival and gross-pathology with any amount of exposure. Generalized edema, hyperemia, and renal hemorrhage were prominent autopsy findings at 1 to 2 days after irradiation in animals exposed within 5 hr after birth. Later gross changes were typical of those that accompany acute radiation deaths. Hemorrhages developed in the cerebrum within the first day and in the cerebellum and medulla after 5 to 7 days. (NSA)

353

Thompson, T. L., Roy B. Mefferd, Jr., and Orville Wyss. THE PROTECTION OF BACTERIA BY PYRUVATE AGAINST RADIATION EFFECTS. *J. Bacteriol.* **62**, 39-43(1951).

The presence of pyruvate in a bacterial suspension protects the cells against the lethal and the mutagenic action of ultraviolet and x rays and against the lethal action of hydrogen peroxide. Upon prolonged exposure to ultraviolet, pyruvate solutions become toxic and mutagenic. The addition of the pyruvate after exposure of the cells or its presence in the plating medium does not modify the biological response to the radiations. In organisms lacking in synthetic ability a rich recovery medium may give higher counts of cells injured by ultraviolet. (NSA)

354

Tullis, John L. RADIORESISTANT CELLS IN CERTAIN RADIOSENSITIVE TISSUES OF SWINE EXPOSED TO ATOMIC BOMB RADIATION. *Arch. Pathol.* **48**, 171-7 (1949).

A report is presented on the morphological changes noted in the radiosensitive tissues of swine following irradiation. These radiosensitive tissues are the lymph nodes, the bone marrow, the intestinal epithelium, the gonads, the spleen, the thymus, the tonsils, lymphoid aggregations in the bowel wall, and lymphocytes in the peripheral blood stream. After irradiation, the lymphocytes undergo a prompt reduction, rapid lysis in some cases and slow degeneration in others; increased erythrophagocytosis also may occur. In the bone marrow the blast cells are easily destroyed, leaving only the reticular cells intact after heavy irradiation. Complete destruction of sections of the bowel epithelium may occur at random locations after radiation expo-

sure; the fibrocytes and the plasmacytes in the lamina propria are relatively uninjured. After injury to the gonads, no sperm cells are apparent, and few spermatogonia and spermatocytes remain; the cytoplasm of the tubular cells becomes granular and vacuolated, but the indifferent cells which line the tubules next to the basement membrane show no alterations. The developing ova in the ovary show vacuolation of the cytoplasm of the follicular cells and other changes, but the primordial ova are more resistant. It is noted that in these organs discussed, the so-called stem cells (reticular cells, primordial ova, etc.) of the highly radiosensitive organs are comparatively radio-resistant; the reason for this is not apparent morphologically. (NSA)

355

Windholz, F. REACTIONS OF CONNECTIVE TISSUES AFTER PROTRACTED FRACTIONATED IRRADIATION OF LARYNGEAL CARCINOMA. *Radiology* **48**, 148-56 (1947).

Microscopic studies of the larynx of patients irradiated with the protracted fractionated method for malignant tumors revealed that, contrary to the general belief, there are profound and extensive changes in the connective tissue. The following 3 stages of connective tissue effect of X-rays may be observed. The first is a bionegative retrogressive period characterized by exudation of fibrin, loss of nuclear staining and frequent changes in the microchemical reaction of subepithelial collagenous fibres. This period is coincidental with fibrinous radiomucositis and disintegration of the epithelial cells and the mucous membrane. The 2nd period might be called a biopositive regenerative phase. Connective tissue fills out the spaces remaining after disintegration of the tumor. The retrogressively changed fibrinoid necrotic collagen of the lamina propria is replaced by hyaline sclerotic layers. Myogenous giant cells indicate the regenerative tendencies of these tissues. Inflammatory reactions of the regenerated connective tissue are markedly reduced as a specific effect of radiation on this structure. In some instances (over exposure or particular sensitivity of the connective tissue) a third retrogressive phase may be observed. The newly formed connective tissue becomes necrotic, the mucous membrane shows ulcerations, and secondary bacterial infections develop and progress into the deep layers of the irradiated larynx. (BA)

356

Windholz, F. PROBLEMS OF ACQUIRED RADIORESISTANCE OF CANCER: ADAPTATION OF TUMOR CELLS. *Radiology* **48**, 398-404(1947).

The article summarizes the various theories so far advanced for the explanation of acquired radioresistance of malignant tumors. The histologic and radiobiologic behavior of the mucous membrane of the larynx as observed by the author forms the basis for his explanation of this phenomenon. The author explains acquired radioresistance as due to adaptation of cancer cells to the environment, changed by irradiation. Tumor cells which are able to adapt themselves to this changed environment maintain their newly acquired properties in successive cell generations. Thus, gradually the author believes the entire tumor becomes transformed into a growth, the radiobiologic properties of which are adapted to the biologic conditions prevailing during and after irradiation. In these new surroundings, the tumor either disintegrates or its radioresistance is increased. (BA)

357

Zirkle, Raymond E. MODIFICATION OF RADIOSENSITIVITY BY MEANS OF READILY PENETRATING ACIDS AND BASES. *Am. J. Roentgenol. Radium Therapy* **35**, 230-7(1936).

Using the spore of the fern *Pteris longifolia* and also *Paramecium*, it was noted that an increase of the acids carbon dioxide and hydrogen sulfide up to a certain concentration increased the radiosensitivity and beyond that point, a decrease, while the base ammonia acted in the reverse manner. These chemicals produced no detectable effects without the irradiation. Clinical application of the above results depends upon whether mammalian tissues will respond in the same way, both to the chemicals and to irradiation, and also whether such response will be without harm to normal tissue. (R)

358

Zirkle, Raymond E. THE INFLUENCE OF INTRACELLULAR ACIDITY ON THE RADIOSENSITIVITY OF VARIOUS ORGANISMS. *J. Cellular Comp. Physiol.* **16**, 301-11(1940).

Drosophila eggs of two ages (2 hours and 4.5 hours) were exposed during x-irradiation to various concentration of a penetrating acid, CO₂. The radiosensitivity of the acidified eggs was deduced from their percentage hatching and the survival curve for normal eggs. When radiosensitivity is plotted against CO₂ concentration in mm of Hg, the resulting curve has maxima at 80, 200, and 350 mm Hg and minima at 150 and 250 mm (temp. 25°). This finding holds for both 2-hour and 4.5 hour eggs. However, the heights of the maxima and minima are widely different for the two age groups. In general, the radiosensitivity of the 2-hour eggs varies over a much greater range. The radiosensitivity curves for the eggs resemble those for fern spores in the occurrence of maxima and minima but these critical points occur at different CO₂ concentrations. Reasons are given for considering the shape of the radiosensitivity-acidity curves to be due to several radiochemical reactions, each of which has a maximum at a characteristic pH. The experimental results are discussed in relation to the radiochemical behavior of proteins at various pH values and to the influence of intracellular acidity on the production of chromosome abnormalities by x-rays. (CA)

359

Zirkle, Raymond E. COMBINED INFLUENCE OF X-RAY INTENSITY AND INTRACELLULAR ACIDITY ON RADIOSENSITIVITY. *J. Cellular Comp. Physiol.* **17**, 65-70(1941).

When germinating fern spores are exposed to X-rays in the presence of graded concentrations of CO₂ and ammonia, their radiosensitivity has maximal and minimal values at definite concentrations of the penetrating acid and base. The heights of the maxima and minima are modified when the intensity of the X-ray beam is varied, and the quantitative change in height is different for the various maxima. The concentrations of acid and base at which the maxima and minima occur are not altered by the X-ray intensity. These results are consistent with the hypothesis that the total radiosensitivity is due to the added effects of several radiochemical reactions which have maximal yields at different pH values. (BA)

360

Zirkle, Raymond E., E. Anderson, E. F. Riley and H. J. Curtis. THE EFFECT OF AGE ON THE RADIOSENSITIVITY OF MICE. *Clinton Labs.* [nd] Decl. Oct. 29, 1946. 6p. (MDDC-418; MonH-89)

Mice of different ages ranging from 1.5 to 12 months were exposed to gamma rays in an effort to determine the change in radiosensitivity with age. The dose necessary to cause 50% killing was determined for each age group and sex. No change in sensitivity with age was observed with either sex, although the experimental error in the case of the males was quite large. The females were found to be more resistant than the males. (ADD)

Comparative Effects

361

Bishop, F. W. COMPARISON OF X- AND BETA RADIATION EFFECTS IN RABBITS. *Univ. of Rochester.* [nd] Decl. Aug. 17, 1948. 12p. (MDDC-203)

The minimal dosage necessary to produce an erythematous reaction in the ear of the rabbit with 30 kv X-rays is in the neighborhood of 1,000 r. A somewhat smaller dose (900 r) was able to cause epilation without erythema. Generally the phenomenon of epilation either appears at a lower dosage level or a higher percentage of the animals are epilated than show erythema for a given dosage. As might be expected, the erythema appears sooner and generally lasts longer at the higher dosage levels and epilation also occurs earlier under these circumstances. Scaliness of the areas treated was a usual accompaniment of the erythema but its appearance time and duration was erratic. The lowest dose of beta rays capable of causing an erythema in the rabbit's ear is near the level of 3,000 rep. Epilation was not observed until a dose of 3,500 rep had been administered and the percentage epilated was less for a particular dose than that developing erythema. Generally the appearance time of the epilation was considerably longer than that of the erythema. Scaliness without any other sequela was noted at low dosage levels but was as variable as in the case of the x-rayed rabbits. These few experiments indicate that from three to five times the dosage is necessary in the case of beta rays to produce a given effect; e.g., it required approximately three times the dose of beta rays as compared with low voltage X-rays to produce a minimal erythema, about four times the dose to cause the first signs of epilation and about four and one-half times the dose to produce epilation in all the animals treated. (ADD)

362

Bonet-Maury, P. and F. Patti. LETHAL IRRADIATION OF MICE WITH HIGH DOSES OF ROENTGEN AND GAMMA RAYS. *Radiology* **57**, 419-23(1951).

Comparison of data was made on mice irradiated over a wide dosage range, under identical conditions, with x and γ radiation. X- and γ-ray doses measured by a graphite-bakelite ionization chamber corresponded fairly well to the energy actually absorbed by the mice and are directly comparable. Though the irradiated animals showed identical symptoms of poisoning, a greater amount of γ energy than of x-ray energy was required in the tissues for similar biological effects. This result was attributed to different primary radiochemical reactions resulting from unequal ion distribution along the electronic path of the two radiations. (NSA)

363

Czech, H., R. Czech, and H. J. Schmermund. A COMPARATIVE STUDY OF THE ACTION OF FAST ELECTRONS AND X-RAYS ON THE CORNEA OF SALAMANDER LARVAE. *Strahlentherapie* **81**, 187-92(1950).

The cornea of the salamander larva was used for a comparative study of the radiobiological action of fast electrons and x-rays. The phenomenon observed was the so-called primary effect of a radiation on the mitotic division of cells. If a cell is irradiated while undergoing division, the effect produced by the irradiation is a primary effect, as distinguished from a secondary one produced by irradiating a cell in the resting stage. No qualitative differences in the disturbances produced by the two kinds of rays were observed. However, the frequency of pathologic changes in the mitosis due to the action of electrons was, per unit

dose, lower than that corresponding to the action of x-rays. These findings are in agreement with the requirements of the "event" or "target" theory of the action of energetic radiations on biological structures. (NSA)

364

Devik, Finn. THE TOLERANCE OF EPIDERMAL CELLS OF MICE TO HEAVY DOSES OF EXTERNAL ALPHA-IRRADIATION. *Acta Pathol. Microbiol. Scand. Suppl.* **91**, 45-7(1951).

The histological and cytological effects of known quantities of external α irradiation on the skin of mice are compared with the effects of local x irradiation. It was concluded that the epidermis contains a number of cells which will survive doses of the order of 100,000 r of α rays. In the histological sections, x irradiation was seen to produce more pronounced changes than were produced by α ray doses of 1 to 2 orders of magnitude above the x-irradiation dose. (NSA)

365

Dieckmann, C. and W. Dittrich. KILLING OF BACTERIUM COLI WITH FAST ELECTRONS OF A 6-MEV BETA-TRON. *Strahlentherapie* **81**, 215,22(1950).

An agar-plate technique was devised for the investigation of the rate of deterioration of *Bacterium coli* commune by fast electrons and x-rays. In agreement with the "event" or "hit" theory of radiobiological processes, 3-Mev electrons were found to be more effective for the above reaction than equal doses of x-rays of 180 kv, 6 ma, 0.27 mm half-value layer and 500 r/min dose rate; the dose range was 500 to 4000 r. The radiobiological effect produced by the electrons is interpreted as a saturation process, in the sense of the above theory; the radio-sensitive volume is composed of about 60 elementary fields of 21 μ average width. (auth)

366

Dobson, R. Lowry. LETHAL RADIATION EFFECTS OF X RAYS, DEUTERONS, AND ALPHA PARTICLES ON THE BACTERIUM ESCHERICHIA COLI. Radiation Laboratory, Univ. of Calif., Berkeley. Feb. 28, 1951. 64p. (UCRL-1140)

Aerobically grown *E. coli* strain B and its naturally occurring radiation resistant mutant strain B/r were irradiated in air with x rays, deuterons, and α particles. In all cases typical exponential survival curves were obtained. In this respect the bacteria behaved as would be expected according to simple target theory. B/r was in all cases more resistant than B. Contrary to expectations based on target theory both strains were killed more efficiently by low-energy deuterons than by high-energy deuterons. This same reversal was found in the case of α rays, low-energy particles being more effective than high-energy particles. When x irradiation was carried out in a N_2 atmosphere, survival was increased over that in air. Such a protection was also demonstrated for argon in the case of strain B bombarded with particles. A modified target hypothesis—that the "target" may be inactivated not only by an ionization occurring within its volume, but also by energy transferred from the track of the ionizing particle through a finite distance in the cell, and further, that the probability of this latter mechanism resulting in target inactivation at a given distance increases with ion density along the track—is proposed. (NSA)

367

Evans, R. D. TOXICITY OF ALPHA AND FAST NEUTRON RADIATION. *Nature* **146**, 621(1940).

The author has described the results of experiments on neutron tolerance in animals in a paper presented at the annual meeting of the U. S. Nat. Acad. of Sci. on April 22-23. He finds that the results cannot be accurately extra-

polated to man because the relative radiation sensitivities are entirely unknown for small doses. Biological effects of neutrons are due to the secondary recoil rays which they produce in the body by collision with hydrogen, carbon, nitrogen, oxygen, and other atoms. The average specific ionization, and hence the ionic effectiveness, of the neutron recoil rays is closer to that of alpha rays than to any other radiation which has been the subject of extensive biological investigations. Data are available from studies of chronic radium poisoning, and of lung cancer produced by radon inhalation, concerning the effects of alpha rays on human tissue. With these data, it is shown that a dosage of 0.01 r per day of fast neutrons may be unsafe if the exposure continues over a period of about 10 years. (S.V.S.)

368

Evans, T. C. and E. H. Quimby. STUDIES ON THE EFFECTS OF RADIOACTIVE SODIUM AND OF ROENTGEN RAYS ON NORMAL AND LEUKEMIC MICE. *Am. J. Roentgenol. Radium Therapy* **55**, 55-6(1946).

The effects of radioactive Na and of whole body roentgen irradiation on white mice have been compared. Results in reduction of white and red blood counts and in shortening of life are similar for the two types of radiation. Mice with enlarged nodes and extremely high leukocyte counts were found especially sensitive to the radiosodium. They were not tested with roentgen rays. The marked response was apparently due to radiosensitivity of the abnormal leukocytes rather than to any selective concentration of the material in lymph nodes. (BA)

369

Gray, L. H. COMPARATIVE STUDIES OF THE BIOLOGICAL EFFECTS OF X-RAYS, NEUTRONS, AND OTHER IONIZING RADIATIONS. *Brit. Med. Bull.* **4**, 11-18(1946).

The author has studied the measurement of neutron energy absorbed in living cells; comparison of the effects of X-rays, gamma rays, neutrons and other ionizing radiations on enzymes, colloids, and numerous plant and animal tissues, both normal and malignant. His experiments are directed toward the treatment of cancer. In this article he discusses: (1) Linear ion density, the distinguishing feature of an ionizing radiation, from the biological standpoint. (2) Ion density produced by different ionizing particles. Figure 1 shows the separation of ion clusters in relation to the size of a virus particle 27 μ in diameter. (3) The influence of ion density on radiochemical yield. (4) Ion density in relation to the inactivation of elementary biologic units. Figure 2 shows the relative efficiency of ionizing radiations for the inactivation of viruses (6 types). (5) The structural changes induced in chromosomes by different types of ionizing radiation (Figure 3). (6) Comparative studies with other biologic material (*Drosophila* eggs, root-tips of *Vicia faba*, animal embryonic tissue, tumor tissue). (7) Neutron therapy. (BA)

370

Gray, L. H. EXPERIMENTAL STUDIES OF THE INFLUENCE OF RADIATION QUALITY, DOSE RATE, AND FRACTIONATION ON THE DIRECT INJURY OF CELLS BY IONISING RADIATIONS. *Acta Unio Intern. contra Cancrum* **6**, 794-8(1949).

The biological effects of equal doses of different ionizing radiations (γ rays, supervoltage x-rays, soft x-rays, neutrons, and α particles) were studied and correlated with the density of ionization along the tracks of ionizing particles, which varies in the extreme from 6 to 4,000 ions/ μ ; the more densely ionizing radiations were found to be either more or less effective in producing gene mutations and in bringing about enzyme inactivation in dilute aqueous solution and, in general, more effective in producing chromo-

some structural changes and in damaging or inhibiting the growth of many tissues including tumor tissue. Experimental data will be presented for a particular tissue (root tip meristems) belonging to this latter class. It was found experimentally, as is commonly observed in radiotherapeutic practice, that the inhibition of growth is markedly dependent on dose rate and fractionation when the radiation employed is x or γ radiation. This is not in general the case with the more densely ionizing radiations; no dose-rate dependence was observed with α radiation. It is concluded that the close interdependence of the effects of varying dose rate and quality can readily be understood by reference to the types of chromosome structural change observed to be produced in the irradiated cells. (NSA)

371

Gray, L. H. and J. Read. COMPARISON OF THE LETHAL EFFECT OF NEUTRONS AND GAMMA RAYS ON MOUSE TUMORS (A) BY IRRADIATION OF GRAFTER TUMORS IN VIVO, (B) BY IRRADIATION OF TUMOR FRAGMENTS IN VITRO. Brit. J. Radiol. 21, 5-10(1948).

The mean lethal doses of neutron and gamma rays on mouse tumours have been compared (a) by irradiation of grafted tumours in vivo, (b) by irradiation of tumour fragments in vitro. (a) Small pieces of carcinoma 2146 were inoculated into the thigh of a mixed strain of mice showing little concomitant immunity. When the tumours reached about 10 mm² in area they were irradiated either by 2.8 Mev (D-D) neutrons or by gamma rays from a 500 mg radium plaque filtered by 0.5 mm Pt and 1 mm brass. The two sources of radiation were so arranged that they gave roughly the same dose distribution throughout a mouse, and a mean lethal dose in about the same time. Eight different neutron doses were given to a total of 33 mice. The mean lethal dose was 65 energy units, standard deviation 12 energy units. The unit is defined as that amount of neutron radiation which releases the same energy per cc in water as 1 roentgen of gamma radiation. Nine different doses of gamma rays were given to 39 mice. The mean lethal dose was 1560 roentgens, standard deviation 64 roentgens. (b) Eight tumour fragments in physiological saline were retained, in the central hole of annular paraffin wax discs 2.5 mm thick, by the waxed paper. Six such cells were stacked in a glass specimen tube so that their distances from the target of the neutron generator gave the desired range of doses. The mean lethal dose was 154 energy units, standard deviation 17 energy units. A similar arrangement was used for the gamma irradiation, a total of 30 fragments receiving four different doses. The mean lethal dose was 1460 roentgens, standard deviation 62 roentgens. The efficiency ratio of neutrons to gamma rays was 24 ± 6.7 for the in vivo irradiation and 9.5 ± 2.3 for the in vitro irradiations. The authors discuss these results in association with their earlier published work on the lethal effect of ionizing radiations on the broad bean root. They support the idea that the tumour regresses by the death of the cells which have sustained chromosome or chromatid breaks resulting in chromosome aberrations. (EM)

372

Hagen, Charles W. Jr. and Raymond E. Zirkle. COMPARATIVE BIOLOGICAL ACTIONS OF CYCLOTRON FAST NEUTRONS AND X RAYS; I. LETHAL ACTION ON MICE AND RABBITS. University of Chicago Metallurgical Lab. Nov. 1950. 26p. (CH-3903)

X-irradiated rabbits exhibited three distinct periods of mortality: (1) "one-day" mortality, the fraction of the total number of animals that died in the first 3 days following irradiation; (2) "ten-day" mortality, the fraction of those rabbits alive at the end of 3 days which died by the 20th day; (3) "late" mortality, the fraction of those rabbits alive at

the 20th day which died on subsequent days. In the first period, weight and sex had considerable effects on survival. The heavier animals were more resistant than lighter ones. Females were more resistant than males during the "one-day" period but less resistant during the "ten-day" period. Following exposure to fast neutrons, the heavier rabbits again showed less mortality, but there were no significant sex differences. After either x or neutron irradiation, the majority of deaths occurred in the 4- to 20-day period. A distinct peak of deaths was evident 10 days after x irradiation, but after neutron exposures mortality during the 4- to 20-day period was divided into two phases with modes at about 8 and 12 days. For rabbits, the 30-day LD₅₀ was 825 r of x rays or 145 n units of neutrons; the x/n ratio was accordingly 5.7. For mean survival times the ratio was 6.3. Mice died in greatest numbers during the first 10 days after exposure to either neutrons or x rays, but the average survival after neutron exposure was about 4 days shorter than after x irradiation. The 30-day LD₅₀ was 540 r or 54 n, the x/n ratio accordingly being 10. (NSA)

373

Heidenthal, Gertrude and Leonard Clark. SURVIVAL RATES OF HABROBRACON EGGS TREATED IN FIRST MEIOTIC METAPHASE WITH LOW AND HIGH VOLTAGE X-RADIATION. Genetics 36, 554(1951).

Studies were made on the survival of haploid eggs treated in first meiotic metaphase with low voltage (124 kv) and with high voltage (50 Mev) x-radiation. Dosage ranged from 100r to 1750r. Standard techniques previously developed by A. R. Whiting were used throughout. Since females were not mated in the first series of experiments, parthenogenetic development occurred among the surviving eggs up to larval stages when the observations were discontinued. The curves for low and high voltage are practically identical, survival following treatment with 400r was 54% for high voltage and 51% for low; at 1500r the viability was about 5% for both types of radiation. The curve for low voltage is essentially a confirmation of that found by A. R. Whiting. — Other studies were made of eggs treated with low voltage but laid by females which were mated following irradiation. Under these conditions it would be expected that if recessive lethals were present, viability should increase. Since the curves for eggs from mated and from unmated females are so very nearly alike, it is tentatively concluded that death of eggs is to be attributed to dominant lethals. (RG)

374

Henshaw, P. S. COMPARATIVE LATE EFFECTS OF PERIODIC DOSES OF FISSION NEUTRONS AND OF GAMMA RAYS. Clinton Labs. June 1946. Decl. Apr. 21, 1947. 90p. (MDDC-1253; MonH-115)

Small daily doses of fast neutrons (0.115 to 13.0 n) and γ rays (1 to 17.2 r) were administered 6 times weekly to the whole bodies of treated animals. Most of the animals died either in a state of atrophy or with leukemia (mediastinal lymphomatosis). The time of death after treatment began, followed a regular pattern and furnished a means of quantitatively comparing the effectiveness of the different treatments and methods of exposure. The fast neutron doses measured in "n" were found to be from 8 to 35 times more effective than γ rays measured in "r". The threshold value for this radiation was found to be below 0.115 n of fast neutrons per day and about 1 r of γ rays. In CF-1 mice about 10 times as much radiation per day was required to produce a threshold change as was required to shorten the life span detectably. Some differences were noted in the responses of different strains of animals to radiation but these were more a matter of degree than of type; no fundamental differences were seen in the different sexes. The quantitative results based on survival time indicate that the degree of

biologic effect varies not only with dose, but also the density of ionization produced. Although the incidence of leukemia was significantly increased in CF-1 animals, the occurrence of lung tumors was only slightly, if any, modified by the treatments given. Only questionable evidence of increased lung tumor incidence was observed in animals which normally show a high spontaneous lung tumor incidence. (ADD)

375

Henshaw, P. S., et al. COMPARATIVE LATE EFFECTS OF SINGLE DOSES OF FISSION NEUTRONS AND OF GAMMA RAYS. Clinton Labs. June 1946. Decl. Sept. 8, 1947. 51p. (MDDC-1254; MonH-116)

Having obtained information about the late effects of small daily doses of fast neutrons and gamma rays (MDDC-1253), the authors now present the results of a study of the late effects caused by the same radiations when single large doses are administered. Experiments were carried out using CF-1 and ABC mice. As a rule more than 100 mice were used for each experimental sample. Single neutron doses of 26, 50, 78, and 90 n and single gamma ray doses of 500 and 700 r were given. Other special experiments to investigate the influence of dosage-rate and of massive doses were also carried out. Acute illness consisting of emaciation and weight loss, lymphopenia and histologic damage to germinal tissues occurred at four days to two weeks. Recovery was rapid in the animals that survived and at three weeks it was difficult to distinguish the experimental from control animals. Such treated animals nevertheless died prematurely more or less in accord with the amount of radiation delivered. Evidence was obtained suggesting that the length of life varied exponentially with dose. It has been noted that 1 n is consistently more effective than 1 r in causing biological injury; the superiority of a fast neutron unit is greater when judged by late effects than when judged by acute lethal action. The incidence of leukemia (mediastinal lymphomatosis) was greatly increased—from 15% in the controls to more than 60% in the case of gamma rays (incomplete results). The findings further substantiate the idea that the higher the concentration of ions the lower the dose of radiation required to produce a particular effect. Other evidence was obtained indicating that a single application of irradiation exposure is sufficient to induce malignant disease. (ADD)

376

Horn, Edward C. RELATIVE BIOLOGIC EFFECTIVENESS OF ROENTGEN RAYS AND NEUTRONS ON REGENERATION OF THE FORELIMB OF AMBLYSTOMA LARVAE. Am. J. Roentgenol. Radium Therapy 46, 727-31(1941).

Report on the comparative effectiveness of neutrons and roentgen rays in retarding and preventing tissue regeneration. Regeneration of an amphibian limb depends primarily on proliferation and cellular differentiation of a mass of undifferentiated cells, the regeneration blastema. This regeneration blastema provides favorable material for a study of the effects of neutrons and roentgen radiation on growth and differentiation. Sufficient doses of neutrons prevent differentiation and hence regeneration of the forelimb of *Amblystoma* larvae. Neutrons are more effective per unit of ionization than are roentgen rays in preventing regeneration. Roentgen dosage 13-14 times neutron dosage, as measured in terms of ionization in a Victoreen 100 r chamber, is necessary to prevent regeneration. (YBR)

377

Jacobson, L. O. and E. K. Marks. COMPARATIVE ACTION OF CYCLOTRON FAST NEUTRONS AND X-RAYS. II. HEMATOLOGICAL EFFECTS PRODUCED IN THE RABBIT BY FAST NEUTRONS. Univ. of Chicago Metallurgical Lab. June 1946. Decl. Oct. 8, 1951. 35p. (MDDC-1372; CH-3839)

Rabbits, weighing approximately 2000 each, were exposed to cyclotron fast neutrons. Hematological studies were conducted on the animals after exposure and at frequent intervals thereafter through 37 days. The range of dosages employed was from 9 to 178 fast neutron units. Detailed information is given on mortality and effects on the hemopoietic system following various doses of n radiation. A comparison of the relative effectiveness of cyclotron fast neutrons and x radiation made on the basis of the degree of heterophil or lymphocyte depression at arbitrarily chosen times after exposure of animals to these radiations gave variable results. The X/n ratios thus derived varied from 6 to 22. The X/n ratios derived from a statistical study of the lymphocyte-heterophil response in rabbits exposed to fast neutrons and X rays are for the lymphocytes 6.4 and for the heterophils 6.3 ± 0.1. (ADD)

378

Depp, Richard Kurt. THE EFFECT OF FAST ELECTRONS FROM A 6 MEV-BETATRON ON HUMAN SKIN, p.165 of INTERNATIONAL CONGRESS OF RADIOLOGY, 6th Congress, London. 1950.

Circular areas, 24 mm. diameter, on the thigh were given a single irradiation with electrons of 3 Mev. The dose was measured with a thin-walled ionization chamber, graduated in r units. The ratio between any given dose and the number of ion pairs produced was recorded photometrically. Doses between 600 r to 1,300 r at intensities of 100 r/minute to 1,600 r/minute were delivered. Doses given at the high intensity produced greater reaction in all cases. By comparing fields which showed the same degree of reaction, although irradiated under different conditions, the effect of protraction was studied and found to be of greater significance with electrons than with X-rays. An explanation of this difference may be the time-sequence of individual "hits". It would seem, therefore, that in order to avoid serious skin damage, the smallest intensity possible of any irradiation should be used.

379

Kepp, Richard Kurt. ACTION OF FAST ELECTRONS ON HUMAN SKIN. Strahlentherapie 81, 201-14(1950).

A comparative study of the effects produced on human skin by hard x-rays and by fast electrons from the betatron of the Siemens-Reiniger plant is described. Fields on the thigh were irradiated with equal surface doses of the two radiations. Unlike the reaction produced by x-rays, that due to electrons is characterized by a rapid development, a high intensity, and a fast healing. Although x-rays produced no exudative reactions, the latter were often quite strong after fast-electron irradiations, and ended with a formation of thick crusts. Even in the case of very strong reactions, the healing took place within three weeks after the beginning of the exudative process. The intensity of reactions produced by electronic radiations grew with the dose, with the energy of the electrons, and with the dose rate (ratio r/min). This dependence of the skin reaction on the dose rate may prove very significant in the therapeutic applications of fast-electron beams. The considerably stronger effect of the latter on the skin, as compared with the action of x-rays, is explained by surmising a gradual increase of the dose under the surface of the skin, which concentrates the main effect in those tissue layers that are responsible for the skin reaction. (NSA)

380

Kepp, Richard Kurt, Kurt Müller, and Herbert Reich. ROLE OF THE TIME ELEMENT IN FAST-ELECTRON IRRADIATIONS OF HUMAN SKIN. Strahlentherapie 84, 225-44(1951).

Test irradiations of human skin with 3-Mev electrons from a betatron showed that, contrary to what is observed with x rays, in the action of fast electrons the time factor

plays a notable part even in the dose-efficiency range 300 to 1800 r/min. This difference is perhaps due to a much less dense ionization in the case of electrons, permitting a partial recovery of the tissue elements if sufficient time intervals between individual hits are given; this recovery effect cannot occur amid the dense ionizations produced by x rays. However, the possible role of the highly fractionated radiation from the betatron also should be taken into account. These results show that, in view of the danger to the skin, fast electrons must be used only in low dose efficiencies. (NSA)

381

Lampe, Isadore and F. J. Hodges. **DIFFERENTIAL TISSUE RESPONSE TO NEUTRON AND ROENTGEN RADIATIONS.** *Radiology* **41**, 344-9(1943).

In 1927, Ferroux and Regaud demonstrated that it is impossible to produce permanent sterilization of the rabbits testis with a single dose of γ rays without severely damaging the scrotal skin. These experiments were repeated by the authors with X-rays and compared with the action of neutrons. The results of the French authors were confirmed. Doses of more than 2,100 r were necessary to produce complete aspermatogenesis and these doses produced at the same time non-healing reactions of the scrotal skin. The neutron irradiation was carried out by using the collimated beam method as described by Aebersold (*Physic. Rev.* **56**: 714, 1939). Measurements were made in arbitrary n units (1 n is the amount of fast neutron radiation necessary to discharge the Victoreen instrument to the same extent, as does 1 r of X-rays). Twenty animals were treated with doses ranging from 356-800 n. With doses of 700 n or more the reaction was that of complete aspermatogenesis and severe cutaneous damage. In the range 513-650 n there was complete aspermatogenesis without permanent skin damage in about half the cases. Although the difference in selective tissue effect between neutrons and X-rays may be slight, the direction of that difference indicates that neutron radiation may hold an advantage over roentgen radiation in the treatment of human neoplasms. (BA)

382

Lawrence, J. H., P. C. Aebersold, and E. O. Lawrence. **THE COMPARATIVE EFFECTS OF NEUTRONS AND X-RAYS ON NORMAL AND NEOPLASTIC TISSUE.** *Occas. Publ. Am. Assoc. Adv. Sci.* **4**, (Suppl. Science 85): 215-19 (1937); *Proc. Natl. Acad. Sci. U. S.* **22** (9), 543-57(1936).

In a previous paper the marked destructive effects of neutrons on the white blood cells of white rats was demonstrated. In this present work whole mice were irradiated with various doses of 200 kv X-rays and neutrons. Qualitatively, the lethal effects of neutrons were similar to those of X-rays, causing destruction of hemopoietic and lymphoid tissues, and of the epithelium of the small intestine, also Sarcoma 80 was irradiated *in vitro* with various doses of 200 kv X-rays and neutrons; neutrons are definitely destructive to this neoplastic tissue. The possibility of an increased differential effect is suggested. (BA)

383

Lawrence, John H, and Robert Tennant. **COMPARATIVE EFFECTS OF NEUTRONS AND X-RAYS ON THE WHOLE BODY.** *J. Exptl. Med.* **66**, 667-87(1937).

Irradiation of the whole bodies of mice with neutron rays in sufficient quantities leads to a clinical, bacteriological and anatomical picture similar to that following roentgen irradiation. Aside from any possible delayed effects upon exposure to small doses over a long period of time, concerning which there is no information, these changes after relatively large doses make it imperative that workers in laboratories generating neutrons protect themselves from exposure by screening. For the same amount of ionization

measured by a small bakelite-walled thimble chamber, neutrons are more biologically destructive than X-rays. The average daily dose to those working with neutrons should not exceed 0.25 of the tolerated dose accepted for X-rays. Also if neutrons are tried therapeutically normal tissue must be protected from undue irradiation. (CA)

384

Lea, D. E. **THE SPATIAL DISTRIBUTION OF IONIZATION IN IRRADIATED TISSUE, AND ITS RELATION TO BIOLOGICAL EFFECTS.** *Brit. J. Radiol.* **16**, 338-9 (1943).

In producing breaks in chromosomes, neutrons are much more effective per ionizing particle than medium wavelength X-rays. The author explains this by the fact that the ionization path of the proton ejected by the neutron is much more dense than that of the electron ejected by the X-ray, except very near the end of the electron path. It is assumed that only the dense and part can produce the chromosome break. The relation between length of dense part of path and X-ray wave length is used to predict relative biological effects for these wave lengths. Experiments confirm the theory. (BA)

385

Marshak, A. **CHROMOSOME ABNORMALITIES PRODUCED IN INTERPHASE NUCLEI WITH X-RAYS AND NEUTRONS.** *Genetics* **26**, 161(1941).

Previous experiments showed the frequency of chromosome abnormalities observed in anaphase at three hours after treatment with x-rays or neutrons to be an exponential function of the dose. Abnormalities observed in *V. faba* root tips at 12 and at 24 hours after neutron bombardment likewise vary exponentially with dose. The slopes of the curves for the 3, 12 and 24 hour intervals are 0.070, .051, .036, respectively. The slope for the *Vicia* x-ray curve at 24 hours is .0025. The ratio of the neutron to x-ray slopes (n/x) at 24 hours is 14.3 as compared with the comparable ratio of 6.6 at 3 hours. Thus chromosomes of the same organism at different stages of the nuclear cycle give different n/x although a constant ratio has been obtained with chromosomes of very different species at the same stage of the nuclear cycle. *Pisum* and *Allium* also give exponential curves at 24 hours, but data are not yet sufficient for obtaining n/x. However the ratio of about 16 obtained by GILES for chromatid dicentric in *Tradescantia* microspores is sufficiently close to the 14.3 for *Vicia* to suggest that a constancy comparable to the one observed for abnormalities induced at the onset of prophase may be found for similar parts of the interphase in different species. (RG)

386

Mateyko, G. M., A. Edelmann, H. A. Charipper, and A. S. Gordon. **EFFECTS OF DIRECT CATHODE RAY PARTICLE IRRADIATION OF THE HYPOPHYSIS AND WHOLE BODY X-IRRADIATION ON THE ADRENOCORTICOTROPHIN, GONADOTROPHINS, AND THYROTROPHIN OF THE PITUITARY GLAND OF THE RAT.** *Am. J. Physiol.* **167**, 808-9(1951) (AECU-1513)

Cathode ray particle irradiation (I- Van de Graaff; $2.23 \times 10^{-3} \mu$ a sec) confined to the volume of the pituitary gland, or whole body x-irradiation (II- 250 kvp, 30 ma, 0.25 mm Cu, 1.0 mm Al; 1,000 r) was given to rats and the adrenocorticotrophic, gonadotrophic, and thyrotrophic titers of the hypophyses were determined by bioassays at 1, 6, and 24 hr after exposure. Following I, the adrenocorticotrophin was elevated at 1 hr and remained at high levels 6 and 24 hr post irradiation. Following II, there was a similar rise at 1 hr, the level starting to fall by 6 hr, and declining to subnormal values within 24 hr. In both groups the gonadotrophins had fallen by 1 hr and remained at subnormal titers

throughout the 24 hr period. Following I, the level of thyrotrophin was elevated at 1 and 6 hr, and fell below normal in 24 hr. A similar, but less marked response, was observed after II. The data suggest that the noxious stimuli of radiation cause an acceleration of adrenocorticotrophic synthesis initially at the expense of the gonadotrophins, and ultimately, of the thyrotrophin. A response was obtained on animals receiving whole body x-irradiation but with their heads shielded. This might indicate an "indirect" effect on the pituitary as contrasted to "direct" effects as seen after I. (NSA)

387

Mottram, J. C. and L. H. Gray. RESPONSE OF THE SKIN OF MICE TO X-RADIATION AND GAMMA RADIATION. *Brit. J. Radiol.* 13, 31-34(1940).

Skin of the tails of inbred mice was exposed to X-rays (2,500-7,000 r) and to γ -rays (4,000 to 8,000 r). It was found that a larger dose is required to induce skin reaction by γ -radiation than by X-rays. The ratio of effectiveness is 1:3 for erythema and desquamation, and 1:6 for epilation and exudation. The difference may be partly attributed to the different absorption of photo-electrons by X- and γ -rays, otherwise it remains unexplained. (EM)

388

Paul, Wolfgang and Gerhard Schubert. PHYSICAL AND BIOLOGICAL PHENOMENA PRODUCED BY IRRADIATIONS WITH FAST ELECTRONS. *Naturwissenschaften* 37, 156-63(1950).

A systematic comparative study of the action of hard x rays (200 kv) and of fast electrons (from a 6-Mev betatron) is being made at the authors' laboratory in Göttingen, Germany. In a general survey of the work done, quantitative differences in the absorption of the two radiations by matter, specific qualitative aspects of their biological action, and the present-day outlook for therapeutic application of fast electrons are examined. 11 figures. (NSA)

389

Paul, Wolfgang and Gerhard Schubert. BIOLOGICAL ACTION OF FAST ELECTRONS FROM A 6-MEV BETA-TRON. *Z. Naturforsch.* 5b, 390-4(1950).

The action of fast electrons (up to 6 Mev) on various biological objects was compared with that of hard x rays (200 kv). In the majority of cases observed (growth inhibition in barley sprouts, mitosis-frequency changes in root-end cells of barley and horse beans, killing of *Drosophila* eggs and pupae) the effect per dose unit is smaller when produced by electrons. On the other hand, no difference is observed in the radiation-induced development of lethal factors in mature or immature male cells of *Drosophila* or in the simpler forms of chromosome breakings produced by radiations in the same insect. Only in the case of the killing of *Bacterium coli* do electrons show the greater effect per unit dose. These results can be interpreted in the light of the "hit" theory. (NSA)

390

Prosser, C. Ladd and Marguerite N. Swift. AN INTER-SPECIES COMPARISON OF THE RADIOTOXICITIES OF X RAY, Sr^{90} , AND Pu^{239} . University of Chicago Metallurgical Lab. June 1949. Decl. Apr. 18, 1950. 10p. (AECD-2828)

The 30-day LD_{50} for Sr^{90} on the basis of injected dose decreases with increasing animal size as shown by 7.8 $\mu\text{c/g}$ for the mouse, through rat and rabbit, to 0.8 $\mu\text{c/g}$ for the dog, and then increases to 1.3 $\mu\text{c/g}$ for the goat. The series is similar when computed on the basis of the dose retained at time of death. Radiation lost outside the body is greater in small than in large mammals, but measurements in mice show such loss to be not more than 3% of total emitted radiation from Sr^{90} . The radiation sensitivity as indicated

by LD_{50} for x-rays follows a different order from Sr^{90} sensitivity, the LD_{50} being highest in the rabbit, least in the dog, and intermediate in the mouse and rat. Calculation of Sr^{90} LD_{50} on the basis of skeletal weight increases the species differences. When the 30-day LD_{50} of Sr^{90} is corrected for retention and relative radiosensitivity (using the radiosensitivity of the mouse as a unit), the following series is obtained in $\mu\text{c/g}$: mouse 3.5, rat 2.48, rabbit 0.57, dog 0.57, and goat 0.98. By extrapolation from this series, the 30-day LD_{50} of Sr^{90} for man would be between 1.0 and 1.5 $\mu\text{c/g}$. The strontium is deposited in bone and has a range (50% of the β rays absorbed) of 0.72 mm in soft tissue. The species differences in LD_{50} are interpreted on the assumption that some volume of marrow needs to be irradiated to cause death. The species series for Pu^{239} , the particles of which have a range of only about 40 μ in soft tissue, shows little variation in toxicity with size. The 30-day LD_{50} on the basis of retained dose in $\mu\text{c/g}$ and corrected for relative radiosensitivity is: mouse 0.0412, rat 0.0399, and dog 0.0375. If the relative radiosensitivity is known, it is possible to extrapolate from one species to another for α -particle dosage, but not for lethal β -particle dosage. (NSA)

391

Sacher, George A. and N. Pearlman. COMPARATIVE ACTION OF CYCLOTRON NEUTRONS AND X-RAYS. PART III. STATISTICAL ANALYSIS OF BLOOD DATA. University of Chicago Metallurgical Lab. June 1946. Decl. Sept. 16, 1947. 29p. (MDDC-1337)

The heterophil and lymphocyte counts of 67 rabbits exposed to fast neutrons, and those of 123 rabbits exposed to 200 kv X-rays, were analyzed. Distributions of counts were normalized in conversion to logarithms. Responses of both blood systems to the two types of radiation were qualitatively similar. The ratio of X-ray and neutron doses for equal effect on heterophil counts was determined by regressions between X-ray and neutron responses at like times after exposure, for various pairs of X-ray and neutron doses. The average of 29 estimates for X/n using this method, with its standard error, is 6.3 ± 0.10 . The above method could not be used in the case of lymphocytes, but an alternative method gives 6.20 as the value for X/n. The authors conclude that the heterophils and lymphocytes do not differ significantly in the X/n ratios, and that the numerical value of the ratio may be taken to be $X/n = 6.3 \pm 0.10$. (ADD)

392

Schaefer, Hermann J. FURTHER EVALUATION OF PRESENT DAY KNOWLEDGE OF COSMIC RADIATION IN TERMS OF THE HAZARD TO HEALTH. Naval School of Aviation Medicine, Pensacola. Aug. 15, 1951. 23p. (NP-3564; U19329)

Data pertaining mainly to the heavy-nuclei component of the primary cosmic radiation and appearing in the literature between Jan. and Dec. 1950 are summarized. There are evidences that about 20% of the incoming primaries are atom nuclei of an atomic no. >1 . Changes in the energy spectrum resulting from the geomagnetic fields at different latitudes are not accompanied by changes in the shape of the mass spectrum. The cut-off mechanism of the geomagnetic field which sets the lower limit of the energy spectrum of the primaries in dependence on the latitudes is discussed. The ionization peak and thin-down phenomena appear to be limited to the polar cap (geomagnetic latitudes of 55° and higher). The values of the specific ionization for the different components of the heavy spectrum cover a range from about 1000 ion pairs per 10 μ of living tissue to more than 1,000,000. The conversion factor for natural α rays (25,000 ion pairs per 10 μ) is 10; that for fission products (2.8 million ion pairs per 10 μ) is 27. Although no accurate interpolation for the different components of the

heavy spectrum can be made, a first approximation seems possible on the assumption of a general conversion factor of 10. The exposure of humans to the primary cosmic radiation at extreme altitude is compared to the corresponding exposures from incorporated radioactive substances. A 15-hr daily exposure continued over weeks and months is expected to produce marked symptoms of radiation injury. A daily exposure of 1.3 hr is estimated to be about equal to the official tolerance limit of 0.1 r in the system. (NRS abst.) (NSA)

393

Schmidt, John W. and E. F. Frolik. **COMPARATIVE EFFECTS OF THERMAL NEUTRON IRRADIATION OF MAIZE POLLEN AND MAIZE SEED ON SUBSEQUENT SEEDLING GROWTH.** *J. Heredity* 42, 173-7(1951).

On the basis of x-ray comparisons, thermal neutrons were ~6 to 12 times as effective on maize seed as on maize pollen in reducing subsequent seedling height. Even if allowance is made for the greater amount of ionization produced in seed than in pollen by equal doses of thermal neutrons, there is still a large difference in the efficiency of these particles on the two plant parts (on the basis of x-ray comparisons). It is, therefore, suggested that ionization alone may not account for all of the biological effects of thermal neutrons and that transmutation of N to C and, or B to Li may also contribute to the biological effects. The susceptibility of maize pollen and maize seed to thermal neutrons was determined through the effects on the subsequent seedling development. (NSA)

394

Schubert, Gerhard. **EFFECTS OF FAST ELECTRONS OF A 6 MEV-BETATRON ON BIOLOGICAL SUBJECTS,** p.164 of **INTERNATIONAL CONGRESS OF RADIOLOGY, 6th Congress, London, 1950.**

The influence of fast electrons on biological substances has been analysed by using the Göttingen-betatron of 6 MeV (Siemens-Reiniger-Werke, Erlangen). Physically equal doses of fast electrons (2 to 6 MeV and X-rays (200 kV.) cause different quantitative effects in biological tissue. The reactions in most instances show a less effect with fast electrons per dose-unit than with X-rays. With some types of biological response the same effect follows each kind of radiation, occasionally fast electrons are more efficient than X-rays. The results obtained with *bact. coli*, *Hordeum*, *Vicia faba*, *Drosophila melanogaster*, *Salamandra maculosa*, chick fibroblasts (heart), rat erythroblasts and Ehrlich's carcinoma are summarized and the mode of action of radiation discussed. The observed quantitative differences between the action of fast electrons and X-rays can be explained by variations in specific ionisation and ion cluster formation. The consequences are considered theoretically in terms of "concentration", "saturation" and "accumulation", and the observed qualitative differences of action between the two kinds of radiation explained on this basis. Differences between the biological effect of fast electrons and high energy X-rays (quantum-energy 2-6 MeV.) are, on this theory, not to be expected.

395

Scott, K. G. **A COMPARISON OF TWO LEVELS OF ROENTGEN AND NEUTRON IRRADIATION ON NORMAL AND LYMPHOMATOUS MICE, USING RADIOPHOSPHORUS AS AN INDICATOR OF CELLULAR ACTIVITY.** *Radiology* 46, 173-5(1946).

Neutron and roentgen rays depress the phosphorus uptake of lymphomatous tissue in mice as measured by radiophosphorus. By the use of this technique another method is available for the study of the effects of various radiations on normal and neoplastic tissues. (BA)

396

Stapleton, G. E. and R. E. Zirkle. **COMPARATIVE EFFECTIVENESS AND ADDITIVITY OF FISSION NEUTRONS GAMMA RAYS, AND BETA RAYS ON DROSOPHILA EGGS.** Clinton Labs. Feb. 1946. 31p. (MDDC-584)

Some investigations have been made to ascertain the similarity of the mechanism of action of radiations which are different in their specific ionization. A suggested approach was to determine if the energies absorbed from the different types of radiation are additive in their lethal effects on biological objects. In an attempt to determine the additivity of ionizing radiations various dose combinations of fast neutrons, gamma rays and beta rays were administered to *Drosophila* eggs. These test objects were chosen because their dimensions are such that they tend to absorb these three radiations uniformly throughout their volume. Although the three radiations were found to vary in their biological effectiveness, per unit energy absorbed, all three were shown to be completely additive in their lethal effect on these organisms. (ADD)

397

Stone, Robert S. **NEUTRON THERAPY AND SPECIFIC IONIZATION.** *Am. J. Roentgenol. Radium Therapy* 59, 771-85(1948).

Neutrons generated by 16 mev and roentgen rays generated by 220 kv show that 1 n (neutron unit) equals 2.5 rep (roentgen equivalent physical). Gross and microscopic studies of mammalian tissues show little or no qualitative difference in the reactions produced by neutron and roentgen ray radiations. Judging by the amount of energy absorbed from the beam in producing a given reaction, the relative biological effectiveness of different radiations vary greatly from 1 test object to another, and from 1 reaction to another in the same tissue. The relative biological effectiveness of radiations on mammalian tissue increased as the specific ionization increased. Neutrons were more effective than roentgen rays per unit of energy absorbed by tissue. The relative biologic effectiveness of neutrons is greater compared to roentgen rays for its late effects rather than early effects. This latter is very important in considering biological effects in treatment of human patients, as the late effects with certain radiations are considerably more marked as compared with X-radiation than the early effects would lead one to expect. (BA)

398

Tobias, C. A., H. O. Hoanger, and J. H. Lawrence. **RADIOLOGICAL USE OF FAST PROTON, DEUTERON, AND ALPHA PARTICLE BEAMS,** p.51-2 of **INTERNATIONAL CONGRESS OF RADIOLOGY, 6th Congress, London, 1950.**

A number of radiological experiments were performed using the Berkeley 184" cyclotron built by E. O. Lawrence and his associates. The 190 MeV deuterons may be brought out into air as a stream of well collimated parallel particles of homogeneous energy. The particles have a well-defined range, approximately 15 cm. in soft tissue and 19.1 g/cm² in Al. Corresponding to their Bragg ionization curve, the peak ionization in tissue is reached about .7 cm. before the end of the range and has about four times the ionization at the point of entry. This beam is thus suitable for selective irradiation of deep lying tissues without overdosing the skin. Using multiple port irradiation the depth dose may be made thirty times the skin dose. Isodose curves will be presented. The 50 per cent lethal dose of high energy deuteron rays on mice is the same as that of 200 kV X-rays, if delivered at the same dose-rate. The 25 per cent of strong mammary carcinoma tumours in "A" mice regressed completely when the beam was directed to the tumours through the body of the mice. All unirradiated tumour controls died. The spe-

cific effect of different energy portions of the deuteron beam was tested using mice and skin effects as criteria. In experiments carried out in association with V; bond a narrow deuteron beam was passed through different body regions of white rats and the acute lethal effect in function of the dosage was measured. In association with R. E. Zirkle experiments were made to study the mechanism of radiation effect on micro-organisms as a function of specific ionization.

399

Wachsmann, F. DIFFERENCES IN THE BIOLOGICAL ACTION OF ORDINARY AND ULTRA-HARD RADIATIONS. *Strahlentherapie* 81, 273-80(1950).

The biological effects of the new radiations furnished by the betatron (ultra-hard x-rays and fast electrons) must differ from those produced by ordinary x-rays, owing both to the more favorable dose distribution in space and to the lower ionization density of the new rays. Furthermore, the differences in the biological action are not just quantitative. Since the ratio of the responses to irradiations of both kinds of rays varies with different irradiated objects, it is permissible to expect a certain "selectivity." A few examples from the author's studies illustrate the point. It can be concluded from the shape of the survival curves of irradiated tadpoles that the biological structures attacked are not the same for the two kinds of radiation. Again, the different ways in which the reticulocyte rate in mice is affected by the radiations point to differences in the mechanism of attack. Finally, tumors inoculated in mice and rats, when treated with 5-Mev electrons, show more satisfactory regression pictures and less deterioration of healthy tissues than in the case of a 200-kv x-ray treatment. (NSA)

400

Zirkle, Raymond E. THE RADIOBIOLOGICAL IMPORTANCE OF THE ENERGY DISTRIBUTION ALONG IONIZATION TRACKS. *J. Cellular Comp. Physiol.* 16, 221-35 (1940).

The role of the linear energy absorption along the tracks of ionizing particles was investigated by irradiating 3 species of small cells. Different values of linear energy absorption E_L were investigated by using various linear portions of α particle tracks, and by comparing the action of X-rays (low E_L) to that of α rays (high E_L). On *Aspergillus* spores the effectiveness of the radiation per unit dose (energy absorbed per cubic micron) increased sharply as the linear energy absorption increased. On vegetative cells of *Saccharomyces cerevisiae* the effectiveness increased only slightly with increase in E_L . Accordingly the radiobiological influence of the linear energy absorption depends both in magnitude and in algebraic sign upon the species of cell irradiated. (BA)

401

Zirkle, R. E. THE RADIOBIOLOGICAL IMPORTANCE OF SPECIFIC IONIZATION. [University of Chicago] Metallurgical Lab. [nd] Decl. Oct. 9, 1946. 30p. (MDDC-444; CH-946)

It is shown that, in the production of injurious effects in both the higher plants and the higher animals, the amount of injury produced per unit of absorbed energy increases with the specific ionization of the radiation. In particular, the injurious action of fast neutrons is greater than that of X-rays or gamma rays by factors ranging up to 20, and the effectiveness ratios are calculated in such a way as to make them conservatively low. Although most of the effects on mammalian tissues show effectiveness ratios ranging from 2 to 3.5, it must be pointed out that to date comparatively few neutron investigations have been carried out on mammalian tissues *in vivo*. It is shown that different effects on

the same biological object may exhibit considerably different effectiveness ratios, therefore a distinct possibility exists that further observation will disclose important injurious effects on mammals which have neutron/X-ray effectiveness ratios ranging up to 10. From the protection standpoint, only one such biological effect, though at present unknown, is a threat. Until extensive and numerous investigations allay this threat by failure to reveal injurious effects extremely sensitive to specific ionization, special precautions seem to be indicated when setting tolerance doses in situations where fast neutrons constitute a sizeable fraction of the total radiation present. These considerations are especially pertinent in case X-ray thimble chambers are used in measuring the total radiation. If uncorrected Victoreen measurements are used in comparing the effectiveness of fast neutrons and X-rays, the apparent effectiveness ratios for the known injurious effects on mammalian tissues range up to more than eight. Carbon-walled chambers are even more misleading. (ADD)

402

Zirkle, Raymond E. RADIOBIOLOGICAL ADDITIVITY OF VARIOUS IONIZING RADIATIONS. *Am. J. Roentgenol. Radium Therapy* 63, 170-5(1950).

A discussion is presented on the problem of additivity of various types of ionizing radiations. A summary is included which outlines the degree of additivity found in various experiments by the author and others through combinations of α , β , γ , fast-neutron and X-rays on the mouse, bean roots, *Drosophila* eggs, *Drosophila* pupae and the human skin. It is concluded from the analysis of these studies that incomplete additivity of two types of radiation indicates some difference in the mechanism of action of the radiations. Complete additivity indicates that the mechanisms of action of the radiations are identical in their most essential feature, the promotion of the same determinative events (one of a succession of unknown relevant events leading to the production of the known biological effect) but are not necessarily alike otherwise. It is concluded that it is probably wise to assume that additivity of fast neutrons and γ rays is the complete type. (NSA)

403

Zirkle, R. E. and P. C. Aebersold. RELATIVE EFFECTIVENESS OF X-RAYS AND FAST NEUTRONS IN RETARDING GROWTH. *Proc. Natl. Acad. Sci. U. S.* 22, 134-8(1936).

Since the biological effectiveness per ion increases markedly with closer spacing in the paths, it seems reasonable to expect that a given number of ions produced by neutrons would be considerably more effective than the same number produced by X-rays. This expectation has been realized in both these experiments (on wheat seedlings) and in the experiments by Lawrence and Lawrence on the rat (*Proc. Nat. Acad. Sci.*, 22: 124(1936)). The authors used wheat seedlings for their experiments, handling them in a manner similar to that described by Failla and Henshaw (*Radiology*, 17: 1-43, (1931)). (S. V. S.)

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This abstract has been intentionally omitted.

405

Zirkle, R.E., P. C. Aebersold, and Everett R. Dempster. THE RELATIVE EFFECTIVENESS OF FAST NEUTRONS AND X-RAYS UPON DIFFERENT ORGANISMS. *Am. J. Cancer* 29, 556-62(1937).

The relative effectiveness of fast neutrons and X-rays, per unit of ionization, was determined for *Drosophila* eggs, wheat seedlings, and fern spores. The neutron-X-ray ratios of effectiveness were, respectively, 2.1, 5, and 2.5. Therefore, the relative susceptibility of various types of cells to

neutrons may differ greatly from their relative susceptibility to X-rays. (BA)

406

Zirkle, R. E. and I. Lampe. DIFFERENCES IN THE RELATIVE ACTION OF NEUTRONS AND ROENTGEN RAYS ON CLOSELY RELATED TISSUES. *Am. J. Roentgenol. Radium Therapy* 39, 613-27(1938).

The authors compared the actions of neutron rays (from the University of Michigan cyclotron) and 200 kv x-rays on the roots and shoots of wheat seedlings, and on three age groups of *Drosophila* eggs. It is impossible to measure the two radiations in terms of the same unit, or to compare them directly. The relative effects of the two on any one tissue were expressed by an X, N ratio, where X denotes the number of roentgens of X-rays producing a given effect, and N the number of arbitrary neutron units producing the same effect. If the X/N ratios for any two tissues were not equal, then the relative action of the two radiations was different for those two tissues. For *Drosophila* eggs of average age 1-1/2, 4, and 6 hours, the ratios were respectively, 2, 3.2, and 2.8. For wheat seedlings the root ratio varied from 6.2 to 11.8, while that for the shoot varied from 5.9 to 9, the former being always greater than the latter in any single experiment. The authors conclude that the relative action of neutrons on closely related tissues is different from that of X-rays. (BA)

407

Zirkle, Raymond E., Dorothy F. Marchbank, and Katherine D. Kuck. EXPONENTIAL AND SIGMOID SURVIVAL CURVES RESULTING FROM ALPHA AND X IRRADIATION OF ASPERGILLUS SPORES. Univ. of Chicago and Argonne National Lab. Mar. 1951. 14p. (ANL-4610)

After samples of air-dry spores of *Aspergillus terreus* had been given graded doses of polonium α particles and of 200-kv x rays, survival fractions were determined, the criterion of a surviving spore being the formation of a germ tube. When survival fraction was plotted against dose, the α -ray curves were exponential, but the x-ray curves were sigmoid, and the experimental points could be fitted fairly well by "two-hit" theoretical curves. It is concluded that, in this particular radiobiological action, the number of entities which must be altered in each cell is quite small, and that, whereas all of them (one or more) are altered by one suitably located α track, two (possibly more) electron tracks are required to produce the same alteration (s). The results also indicate that the decisive events of the radiobiological action occur very early, i.e., before each relevant ionization track loses its original configuration by diffusion of the initially activated molecules or their chemical derivatives. (NSA)

408

Zirkle, Raymond E. and Mary Ellen Parrish. COMPARATIVE LETHAL ACTION OF X RAYS AND CYCLOTRON NEUTRONS ON DROSOPHILA EGGS. Univ. of Chicago Metallurgical Lab. Dec. 1950. 6p. (CH-3904)

The x rays were generated at 200 kv and 5 ma and were filtered by 0.5 mm of Cu and 1 mm of Al. The target-to-object distance was adjusted to give a dose rate of about 10 r/min. The fast neutrons were generated by 8-Mev deuterons impinging on a Be probe in the University of Chicago cyclotron. The eggs were exposed in a lead-walled chamber which was so constructed that radiation directly from the probe was filtered through 4 in. of Pb, while scattered radiation from other directions was filtered through at least 2 in. Various lots of eggs were given graded doses of x rays, of fast neutrons, and of mixed neutrons and γ radiation. The LD₅₀ of x rays is 170 r, that of fast neutrons is 31 n, and that of the mixed cyclotron emission is 43 Victoreen scale units. Accordingly the x/n dosage ratio is 170/31 or

5.5, whereas the apparent x/n ratio, from data obtained when γ rays were present, is 170/43 or 4.0. (NSA)

409

Zirkle, R. E., J. R. Raper, E. F. Riley, and G. E. Stapleton. ADDITIVITY OF FAST NEUTRONS AND GAMMA RAYS IN THEIR ACUTE LETHAL ACTION ON MICE. Clinton Labs. June 5, 1945. Decl. Sept. 17, 1948. 19p. (AECD-2328; CH-2571)

By exposing various groups of mice to graded doses, the median lethal dose (LD-50) of each of the following radiations was determined: (a) fast neutrons from the Clinton pile; (b) Radiation G, consisting of gamma rays contaminated with fast neutrons; (c) Radiation M, a mixture of fast neutrons and Radiation G. The LD-50 of Radiation M was found to consist of 0.52 times the LD-50 of fast neutrons plus 0.55 times the LD-50 of Radiation G. Theoretically, the sum of these two fractions should be unity if fast neutrons and Radiation G are radiobiologically additive. Since the experimental deviation from unity (7%) is within the error of the measurements, it is concluded that complete additivity of these two radiations has been demonstrated. It is assumed that this conclusion concerning additivity of fast neutrons and Radiation G may be extended to additivity of fast neutrons and pure gamma rays. The LD-50 of fast neutrons, directly determined, was 91 n. The LD-50 of pure gamma rays, indirectly determined from the experimental data, was 812 r. In another experiment, performed later for a different purpose, a corresponding value of 840 r was obtained. (NSA)

Pathology

410

Barrow, Jack and John L. Tullis. THE SEQUENCE OF CELLULAR RESPONSE TO INJURY IN MICE EXPOSED TO 1100 r TOTAL BODY X-RADIATION. Naval Medical Research Inst. July 6, 1949. 23p. (NP-1411; NM-007-039)

Following a single lethal dose (100% in approximately 96 hours) of 1100 r total body x-radiation, 880 mice were killed 10 at a time at hourly intervals. Microscopic observations of spleen, mesenteric lymph nodes, bone marrow, intestines, and testis were made to determine the sequence of cellular response to the injury. Fragmentation and lysis of lymphoid elements were well established one hour after exposure. The extent and rapidity of progression of destruction were of equal intensity in the lymphoid elements in the spleen mesenteric lymph nodes, and lymphoid aggregations in the intestinal wall. The erythropoietic elements also were almost as radiosensitive as the lymphoid tissues. Slightly less radiosensitive were the myelopoietic and megakaryocytic elements in that order. The reticulo-endothelial cells remained morphologically intact. In the testis the spermatogonia disappeared by 66 hours, but the spermatocytes and particularly the spermia and Sertoli cells were more radioresistant. The crypt epithelium of the small intestine and to a lesser extent the basal portions of the glands of the large intestine were damaged early, but repair of these organs was accomplished by the 85th hour. (NSA)

411

Bigelow, R. R., J. Furth, M. C. Woods, and R. H. Storey. ENDOTHELIAL DAMAGE BY X-RAYS DISCLOSED BY LYMPH FISTULA STUDIES. *Proc. Soc. Exptl. Biol. Med.* 76, 734-6(1951).

The degree of capillary permeability was assayed in dogs and rats by studying the appearance of components of the blood in the lymph. Marked capillary permeability was indicated in dogs and rats exposed to approximately LD₅₀

doses of x rays by the appearance of large numbers of erythrocytes in the lymph. The data indicate that the reduced red-cell counts after irradiation are due to the flooding of the lymph compartments and tissue spaces by erythrocytes. The massive erythrophagocytosis and hemosiderosis in sinuses of lymph nodes, if irradiated hosts, indicate that many of the erythrocytes leaving the blood capillaries are destroyed. Loss of erythrocytes caused by capillary damage and death of aging erythrocytes with inhibition of erythropoiesis are the main causes of radiation anemia. (NSA)

412

Borak, J. RADIATION EFFECTS ON BLOOD VESSELS. *Radiology* 38, 481-92, 607-17, 718-27(1942).

This review considers various effects of radiations and their relation to blood vessels. The discussion is centered around the author's own theory that the observations on capillaries are to be explained as direct effects of the radiation on the epithelial cells. The material discussed is divided in three parts: Part I deals with skin erythema and edema. In Part II, inflammation produced by irradiation, degeneration, suppression of growth capacity of the capillaries, retrogression of blood vessels and radionecrosis are discussed. Part III deals with the etiology of telangiectasis and the effects on lymph vessels. (BA)

413

Campbell, Berry, Stanley C. Peterson, and Rosalind Novick. EARLY CHANGES INDUCED IN PURKINJE CELLS OF RABBIT BY SINGLE MASSIVE DOSES OF ROENTGEN RAYS. *Proc. Soc. Exptl. Biol. Med.* 61, 353-5 (1946).

Immediate and severe changes were seen in Purkinje cells of cerebellum immediately after exposure to doses of 1000-4000 r. Chromatolysis, vacuolization, and the appearance of a clear marginal zone were seen immediately following irradiation. These changes were transient and were replaced in 24 hours by pyknosis and neuronophagia. (BA)

414

Carter, Robert E. SPLENIC CHANGES IN CF1 FEMALE MICE OVER A FORTY-ONE DAY PERIOD POST X-IRRADIATION. Los Alamos Scientific Lab. [nd] 9p. (AECU-709)

This study was undertaken to determine if, at any time in the immediate post exposure period, weight changes in the spleen or white pulp atrophy of CF1 female mice could be related to the amount of x-irradiation the animals received. Splenic weight changes and white pulp-red pulp ratio changes over a 41-day period post irradiation are presented. Initial studies of splenic weight changes indicate that between three and eight days post irradiation the decrease in splenic weight may serve as a remarkably accurate indication of the radiation received. The changes in the pulp ratios of the spleen were not deemed of sufficient promise to warrant further investigation. Possible applications of this phenomenon to the field of radiation and biology are mentioned. (NSA)

415

Denniston, Rollin Henry, II. THE INFLUENCE OF ROENTGEN-RAY TREATMENTS OF THE HYPOPHYSIS ON REPRODUCTION SYSTEMS OF THE GROUND SQUIRREL AND RAT. *J. Exptl. Zool.* 91, 237-63(1942).

Annual-breeding ground squirrels *Citellus tridecemlineatus*, were x-rayed on the pituitary at various times during the annual cycle with doses ranging from 7 to 4000 roentgen units. Adult and immature rat pituitaries were also rayed. No evidence for a "stimulating dose" of x-ray was found in gross or cytological studies of ground squirrel tissues fol-

lowing pituitary x-radiation in the yearly quiescent phase. Gonads and pituitaries of quiescent animals proved resistant to massive x-radiation. Gonadotrophic hormone secretion of the inactive pituitary did not effect recovery or rayed testis within 40 days. Age-correlated effects follow x-radiation of rat pituitaries: 1000 r reduce the growth rate of young rats 50%; 2000 r inhibit spermatogenesis in same age animals; 6000 r are necessary to affect gametogenesis in adults. "Signet-ring castration cells" appear in these adult pituitaries at lower dose levels than those necessary to produce effects on the germ line. (BA)

416

Devik, Finn. HISTOLOGICAL AND CYTOLOGICAL CHANGES PRODUCED BY ALPHA-PARTICLES IN THE SKIN OF MICE. *Acta Radiol.* 35, 149-64(1951).

The histological and cytological changes in the skin of a hairless strain of mice following external α irradiation are described. It is found that the epidermis contains cells that are able to survive doses of the order of 100,000 r. The effects of the α rays, which mainly are localized in the epidermis, have been compared to the effects caused by roentgen rays in the skin. This comparison stresses the great importance of the indirect effects brought about by the stroma-vascular bed, when the latter also is irradiated. 18 references. (NSA)

417

Ellinger, F. RESPONSE OF THE LIVER TO IRRADIATION. *Radiology* 44, 241-54(1945).

The author discusses the response of the liver to irradiation. It is considered that the liver cells are radiosensitive, but are less so than those of the spleen. An attempt is made to analyze the experimental results of liver irradiation in various animals. Morphological changes are difficult to assess because of the rapid recuperative capacity of liver cells. All animal species show a decrease in glycogen and an increase in sudanophil fat content, the former occurring early after exposure, the latter usually appearing at a later date. (BEMP)

418

Engelstad, R. B. and O. Torgersen. EXPERIMENTAL INVESTIGATIONS ON THE EFFECTS OF ROENTGEN RAYS ON THE SUPRARENAL GLANDS IN RABBITS. *Acta Radiol.* 18, 671-87(1937).

The authors have examined the suprarenal glands of 41 rabbits four hours to six months after roentgen radiation with doses of 2,200 r-2,500 r administered in one session, and of 17 normal control animals. These doses produce marked degeneration in the cortex, hyperaemia and in some cases inflammatory infiltration. The radio-sensitivity of the suprarenal glands shows a very good accord with the skin tolerance in rabbits. The degeneration is most constant and most pronounced in the zona fasciculata and zona reticularis. In the medullary substance no sure degeneration is proved. The reaction curve shows an initial hyperaemia beginning within the first 10 hours after the radiation and receding during the course of the first 2-3 days. A pronounced degeneration (the main reaction) is first found on the sixth day after the radiation; it is accompanied by hyperaemia and, in a number of cases, slight lymphocytic infiltration. The changes seem to be greatest and most constant three months after the radiation, but also six months after a clear degeneration can be seen. The lipid distribution seems to be very irregular in the irradiated suprarenal glands. (auth)

419

English, James A. and John L. Tullis. ORAL MANIFESTATIONS OF IONIZING RADIATION. PART I. ORAL LESIONS AND EFFECT ON DEVELOPING TEETH OF SWINE EX-

POSED TO 2000 KV TOTAL BODY X-RADIATION. Naval Medical Research Inst. Bethesda. Dec. 29, 1950. 10p. (NP-3162; U17518; NM-006-012.04.34)

Oral tissues, salivary glands and developing teeth of 41 young swine were studied grossly and histologically to observe pathologic changes resulting from X-radiation. These swine were selected from 120 animals which were exposed to 2000 kv total body X-radiation in doses of about 250 to 800 roentgens in air. Undecalcified teeth and jaws were cut in thin sections by high speed, water cooled hard rubber discs or steel circular saws. Gross changes in the oral mucosa consisted of petechial and ecchymotic hemorrhages in 49 per cent of the animals and marked ulceration in 9.8 per cent. Histologic study revealed irregular erosions of the mucosa in about 30 per cent of the animals and either petechial or massive hemorrhage around developing teeth of 70 per cent of the swine. Regional lymph nodes showed a high degree of sensitivity to X-radiation by exhibiting hemorrhage and depletion of lymphoid cells. Salivary glands were among the less sensitive tissues, with regard to morphologic change. However, a definite decrease of basic staining granules was observed in acute stages of radiation sickness, with complete recovery in 30-day survivors. A characteristic kind of hypoplasia of the enamel of developing molar teeth was observed among swine which received more than 400 r. Ameloblasts actively producing enamel matrix appeared to be sensitive to irradiation. Other portions of the teeth showed minimal effects. (auth)

420

Eschenbrenner, Allen B. **FURTHER STUDIES OF THE EFFECT OF TOTAL-BODY IRRADIATION ON THE TESTES OF MICE**, p.28-35 of **BIOLOGICAL AND MEDICAL DIVISIONS, QUARTERLY REPORT, AUGUST, SEPTEMBER, OCTOBER, 1948**. Argonne National Lab. Nov. 1, 1948. 7p. (ANL-4227(p.28-35))

Author reports the course of injury and recovery of the testes following total-body radiation, as reflected in testes weights. It is noted that the minimum weights of testes observed is dependent upon dosages-also that the time required to effect the minimum weights as well as the time required for the weights to return to normal are functions of dosage. The author also reports observations on the recovery pattern of the testes from a second acute exposure following recovery from the first. The results of microscopic examination of the testes of mice exposed to 400 r are summarized in a table. These data indicate that the decrease of testes weights following acute irradiation is primarily due to marked retardation in rate of production (multiplication of spermatogonia for a period of approximately two weeks). In previous studies (ANL-4184) it was tentatively concluded that the over-all decrease in spermatogenic elements was primarily due to retardation in the rate of multiplication of spermatogonia. The present studies support this conclusion. (S.V.S.)

421

Eschenbrenner, A. B. and E. Miller. **QUANTITATIVE HISTOLOGIC ANALYSIS OF THE EFFECT OF X-RADIATION ON THE INTERSTITIAL TISSUE OF THE TESTES OF LAF-1 MICE**. J. Natl. Cancer Inst. 6, (6) 343-8(1946).

The exposure of mice to doses of X-radiation sufficient to produce severe damage of spermatogenic elements resulted in an apparent increase of interstitial tissue. Chalkley's method for the quantitative morphologic analysis of tissues was used in a study of the testes of normal and irradiated mice. It was found that the apparent increase of interstitial tissue in the testes of irradiated mice is relative and not absolute. (BA)

422

Eschenbrenner, Allen B. and Eliza Miller. **QUANTITATIVE HISTOLOGIC ANALYSIS OF THE TESTES OF MICE FOLLOWING A SINGLE TOTAL-BODY EXPOSURE TO X RAYS**, p.42-6 of **BIOLOGICAL AND MEDICAL DIVISIONS QUARTERLY REPORT FEBRUARY, MARCH, APRIL, 1950**. Argonne National Lab. [nd] 5p. (ANL-4451(p.42-6))

Groups of LAF₁ male mice were given single total-body exposures to 400 r of radiation. Irradiated and nonirradiated mice were sacrificed and the testes were removed at weekly intervals for 12 weeks after x irradiation. Chalkley's method (J. Natl. Cancer Inst. 4, 47-53(1943)) was used for quantitative analysis of the testes and the various cellular elements were identified according to his criteria. There appeared to be no evidence of morphologic cell death even when the testes' weights were reduced to 40% of normal. The weight decrease was due to a decrease in quantity of the spermatogenic elements, the interstitial tissue and supporting stroma remaining normal in total amounts. This depopulation of spermatogenic elements was due to the radiosensitivity of the spermatogonia. The depopulation was not a result of the destruction of spermatogonia but of the inhibition of mitosis which lasted for a period ranging between 2 and 3 weeks. Mitotic activity of spermatogonia in which they reproduce their own kind is considered to be similar to mitotic activity in somatic cells. If this is true, a similar irradiation effect should be seen in other irradiated somatic cells. Studies are under way to determine this. (NSA)

423

Eschenbrenner, Allen B. and Eliza Miller. **EFFECT OF ROENTGEN RAYS ON THE TESTIS. QUANTITATIVE HISTOLOGICAL ANALYSIS FOLLOWING WHOLE-BODY EXPOSURE OF MICE**. Arch. Pathol. 50, 736-49(1950).

LAF₁ mice were exposed to 50, 100, 200, 300, and 400 r of 186-kv x rays directed to the whole body at 3 months of age. The course of damage and recovery of the testes was studied. The damage and recovery pattern can be explained on the basis of a selective effect of radiation on a single stage of spermatogenesis, the spermatogonia. The course of damage and recovery following exposure to a second dose of radiation is the same as that of damage and recovery following an initial exposure. The pattern of loss and recovery of weights of the testes of mice exposed to 10-Mev x rays is the same as that following exposure to 186-kv x rays. (NSA)

424

Eschenbrenner, Allen B., Eliza Miller, and Egon Lorenz. **QUANTITATIVE HISTOLOGIC ANALYSIS OF THE EFFECT OF CHRONIC WHOLE-BODY IRRADIATION WITH GAMMA RAYS ON THE SPERMATOGENIC ELEMENTS AND THE INTERSTITIAL TISSUE OF THE TESTES OF MICE**. J. Natl. Cancer Inst. 9, 133-47(1948).

LAF-1 male mice were exposed to 8.8 r, 4.4 r, or 1.1 r, respectively, whole-body γ -radiation given in 8 hr daily beginning at 2 months of age. Four mice on each dose level and 4 nonirradiated mice of the same age were killed at intervals of 2 months after 2 to 16 months of irradiation. Only the findings in the testes of these mice are reported. In mice exposed to 4.4 r and 8.8 r daily there was a sharp decrease of testes weights after 2 and 4 months of irradiation. Thereafter the weight curves leveled off at different values for the different dose rates. The relative amount of interstitial tissue increased in proportion to decrease of testes weights. Quantitative histologic analysis showed this relative increase was not an absolute one, the quantity of interstitial tissue per testis remaining the same as that of the testes of nonirradiated mice. Analysis of the mor-

phology of the kidneys revealed no evidence of measurable decrease of hormone output of the testes of irradiated mice. Despite marked decrease of total quantity of spermatogenic elements in the testes of irradiated mice, the proportion of these cells in different stages of spermatogenesis was normal in mice exposed to 1.1 r and 4.4 r daily for as long as 16 months. In mice exposed to 8.8 r daily, it was normal for four months, while after six or more months of irradiation, there was failure of completion of spermatogenesis, and this was associated with degeneration of Sertoli cells. Some theoretical implications of the data are discussed, and the practical value of the mouse testis as a test object in quantitative experiments on the biologic effect of radiation is indicated. (NSA)

425

Essenberg, J. M. and R. J. Karrasch. AN EXPERIMENTAL STUDY OF THE EFFECTS OF ROENTGEN RAYS ON THE GONADS OF THE SEXUALLY MATURE DOMESTIC FOWL. *Radiology* **34**, 358-65(1940).

A total of 71 animals was used, 10 of which served as controls. Initial injury to the ovarian follicle was produced by 400 r, follicular disintegration by 800 r and total destruction of the follicles by 1800 to 2200 r. Initial injury to the germinal epithelium occurred with 400 r, total destruction with 1200 r. Acclimatization to the effects of cumulative doses of X-rays was noted in both testes and ovaries of treated birds. The gonads of birds appear to be more resistant to the effects of X-rays than the gonads of mammals. (BA)

426

Fogg, Lloyd C. and Russell F. Cowing. THE CHANGES IN CELL MORPHOLOGY AND HISTOCHEMISTRY OF THE TESTIS FOLLOWING IRRADIATION AND THEIR RELATION TO OTHER INDUCED TESTICULAR CHANGES. I. QUANTITATIVE RANDOM SAMPLING OF GERMINAL CELLS AT INTERVALS FOLLOWING DIRECT IRRADIATION. *Cancer Research* **11**, 23-8(1951).

Testes of pure line C57 black mice 18-25 g were subjected to a single dose of 300 r. The effect produced on the germinal cells by x-radiation produced at 100 kvp having a half-value-layer of 2.6 mm. Al, dosage of 187 r/min in air at 20 cm. target-skin-distance was investigated. Evaluation was based on a quantitative random sampling of the germinal elements of the testis, made with respect to frequency of cell population types plotted against time after radiation. A small percentage of all germinal elements persists after a dose of 300 r. The period of least number of spermatogonia is from 5 to 7 days post-radiation, that of least frequency of spermatocytes is around 14 days; of spermatids and sperm 28 days. It takes 21 days for spermatogonia to develop into spermatozoa. The slopes of the curves in terms of time and progressive loss of each of the germinal elements are roughly the same. This suggests that each of the germinal elements are affected at the same degree but at different intervals. The period of greatest biological variation is from 10 to 28 days for each of the 4 germinal elements. A single dose of 300 r does not cause the disappearance of Sertoli cells or interstitial cells, nor is connective tissue markedly affected. (auth)

427

Fogg, Lloyd C. and Russell F. Cowing. THE CHANGES IN CELL MORPHOLOGY AND HISTOCHEMISTRY OF THE TESTIS FOLLOWING IRRADIATION AND THEIR RELATION TO OTHER INDUCED TESTICULAR CHANGES; II. COMPARISON OF EFFECTS OF DOSES OF 1,440 r AND 5,050 r WITH 300 r. *Cancer Research* **11**, 81-6(1951).

Evidence is presented to show that a dose of 1440 r does not destroy all the germinal elements at any time; there is

a sequence for radiation reaction from gonium to sperm, and there is an eventual reduction of production. In comparison to 300 r, it is indicated that a single dose of 1440 r further reduces the frequency of the appearance of the germinal cells and delays the time of recovery for spermatogonia and spermatocytes. There is also less evidence of numerical variation in the spermatogonia and spermatocytes and less marked peaks and depressions in the figures. An acute dose of 5050 r destroys all the germinal elements, but all these elements do not disappear at the same time. The gonad disappears first, followed by the spermatocytes, spermatids, and sperm. Once each of the types of germinal elements starts to disappear, the rate is approximately the same, regardless of the dose. The degree of injury is relative to the magnitude of the dose. No marked pathological changes were noted in cells or tissues other than in the true germinal cells. (NSA)

428

Frederic, J. HISTOLOGICAL AND HISTOCHEMICAL STUDIES OF THE SKIN OF GUINEA PIGS TREATED WITH X-RAYS. *Compt. rend. soc. biol.* **142**, 850-3(1948).

Eleven guinea pigs received radiation of 3,000 r, filtered through 1 mm Al, and 10 others received 1,500 r and 1,000 r doses. Epidermal morphology was followed in all animals for 30 days for appearance of lesions, various cytological abnormalities, and restitution. The presence of sulphydril groups in the regenerating areas indicates, the author concludes, that these play a role in the restitution of cells which have been damaged by radiation. (NSA)

429

Frederic, J. STUDY ON REGENERATION AND ON -SH GROUPS IN X-RAYED GUINEA PIG SKIN, INCLUDING CHANGES SEEN IN TISSUES OUTSIDE THE FIELD OF DIRECT RADIATION, p. 39 of INTERNATIONAL CONGRESS OF RADIOLOGY, 6th Congress, London. 1950.

A histological study of the guinea pig skin after X-radiation has been made, including a study of -SH groups in irradiated epithelium and in unirradiated epidermis of the same animal. Doses of 3,000, 2,000 and 1,500 r. were given to the skin of the hind legs, the rest of the animal being protected by thick lead sheets. After a dose of 3,000 r. the epidermis is destroyed but regenerates very actively, becoming much thicker than the original and presenting a very abnormal appearance. After 2,000 r. the epidermis is not completely destroyed and regeneration begins earlier but proceeds more slowly. After 1,500 r. the regenerated epithelium is thicker than before but structurally normal. X-rays do not appear to have a direct influence on keratinisation. During the period when the destructive action of radiation on the epithelium is most marked, -SH groups of the stratum granulosum do not appear to be modified as long as this layer is distinguishable; in the stratum germinativum, on the other hand, -SH groups fade out progressively; it seems that the metabolism of the cells in this layer is affected by X-rays. There is also a diminution of -SH groups in this skin layer in unirradiated and protected epithelium of the same animal, indicating a distant effect in addition to the local lesion. In this respect, the epidermis appears to react "as a whole". During the period of regeneration the concentration of -SH groups increases progressively to a higher level than normal. In unirradiated epithelium, -SH groups increase more slowly and never exceed the normal.

430

Freed, John H., Edmond J. Farris, Douglas P. Murphy, and Eugene Pendergrass. EFFECT OF LOW DOSAGE ROENTGEN RADIATION ON THE GONADOTROPIC FUNCTION OF THE HYPOPHYSIS OF THE MATURE AND IM-

MATURE FEMALE ALBINO RAT. *J. Clin. Endocrinol.* **8**, 461-81(1948).

Five sexually mature female Wistar albino rats given single doses varying from 100 to 200 r on the third day of their oestrus cycles did not appear to be affected. A second group of 57 rats given single or multiple doses varying from 5 to 300 r on the second day of their oestrus cycles showed no change in running activity or periodicity of the oestrus cycle. Gross anatomical studies and weight determination made of the pituitaries, ovaries, and uteri of six of the two-day treated rats and seven controls showed the pituitary weights of the treated rats to be significantly greater, the uterine weights only slightly greater, and the ovarian weights similar. Sixteen immature rats given single or five successive daily treatments of 5 to 100 r per treatment matured sexually within the normal age limits. In gross appearance and weight their pituitary, ovarian, and uterine organs differed in no way from their control. It is concluded that low dosage radiation produces only a transient effect on the normal pituitary function and has no evident harmful effect. (NSA)

431

Geist, S. H., J. A. Gaines, and G. C. Escher. **VAGINAL ESTRUS IN IRRADIATED MICE. RELATIONSHIP OF VAGINAL ESTRUS TO OVARIAN CHANGES AND PRODUCTION OF BIOLOGICALLY ACTIVE OVARIAN TUMORS AFTER ROENTGEN IRRADIATION.** *Endocrinology* **29**, 59-63(1941).

The effects of roentgen irradiation upon the estrous cycle of female mice were studied in 23 animals by daily smears over a period of 14½ months. The changes noted within the vagina reflect those within ovaries and are described in correlation with them. The destructive effects of X-ray upon the ovarian follicular system of female mice in the first 4-8 weeks after irradiation are accompanied by a temporary abolition of estrus during that time. The luteal changes within the residual ovarian parenchyma which then develop result in the elaboration of sufficient estrogenic hormone to reestablish vaginal estrus in 100% of the animals. The estrous cycle is found to be totally irregular, with marked variations in the duration of continuous estrous period (1 to 222 days). Individual differences are apparently related to the degree and duration of functional activity within the luteinized ovarian parenchyma. From six months to one year after irradiation, surface epithelial proliferation and downgrowth replace a good portion of the ovarian cortex, with diminution of luteinized tissue and increased evidence of degenerative change. During this time, the extent of vaginal stimulation is found to be decreased and the number of mice showing acyclical estrus is reduced from 100% to 37%. After one year following irradiation, a prolonged absence of estrus may be correlated with senescent changes within the ovary. Those mice, however, which develop biologically active, luteinized granulosa or theca cell tumors once more exhibit increased estrogenic secretion expressed in irregular prolonged estrous periods. (BA)

432

Gersch, Manfred and Wilfried Mobius. **BIOLOGICAL EFFECTS OF SHORT WAVE RADIATIONS. INVESTIGATIONS ON INVERTEBRATES.** *Strahlentherapie* **85**, 565-80(1951).

Radiation experiments were carried out on Enchytraeae (oligochaete worms) and the gnat larva *Corethra*. The oligochaetes were very resistant and showed no radiation injuries after administration of 90,000 r three times in succession. *Corethra* showed injuries to intestinal cells after being submitted to radiations of medium strength; higher doses resulted, in addition, in degeneration of

pericardial cells (20 to 30 days after radiation) and of some thoracic cell complexes. Irradiation with 25,000 r caused great mortality and physiological injury to muscles, tracheal pigment cells, and the hypodermis. The cytological effects of radiation on the cells are described. It seems possible to use the pericardial cells as test cells whereby the action of short-wave radiations on the whole organism can be judged. (NSA)

433

Halberstaedter, L. and M. Ickowicz. **THE EARLY EFFECTS OF X-RAYS ON THE OVARIES OF THE RAT.** *Radiology* **48**, 369-73(1947).

The authors have set out to determine whether changes can be demonstrated in the ovary of the rat as early as four hours after irradiation by X-rays. Doses varying from 50 to 2,000 roentgen units were used, on some rats to the abdomen only, on others to the head and thorax only, while others were totally irradiated. There were four non-irradiated controls. Serial sections of the ovaries were examined, the animal in each case having been killed four hours after irradiation. In the follicles of the non-irradiated ovaries some pyknosis of the granular layer cells can usually be seen, but this is confined to follicles in which the ovum is in a state of division with the nucleus showing mitosis. Those with resting ova show very few pyknotic cells. In the irradiated series no difference was noted in the rats receiving 50 to 200 roentgen units. After a dose of 400 units and more, however, numerous pyknotic cells were observed in all follicles, both among the follicular cells and those in the granular layer. This appears to happen irrespective of the state of the ova. These findings applied only to the animals receiving direct abdominal irradiation or total irradiation. No abnormality was noted where the abdomen had been protected and the thorax only irradiated. Degenerative changes in the ovaries as early as four hours after irradiation, with doses exceeding 400 roentgen units, are thus demonstrated. Photomicrographs are given. (AWM)

434

Henshaw, P. S. **EXPERIMENTAL ROENTGEN INJURY. I. EFFECTS ON THE TISSUES AND BLOOD OF C₃H MICE PRODUCED WITH SINGLE SMALL WHOLE-BODY EXPOSURES.** *J. Natl. Cancer Inst.* **4**, 477-84(1944).

Tissue and blood changes were followed in C₃H mice after the application of a single acute 50 r dose of x-rays to the whole body. A slight leukocytosis developed in 2 to 4 hours, followed within 6 to 12 hours by a mild or persisting leucopenia which was found to consist mainly or entirely of lymphopenia. A small amount of nuclear debris was seen in the lymph nodes at 204 hours, which disappeared and a mild hyperplasia developed in 8 to 12 hours. Seminiferous tubules of the testis showed a reduction in spermatogonia and primary spermatocytes at one week and of secondary spermatocytes at two. The tubules appeared normal again in 4 to 6 weeks. (BA)

435

Henshaw, P. S. **EXPERIMENTAL ROENTGEN INJURY, II. CHANGES PRODUCED WITH INTERMEDIATE-RANGE DOSES AND A COMPARISON OF THE RELATIVE SUSCEPTIBILITY OF DIFFERENT KINDS OF ANIMALS.** *J. Natl. Cancer Inst.* **4**, 485-501(1944).

Doses of 50, 100, 200, and 400 r were applied to the whole bodies of C₃H mice, LAF₁ mice, and to guinea pigs. The hematologic and histopathologic changes following exposure were studied; the histologic studies pertained to the lymphoid organs, bone marrow, and testis for the most part. In a general way tissue responses consisted of a parenchymatous-cell loss, followed by a slow return to normal if the damage was not too severe. Regeneration started from

primitive cell forms that had survived irradiation fatal to other cells. Leukocyte reserves appeared to prevent the peripheral blood picture from reflecting the condition of the hematopoietic tissue when the damage is slight. The problems of the organism after moderate doses of radiation appear to depend largely upon injury to the stem cells of regenerative tissues. (BA)

436

Henshaw, P. S. EXPERIMENTAL ROENTGENOLOGICAL INJURY. III. TISSUE AND CELLULAR CHANGES BROUGHT ABOUT WITH SINGLE MASSIVE DOSES OF RADIATION. *J. Natl. Cancer Inst.* 4, 503-12(1944).

Application of 50,000 r doses of X-rays to the whole bodies of guinea pigs, rabbits, and mice was followed by death in a few hours. Guinea pigs were dead at the end of treatment (three hours), rabbits within three to six hours after treatment, and mice within 24-48 hours. Death appeared to result from distinctive type of shock, symptoms of which were generalized toxemia, hyperthermia, hyperesthesia with intermittent seizures, and cyanosis. Hemocentration was not seen in the acute cases. Widespread tissue destruction occurred during these short intervals. Tissue sections showed extensive nuclear and cytoplasmic degeneration followed by extensive parenchymatous-cell loss. (BA)

437

Henshaw, P. S. EXPERIMENTAL ROENTGEN INJURY: IV. EFFECTS OF REPEATED SMALL DOSES OF X-RAYS ON BLOOD PICTURE, TISSUE MORPHOLOGY AND LIFE SPAN OF MICE. *J. Natl. Cancer Inst.* 4, 513-22(1944).

Small daily doses of 5, 10, 15, 20, and 25 r/day were applied to the whole bodies of C H mice. There was a fall in leukocyte level, owing mainly to lymphocyte loss. The amount of fall varied progressively as treatments proceeded and directly with the size of the daily dose. Extensive parenchymatous tissue damage was seen in lymph nodes, spleen, bone marrow, and testis; the degree of which varied with size of daily dose. The life span was shortened, the amount varying directly with daily dose. Leukemia developed in some of the mice receiving 15 and 20 r daily. (BA)

438

Henshaw, P. S. and R. S. Snider. HISTOPATHOLOGICAL EFFECT. CORRELATION OF TISSUE RESPONSES FOLLOWING EXPOSURE TO PENETRATING RADIATIONS. Clinton Labs. July 1946. Decl. Dec. 16, 1946. 19p. (MDDC-569; MonH-144)

A review has been made of the available information concerning tumor formation and the accompanying changes in mammalian forms that take place following exposures to penetrating radiations. The tissues in the order of increasing resistance to radiation may be listed as follows: lymph nodes (small lymphocytes), germinal epithelium of the testis, erythrocytes and myeloblasts, gastrointestinal epithelium, ovary, skin, connective tissue, bone, liver, pancreas, kidney, nerve, brain, and muscle. It was pointed out that the most radiosensitive tissues are of the generative type—i.e., those which in life are continually proliferating new cells which undergo maturation, serve a useful function for a limited period and then die. The skin, testis, hemopoietic organs, gastrointestinal epithelium and perhaps other tissue series show a parallel type of differentiation with these features in common. In all cases, certain parent cells (but not the most primitive types), were found to be the most susceptible to radiation. It is plain that partial damage to a particular tissue series results in a limited period during which mature cells are being formed, whereas complete damage results in sterilization. Stress was laid on the fact that recovery to an apparently normal con-

dition takes place even when the acute histologic destruction has been almost complete. (ADD)

439

Henshaw, P. S. and R. S. Snider. THE GENERAL PICTURE OF IRRADIATION DAMAGE TO TISSUES, PART I. SUPERFICIAL RADIATION (BETA RAYS); PART II. PENETRATING RADIATIONS (NEUTRONS, GAMMA RAYS). Clinton Labs. July 8, 1947. Decl. July 18, 1950. 29p. (AECD-3009; MonH-288)

Part I. Radiation absorbed in the skin causes damage primarily in the germinal layer. When the damage to this layer is partial, the effect is a skin failure and repair takes place from the floor of the damaged area from living germinal cells that remain. When damage to the germinal layer is complete the effect is skin sterilization and healing must be from the edge.

Part II. The most radiosensitive tissues are of the generative type, that is, those which are continually proliferating replacement cells. In all cases (with the possible exception of lymphocytes), certain parent cells (but not necessarily the most primitive types), were found to be the most susceptible to radiation. Partial damage to a particular tissue series results in a limited period during which no mature cells are being formed. Recovery to an apparently normal condition takes place even when the acute histological destruction has been almost complete. Subliminal damage in the case of daily exposure may hold an animal nearer to a state of exhaustion so that he is less able to cope with a crisis. When penetrating radiations are applied generally to the whole body, leukemia is the predominant tumor type obtained. (NSA)

440

Jadassohn, W., E. Bujard, R. Paillard, P. Wenger, and P. Gaudin. THE EFFECT OF ROENTGEN, GAMMA AND BETA RAYS ON THE EPIDERMAL CELL. EXPERIMENTS ON THE 'NIPPLE TEST' ASSOCIATED WITH THE DUSTIN REACTION. *Acta Radiol.* 34, 469-87(1950).

The combined action of radiation therapy and treatment by estrogenic hormones on the nipple of the male guinea pig has been studied and controlled by Dustin's colchicine reaction. Roentgen, γ , and β rays administered in sufficiently large doses inhibit mitosis of the epidermal cells of the nipple. This action is also maintained if estrogenic hormones are administered after irradiation. This effect of irradiation is more evident when the irradiation is combined with the application of an estrogen, as the control nipple presents more mitoses. A dose of 200 r has no appreciable effect; on the other hand, 400 r or still larger doses are effective. A single dose 2400 r given under varying physical conditions and consequently for varying lengths of time (from 4 min 26 sec to 153 min 27 sec) is effective regardless of the type of rays used. The effect of 2400 r decreases if this total dose is applied in fractional doses of 200 r per day over 12 days. Irradiation has the same effect on the nipple showing acanthosis produced by the administration of estrogenic hormones prior to irradiation. Estrogenic hormones cause a thickening of the epidermis of the nipple, i.e., acanthosis, through mitosis and a mild degree of simple hypertrophy of the cells. A few mitotic figures are also seen if estrogenic hormones are administered after irradiation. It is evident that irradiation therapy does not totally destroy the capacity of the epidermal cells to divide. However, the number of mitotic figures is too small to explain the thickening of the epidermis after irradiation. The action of estrogenic hormones administered after irradiation produces a simple hypertrophy involving similarly the nuclei and the cytoplasm, and a certain degree of imbibition of the epidermis,

the combination of which we call pseudoacanthosis. (NSA)

441

Jolles, B. STUDY OF CONNECTIVE-TISSUE REACTION OF RADIATION. THE SIEVE OR CHESS METHOD. *Brit. J. Cancer* **3**, 27-31(1949).

The author describes a new technic for the study of connective-tissue reaction to radiation, consisting in the irradiation of accessible tumors (breast, skin) through a lead sieve with circular or square apertures of diameters 1.0 to 2.0 cm. On the basis of 9 cases studied thus far, the following preliminary conclusions are reached: The "sieve-chess" technic is a workable one for the study of direct and indirect effects of irradiation. The connective-tissue reaction takes place not only in the irradiated areas, but also in the neighborhood protected from the direct irradiation. There are visible effects on cells not directly exposed to the radiation. The pattern of connective-tissue destruction and regeneration can be studied. As a general inference, it can be said that the irradiation affects the connective-tissue cells and induces a kind of "over-differentiation." This consists chiefly in the deposition of an excessive amount of collagenous fibrils, which are organized into solid, coarse bundles in the exposed parts where the fine connective-tissue network is grossly altered. Lymphatic channels and blood capillaries are greatly affected, compressed, and blocked. This has a considerable effect on tumor nourishment, the lack of which enhances tumor tissue degeneration. (R)

442

Knowlton, Norman P., Jr., Louis H. Hempelmann, and Joseph C. Hoffman. THE EFFECTS OF X-RAYS ON THE MITOTIC ACTIVITY OF MOUSE EPIDERMIS. *Science* **107**, 625(1948).

The mitotic index of the skin of the mouse has been studied as a means of measuring the biological effect of X-rays at doses of 35 and 325 r. As little as 35 r of 250 kv X-rays produce a drop in the mitotic index to zero within one to two hours after radiation. The number of mitoses returned to normal within a few hours after radiation. The time required for the number of mitoses to return to normal increases greatly with increased radiation dosage. It is believed that the time required for the mitotic index to return to normal will provide an excellent basis for rating the biological effectiveness of radiation of different types and different energies. With 325 r of X-rays the mitotic index required six days to return to normal and continued to increase to more than twice normal. This is believed to be an over compensation phenomena which may also be used as an index of radiation damage. (NSA)

443

Krebs, A. T. and I. L. Gierlach. VITAL STAINING WITH THE FLUOROCHROME ACRIDINE ORANGE AND ITS APPLICATION TO RADIOBIOLOGY I. ALPHA-RAY EFFECTS. *Am. J. Roentgenol. Radium Therapy* **65**, 93(1951).

Using the acridine orange vital staining technique, the results of earlier preliminary investigations have been confirmed and extended. The findings are (1) cells and cell groups inactivated before staining and also irradiated stained cells demonstrate the radiation effect by a color change in the emitted fluorescent light as they became non-viable. When normal, the cells have a green fluorescence. When completely destroyed, the cells have a light red fluorescence; (2) intermediate stages or degrees of radiation damage are characterized by shades of yellow or orange fluorescence; (3) These changes occurring in cells under alpha radiation have been fixed on color film; (4) the amount of irradiation necessary to kill cells can be readily quantitated. By this means it is possible to study

some of the details of radiation damage. The results reported together with the photomicrographs amply justify the use of the acridine orange vital staining method in radiobiology. (auth)

444

Lamson, Baldwin G. and John L. Tullis. THE PROGRESSION OF MORPHOLOGIC LESIONS IN SWISS MICE EXPOSED TO 625 r, 2000 KVP, TOTAL BODY X-RADIATION. Naval Medical Research Inst. Bethesda. July 31, 1951. 27p. (NP-3667; R-6089; NM-006-012.04.37)

One thousand Swiss male mice were exposed to 625 r, 2000 kv total body x-radiation. Nine hundred ninety of these mice were sacrificed serially, ten mice each hour for the succeeding 99 hours. Microscopic studies of the spleen, lymphoid tissue, bone marrow, intestines, liver and testes were made to observe the tissue response to this injury. Damage to lymphocytes, immature erythropoietic tissue and selected epithelial cells of the small bowel mucosa was observed one hour after exposure. Reduction of cellularity of myeloid tissue occurred more gradually. Damage to lymphoid tissue reached a peak between 7 and 12 hours, and regeneration was generally evident by 60 hours. Erythropoietic tissue could not be found after 14 hours, yet regeneration was seen sporadically between 66 and 99 hours. Peak injury to small bowel mucosa extended over the 8 to 32 hour period, whereas repair was completed by 60 hours after radiation exposure. Complete repair of lymphoid, erythropoietic and myeloid tissue did not occur during the 99 hours observation period. Mitotic activity was reduced for a period following irradiation in all organs studied with the exception of the testes. Selective damage to spermatogonia of the testes was not seen during the period of this study. (auth)

445

Lasnitzki, I. A QUANTITATIVE ANALYSIS OF THE DIRECT AND INDIRECT ACTION OF X-RADIATION ON MALIGNANT CELLS. *Brit. J. Radiol.* **20**, 240-7(1947).

This research determined quantitatively the direct and indirect action of x radiation *in vitro* and *in vivo* following a dose large enough to involve the circulatory system. Mouse adeno-carcinoma 63 was grown in the right thigh of 2 to 3-month-old hybrid mice, and the tumors were irradiated through a hole in a Pb shield about 12 days after inoculation, when they had reached the size of a small cherry. Following the exposure the irradiated tumors were excised for histological examination at various intervals from 80 min. to 10 days. Tissue cultures were prepared from small fragments taken from the viable tumor edge, grown by the hanging drop method, irradiated 24 hr after explantation, and returned to the incubator for periods ranging from 80 min. to 10 days before fixation. An X-ray dose of 2,000 r was given in 20 min., both to the tumors and to the tissue cultures, generated at 160 kv with 12 mm Al filtration. The effect of the radiation was assessed by cell counts. Several fields near the skin surface of the tumors in the young growing parts of the periphery only, and in the zone of growth of the tissue cultures, were selected, and all of the cells present were counted and classified as dividing, resting or degenerate cells. In each tumor and culture 300-500 cells were counted, and each observation represented the average of at least three tumors and four to six tissue cultures. The curative dose for carcinoma 63 was 2,500 r; 2,000 r caused temporary retardation of growth. A slight dilatation of blood vessels in the tumor and adjoining skin was seen almost immediately; the reaction was marked after 24 hours, increased for four days, and was still present 10 days after the irradiation. Mitosis was absent in both tumors and tissue cultures 80 min. after the exposure. It reappeared *in vivo* after 3 hours,

but not before two days *in vitro*, most of the cell divisions in both cases being abnormal—multipolar mitoses, clumping, fragmentation of chromosomes, and chromosome bridges. Increase in cell size occurred in both cases, but was much more marked and of longer persistence in the cultures. Degenerate cells appeared shortly after exposure in both cases, being qualitatively similar to each other and to irradiated normal tissue—hyperchromatosis and pyknosis of nuclei followed by disintegration of the cytoplasm and chromatolysis. Degeneration sometimes began in the resting nucleus. The *in vivo* and *in vitro* results were qualitatively the same, but *in vivo* a large group of degenerate cells appeared between 2 and 7 days after irradiation, which did not occur *in vitro*. Mitosis *in vitro* was much less affected than *in vivo*, suggesting that the degenerate cells seen in the tumor replaced the cells seen in mitosis in the cultures. The big group of degenerate cells in the tumor was coincident with the appearance of vascular changes. It is assumed that these cells broke down on reaching division because of the interference with their blood supply. On the other hand it is concluded that the changes seen on the first day were due to the direct action of the radiation on the cell and the early mitotic recovery in the tumor was due to the still intact circulation. (EM)

446

Lorenz, Egon and Thelma B. Dunn. OCULAR LESIONS INDUCED BY ACUTE EXPOSURE OF THE WHOLE BODY OF NEWBORN MICE TO ROENTGEN RADIATION. Arch. Ophthalmol. 43, 742-9(1950).

Twenty-four male and 32 female mice of strain A were given at birth a single whole-body dose of 400 r delivered by a 186-kv machine at 50 cm target distance. The experiment was terminated 12 months later. Seventeen males and 22 females survived; all showed lesions in one or both eyes. These lesions consisted of opacity of the lens, partial opacity and vascularization of the cornea, and atrophy of the retina, which was only a small fraction of its normal thickness. The difference in radiosensitivity of the eye of young and that of old animals is discussed. (NSA)

447

Mason, K. E. and S. L. Shaver. THE DEGENERATIVE CHANGES IN THE TESTES OF THE ADULT RAT AFTER X-IRRADIATIONS, p.16-28 of QUARTERLY TECHNICAL REPORT, JULY 1, 1950 THROUGH SEPTEMBER 30, 1950. Atomic Energy Project, University of Rochester. Nov. 1, 1950. 13p. (UR-142(p.16-28))

The report deals mainly with (a) a study of the degenerative changes in the testes of the adult rat after x irradiation of 500 r total body, (b) the influence of vitamins A, D, and E upon the sensitivity of rats and their genital organs to irradiation, (c) the morphological stages of degeneration in the testes of the rat after the administration of 1005 r locally, (d) the study of the 'indirect' factor and its relation to testicular degeneration, and (e) a survey of testicular damage in different strains of rats. It is concluded from the work performed upon this series of animals that with the dose of 500 r administered total body there are no strain differences in the three strains of rats used and that there is very little or no secondary effect upon the testes of these animals. Yet when animals were irradiated locally in this laboratory with the dosage of 500 r, no morphological degeneration was observed in routine histological sections. Therefore the possibility exists that the degeneration of the testes in the rat after 500 r total body may be due to a combined effect of a secondary mediator and the direct effect of the irradiation, neither of which will produce an observable degeneration alone. (NSA)

448

Metcalf, R. G., R. J. Blandau, and T. B. Barnett. THE PATHOLOGICAL CHANGES EXHIBITED BY ANIMALS EX-

POSED TO SINGLE DOSES OF X-RADIATION. Atomic Energy Project, University of Rochester. July 17, 1950. 44p. (UR-123)

Albino rats were exposed to a single dose of 550 r of whole-body x radiation and were sacrificed at intervals from 15 min to 42 days after exposure. Sections of selected organs were examined microscopically, and studies were done on the peripheral blood and bone marrow and on sperm from the vas deferens. 33 figures. 28 references. (NSA)

449

Montag, C. ON THE EFFECT OF METHYLTHIOURACIL AND X-RAYS ON THE THYROID GLAND. Strahlentherapie 81, 1-38(1950).

An investigation of the effect of x-rays on the thyroid glands of rats was carried out with the use of methylthiouracil, a chemical substance which results in a pronounced histological change and makes it possible to influence the functioning of the thyroid gland in a measurable manner. Upon irradiation of the thyroid gland with approximately 1500 r, degenerative changes were found in the nervous terminal apparatus (preterminal plexus and nervous terminal reticulum) and in the nuclei of follicular cells. An effect on the protoplasm and the surface areas of the follicular cells is probable. The nuclear changes had previously been unobserved because they become apparent only during cell division. They are made visible by accelerating the mitosis by the administration of methylthiouracil. (NSA)

450

Murray, Raymond, Mila Pierce, and Leon O. Jacobson. THE HISTOLOGICAL EFFECTS OF X-RAYS ON CHICKENS WITH SPECIAL REFERENCE TO THE PERIPHERAL BLOOD AND HEMOPOIETIC ORGANS. Univ. of Chicago Metallurgical Lab. Mar. 2, 1948. 81p. (AECD-2303; CH-3873)

Chickens, 3 to 11 weeks old, were treated with doses of 200 kv x-rays, ranging from 2 r to 1,200 r. The median lethal-dose for 3-week-old chickens appeared to lie between 400 r and 800 r. Histopathologic changes in the 11-week chickens paralleled those reported for mammals of comparable maturity, with the exception of damage to neurilemma sheath cells in the chickens. The 3-week-old chickens suffered additional damage to immature structures, but the threshold of observable damage to the lymphatic tissue (25 r) was comparable to that reported for mammals. By application of a slight modification of Kyes' method for peripheral blood counting of fowl, dramatic decrease in blood constituents, paralleling those reported elsewhere for mammals, were seen in 3-week-old and 5-week-old chickens after treatment with 600 r and 800 r, respectively. Numerous degenerating cells were observed in dry smears made during the first week after irradiation, in contrast to the scarcity of such findings in smears of mammalian blood at the same period. Although the normal values for leukocytes of chicken blood were found to be several times those of mammalian blood, this difference could account only in part for the greater degeneration observed in the chickens. (NSA)

451

Nettleship, A. TISSUE CHANGES PRODUCED IN C₃H MICE BY 50 r WHOLE BODY EXPOSURE. Radiology 42, 64-70(1944).

Young adult male mice of an inbred C₃H colony were given whole body exposures of 50 r (measured in air) each of filtered 200 kv X-rays. Blood counts were made and tissues fixed at 1, 2, 4, 8, 12, and 24 hours, 2, 4, 7, 10, and 14 days, three animals being examined for each count and each tissue fixation. Curves showing white blood counts indicate an abrupt rise followed by a sharp fall in both lymphocytes and neutrophils to below normal in a few hours

and reaching a minimum on the fourth or fifth day. Lymphocytes failed to recover before the fourteenth day, but neutrophils quickly returned to normal or even slightly above normal. Earliest discernible tissue changes were eosinophilia, cloudy swelling of cytoplasm, and poor staining of nuclei, observed in all tissues within one hour, and disappearing at various times up to 24 hours. In lymph nodes and spleen, multiple flecks of necrosis appeared in germinal follicles within four hours and persisted until 8 to 12 hours. Multi-nucleated giant-cells were seen in from four hours to three days. No clear mitotic wave was found. Changes in bone marrow were less pronounced and occurred later. At 12 hours there were abundant megakaryocytes and an increase in myeloblasts. Increased alkalinity lasted two to four days. In the ileum pronounced oedema appeared within two to four hours with return to normal at eight to twelve hours. The testes showed general swelling, with ragged and pyknotic germinal cells in some tubules. However, even at the height of the reaction the majority of the tubules showed normal spermatogenesis. By the end of three weeks the tubules had returned to normal. No significant changes were seen in any other tissues. None of the changes described could be found in an adequate control material. (EM)

452

Pape, R. HISTOLOGICAL FINDINGS AFTER VERY SMALL DOSES OF IRRADIATION, p.162-3 of INTERNATIONAL CONGRESS OF RADIOLOGY, 6th Congress, London. 1950.

After exposure of lymphoid tissue of the rat spleen to single doses of a few roentgens (1-20) given as total body irradiation, loosely arranged cells are seen with a bubbly structure in the nuclear protoplasm. After repeated doses the "Seemann syndrome of the stimulated spleen" is frequently observed, often others associated with a lymphocytosis. After daily doses of 0.25 r extending over one year, there is an increase of lymphocytes up to three times the normal value. The best histological results are obtained when the initial irradiation consists of very small doses followed some days later by doses of the order of 300—600 r. Under these circumstances the follicles of the spleen are better preserved and richer in cellular elements including mitotic figures. Similarly, after an initial irradiation, the spermatogonia of the testis show mitotic activity following a further exposure of 600 r.

Inflammatory processes in the granulation tissue of healing wounds, recovery processes from artificial pneumonia caused by staphylococci and from intraperitoneal infections with tubercle bacilli, all show, after small preliminary doses of radiation, a reduction in the amount of exudate which is characteristic of the response to the usual X-ray doses. There is also an increase in the perivascular cells, an acceleration of fibroblast formation and of the process of healing and a localisation of the lesion. In tubercle infection there is a diminished tendency to caseation. To sum up, small doses of irradiation have a protective effect upon cells, increasing their resistance to radiation and enabling mitotic activity to be maintained.

453

Pape, R. NEW OBSERVATIONS AND EXPERIMENTAL FINDINGS ON THE EFFECT OF VERY SMALL ROENTGEN DOSES Radiol. Austriaca 4, 35-51(1951).

Following single or repeated irradiations with small doses (1-20 r) changes are seen in the nucleus a few hours later. The nucleus is larger and may have a foamy appearance. Epithelioid cells are seen surrounding the malpighian follicles in the spleen. In rats irradiated with 312×0.25 r the number of leucocytes was increased 3 times. By combined irradiation the spermatogenesis in

rats did not decrease but rather increased. The period between the irradiation with small doses and a large dose can be extended 4 weeks. The smaller dose can be either 1 r or 5×20 r. Increased growth and decreased exudation is seen in granular tissue, but with doses over 150 r the exact reverse is seen. In tb in guinea pigs proliferative alteration is seen but not exudative alterations. The effect of the irradiation with small doses is not only activation of the reticulo-endothelial system, but also decrease of the exudation and increase of the cell resistance. One hour after the irradiation the number of leucocytes decreases slightly ('hour reaction'). The decrease does not depend on volume dose, but on the area of treatment and its sensitivity. The effect is not specific, but depends on neurohumoral reactions. In experiments with growing plants even doses short of 14 accomplished effects on growth and protection. By variation of dosage 3 different levels were established: (1) cell destruction with 20 r and above; (2) neurohumoral reflex reactions down to 3 r; (3) activation of cell partition and resistance with 1 r and below. (EM)

454

Pape, R. and N. Jellinke. IMPORTANT VARIATIONS IN THE ORGANIC FINDINGS AFTER TOTAL AND LOCAL IRRADIATION AND THE PARTICULAR EFFECTS OF SMALL SCALE DOSAGES. THE SPLEEN AS A TEST FOR VARIOUS RADIATION EFFECTS. Radiol. Austriaca 3, 43-62(1950).

The response of the spleen (rat) to X-rays was investigated under various conditions. After local application of 100 r (or more) definite signs of destruction were observed, but after 30 r (or less) no destructive changes were observed. However, 3 hours after the application of 2-5 r lymphoblasts showed some departure from normal nuclear structure. With larger doses, the histological appearance of the spleen showed distinct differences after total and after local irradiation. After local exposure recovery occurs rapidly from the influx of mature lymphocytes from undamaged depots through blood vessels, whereas after total irradiation, true regeneration is extended over several weeks or even months. Most interesting results were obtained with preliminary irradiation of 3 to 20 r daily and subsequent exposure to 300 r. After a single exposure to 300 r, destruction was always found, but it failed to appear in all cases when preliminary small doses had been given. Apparently the preliminary small dose exercises some sort of protection against further radiation damage. This is ascribed to acceleration of cell regeneration. The fundamentals of G. Rickers' theories are referred to in relation to the results reported. (EM)

455

Pohle, E. A., G. Ritchie, and W. W. Moir. STUDIES OF THE EFFECTS OF ROENTGEN RAYS ON HEALING OF WOUNDS. III. HISTOLOGICAL CHANGES IN SKIN WOUNDS IN RATS FOLLOWING POSTOPERATIVE IRRADIATION WITH VERY SMALL AND MODERATE DOSES. Radiology 52, 707-13(1949).

The effect of roentgen rays in doses of 10, 25, 150, 300, 350, and 700 r on the healing of skin incisions was studied macroscopically in 18 and macroscopically and microscopically in 122 white rats. The radiation doses were administered by a 100-kv machine, through a 2 mm Al filter, at a target distance of 30 cm and at the rate of 45 r/min. Although all wounds were examined daily, no consistent difference in the healing time between the irradiated and the non-irradiated portions of the wound could be detected macroscopically. Histologically, no true stimulative effect on the healing—even with the lowest doses used—could be found. Any slight difference in the healing process in favor of the irradiated portion (small

doses only) was considered to be due to a reduction in the amount of exudate, which in turn decreased the amount of fibrin replaced by the scar tissue. (NSA)

456

Raynaud, Albert and Marcel Frilley. **THE HISTOLOGICAL STRUCTURE OF THE TESTICLES OF FETAL MICE AFTER DESTRUCTION OF THE HYPOPHYSIS BY X-RADIATIONS.** *Compt. rend. soc. biol.* **143**, 954-8(1949).

A total of five fetuses, with their hypophyses destroyed by means of elevated doses of X-rays (up to 200,000 r), were examined to determine the effects on the histological structure of the testicles. The x-radiations were delivered in one dose of 100,000 r at the age of 12 days and an additional 100,000 r dose at 13 days, localized in an area with 2.5 mm diameter; the fetuses were sacrificed at the age of 18 days and examined histologically. It was found that the testicles were differentiated sexually; the relative growth and dimensions of the testicular tubules were not perceptibly modified, however. The interstitial gland of the testicle was relatively well developed. The studies indicate that if the destruction of the hypophyseal line occurs rapidly and completely the testicular growth and the development of interstitial gland may then be accomplished in a nearly normal fashion. (NSA)

457

Raynaud, Albert and Marcel Frilley. **THE HISTOLOGICAL STRUCTURE OF THE OVARIES OF FETAL MICE AFTER THE DESTRUCTION OF THE HYPOPHYSIS BY X-RAYS.** *Compt. rend. soc. biol.* **143**, 959-63(1949).

The hypophyseal line was destroyed in five female mice by irradiating the base of the cranium at the age of 12 or 13 days with a narrow localized beam of X-rays for a total dose of 150,000-200,000 r; the irradiated and control animals were sacrificed when 18 days old. It was found that after the hypophyseal destruction the general growth of the ovaries was not affected noticeably; the germinal cells were entering the mitotic prophase. It is concluded that if the destruction of the hypophysis in each animal can be assumed to be done completely and quickly upon irradiation, the ovarian growth must be independent of fetal hypophyseal secretions. (NSA)

458

Schrek, Robert. **STUDIES IN VITRO ON CELLULAR PHYSIOLOGY, THE EFFECT OF X-RAYS ON THE SURVIVAL OF CELLS.** *Radiology* **46**, 395-410(1946).

Cellular suspensions were prepared from thymus, spleen, bone marrow and testis of rabbits and from leucocytes of normal and leukemic blood of men. The suspensions were irradiated with doses of X-rays varying between 20 and 5000 r/air (Factors: 250 kv, 10 ma, 50 cm. distance, 1 mm Al filter, 120 r/min HVL 0.7 mm. Cu). After exposure the suspensions were incubated at 37°C for 1-7 days. The irradiated and non-irradiated control suspensions were examined at periodic intervals by the method of unstained cell counts (resistance to eosine) and by stained smears. Exposure of thymic and splenic suspensions to 1000 r caused no perceptible change in the number of eosine resistant (i.e., viable) cells in the first 3 hours of incubation but produced a relatively rapid decrease in the unstained cell counts after a short latent period. Irradiated leucocytes from normal blood and from lymphatic leukemic blood had shorter survival periods than non-irradiated cells. Irradiation and incubation of suspensions from bone marrow from myelogenous leukemic blood and from the testicle had no effect on the number of eosine resistant of viable cells when compared to non-irradiated suspensions. (BA)

459

Schrek, Robert. **CYTOLOGIC CHANGES IN THYMIC GLANDS EXPOSED IN VIVO TO X-RAYS.** *Am. J. Pathol.* **24**, 1055-64(1948).

Intranuclear, acidophilic vacuoles were observed in many cells of thymic tissue of the rat and rabbit, three hours after irradiation with 1,000 r of X-rays. On dark-field examination of the suspension of the irradiated thymic tissue, many of the cells had single or multiple primary vacuoles with or without vacuolar walls. Thymic tissue, five hours after irradiation, had, on histologic examination, many pyknotic and fragmented nuclei. Suspensions of this tissue had many cells with secondary vacuoles and many fragments of cells. Nonirradiated thymus also had a few cells with intranuclear vacuoles and pyknotic nuclei. The spontaneous and X-ray induced degeneration of lymphocytes was associated with the formation of intranuclear vacuoles, pyknosis, and fragmentation. Primary intranuclear vacuoles are seen in a higher percentage of cells by dark-field methods than by routine histologic technique. (NSA)

460

Shaver, Samuel L. and Karl E. Mason. **SELECTIVE TESTICULAR DAMAGE IN RATS DUE TO X-RAYS.** University of Rochester. [nd] 1p. (AECU-747)

The document is in abstract form; it is reproduced below in its entirety.

A dosage of 500 r total-body x-irradiation, administered in approximately 8 min, has proved most suitable for producing minimal but selective effects upon the testis of the rat.

In 52 rats given this dose there was negligible cell damage in the germinal epithelium when testis smears were studied supravitaly and by fixation and application of histochemical methods for glycogen, lipids, and mitochondria. However, in histological sections of testes taken at frequent intervals during the first 2 weeks after irradiation, there occurs a progressive diminution in, and ultimately almost a complete loss of, spermatogonia; yet spermatogenesis continues normally. During the following 2 weeks, primary spermatocytes gradually diminish, and cells in advanced phases of spermatogenesis predominate. Approximately 10 days later there is evidence of early regeneration in the basal layers.

The infrequent occurrence of necrosis or pycnosis in spermatogonia and other germ cells, the abundance of mature sperm usually uncontaminated with sloughed germ cells in the epididymis, and the fact that the time required for these phenomena approximates the duration of the spermatogenic cycle (about 26 days) suggest a specific but temporary inhibition of the somatic mitotic divisions in the spermatogonia. This is further supported by observations on prepubertal rats given the same dosage and on adult rats showing a similar degree of testis injury after 1,005 r irradiation applied locally to the testis. (NSA)

461

Smith, Christianna and Lois A. Loewenthal. **A STUDY OF ELASTIC ARTERIES IN IRRADIATED MICE OF DIFFERENT AGES.** *Proc. Soc. Exptl. Biol. Med.* **75**, 859-61 (1950).

Changes comparable to those of physiological aging were induced by x radiation in the tunica media of elastic arteries of mice of different ages. In the elastic arteries of 20-to-30-day- and 80-to-100-day-old irradiated mice there were increased amounts of ground substance, increased numbers of interlamellar fibers, and premature raggedness and fraying of the elastic membranes. No changes attributable to irradiation were seen in the arteries of the old mice. (NSA)

462

Spargo, B., J. R. Bloomfield, D. J. Glotzer, E. Leiter Gordon, and O. Nichols. HISTOLOGICAL EFFECTS OF LONG-CONTINUED WHOLE-BODY GAMMA-IRRADIATION OF MICE. *J. Natl. Cancer Inst.* 12, 615-56(1951).

Chronic effects of repeated low doses of external γ radiation on mice sacrificed at bimonthly intervals from 2 to 16 mo are reported.

463

Strelin, G. S. HISTOLOGICAL CHANGES PRODUCED IN THE EPITHELIUM OF THE FROG'S CORNEA BY TOTAL AND PARTIAL IRRADIATIONS WITH X-RAYS. *Doklady Akad. Nauk S.S.S.R.* 73, 1283-6(1950).

The influence of irradiated portions of tissues on the neighboring nonirradiated ones, and vice versa, was illustrated by observing the depressing action of x rays on the mitotic division in the cornea epithelium of frogs; partial irradiations were obtained by using a lead grid 0.5 mm thick as a filter. The doses used varied between 450 and 7200 r (350 r/min); the histological observations were made on material fixed at various intervals after the irradiation (up to 10 days). The results showed that partial irradiations with 3600 r produced the same effect as total irradiations with 900 r, and that at lower doses the healing effect of protected strips on the irradiated ones was very apparent, as was also the reverse (depressive) action at higher doses. These influences should be ascribed to chemical interactions between cells rather than to cell migrations. The foregoing observations point to possible applications of grid-shaped filters for the protection of the skin in depth therapy, as has been recommended by several authors. (NSA)

464

Tansley, K., L. H. Gray, and F. G. Spear. A PRELIMINARY NOTE ON SOME BIOLOGICAL EFFECTS OF ALPHA RADIATION ON THE FROG TADPOLE. *Brit. J. Radiol.* 21, 567-70(1948).

Mitotic and degenerate cell counts were made on the eye and brain of frog tadpoles exposed to three different doses of α -rays and the results compared with those already known for a small dose of γ -rays. Whereas with the lowest α -ray dose the relation between mitosis and degeneration does not differ from that which would be expected to follow a relatively small dose of radiation, after the two larger α -ray doses degeneration far exceeds this amount. It would seem that α -rays cause the degeneration of potential dividing cells in considerable numbers. (NSA)

465

Tullis, John L. THE SEQUENCE OF PATHOLOGIC CHANGES IN SWINE EXPOSED TO THE LD100/30 OF TOTAL BODY SUPER-VOLTAGE X-RADIATION. *Naval Medical Research Inst. Bethesda.* Aug. 24, 1951. 17p. (NP-3600; NM-006-012.04.38)

Eighteen 140-pound barrows five to seven months old were subjected to 600 r total body X-radiation administered 300 r to each lateral aspect of the animal at two meters target-skin distance from the 2000 KVP source. The swine were killed at intervals from 50 minutes to 164 hours (seven days) after irradiation and their tissues were studied grossly and histologically from morphologic X-ray-induced changes. Lymphoid cells in the several lymphoid organs of the body had undergone degenerative changes in the swine examined 50 minutes after irradiation. The degenerative processes increased for a while, then ceased. The debris was removed by phagocytosis after which the lymphoid organs appeared quiescent and depleted of lymphocytes. After 36 hours, regeneration and gradual repopulation took place. Immature erythroid elements in the marrow reacted

early and progressed to almost complete depopulation with no evidence of regeneration in the seven-day observation period. Immature myeloid elements lagged behind the erythroid elements, but with a similar end result. Mature blood cells and megakaryocytes were more radioresistant. Lesions in the small intestine were limited to early necrosis with rapid regeneration of the epithelium in the deep glands of the mucosa, depletion of the lymphocytes in the lamina propria and solitary nodules, and the congestion of blood vessels. Other lesions in the gastro-intestinal tract included hemorrhages in two swine after 128 hours and shallow ulcerations in the rectal mucosa in the swine at 92 hours. In a few instances endothelium of the arterioles appeared swollen and distorted. Other tissues examined were not remarkable. (auth)

Carcinogenesis

466

Boyland, E. CHEMISTRY OF NEOPLASTIC TISSUE. *Ann. Rev. Biochem.* 18, 217-42(1949).

This article is a review of recent work in the field based on a thorough compilation of the literature. Included are the treatment of cancer by radioisotopes (P^{32} and I^{130}), the cancer producing properties of radioactive fission products (plutonium and Y^{91}), the inhibition of skin cancer due to radiation by the use of chemicals, and the effect of cosmic radiations on carcinogenesis. 170 references. (NSA)

467

Brent, Robert L. and H. Charles Jordan. POSSIBLE LATE TUMOR DEVELOPMENT IN RAT EMBRYOS IRRADIATED WITH 100 r OF X-RADIATION ON THE 9TH DAY OF GESTATION. *University of Rochester.* Jan. 19, 1951. 1p. (UR-150)

The report is reproduced here in its entirety.

Rat embryos were isolated in utero and given 100 r of x radiation. In one series sacrificed at intervals up to and including 15 days gestation, groups of tumor cells apparently originating from neutral tissue were observed in the cephalic portion. These tumors vary in size, differentiation, and position; some are associated with brain tissue, others with the skin, and many are distributed in the intervening mesenchymal tissue.

A second series of embryos were subjected to the same procedure and sacrificed at intervals from 15 days gestation until term. Gross observations have revealed tissue masses of such size as to prevent closure of the mid-sagittal suture. The largest of these growths were observed at 15, 16, and 17 days, while growths observed at term are uniformly smaller. This apparent failure of embryos bearing the larger growths to survive may account for the sharply increased incidence of resorption seen at term as compared with 16 days. Histologic studies are in progress to determine whether these masses are identical with the above-mentioned types of tumor or are distortions of the brain wall. (NSA)

468

Brues, Austin M. CARCINOGENIC EFFECTS OF RADIATION, p.171-91 of ADVANCES IN BIOLOGICAL AND MEDICAL PHYSICS, John H. Lawrence and Joseph G. Hamilton, eds. Volume 2. New York, Academic Press Inc. 1951.

A review of the carcinogenic effects of ionizing radiation including sections on (1) carcinogenic effects of total-body irradiation; (2) carcinogenesis by locally directed irradiation; (3) carcinogenesis by absorbed radioelements; and (4) mechanism of radiation carcinogenesis. 106 references. (S.V.S.)

469

Brues, Austin M., H. Lisco, and M. P. Finkel. CARCINOGENIC ACTION OF SOME SUBSTANCES WHICH MAY BE A PROBLEM IN CERTAIN FUTURE INDUSTRIES. *Cancer Research* 7, 48(1947).

An investigation is under way to test the late or chronic effects of exposure to plutonium and products of U fission on rats, mice, rabbits, and dogs. Effects of Ra were also studied for comparison. Sr^{90} , with a 55-day half life and a tendency to become concentrated in bone, produced bone tumors, slightly increased the incidence of lymphoma, and did not affect mammary tumor incidence. Ra produced bone tumors and heavy calcification in the media of the larger arteries and certain other sites. Ce^{144} - Pr^{144} caused bone sarcoma and atrophy of the liver except in the marginal areas where ionization was less and regeneration could proceed. Y^{91} , fed by stomach-tube, was virtually unabsorbed; 0.1 of the acute lethal dose was fed daily for three months with no measurable detriment, but animals surviving this treatment as well as those surviving a single acute dose of 20-30 mc./kg. showed after several months a variety of intestinal lesions with obstruction. Plutonium (Pu^{239}), injected intravenously, became most concentrated at first in liver and spleen, was later translocated to bone. Acute plutonium was similar to acute total body radiation sickness, with the addition of splenic atrophy and gross liver changes. Chronic plutonium involved hair graying, progressive liver damage, and bone sarcoma. After subcutaneous injection of 1 γ of Pu^{239} , local fibro-sarcomas appeared within one year, and local epilations, ulceration, keratoses, and spontaneous amputation also occurred. (GPR)

470

Brues, Austin M., George A. Sacher, Miriam P. Finkel and H. Lisco. COMPARATIVE CARCINOGENIC EFFECTS BY X-RADIATION AND P^{32} . *Cancer Research* 9, 545(1949).

This paper is an abstract and is presented here in its entirety.

Production of lymphoma has been studied in CF1 female mice, using total body x-ray and P^{32} . Control mice show an exponentially increasing susceptibility to the spontaneous disease, with doubling of the tumor expectancy about every 75 days, until 700 days of age. Beyond this time, the rate fails to increase further. Using different patterns of x-ray treatment, it is found that 400 r total body x-ray is more effective if divided over a 10-day period than if it is either given as a single dose or divided over 40 days. Increasing doses are more effective until a saturation value is reached, which appears to be at a probability of approximately 0.01 lymphomas per mouse per day. This is about the same as the saturation value reached in old age (after 700 days). There is also evidence for a threshold dose or dose rate below which early tumors are not induced. P^{32} is a comparable carcinogenic stimulus and, again, a threshold dose or dose rate is encountered. The rate of tumor production with both agents is roughly proportional to the respective lethal doses. P^{32} is effective, whether given in a single dose or in monthly divided doses.

471

Burrows, H. and W. V. Mayneord. A NOTE ON TUMORS IN MICE. *Am. J. Cancer* 31, 484-5(1937).

Spindle cell sarcoma were produced in mice injected subcutaneously with cholesterol which had been irradiated with x-rays in doses of 2000-110,000 roentgens. (CA)

472

Butterworth, J. S. OBSERVATIONS ON THE HISTOGENESIS OF OVARIAN TUMORS PRODUCED IN MICE BY X-RAYS. *Am. J. Cancer* 31, 85-99(1937).

Ninety-one female mice were irradiated over the entire body in groups of 15 to 25. The irradiation factors were as follows: 190 kv, 30 ma, 50 cm distance, 0.5 mm Cu + 1 mm Al. The ovaries of these mice and of control mice were studied at various ages from 5 weeks to 25 months to determine the histogenesis of tubular adenomata, granulosa-cell tumors, and luteomata. In irradiated mice, tubular adenomata are formed by down-growths of the germinal epithelium of the ovary. The earliest down-growths appear about six months after irradiation. Granulosa-cell tumors are derived from nests of follicle cells which form at the periphery of the ovary after irradiation and in senile mice proliferate to form tumors. These nests of cells are probably derived from normal follicles following degeneration of the ova. Luteomata are usually formed indirectly by luteinization of granulosa-cell tumors, but it is possible that they are occasionally formed directly by division and proliferation of lutein cells. Granulosa-cell tumors and luteomata of mice are similar to those of women and it is unnecessary to postulate embryonic rests of granulosa cells to account for the histogenesis of granulosa-cell tumors. (S.V.S.)

473

Cloudman, Arthur M., S. Phyllis Stearner, Katherine Hamilton, John Sackis, and Dorothy Vining. PROGRESS REPORT (HISTOPATHOLOGY), p.102-15 of BIOLOGICAL AND MEDICAL DIVISIONS QUARTERLY REPORT, NOVEMBER 1948 TO FEBRUARY 1949. Argonne National Lab. Feb. 1, 1949. 13p. (ANL-4253(p.102-15))

The first section of this progress report is a bioassay of the combined effects of the simultaneous exposure to methylcholanthrene (MC) and a beta emitter. CF-1 mice were used. One series received P^{32} and MC on the skin surface. A second series received subcutaneous exposure to cholesterol pellets containing Y^{91} and/or MC. Observed tumors were grouped according to distribution at the treatment site, immediately adjoining treatment site, and in other body regions. Data were tabulated at 10-week intervals for the first 50 weeks. The number of tumorous mice and the frequency per animal are given. There is a strong indication of a synergistic effect in the production of certain types of tumors. In chicks, the lethal effects of exposure to a given dosage of x-radiation has been shown to depend on the age of the animal as well as on the rate at which the exposure is made. (ACD)

474

Elson, L. A. and L. F. Lamerton. THE INFLUENCE OF THE PROTEIN CONTENT OF THE DIET ON THE RESPONSE OF WALKER RAT CARCINOMA 256 TO X-RADIATION. *Brit. J. Cancer* 3, 414-26(1949).

After whole-body radiation (100 r/day for 8 days beginning 1 day after tumor implantation) or localized irradiation of an established tumor (400 r total in dose of 250 r daily beginning 6 days after tumor implantation) tumor inhibition was greater in rats on a 5% protein diet than in those on a 20% protein diet. No complete regression of the tumor was obtained. With localized irradiation of the tumor when 4000 r was applied in large daily doses complete regression of tumors was obtained in 90% of the rats on the 20% protein diet but in only 15% of those on the low protein diet. (CA)

475

Figge, Frank H. J. COSMIC RADIATION AND CANCER. *Science* 105, 323-5(1947).

An experiment is described which involved the attempt to intensify cosmic radiation effects by means of various combinations of lead plates and the comparison of the rate of carcinogenesis in mice receiving the intensified cosmic radiation with the rate of carcinogenesis in mice re-

ceiving non-intensified (normal) cosmic radiation. The rate of induction of cancer in mice kept under the lead plates was found to be consistently and definitely higher than that in the controls. All the mice had been injected with methylcholanthrene. It is suggested that the cosmic radiation is intensified by production of showers or bursts of ionizing radiations occurring when the rays pass through the thin metal plates, and that the methylcholanthrene induces cancer by converting some of the energy of the cosmic radiation into carcinogenic stimuli. (BA)

476

Figge, Frank H. J. STUDIES ON THE INFLUENCE OF PENETRATING RADIATIONS ON CARCINOGENESIS. *Acta Unio Intern. contra Cancrum* 6, 782-6(1949).

In order to test the possible influence of cosmic radiation of carcinogenesis, lead plates were placed 5-8 cm above male mice injected with 0.5 g of methylcholanthrene; the frequency of showers of cosmic radiation was thereby increased. The latent period for the induction of tumors was decreased for this group as compared with controls; repetition of this experiment using a different strain of mice gave essentially similar results; the possibility of lead toxicity as a contributing factor was tested and ruled out. Mice were also placed in coal mines at various levels; one group at 300 ft, one at 600 ft, and other groups at 1,035 ft underground. It was found that while the cosmic radiation decreased as the depth in the mine shaft increased, in this mine at least, the γ radiation increased; a group of 40 mice at the 1,035 ft level were placed in a lead cage to partially eliminate the γ radiation factor. From the results of this and related experiments there was some evidence that the cosmic particles and photons of γ radiation are synergistic and additive but not equivalent as co-carcinogenic agents. The mice shielded only in wire cages at various levels in the mine required longer latent periods for the development of the cancer in the order given: 300, 600, and 1,035 ft. It is concluded that the potency of such powerful carcinogens as methylcholanthrene may be altered by slight variations in the intensity of penetrating environmental radiations. (NSA)

477

Furth, J. FACTORS OF INDUCTION OF OVARIAN TUMORS BY X-RAYS: TYPES, CHARACTER AND HISTOGENESIS OF THESE GROWTHS. *Acta Unio Intern. contra Cancrum* 6, 785-6(1949).

Following the irradiation of four to six weeks old mice with 87 r, 175 r, or 350 r, ovarian tumors began to appear when the mice were about 11 months of age. The frequency of these neoplasms increased with time and almost every mouse that lived 17 months developed a unilateral or bilateral ovarian growth irrespective of the dose of irradiation; these growths were transplantable and metastasizing and usually complex: granulosa, luteoma, glandular, and other types. The granulosa tumors caused estrogenization and hypervolemia, while the neoplastic lutein cell masses masculinized (caused atrophy of adrenal cortex and often obesity). It is stated that the histogenesis of these and other tumors induced by x-rays will be discussed. (NSA)

478

Furth, J. RELATION OF PREGNANCIES TO INDUCTION OF OVARIAN TUMORS BY X-RAYS. *Proc. Soc. Exptl. Biol. Med.* 71, 274-7(1949).

It was found that mice exposed to 50-200 r of X-rays can have one or several normal pregnancies and still be liable to the development of ovarian tumors in a stock in which this neoplasm is extremely rare. Irradiation at 1-3 days of life with 150 r sterilized only one-third of the mice, while ovarian neoplasms appeared in about 76%. Irradia-

tion at 1-3 days did not hasten the onset of ovarian neoplasms as compared to irradiation at 4-10 weeks. In both groups the tumors developed in middle-aged and old mice. The author postulates the existence of a specific delayed x-ray effect coupled with a hormonal imbalance provoked by X-rays leading to the development of ovarian tumors. (EM)

479

Furth, J. and O. B. Furth. NEOPLASTIC DISEASES PRODUCED IN MICE BY GENERAL IRRADIATION WITH X-RAYS. I. INCIDENCE AND TYPES OF NEOPLASMA. *Am. J. Cancer* 28, 54-65(1936).

Mice were exposed to a single dose or repeated doses of X-rays at the age of approximately 5-12 weeks; 775 mice were irradiated, and 1,290 were kept as controls. Irradiation caused an increase of ovarian tumors to 15 times as many as in the controls of myelosis to 8 times, of mediastinal lymphosarcoma of 7 times. There was a slight but definite rise in the incidence of several other neoplasms, but those of the breast decreased by half. The occurrence of breast cancer appears to be conditioned by ovarian hormonal activity, which is decreased by irradiation but apparently increased with the development of ovarian new growths, in irradiated mice. The high incidence of breast cancer with ovarian neoplasms and the associated endometrial hyperplasia suggest that some ovarian tumors produce hormone. The X-ray induced tumors are indistinguishable from those occurring spontaneously and appear at a somewhat earlier age than the similar tumors of unirradiated mice. It is suggested that X-rays so alter the constitution of certain cells that they or some of their offspring undergo malignant transformation several months after irradiation. (BA)

480

Gardner, W. V. OVARIAN AND LYMPHOID TUMORS IN FEMALE MICE SUBSEQUENT TO ROENTGEN-RAY IRRADIATION AND HORMONE TREATMENT. *Proc. Soc. Exptl. Biol. Med.* 75, 434-6(1950).

Mice irradiated with 280-380 r and then given weekly injections of 16.6 γ estradiol benzoate did not have ovarian tumors whereas those irradiated and given 1.25 mg testosterone propionate weekly or plain sesame oil injections did. Many of the mice developed lymphomas, the incidence was lower in the group given testosterone propionate than in the other 2 groups. (CA)

481

George, E. P., M. George, J. Booth, and E. S. Horning. INFLUENCE OF COSMIC RADIATION ON INDUCED CARCINOGENESIS IN MICE. *Nature* 164, 1044-5(1949).

The influence of cosmic radiation on carcinogenesis in mice was studied at Jungfrauoch. Mice receiving 0.25 mg of 20-methylcholanthrene were divided into three equal groups; the controls in a tunnel under 60 m of rock, the second group in the cosmic ray cabin and the third under a 2 cm lead screen in this cabin. The results were not conclusive and the repeated experiments on the roof of the London School of Hygiene and Tropical Medicine gave a random variation and differed from Frigge's results. (EM)

482

Henshaw, P. S. LEUKEMIA IN MICE FOLLOWING EXPOSURE TO X-RAYS. *Radiology* 43, 279-85(1944).

C-57 black mice received single doses of 200 r/air of X-rays over the whole body, repeated at four week intervals as long as this could be done without too severe an effect on the health of the animals. The radiation factors were: 200 kv, 20 ma, 0.5 mm Cu and 1.0 mm Al filtration, distance 38 cm. During exposure the mice were kept in a shallow light-weight celluloid tray. Following treatment,

they were kept under constant observation (blood counts) until death, at which time they were examined grossly and histologically for leukemia. Continuous blood records showed a general depression of leucocyte level during treatment, followed by a slow return to normal after treatments were discontinued. In some animals, the recovery extended into marked leucocytosis, and these animals at death were invariably found to have leucemic infections. Hyperplasia of hematopoietic organs was seen in all animals recorded as positive, but the distribution of such conditions varied from animal to animal. (BA)

483

Henshaw, Paul S. and James W. Hawkins. INCIDENCE OF LEUKEMIA IN PHYSICIANS. *J. Natl. Cancer Inst.* 4, 339-46(1944).

A comparison was made of the incidence of leukemia in physicians and in the general population. Data were obtained from the death list of the J. A. M. A. from the mortality reports of the U.S. Bur. of the Census, and an unpublished compilation of the U. S. Public Health Service. Comparisons were made on the basis of (1) the ratio of deaths from leukemia to deaths from cancer, (2) ratio of deaths from leukemia to total death rates, and (3) death rates from leukemia. Leukemia was recognized approx. 1.7 times more frequently among physicians than among white males in the general population. Possible discrepancies are discussed. While these observations furnish no direct proof that radiation acts to incite leukemia in human beings, they are in accord with the findings on experimental animals in which exposure to X-rays has been found to increase the incidence of leukemia. (BA)

484

Henshaw, P. S., E. F. Riley, and G. E. Stapleton. THE CARCINOGENIC EFFECT OF PILE RADIATIONS. (*Am. Assoc. Adv. Sci., Section on Chem., Gibson Island Research Conference on Cancer, 1946*), *Cancer Research* 7, 48(1947).

Mice and rats exposed to penetrating radiations (fast and slow neutrons, γ -rays) from the U chain reaction in a pile reactor developed neoplasms (mainly mediastinal lymphomas), the incidence of which was less than 15% in the controls, more than 60% in some of the experimental groups), lowered leucocyte level, emaciation, and loss of weight and died prematurely. When the animals were exposed to nonpenetrating radiations (β -rays) from the pile, the effects were limited mainly to skin abnormalities of all types, appearing several months after single massive doses; in strains that rarely showed skin lesions of any type, the incidence of carcinoma was raised to 100%, and loci per animal were great as 50-100. Fast neutrons were more active than γ -rays in producing the late effects. Daily threshold levels for shortening life were in the range of 1 r of γ -rays, and something well less than 0.1 r (of fast neutrons?). Length of life varied inversely with the amount of exposure, and the amount of effect varied directly with the concentration of ions in space and time. (CA)

485

Henshaw, Paul S. and R. S. Snider. REVIEW OF INFORMATION BEARING ON THE TUMOR INDUCTION ACTION OF SUPERFICIAL RADIATIONS, p.229-37 of BIOLOGICAL EFFECTS OF EXTERNAL BETA RADIATION. New York McGraw-Hill Book Company, Inc., 1951. (NNS Volume 22E, Chapter 16)

The pertinent facts associated at this time with induction of skin tumors with superficial radiations may be indicated as follows: It is important to remember that skin consists of layers of cells with the germinal layer at the base, and that the germinal layer proliferated other germinal cells and cells which became differentiated first to form an intermediate layer and finally the dead corneal layer. In the

skin there must continually be a residuum of active germinal cells and a process of maturation to death of cells in order to have normal skin function. Skin abnormalities consist of three types: (1) failures manifested as drying, scaling, fissuring, lessened resiliency, and reduced regenerative capacity, (2) anomalies such as badly formed nails, poor quality of hair, and poorly developed teeth; and (3) excesses involving overgrowth and overfunction as in neoplasia. Radiation absorbed in the skin causes damage primarily in the germinal layer. When the damage to this layer is partial, the effect is a skin failure; the germinal layer is unable to proliferate enough cells to maintain the integument with the result that there is drying, scaling, fissuring, possible loss of hair, etc. Repair takes place from the floor of the damaged area, however, from living germinal cells that remain. When damage to the germinal layer is complete the effect is skin sterilization; not only is there drying and scaling, but also there is exudation, sloughing, and ulcer formation. In this case healing must be from the edges as no germinal elements remain. Skin tumors often arise out of such wounds that have become refractory. In the case of superficial radiations skin tumors (of practically every type) have been observed to appear in animals that display little or no gross evidence of skin break down. Single applications of beta rays have been observed to be carcinogenic, as many as 50 to 100 loci of tumor growth being produced on rats that ordinarily show no skin lesions. (ADD)

486

Hoch-Ligeti, Cornelia. EFFECTS OF REPEATED X-RADIATION OF THE WHOLE BODY ON THE DEVELOPMENT OF TUMORS IN RATS DUE TO FEEDING p-DIMETHYLAMINOAZOBENZENE. *Brit. J. Cancer* 3, 562-9 (1949).

Forty male and 10 female Wistar rats were fed ad lib a semi-synthetic diet, containing 0.07% p-dimethylaminoazobenzene, and 20 of the male rats were given soft x-radiations, while 10 male and 10 female rats received penetrating x-radiations. The irradiations were begun on the same day as the feeding of the carcinogenic compound and similar techniques of application were utilized. The penetrating radiations were delivered by a 180-kv machine with a 0.75 mm Cu and 1 mm Al filtration at a focal distance of 30 cm, while the soft radiations were delivered at 45 kv with no added filtration and at a focal distance of 20 cm. At the beginning of the experiment, each rat received 10 r once weekly, delivered to the liver as a 10 r dose in the case of the penetrating radiations (with a dorsal skin dose of 13 r), and as a dose of 0.3 r to the liver for the soft radiations. Each rat was irradiated individually and the intervals between irradiations were extended to two weeks and occasionally three to four weeks. The rats treated with hard radiations received a total of 310 r in the liver, while the soft radiation group received a total of 10 r. All nonirradiated rats receiving p-dimethylaminoazobenzene developed hepatic tumors, but the development of tumors was prevented, or their rate of growth retarded, in rats treated with soft radiation. The growth of hepatic tumors was slightly retarded in rats treated with penetrating rays and skin tumors developed in two of these rats. The adrenals of rats receiving soft x-rays were significantly enlarged. (NSA)

487

Kaplan, H. S. OBSERVATIONS ON RADIATION-INDUCED LYMPHOID TUMORS OF MICE. *Cancer Research* 7, 141-7(1947).

Strain A mice in groups of various ages yielded a maximum incidence of lymphoid tumors in animals irradiated at one month of age with a sharp decrease at two months

and later. Thymectomy of strain A mice irradiated at two to three months of age resulted in a considerable increase in the latent period and a very slight decrease in the incidence of lymphomas as compared with the low incidence in intact irradiated control mice of the same age. In a parallel experiment, splenectomy was followed by a slight decrease in incidence without change in latent period. The tumors are lymphocytic lymphomas which, in most instances, appear to rise in the thymus, to disseminate to the spleen, lungs, liver, kidneys, and lymph nodes, and to cause leukemia in a considerable percentage of animals. Incidental observations on radiation-induced ovarian tumors and on inhibition of spontaneous mammary tumors following X-ray treatment are presented. (auth)

488

Kaplan, Henry S. **PRELIMINARY STUDIES OF THE EFFECTIVENESS OF LOCAL IRRADIATION IN THE INDUCTION OF LYMPHOID TUMORS IN MICE.** *J. Natl. Cancer Inst.* **10**, 267-70(1949).

In order to test the theory that incident radiation acts locally and directly upon the cell or tissue to produce alterations in the cellular behavior manifested as tumorous growth, the three experiments described here were performed. In the first experiment, strain A mice were immobilized and irradiated over one of four dorsal regions through a circular portal of 1 cm. in diameter; the radiations were 600-750 r. The second experiment consisted of the irradiation of mice of the C-57 strain by a single dose of 1000 r, delivered to a transverse body section 4 mm. in thickness. In the third experiment, 1000 r was delivered in five daily treatments in two consecutive weeks to mice of the strain C-57; some of the mice were treated over the entire upper half of the body, and others over the entire lower half. The results show that the induction of the lymphoid tumors occurred without significant frequency and indicate that their production is, the authors state, probably not solely the result of a simple direct action of radiation upon the susceptible cell or tissue of origin. (NSA)

489

Kaplan, Henry S. **LOCAL IRRADIATION AND THE INDUCTION OF LYMPHOID TUMORS IN MICE.** *Cancer Research* **9**, 621(1949).

This paper is an abstract and is presented here in its entirety.

Whole-body exposure of mice to roentgen rays in adequate dosage has long been known to yield lymphoid tumors. Strain A mice, which are moderately susceptible, and strain C57 black mice, which are highly susceptible to whole-body irradiation, have been studied following local exposure. Strain C57 black mice one month of age were treated over the anterior or posterior half of the body with daily doses of 100 r for 10 days. After 17 months, only 2 of 55 mice (4%) irradiated over the upper half, and 1 of 55 mice (2%) irradiated over the lower half of the body have developed lymphoid tumors. In previous experiments the incidence of such tumors following whole body exposure of young mice of this strain to the same total dose has averaged about 65% at 10 months. No exact data are available for half of this total dose delivered to the whole body, but extrapolation indicates that a significantly higher incidence might be expected than was observed after half body irradiation. Larger doses sharply localized to the region of the mediastinum or upper abdomen have produced no lymphoid tumors in either strain, and mice of strain A have also been completely refractory to local treatment over the skull or lower abdomen. These results suggest that shielding one half or more of the body

from roentgen rays confers a considerable degree of protection against the induction of lymphoid tumors in mice.

490

Kaplan, Henry S. **INFLUENCE OF OVARIAN FUNCTION ON INCIDENCE OF RADIATION-INDUCED OVARIAN TUMORS IN MICE.** *J. Natl. Cancer Inst.* **11**, 125-32(1950).

Irradiated ovaries implanted intramuscularly into irradiated and nonirradiated groups of spayed LAF₁ hybrid mice gave rise to many granulosa-cell tumors, luteomas, and related neoplasms. No such tumors occurred when irradiated ovaries were implanted into nonirradiated, nonovariectomized mice. It is concluded that intact ovarian endocrine function inhibits the development of tumors in irradiated ovarian grafts, confirming the reported observations of Lick, Kirschbaum, and Mixer. (*Cancer Research*, **9**: 532-536(1949)) (NSA)

491

Kaplan Henry S. and Mary B. Brown. **INHIBITION BY TESTOSTERONE OF RADIATION-INDUCED LYMPHOID TUMOR DEVELOPMENT IN INTACT AND CASTRATE MALE MICE.** *Cancer Research* **11**, 262(1951).

Strain C57 black male mice were distributed as litter mates among four groups of about 50 mice each. Two groups were maintained intact, the other two castrated at 2 months of age. Whole-body irradiation was started 3 to 4 days later; all groups received a total of 675 r in 4 equal fractions at 4-day intervals. One castrated and one intact group received intramuscular injections of testosterone starting on the first day of irradiation, while the other two groups were injected with the aluminum phosphate suspension (placebo) alone. The injection volume was 0.02 cc of either material given twice weekly for 10 weeks. To date, lymphoid tumors have been observed in only 3 of 49 intact, testosterone-treated animals (6%), and in 4 of 50 castrated, testosterone-treated animals (8%), as contrasted with an incidence of 71 and 83% among intact and castrated placebo-treated mice, respectively. Thus, testosterone exerts a striking inhibitory effect on the development of lymphoid tumors in irradiated male mice. Under the conditions of the present experiment, castration of mature male mice did not significantly modify lymphoid tumor incidence. (NSA)

492

Kaplan, Henry S. and Mary B. Brown. **EFFECT ON LYMPHOID TUMOR INCIDENCE OF CHANGES IN TOTAL DOSE, FRACTIONATION, AND PERIODICITY OF WHOLE-BODY ROENTGEN IRRADIATION.** *Cancer Research* **11**, 262(1951).

(This paper is an abstract and is presented here in its entirety.)

A total of 1733 black mice of both sexes was assigned by randomization of litters to 32 groups, all of which were irradiated at 33 ± 3 days of age. Successive groups received systematic increments of total dose, administered either as a single treatment or in 2, 4, or 8 equal daily fractions. Equivalent total doses were also given in fractionated treatments at intervals of 4, 8, and 16 days. Lymphoma incidence roughly paralleled total dose, within the range investigated, for either a single exposure or fractionated exposures at daily intervals. Response to equal total doses was not modified by the degree of fractionation. For a given total dose, however, there was a striking increase in incidence when an interval of 4 to 8 days occurred between treatments. Response was no greater than for daily treatments when the interval was increased to 16 days. In contrast, mice exhibited a pronounced ability to recover from the lethal effect of a given total dose with either increasing fractionation or, in particular, the interposition of an in-

creasing interval between treatments. The difference in dose-response characteristics indicates that roentgen radiation operates through different mechanisms in eliciting lethal and leukemogenic responses in mice. (NSA)

493

Kaplan, Henry S. and Mary B. Brown. FURTHER OBSERVATIONS ON INHIBITION OF LYMPHOID TUMOR DEVELOPMENT BY SHIELDING AND PARTIAL-BODY IRRADIATION OF MICE. *J. Natl. Cancer Inst.* **12**, 427-35(1951).

Previous evidence that local irradiation is ineffective in the induction of mouse lymphoid tumors and that an indirect systemic mechanism must therefore be implicated was confirmed by partial-body irradiation and mediastinal shielding experiments. There was no evidence of an effect attributable to shielding or transplanted ovaries, while shielding of an indifferent area of the body such as the thigh significantly inhibits the genesis of lymphoid tumor. (NSA)

494

Kaplan, Henry S., Mary B. Brown, and Sumner N. Marder. ADRENAL CORTICAL FUNCTION AND LYMPHOID TUMOR INCIDENCE IN IRRADIATED MICE. *Cancer Research* **11**, 262-3(1951).

Experiment I.—Groups of C57 black mice received local or whole-body irradiation and/or cortisone in various combinations. In the dose administered, whole-body irradiation yielded lymphomas in 41 of 50 mice. When cortisone injections were started simultaneously with irradiation, only 18 of 48 mice developed these tumors, and when cortisone treatment was deferred until 6 weeks after irradiation only 6 of 23 animals responded. Cortisone alone yielded no tumors. Irradiation over the mediastinum alone, or over the rest of the body with the mediastinum shielded, failed to elicit lymphomas whether or not cortisone was also given. **Experiment II.**—Two groups of C57 black mice were adrenalectomized and a third subjected to sham operations. Group I received no further treatment; the other adrenalectomized group and the sham-operated group received fractionated whole-body irradiation in four treatments at 2-week intervals. Initial mortality was 20, 67, and 3%, respectively. Lymphoid tumors occurred among 0 of 24, 13 of 20, and 12 of 59 surviving mice, respectively, indicating a significant increase in susceptibility to lymphoma induction among adrenalectomized mice. (NSA)

495

Kaplan, Henry S. and Edwin D. Murphy. THE EFFECT OF RADIATION ON THE BIOLOGICAL BEHAVIOR OF A MOUSE MAMMARY CARCINOMA. *Acta Unio Intern. contra Cancrum* **6**, 810-11(1949).

In four separate experiments, a transplantable mouse mammary adenocarcinoma (tumor 755) was inoculated in the hind legs of groups of 40-50 mice of C57 black strain. When the tumors reached the diameter of about 1 cm, half of the animals were treated locally with doses of 400-1,000 r with the remainder of the body carefully shielded. Animals of both the irradiated and untreated groups were sacrificed simultaneously and pulmonary metastases were found in 27 of 62 mice bearing irradiated tumors, and in five of 52 controls. Collaterally, irradiated and control tumors were removed from their hosts and inoculated subcutaneously into several alien strains of mice and into the anterior ocular chamber of guinea pigs. It was found that the irradiated tumors grew progressively in 7 of 77 alien mice and that the untreated tumors grew in 2 of 108 mice, no progressive growth was observed in guinea pigs. It is suggested that roentgen irradiation in moderate doses may

alter the behavior of a tumor in the direction of increased autonomy. (NSA)

496

Kirschbaum, A., J. R. Shapiro, and W. H. Mixer. SYNERGISTIC ACTION OF ESTROGENIC HORMONE AND X-RAYS IN INDUCING THYMIC LYMPHOSARCOMA OF MICE. *Proc. Soc. Exptl. Biol. Med.* **72**, 632-4(1949).

Synergistic lymphogenic effects were obtained when estrogenic hormone and X-rays were administered simultaneously to mice of the Bagg albino and CBA strains. Thymic lymphoid tissue appeared to be more sensitive than other lymphoid tissue. This was also true when X-rays and methylcholanthrene acted synergistically in the dba stock. (BA)

497

Koletsky, Simon, Frederick J. Bonte, and Hymer L. Friedell. PRODUCTION OF MALIGNANT TUMORS IN RATS WITH RADIOACTIVE PHOSPHORUS. *Cancer Research* **10**, 129-38(1950).

Adult white male rats of the Wistar strain, weighing about 150 g, were used in experiments in which the incidence of neoplasms was observed following either the injection of a LD-50 dose of P^{32} (4.5 μ c/g of body weight) or repeated injections of P^{32} (1.5 μ c/g body weight every three weeks) for a total dose of 9 or 12 μ c/g; spontaneous bone tumors have not been observed among control animals of this strain. Complete autopsies were performed on all rats which died or were sacrificed, and in almost all the animals routine microscopic sections of the femur and vertebrae were taken. Of the 19 animals in the first group, nine developed malignant neoplasms but were otherwise in good condition, except for the last few weeks of life. Of 15 rats in the second group, 4 were discarded, and of the remaining 11, 4 developed neoplasms. Of the total of 13 neoplasms, 3 were squamous-cell carcinoma involving the face and were associated with exophthalmos; 10 were osteogenic sarcomas, 4 of which were located in the jaw, 2 in the spine, 2 in the tibia, and 1 each in the femur and pelvis; 4 of these latter tumors metastasized to the lungs. The incidence of tumor development was about 40%. A typical proliferation of bone was usually found in the rats and the lesions, it is concluded, may have served as a precursor to malignant change. (NSA)

498

Lick, Louis, Arthur Kirschbaum, and Harry Mixer. MECHANISM OF INDUCTION OF OVARIAN TUMORS BY X-RAYS. *Cancer Research* **9**, 532-6(1949).

The results of experiments to determine whether X-rays induce tumors in mice in the presence of normal ovarian function are discussed. The Bagg albino stock of mice was used. The ovaries were irradiated with a Phillips Contact Therapy Machine at 45 kv through 1 mm. Al filtration at a 19 mm target distance and at a rate of 1,500 r per minute. Practically all the females receiving 200 r whole body irradiation at 8-10 weeks of age developed bilateral ovarian tumors if they survived 16 months after the irradiation; mice receiving 200 r irradiation to one ovary after the extirpation of the other ovary demonstrated 100% tumor development; mice receiving 200 r locally to one ovary with the other protected and intact developed no tumors in the irradiated ovary. However, a granulosa cell tumor did develop spontaneously in a non-irradiated ovary. Larger doses of x-radiation produced results similar to the 200 r irradiation. (NSA)

499

Lorenz, E., W. E. Heston, M. Deringer, and A. B. E. Eshenbrenner. INCREASE IN INCIDENCE OF PULMONARY TUMORS IN STRAIN-A MICE FOLLOWING LONG-

CONTINUED IRRADIATION WITH GAMMA-RAYS. *Cancer Research* 6, 485(1946); *J. Natl. Cancer Inst.* 6, 349-53(1946).

Sixty mice of strain A (35 males and 25 females) were exposed daily for eight hours to γ radiation from a 1-g Ra source filtered by 0.5 mm of Pt. The daily dose was $8.8 \pm 10\%$ r. The same number of controls were kept. The animals were 1-2 months old at the beginning of the experiment. Exposure was terminated after 287 days when the experimental animals had received a total dose of $2500 \pm 10\%$ r. The incidence of lung tumors in the experimental animals was 77% and in the controls 47%, a statistically significant difference. (NSA)

500

March, H. C. LEUKEMIA IN RADIOLOGISTS. *Radiology* 43, 275-8(1944).

For some years there has been an impression that exposure to radiation might cause leukemia. Twenty-three cases of leukemia following irradiation have been reported in the world literature but in some of these details were lacking and the causal relationship was not established. The author was impressed by the death of three radiologists from leukemia during 1943. He therefore made a study of the death of radiologists reported in the *Am. J. Roentgenol.* and in *Radiology* for the past 15 years and found that among 175 deaths, the cause of which was reported in 173, eight deaths had been caused by leukemia. This gives an incidence of 4.57% for all types of leukemia in radiologists in the past 15 years. The incidence of deaths from leukemia among physicians not practicing radiology during this same period was 0.44%. The incidence of leukemia therefore among radiologists was more than 10 times that among physicians not practicing radiology. A statistical analysis shows that there is only one chance in a million of getting eight cases of a condition by chance alone in a group of 175 cases, when the standard rate of incidence is 0.441%. The author suggests that the deaths and major illnesses of all radiologists be recorded by some central agency so that the relationship between prolonged irradiation and various pathological conditions may be established. (AJR)

501

March, Herman C. LEUKEMIA IN RADIOLOGISTS IN A 20-YEAR PERIOD. *Am. J. Med. Sci.* 220, 282-6(1950).

The study of the incidence of leukemia in radiologists has been extended to cover a 20-year period. It has been shown that during this time leukemia has occurred more than nine times as frequently in radiologists as in nonradiological physicians. This difference has statistical significance. It is suggested that the increased incidence of leukemia in physicians as a whole (compared with the adult male white population) might be due to the same factor of exposure to ionizing radiation. The experimental work showing an increased incidence of leukemia in mice exposed to roentgen irradiation has been reviewed. (NSA)

502

Martland, Harrison S. THE OCCURRENCE OF MALIGNANCY IN RADIOACTIVE PERSONS. *Am. J. Cancer* 15, 2435-2516(1931).

There have been 5 deaths from osteogenic sarcoma in a total of 18 originating in occupational poisoning by radioactive substances in former dial painters from the New Jersey plant, an incidence of 27%. As the incidence of the ordinary variety of primary osteogenic sarcoma is only about 0.07%, this is overwhelming evidence that the radioactivity of these dial painters is the true cause of the sarcoma. Symptoms and histopathological developments occurred during the various stages of osteogenic sarcoma are

described to some detail. Attention is called for the first time to the difference in biological effects on the human bone marrow of external penetrative irradiation and internal α radiation as seen in these cases. In this respect attention is called to the fact that anemias developing from undue exposure to external radiation are considered by most authorities as of the aplastic type, whereas anemias caused by internal α radiation are of the regenerative, hyperplastic, or megablastic type. That radioactivity in the human body may play an important part in the production of other forms of malignancy in no way connected with Ra dial painting is suggested; the high incidence of primary carcinoma of the lungs in the Co miners of Schneeberg and in the pitchblende mines of Joachimsthal being noted. The multiplicity of lesions and diseases produced by irradiation from external exposure to Ra and X-rays, and radiation from intern. bombardment by the α particle is noted. Such a variety of lesions produced by a single agent might indicate that many of the lesions are closely interrelated and are only manifestations of various degrees of injury to, or stimulation of exhaustion of, certain normal body tissues. (S.V.S.)

503

Mayneord, W. V. and L. Dorothy Parsons. THE EFFECT OF X-RADIATION ON TUMOR PRODUCTION BY A CHEMICAL COMPOUND IN MICE AND THE ASSOCIATED BLOOD CHANGES. *J. Pathol. Bacteriol.* 45, 35-8(1937).

Irradiation of mice either previous to or during the injection of Na 1,2,5,6-dibenzanthracene-9,10-endo- α , β -succinate accelerates tumor formation and gives rise to a greater number of sarcomas. All irradiated mice show a constant blood change immediately following irradiation, i.e., an initial fall in total white count with a subsequent rise, an absolute fall in lymphocytes and a corresponding rise in polymorphs. (CA)

504

Mendeleeff, P. THE ADDITIVE ACTION OF METHYLCHOLANTHRENE AND X-RAYS ON THE GUINEA PIG. *Compt. rend. soc. biol.* 144, 301-2(1950).

Previous attempts by the writer to induce cancer in guinea pigs with methylcholanthrene were unsuccessful. Massive doses of X-rays or radium alone would only produce radiodermatitis which occasionally would be transformed into a malignant tumor. The author injected four guinea pigs subcutaneously with 30 mg. methylcholanthrene and exposed them five to six days later to 400 r at 85 kv at the place of injection. Three of the animals exhibited tumors, two of which were cancerous. These tumors occurred with prior radiodermatitis. (NSA)

505

Moshman, Jack. ON THE INCIDENCE OF CANCER IN OAK RIDGE, TENNESSEE. Office of the Medical Adviser (ORO, AEC). July 2, 1948. 28p. (TID-77)

Since the full nature of the extent of operations at Oak Ridge was reached after the dropping of the first atomic bomb on Hiroshima, there has been a great deal of speculation concerning the hazards of employment, or residence, in the "Atomic City". To many, radioactive chemicals suggest cancer and one of the hitherto unanswered questions was "are Oak Ridge employees, or residents, more susceptible to cancer than is the general population?" In order to provide a factual, statistical answer to these questions the Medical Advisor's Office of the ORDO of the U. S. A. E. C. conducted an exhaustive, statistical study of this problem at Oak Ridge. Conclusions follow: The age standardized incidence rate of cancer among the Oak Ridge employees and their resident dependents is 123 cases an-

nually per 100,000. This is significantly lower than the accepted national rate of 230 per 100,000 annually. The proportion of employees who have possibly been exposed to radioactive chemicals and who have developed cancer is approximately equal to their proportion in the entire population indicating that there is no reason to believe that they are more susceptible to cancer. The low cancer rate is in harmony with the low death rate in Oak Ridge from most diseases and within the accepted tolerance limits of the ratio of cases of cancer to cancer-caused deaths. The relative proportion by primary sites of occurrence among white females with cancer is not significantly different from the nationally based expected values. Among white males a significantly higher proportion of cancer of the respiratory system was found than might be expected by chance from the 1938 national averages. A tentative explanation on the basis of a long-established upward trend in cancer of the respiratory system among males was offered. Reference was made to other authorities who offer evidence of the relationship between one's socio-economic group and his susceptibility to cancer. (ACD)

506

Mottram, J. C. PRODUCTION OF EPITHELIAL TUMORS BY IRRADIATION OF A PRECANCEROUS SKIN LESION. *Am. J. Cancer* **30**, 746-8(1937).

Application of γ -radiation to a precancerous skin lesion in doses of about 1,000 r, or insufficient to destroy the epidermis is followed by a greater number of epithelial tumors than would have occurred had no radiation been applied. This is a corollary to Cramer's finding that doses destructive to the epidermis inhibited epithelial tumors under similar conditions. The similarity between these experimental findings and the results of a stimulating dose occasionally seen clinically is discussed. The danger of treating precancerous lesions with radiation unless a destructive dose can be given to the whole area, is stressed. The importance of these findings with regard to the mutation hypothesis is considered. (auth)

507

Park, Harold F. ROLE OF THE UNPAIRED ELECTRON IN CARCINOGENESIS. *J. Phys. & Colloid Chem.* **54**, 1383-4(1950).

Azo dyes, complex hydrocarbons, organic amines and their derivatives, actinic radiation, x-rays, and radiations from radioactive materials are capable of initiating neoplastic tissue transformations and also of forming free radicals. Free radicals can be destroyed only as the result of an electron pairing reaction. Substances which initiate cancer are identical or similar to the substances which alleviate it. Thus cancer seems to be the result of a free radical reaction. (CA)

508

Rajewsky, B. ON THE MUTATION THEORY OF THE ORIGIN OF CANCER. *Z. Krebsforsch.* **55**, 274-84(1949).

The cancerogenic properties of ionizing radiations were examined, in the light of the cell-mutation theory, on white mice submitted to the action of x rays and α particles. The latter were introduced into the animals' bodies by adding radon, in various concentrations, to the air of the cage. The main result was the discovery of the strong tumor-producing effect of very small doses of α rays. With increasing time of exposure to feeble α radiations, a whole series of tumors from benign adenoma to adenocarcinoma and bronchial cancer was obtained. (NSA)

509

Ross, Joan M. THE CARCINOGENIC ACTION OF RADIUM IN THE RABBIT: THE EFFECT OF PROLONGED IRRADIATION WITH SCREENED RADIUM. *J. Pathol. Bacteriol.* **43**, 267-76(1936).

Radium-filled platinum tubes of 1.0 cm. overall length, filtration 0.55 platinum and content 0.1 mg radium element, were implanted into the tissues of 9 rabbits; 7 of the rabbits developed malignant new growths in immediate relation to the tubes. Five of the tumors were sarcoma and 2 were squamous cell carcinoma. It was concluded that γ radiation of weak intensity but prolonged duration (97-167 weeks) was the carcinogenic factor in these cases and that the type of growth produced depends on the nature of the tissue in which the tube is embedded. (auth)

510

Vesin, M. S. PULMONARY CANCER PRODUCED BY RADIOACTIVE EMANATIONS. *Arch. maladies profess. md. travail et scurit sociale* **9**, 280-3(1948).

A discussion is presented on the effects of radioactive emanations on the lungs of mine workers in Jachymow. It is claimed that other predisposing factors toward the development of carcinoma of the lungs in miners are the lack of oxygen, the excess of carbon dioxide, and, possibly, silicosis and arsenic dust. Prophylaxis requires better ventilation of the mines; work in the mines, it is concluded, should be restricted to 5 to 10 years per person. (NSA)

511

Williams, George Z., Nelson F. Young, and Jeffries P. Moore. THE EFFECT OF IRRADIATION ON AZO DYE NEOPLASIA IN THE RAT LIVER. I. INFLUENCE OF X-RAY AND RADIO-GOLD ON THE INCIDENCE OF HEPATOMA AND THE HISTOLOGY OF THE LIVER IN RATS FED DIMETHYLAMINOAZOBENZENE. *Cancer Research* **11**, 289(1951).

Sprague-Dawley albino rats were maintained 24 weeks on a synthetic diet containing 0.04% m'-methylaminoazobenzene. Controls fed the basal diet and the azo dye only yielded nine tumors in 38 rats (24%), which survived 6 months or longer. The diet plus m' meDMB and 200 r x rays 3 times weekly for 6 weeks, with a total dose of 3,600 r, resulted in 20 liver tumors in 37 animals (55%); 20 r x rays 3 times per week for only 3 weeks (total of 1,600 r), followed by intrasplenic injection of radioactive gold colloid the fourth week of azo dye diet, caused 10 tumors in 15 rats which survived 6 months or longer (66%). In animals receiving x rays or radio-gold, the tumors were larger, occurred earlier, and were multicentric. An unusual cytologic pattern found in many irradiated livers is described. It is concluded that x-ray or Au¹⁹⁸ (chiefly β) irradiation produces a nonspecific liver-cell damage which increases the incidence of tumors produced by m'-methyl-dimethylaminoazobenzene. (NSA)

512

Wilson, James G., Robert L. Brent, and H. Charles Jordan. NEOPLASIA INDUCED IN RAT EMBRYOS BY ROENTGEN IRRADIATION. University of Rochester. Sept. 5, 1951. 30p. (UR-183)

Rat embryos x-irradiated on the 9th day of gestation developed discrete tumor-like growths in and around the brain. The incidence of such tumors was directly related to the dosage of x rays. They first appeared on the 2nd day after irradiation and thereafter exhibited varying capacities for growth and differentiation. Some grew for 1 or 2 days and then disappeared as a result of dispersal of the cells, others grew rapidly until the 5th and 6th postirradiation day and then became atrophic, and still others continued to grow slowly until the 7th or 8th day and then became static or underwent atrophic regression. Few remained in term animals and these were small and gave no evidence of proliferative activity. Although the tumor-bearing animals had a somewhat higher mortality than the nonirradiated controls, neither prenatal nor postnatal death could be attributed to the presence of the tumors. (NSA)

513

Young, Nelson F. and George Z. Williams. **THE EFFECTS OF IRRADIATION ON AZO DYE NEOPLASIA IN THE RAT LIVER. II. CATALASE, ALKALINE PHOSPHATASE, ARGINASE, AND RIBOFLAVIN LEVELS OF THE LIVER FOLLOWING X-RAY AND RADIO-GOLD IRRADIATION OF RATS FED DIMETHYLAMINOAZOBENZENE.** *Cancer Research* **11**, 291(1951).

Sprague-Dawley albino rats were maintained for 24 weeks on a synthetic diet containing 0.04% m'-methyl-dimethylaminoazobenzene. Groups were treated with (a) 250 r (x ray) at 250 kv 3 times weekly to 3,600 r, (b) intrasplenic injections of 2.0 mc or 0.6 mc. radioactive gold colloid, and (c) combination of 1,600 r x rays and 2.0 mc of intrasplenic radioactive Au colloid. Alkaline phosphatase ranged between 40 and 100 Bodansky units with diet and dye only. In livers containing tumors but without irradiation, it ranged from 75 to 110 (1 at 378), and in the livers containing tumors and subjected to irradiation, levels were from 75 to 180 with 3 above 325. Catalase was low during periods on the riboflavin-deficient diet but rose to normal levels after the animals were returned to stock diet. Irradiation produced no significant changes, and the levels were generally higher in the livers containing tumors. The riboflavin content of the livers was low (10 to 12 µg/g) with basal riboflavin-deficient diet and azo dye, and returned to normal levels of 20 to 30 µg on stock diet. The majority of livers of irradiated and tumor-bearing animals contained less riboflavin than normal appearing livers without irradiation. Irradiation produced no changes in arginase levels. It is concluded that ultimate dietary changes in catalase and riboflavin levels are not influenced by irradiation in the doses applied, and the possible significance of the changes in alkaline phosphatase is discussed. (NSA)

Effects on Immunity of Organisms

514

Becker, Robert M. **SUPPRESSION OF LOCAL TISSUES REACTIVITY (SHWARTZMAN PHENOMENON) BY NITROGEN MUSTARD, BENZOL, AND X-RAY IRRADIATION.** *Proc. Soc. Exptl. Biol. Med.* **69**, 247-50(1948).

Male albino rabbits were intradermally injected with 0.3 cc. of a solution of avirulent type I meningococcus filtrate or endotoxin in three areas, the epigastrium and the right and left lower quadrants. From 20 to 26 hours later, 2 cc. of undiluted meningococcus endotoxin/rabbit or 2 cc. of the undiluted meningococcus filtrate/kg. body weight was injected intravenously through the ear vein. The effects of various agents were studied to determine their suppressive action on the Shwartzman phenomenon produced by the meningococcus. When 13 rabbits were exposed once to 800 r of total body x-irradiation 3 to 7 days before the meningococcal injection there was almost a complete suppression of the reaction in 7 of the rabbits and complete suppression in the other 6; one animal which received 300 r three days before injection showed no suppression and two animals which received 800 r of the total body irradiation immediately before the injection also demonstrated no suppression. Benadryl, urethane, crude penicillin extract, penicillin G, streptomycin, mapharsen, BAL, vitamin C, α tocopherol, thyroidectomy, and partial exsanguination had no suppressing effect, but pretreatment with nitrogen mustard or benzol caused complete suppression of the reaction. It is suggested that this study may serve as a basis for a new therapeutic concept in the treatment of diseases involving tissue and vascular reactivity. (NSA)

515

Bennett, L. R., Vera Collier, Marion Kresage, and Paul E. Rekers. **A STUDY OF BLOOD AND SALIVARY LYSOZYME IN THE X-IRRADIATED DOG.** *Atomic Energy Project, University of Rochester.* Nov. 1, 1948. 13p. (UR-46)

Blood and salivary lysozyme activity has been studied in dogs receiving 350 r total body, single dose, roentgen irradiation. The depression of blood lysozyme activity parallels the depression of the white blood cell count post-irradiation and reaches near zero levels by the 12th day in animals that did not survive. The depression in leukocyte values and lysozyme activity is less pronounced in surviving animals. The salivary lysozyme shows no significant change following irradiation. (NSA)

516

Bisgard, J. D., H. B. Hunt, and R. H. Dickinson. **EFFECT OF X-RAY IRRADIATION UPON BACTERIAL TOXEMIA IN RABBITS.** *Radiology* **43**, 330-2(1944).

Irradiation causes the production or elaboration of a nonspecific antitoxin, produced by the tissues (but not by plasma or whole blood), irrespective of the position of the body irradiated. The minimal dose is 20 r to produce an effective quantity of antitoxin in rabbits. (CA)

517

Bond, V. P., I. L. Schechmeister, M. N. Swift, and M. C. Fishler. **THE EFFECTS OF X-IRRADIATION ON A NATURALLY OCCURRING ENDEMIC INFECTION.** *Naval Radiological Defense Lab.* Nov. 29, 1950. 17p. (AD-273-(B))

The effects of x irradiation on animals from a laboratory colony in which a pulmonary infection was endemic were studied. The results indicate that irradiation increases the rate of spread of the disease, or "activates" infection that otherwise might remain latent in unirradiated animals, and that the LD₅₀ for rats showing gross evidence of a disease that in itself does not kill immediately is reduced considerably below that for apparently normal animals. The necessity of maintaining a healthy experimental animal colony, particularly where investigations may extend over several weeks and involve a debilitating agent such as x ray, is emphasized. (NSA)

518

Borowskaja, D. **EFFECT OF ROENTGEN IRRADIATION ON THE SERUM CONTENT OF HAEMAGGLUTININS IN HUMAN BLOOD.** *Nature* **158**, 269(1946).

The author studied the possible influence of radiological stimulation of the reticulo-endothelial system on the titre of anti-sheep agglutinins. Thirty-two persons were observed who received roentgentherapy for various causes (cancer, leukemia, inflammatory states, etc.). Dosages varied from 50 r to 6,000 r. In no case did the titre of sheep agglutinins after irradiation rise above the dilution of 1:10. Since the standard titre in normal individuals is generally equivalent to the dilutions 1:4-1:8 of the serum, the author concludes that the titre of sheep agglutinins after irradiation remained normal. These observations show that X-rays do not influence the behavior of normal anti-sheep agglutinins; hence the rise of the titre in some conditions probably does not depend on the stimulation of the reticulo-endothelial system, but on active immunization. (S.V.S.)

519

Bukantz, S. C., F. J. Dixon, G. J. Dammin, and D. W. Talmage. **METABOLISM OF ANTIGENIC I⁺ PROTEINS; EFFECT OF ANTIGEN AND HOST ALTERATION.** *Washington Univ., St. Louis, School of Medicine.* [nd] 2p. (AECU-1239)

This report is reproduced here in its entirety.

The mechanisms involved in the metabolism of antigens have been investigated (1) in normal rabbits with tracer-labeled I* bovine serum albumin, I* bovine gamma globulin (I*-BGG), and with I*-BGG altered chemically by azo conjugation or iodination to saturation; and (2) with I*-BGG injected into animals after whole-body irradiation, active immunization, passive immunization, and in a specific anamnestic response. I*-BGG disappeared from the circulation in three phases (75% in 24 hr, 92% in 96 hr, and virtually 100% in 9 days) and was never retained in or concentrated by tissues. Complement fixing antibody appeared by the 7th day, was maximal at the 10th, and disappeared by the 20th day. By contrast, R-salt-azo-biphenyl-azo I*-BGG and P-amino benzoic acid-azo-I*-BGG disappeared from circulation precipitously (90% loss in 6 hr and 99% loss in 24 hr) and was retained in the RE macrophages of several organs, notably spleen, liver, and lymph nodes, with an approximate tissue half-life of 3 to 7 days. The I-saturated antigen left the circulation as rapidly as azo antigens, with less tissue retention. Urine excretion of I¹³¹-containing protein breakdown products reflected the blood and tissue elimination of antigen. X rays (300 or more r) did not effect the nonimmune rate of elimination of antigen, although the immune response was suppressed. The intravenous injection of antibody to I*-BGG produced a prompt decrease in circulating antigen in proportion to the amount of antibody injected. Finally, in a specific anamnestic response, antigen disappearance during the first 2 days was at the usual nonimmune rates, and a typical immune rate began at the 3rd day. (NSA)

520

Burrows, William. EFFECT OF X-IRRADIATION ON ENTERIC CHOLERA AND COPROANTIBODY RESPONSE IN THE GUINEA PIG, p.131 of BIOLOGICAL AND MEDICAL DIVISIONS; QUARTERLY REPORT, AUGUST, SEPTEMBER, OCTOBER 1949, Austin M. Brues and Herman Lisco, eds. Argonne National Lab. [nd] 1p. (ANL-4360(p.131))

This report superseded by the paper abstracted as 522.

521

Burrows, William, Norma G. Deupree, and Dorothy Moore. EXPERIMENTAL ENTERIC CHOLERA IN THE X-IRRADIATED GUINEA PIG, p.110 of BIOLOGICAL AND MEDICAL DIVISIONS QUARTERLY REPORT, FEBRUARY, MARCH, APRIL 1950, Austin M. Brues, ed. Argonne National Lab. [nd] 1p. (ANL-4451(p.110))

This report is superseded by the paper reviewed in the following abstract.

522

Burrows, William, Norma G. Deupree, and Dorothy E. Moore. THE EFFECT OF X-IRRADIATION ON EXPERIMENTAL ENTERIC CHOLERA IN THE GUINEA PIG. J. Infectious Diseases 87, 158-68(1950).

The effect of x-irradiation in doses of 100-200 r on enteric cholera in the guinea pig was assayed by two methods, autopsy culture of animals sacrificed periodically, and as numbers of vibrios and titer of antibody excreted in the feces. The period of deaths produced by doses of 150 r was associated with generalized bacterial infection in the majority of animals examined, a coincidence consistent with the belief that a bacteremia of intestinal origin is a part of radiation sickness. Of the animals examined at autopsy 63% were so infected, and of these 44% were infected with the cholera vibrio, and the remainder with hemolytic streptococci and staphylococci. Whole body irradiation with x-ray in this dosage, then, resulted in a generalized tissue invasion by the cholera vibrio from a focus in the bowel which is not observed in the infected nonirradiated animal. The course of the infection was also significantly altered by x-irradiation. With doses of 150

and 200 r the intensity of the infection was reduced in the first 3 days following inoculation concurrent with a stimulus of coproantibody response, but subsequently the antibody titer declined and the intensity of the infection increased in the period during which tissue invasion occurred. While the infection was appreciably reduced in its intensity in its early stages by doses of 100 r, coproantibody response was not effectively inhibited and both intensity and duration of the infection were reduced over that in the nonirradiated animal to give an over-all therapeutic effect of x-ray in this dose. The observed inverse relation between coproantibody on the one hand, and the intensity and tendency for generalization of the enteric infection on the other, provide additional support for the hypothesis that effective immunity to enteric infection is in part a function of coproantibody. If it be assumed that natural immunity to bacteria of the intestinal flora is also related to coproantibody response, the inhibition of this immune response by lethal doses of x-ray may account for bacteremia of intestinal origin in radiation sickness. (Authors' Summary)

523

Burrows, W., Norma G. Deupree, and Dorothy E. Moore. THE EFFECT OF X-IRRADIATION ON FECAL AND URINARY ANTIBODY RESPONSE. J. Infectious Diseases 87, 169-83(1950).

The effect of pre- and postimmunization irradiation with x-ray in doses ranging from 50 to 200 r on the immune response of guinea pigs to cholera 0 vaccine was assayed as serum, fecal, and urinary antibody (agglutinin). Irradiation following immunization did not affect serum antibody titer appreciably, but in doses of 100 and 150 r partially or completely inhibited the excretion of fecal and urinary antibody, and the excretion could be partially restored by booster inoculation. Preimmunization irradiation resulted in sharply reduced serum antibody titer, but produced a transitory stimulus of fecal and urinary antibody, apparent when immunization was begun at one day, but not 3 days, after irradiation. (Authors' Summary)

524

Clemmesen, J. THE INFLUENCE OF ROENTGEN RADIATION ON IMMUNITY TO SHOPE FIBROMA VIRUS. Am. J. Cancer 35, 378-85(1939).

Shope fibroma virus injected into rabbits treated with a general roentgen irradiation produces results similar to those described by Andrewes and others in rabbits injected with tar, namely prolonged growth of the resultant fibromata, prolonged resorption, and generalized fibromatosis after intravenous inoculation. The development of immunity to repeated inoculations with this virus is delayed in x-rayed rabbits. The effects of a general roentgen irradiation on transplantation of tumor and normal cells, inoculation of fibroma virus, and artificial carcinogenesis, have their parallels in the effects of injections of tar and of trypan blue. All these procedures probably act through the reticuloendothelial system. (BA)

525

Clemmesen, Johannes, and Else Krag Andersen. INFLUENCE OF FRACTIONED ROENTGEN RADIATION ON BACTERIAL AGGLUTINATION TITRE. Acta Pathol. Microbiol. Scand. 25, 611-14(1948).

Rabbits were given total body irradiation in effective doses of 120 r five times in this investigation of the possibilities offered by X-ray irradiation as a means of lowering the resistance of experimental animals to inoculations of various kinds. Immunization was carried out by a single intravenous injection of 0.1 cc H-Antigen of B. paratyphus B (formolized broth-culture). From the agglutination titer curves and their general experience the authors conclude: (1) Fractioned doses are more effective for lowering of

resistance than single doses. (2) It seems possible to prevent development of immunity without serious damage to the general health of the animals. (3) A dose of rays which if given before immunization will delay the development of immunity does not show the same effect if applied after immunization. (4) If an insufficient part of the radiation has been applied before immunization, the remaining dose given after the latter will be more effective than the total dose given at the same period. Even an immunity otherwise apparently refractory to radiation may in this way be prevented from developing. (5) The effect may be visualized as a blockage of the reticuloendothelial system which must be established at the appearance of antigen and must be repeatedly renewed in the presence of the latter. 3 tables and 6 references. (NSA)

526

Cohen, Sheldon G., Lloyd D. Mayer, and Leo H. Crip. **THE EFFECT OF X-RADIATION ON EXPERIMENTALLY PRODUCED CUTANEOUS SENSITIVITY.** *J. Invest. Dermatol.* **16**, 91-6(1951).

Albino guinea pigs were sensitized by the daily injection for 7 days of 0.1 ml. 0.1% p-phenylenediamine into the skin. Of these test animals 19 were then exposed to 175 roentgens of total body irradiation filtered through 0.5 mm Cu and 1 mm Al, at a focal distance of 64 cm, and after 16-24 hours again tested for skin sensitivity to the reagent; 5 animals exhibited a positive reaction, 11 an attenuated response, and 5 a negative skin reaction, while of 18 sensitized but not irradiated animals, 14 showed a marked positive reaction and 4 and attenuated reaction. The modification of the degree of severity of cutaneous hypersensitivity is accompanied by a destruction of lymphoid cellular elements. (CA)

527

Craddock, Charles G. Jr. and John S. Lawrence. **THE EFFECT OF ROENTGEN IRRADIATION ON ANTIBODY FORMATION IN RABBITS.** *J. Immunol.* **60**, 241-54(1948).

The new importance placed on the role of lymphoid tissue and circulating lymphocytes in antibody production, and the well-known detrimental effects of X-rays on lymphoid tissue morphologically led to this study in which the attempt is made to correlate the influence of roentgen irradiation on antibody production with that on lymphoid tissue. Rabbits were exposed to 250 r whole-body irradiations and given pre- or post-irradiation injections of antigen. Antibody production was markedly decreased when injections were made following irradiation. This is of a transient nature and the animals regained their ability to respond normally to antigen injection 40 days after exposure to X-ray. Irradiation, however, after the onset of antibody production does not impair ability to produce circulatory antibodies. The reason for this remarkable difference is not apparent, but it is suggested that reserve sources of tissue must be capable of carrying out antibody formation once it has begun even though the major portion of lymphoid tissue has been damaged. (NSA)

528

Craddock, Charles G., Jr., William N. Valentine, and John S. Lawrence. **THE EFFECT OF MASSIVE WHOLE BODY X-RAY ON THE ANTIBODY CONTENT OF LYMPH, p.166-9 OF THE LYMPHOCYTE STUDIES ON ITS RELATIONSHIP TO IMMUNOLOGIC PROCESSES IN THE CAT.** *J. Lab. Clin. Med.* **34**, 158-77(1949).

Lymph specimens were collected every two hours for eight hours following irradiation by a single total body dose of 1,500 r. In spite of widespread destruction of lymphoid cells, no appreciable alteration in antibody concentration of the lymph was detected. No consistent correlation was found to exist between the height of the serum antibody

titer and that of the lymph. Thus, in several instances no antibody could be detected in the lymph, in spite of a significant serum antibody titer. The concentration of serum antibody at the end of the experiment was higher than that of the lymph in all cases except one. (NSA)

529

Criep, Leo H., Lloyd D. Mayer, and Sheldon G. Cohen. **EFFECT OF X-RAY RADIATION ON HYPERSENSITIVE-NESS.** *J. Allergy* **21**, 269(1950).

This paper deals with the authors' experience in the evaluation of the effect of x-ray radiation on the development of diffuse vascular disease (collagen disease), on the Arthus phenomenon, on the Schultz-Dale reaction, and on the production of precipitins in sensitized animals. The experiment indicates that interference with the function of the reticulo-endothelial system depresses precipitin titers, completely abolishes the Arthus phenomenon, and interferes with the production of diffuse vascular changes so obviously present as a result of sensitization in untreated animals. (NSA)

530

Dixon, F. J., S. C. Bukantz, and G. J. Dammin. **THE EFFECT OF SENSITIZATION AND X-RADIATION ON THE METABOLISM OF IODINE 131-LABELED PROTEINS.** *Science* **113**, 274-6(1951).

Rabbits immunized by an intramuscular injection 325 mg bovine γ -globulin (BGG) eliminate injected I^{131} -BGG much more rapidly than controls although x-radiation interferes with the development of an immune state. Fifty % of the injected activity is found in the urine of immunized rabbits by the third day, of the control group by the fourth day, and of the x-radiated group by the sixth day. In fatal anaphylaxis there is rapid loss of activity from the blood and rapid accumulation in the lungs. (CA)

531

Dixon, F. J., D. W. Talmage, and S. C. Bukantz. **RADIO-SENSITIVE AND RADIORESISTANT PHASES IN ANTIBODY PRODUCTION.** Washington Univ., St. Louis, School of Medicine. [nd] 2p. (AECU-1241)

The report is reproduced here in its entirety.

The radiosensitivity of the antibody response is well known, but the time relationships of radiation, antigen administration, and antibody suppression or response have not been completely explored. The following observations were made in rabbits using I^{131} -labeled bovine gamma globulin as antigen. Antibody was determined by complement fixation, employing four 50% units. (1) Antibody response to initial antigen exposure is completely suppressed by 300 r or more whole-body radiation given 40 hr before injection of antigen. With 500 r this suppression is evident for 6 weeks. (2) However, no suppression of initial antibody response is noted following 500 r given simultaneously with antigen, and only partial antibody suppression follows 500 r given $2\frac{1}{4}$ hr before the antigen. (3) The specific anamnestic response, unlike the initial antibody response, is not prevented by 500 r 40 hr before the second injection of antigen. It is apparent that within a matter of hours after 300 to 500 r radiation an animal loses a substance necessary for the production of antibody. However, since simultaneous radiation and antigen administration does not diminish antibody production in spite of the fact that the necessary radiosensitive substance can persist for only a matter of hours, it would appear that the radiosensitive portion of the antibody response lasts only a few hours. The remainder of the antibody response, during which the antibody protein is actually produced, lasts several weeks and can be carried on undiminished in spite of radiation. The complete radioresistance of the specific anamnestic response indicates a lasting orientation of antibody-

producing sites to the specific antigen, so that on second antigen administration the radiosensitive initiation phase of antibody production is unnecessary. (NSA)

532

Ephrati, Erela. MECHANISM OF THE EFFECT OF X-RAYS ON BACTERIAL TOXINS. *Biochem. J.* **42**, 383-9 (1948).

Staph. hemolysin is much more sensitive to destruction by x-rays than tetanus toxin, and purification of the toxin greatly increases its sensitivity. In either case antigenicity and toxicity are destroyed simultaneously. The effect of x-rays is indirect, through ionization, leading either to oxidation or reduction. In the case of toxins all the facts indicate that an oxidation is responsible for the destruction. Various proteins, reducing amino acids, glutathione, thio-glycolic and ascorbic acids are all effective as protective agents. Oxidizing substances were ineffective. (CA)

533

Evans, R. Winston. THE ANTIBODY RESPONSE IN CASES OF RADIATION LYMPHOPENIA, AND IN THE RETICULOSSES. *J. Pathol. Bacteriol.* **60**, 123-30(1948).

The antibody response was tested in a series of 30 patients exhibiting a radiation-induced lymphopenia and in a control group of 17 individuals with a normal blood-lymphocyte level. A suspension of *Bact. paratyphosum* A(H) was used as antigen. A lower level of antibody production was recorded in patients showing a low lymphocyte count. The significance of this finding is related to the immunological function of the lymphocyte. A series of reticulo-endothelioses comprising cases of myelocytic and lymphatic leukaemia, Hodgkin's disease, lymphosarcoma and lymphofollicular reticulosis was also tested for agglutinin response, which was found to be very poor except in the myelocytic leukaemias. This poor response is attributed to the degree of disorganization of the lymph glands in these conditions. (NSA)

534

Fischel, Edward E., Marjorie LeMay, and Elvin A. Kabat. THE EFFECT OF ADRENOCORTICOTROPHIC HORMONE AND X-RAY ON THE AMOUNT OF CIRCULATING ANTIBODY. *J. Immunol.* **61**, 89-93(1949).

Experiments initiated to determine whether X-rays and the adrenocorticotrophic hormone are able to cause an anamnestic or secondary response in circulating rabbit antibodies are described. One group of rabbits received 25 mg. of 75% potent ACTH subcutaneously, while the other group received 50 r, spray radiation with 184 kv and 25 ma, at a distance of 35.25 cm. with 2 mm Cu and 1 mm Al filters. Bleeding times and white cell counts were obtained at 6, 12, and 48 hours after the administration of the ACTH and the X-rays. The results are presented in two tables. A fall of more than 50% in the total number of circulating lymphocytes occurred after the treatments for a corresponding change in the total white count either in the same or in the opposite direction. The serum antiovalbumin content was either the same or diminished in all of the rabbits. Therefore, the expected anamnestic change was not demonstrable by the quantitative precipitin-method used. (NSA)

535

Fredell, H., et al. THE EFFECT OF X-RAYS UPON ANTIBODIES (A STUDY OF HEMOLYSIN TITRATIONS IN SENSITIZED IRRADIATED RABBITS). Argonne National Lab. Aug. 1, 1947. Decl. May 26, 1948. 172p. (AECD-2024)

Experiments were conducted using the rabbit as a test animal and measuring the antibody production in terms of hemolysins produced by sheep cell antigen. A group of 16

rabbits was sub-divided into four groups of four animals each. The first group served as control; the second group was irradiated at the peak of the antibody response, approximately 10 days after antigen administration; the third group was irradiated on the day of antigen administration; and the fourth group was irradiated on the day of antigen administration and reirradiated at the peak of antibody response. All irradiated animals received about 550 r at dosage rates of 16 to 17.7 r/minute, using 0.5 mm Cu and 1.0 mm Al filters. In addition, the animals in group four received a second dose of 550 r. A single dose of 550 r total body x-radiation depressed sheep cell antibody production in rabbits. When 550 r was administered at the time of sensitization, antibody production 10 days later was, for all practical purposes, completely inhibited within the period of study. (NSA)

536

Glenn, John C., Jr. FURTHER STUDIES ON THE INFLUENCE OF X-RAYS ON THE PHAGOCYTTIC INDICES OF HEALTHY RABBITS. *J. Immunol.* **53**, 95-100(1946).

A preliminary study with 18 rabbits showed that the phagocytic indices of healthy rabbits tested with *Staphylococcus aureus* increased significantly 48 to 96 hr following radiation by 100 r (measured in air) delivered at 140 kv over a small area of normal skin. In a second experiment using 35 rabbits, all treated animals received radiation generated at 140 kv through a 6 x 6-cm port over the inner surface of the unshaven and unclipped right hind thigh of from 50 r up to 1,000 r, given either in single or in repeated doses. It was found that the phagocytic index of the white rabbit can be most effectively increased by a dose of 100r. The maximal increase occurs 48 hr after treatment. Repetition of the optimal dose produces an increase in the phagocytic index which is only moderately higher than that obtained with a single dose, but the index may be maintained at a high level for a short time. There is a definite tolerance of the animals to x rays for producing an increase in the phagocytic index, beyond which point a depression occurs. Previously irradiated animals show a return of the phagocytic index to normal at varying lengths of time following treatment, so that subsequent treatments following this event again institute a rise in the phagocytic index which is identical with that observed in untreated animals. TIS

537

Goldman, M. O., Leon O. Jacobson and Melba J. Robson. PRELIMINARY REPORT; THE EFFECT OF SPLEEN AND APPENDIX PROTECTION ON THE SHWARTZMAN REACTION, p.32-5 of BIOLOGICAL AND MEDICAL DIVISIONS; QUARTERLY REPORT FEBRUARY, MARCH, APRIL, 1950. Argonne National Lab. [nd] 4p. (ANL-4451(p.32-5))

In rabbits the administration of an intradermal injection of meningococcus endotoxin followed 24 hr later by an intravenous injection of the same material results in a severe hemorrhagic necrotic reaction at the intradermal site within 2 to 6 hr after the second injection. This phenomenon is known as the Schwartzman phenomenon. It may be suppressed by such agents as nitrogen mustard, x rays, and benzol if these are administered in large doses prior to intradermal injection. Experiments are in progress to investigate the possibilities of altering this suppressive action with the view of finding explanations for the Schwartzman phenomenon. It was found that local irradiation (800 r) administered to the skin of rabbits did not suppress the reaction. Data indicate that suppression of this phenomenon by total-body x irradiation is dependent upon some generalized change throughout the body, that Pb pro-

tection as such does not alter this condition, but that trauma to the abdominal viscera at the time of irradiation does prevent the full suppressive action. (NSA)

538

Gowen, John W. **MODIFYING DISEASE RESISTANCE THROUGH RADIATION**, p.55-8 of **CONFERENCE ON BIOLOGICAL APPLICATIONS OF NUCLEAR PHYSICS**. Brookhaven National Lab. July 1948. 3p. (BNL-C-4)

Author discusses host variability toward resistance or susceptibility, bacterial variation in disease, hereditary variation in acquired immunity, phenotypic mechanism by which resistance is accomplished, and x-ray effects on resistance. (S.V.S.)

539

Gowen, John W. **RADIATION EFFECTS ON MICE AS RELATED TO SURVIVAL**. *Genetics* **35**, 112(1950).

The effects of acute irradiations on the subsequent lengths of life of the exposed individuals have evolutionary, as well as current, interest. Genetic variations exist in different hosts; genetic diversity is found in the organisms initiating a disease; and the environmental setting in which the disease is to occur is subject to variation. The type and character of the radiation to which either the hosts or the pathogens are exposed may be considered environmental variations. In examining the interactions of these factors, the discussion will be limited largely to the mouse and its typhoid disease caused by Salmonella typhimurium. Six inbred mouse strains of characteristically different typhoid susceptibility (8 to 90%) and leucocyte counts were exposed to X-rays in doses from 0 to 700 roentgens/cm² of body surface. All six strains reacted alike. Radiation throughout decreased resistance. The decrease in resistance was an exponential function of the dosage of X-rays to which the mouse was exposed. The data, while quite irregular due to limited numbers, show the same rate of decrease in resistance for each of the strains. Resistance at 600 r exposure was decreased to about 43% of that expected with no radiation. These results are explained by the exponential destruction of the phagocytic cells by the acute irradiation. Mice were blood counted, irradiated, and the cell counts taken again at one and two weeks after treatment. The results show a corresponding decrease in leucocyte numbers for each of the strains. The decrease, like that for survival to typhoid, is exponential. (RG)

540

Hollingsworth, J. W. **EFFECTS OF X-IRRADIATION ON PASSIVELY TRANSFERRED ANTIBODY**. *Proc. Soc. Exptl. Biol. Med.* **75**, 477-9(1950).

X irradiation in dosage of 300 r had no effect on the rate of destruction of passively transferred homologous or heterologous antisera given intravenously to rabbits 24 hr after irradiation. This x-ray dosage was sufficient, however, to decrease, but not totally prevent, the formation of antibody to the heterologous serum proteins. (NSA)

541

Jacobson, Leon O., Melba J. Robson, and Edna K. Marks. **THE EFFECT OF X-RADIATION ON ANTIBODY FORMATION**. *Proc. Soc. Exptl. Biol. Med.* **75**, 145-52(1950).

Experiments in which rabbits have been exposed to 800 r of x radiation have confirmed previous findings (Hektoen, J. *Infect. Dis.*, **17**: 415(1915)) that antibody formation is suppressed by total-body x radiation. It has been demonstrated, in addition, that if the spleen or appendix of the rabbit is protected by lead shielding during total-body irradiation, the capacity to produce antibodies to an injected particulate antigen is retained to a marked degree even though lymphatic tissue elsewhere in the body is temporarily destroyed. (NSA)

542

Jacobson, L. O., M. E. Robson, E. K. Marks, and M. C. Goldman. **THE EFFECTS OF X-IRRADIATION ON ANTIBODY FORMATION**. *J. Lab. Clin. Med.* **34**, 1612-13 (1949).

This communication describes an attempt to study the capacity of the rabbit to form antibodies during a period in which all lymphatic tissue of the body, with the exception of the spleen or appendix, is essentially destroyed. Young rabbits were given 800 r total body x-irradiation (exclusive of the lead-protected spleen or appendix) at 250 kv 24 hours prior to an intravenous immunization with sheep cells (1 cc. of a 2% suspension). Hemolysin titers were determined on serum obtained before immunization and on samples taken 7, 14, 21, and 28 days after immunization. Normal titers were 1 to 5120 14 days after the injection; in the irradiated animals titers of 1 to 5120 were not observed until the 21st day after the injection. It is concluded that these experiments corroborate Hektoen's findings that antibody formation is suppressed by total body irradiation and also show that the capacity to produce antibodies to an injected particulate antigen is not lost when some part of the body such as the spleen or the appendix is protected from radiations which destroy lymphatic tissue. (NSA)

543

Jude, A., P. Bonet-Maury, and P. Servant. **ACTION OF IONIZING RAYS UPON ANTIGEN Vi OF SALMONELLA TYPHY (INAGGLUTINABLE O AND AGGLUTINABLE Vi)**. *Compt. rend. soc. biol.* **144**, 214-16(1950).

In this note the action of the α particles of Rn upon antigen Vi of *Salmonella typhi* is recorded. Antigen Vi preserved its serological characteristics even at elevated doses of radiation. Radiation dosages up to 40 μ cd/cm², nearly 3 times the sterilizing dose, were used. Neither inagglutinable antigen O nor agglutinable antigen Vi were destroyed. (NSA)

544

Kohn, Henry I. **THE EFFECT OF TOTAL-BODY X-IRRADIATION UPON THE HEMOLYSIN RESPONSE OF THE RAT TO SHEEP ERYTHROCYTES**. *J. Immunol.* **66**, 525-33(1951) (ORNL-391)

X-rays were administered to rats at various times during the week before and the five days after a single injection of sheep erythrocytes. When given at any time during this interval, 300 r (LD-50, 725 r) depressed the hemolysin titer, which is defined as the reciprocal of the dilution of plasma causing 50% hemolysis in a 0.7% suspension of sheep erythrocytes. A given dose of X-rays (175-850 r) became progressively less effective as the time of its administration was delayed after the injection of the antigen. The data show that x-rays given either before or after immunization can inhibit antibody production. The effect of the X-rays upon antibody production always involved a decrease in the peak titer; and under certain conditions, the development of the depressed peak was delayed. Therefore in certain instances, the titer in the irradiated animal, at first below the control level, exceeded the control when the latter subsequently declined. (NSA)

545

Lecomte, J. and P. Fischer. **CIRCULATING ANTIBODIES AND THE ALARM SYNDROME BROUGHT ON BY X-IRRADIATION**. *Compt. rend. soc. biol.* **143**, 878-9(1949).

Studies were carried out to determine whether the destruction of lymphocytes by X-irradiation is followed, in the sensitized rabbit, by an increase in the amount of circulating antibodies. The authors point out the importance of the lymphatic ganglia and the lymphocytes in the production and accumulation of antibodies; the injection of any

antigen is followed swiftly by the appearances of antibodies in the lymphatic ganglia draining the region. Four rabbits (the serum of which had been rendered greatly precipitant with respect to horse serum) were irradiated with 200 r on their hind legs, after the withdrawal of a control sample of blood; samples were also taken three hours after, and four days after the irradiation. It was discovered that the destruction of the lymphocytes which accompanied the alarm syndrome caused by the administration of the X-rays was not followed by a simultaneous increase in the amount of circulating antibodies. (NSA)

546

Richards, O. W. **YEAST GROWTH: A POSSIBLE TEST ORGANISM FOR X-RADIATION.** *Radiology* **34**, 317-26 (1940).

Populations of a pure strain of *Saccharomyces cerevisiae* were radiated with from 9500 to 28,500 r at 70 kv, and with from 200 to 38,000 r at 200 kv under carefully controlled, established conditions for yeast growth. The increase in numbers of cells per unit volume is retarded by the x-rays. Increased optical densities of the populations were observed with a nephelometer for dosages up to 15,000 r, and decreased density for greater dosages. Recovery takes place gradually, and the irradiated cultures reach about the same equilibrium level as the controls by the end of the growth cycles. Percentages of buds and of cells staining with methylene blue are given. While a single criterion of growth may be useful, the analysis of the effect of x-radiation on yeast growth requires the information gained from the simultaneous use of several different criteria and methods for the measurement of the growth of yeast populations. (BA)

547

Sarian, Jirair N. **EFFECT OF PHYSICAL AND CHEMICAL FACTORS IN PHAGOCYTOSIS IN THE PRESENCE OF IRRADIATED HUMAN BLOOD AND PLASMA.** *Am. J. Roentgenol. Radium Therapy* **65**, 465-71 (1951).

Anticoagulation measures, particularly citration, handicap phagocytosis in the presence of both normal and irradiated blood and plasma. Normal blood and plasma irradiated with 50 and 100 r, respectively, did not lose their increased phagocytosis-enhancing properties after storing at 0°C for 48 hours. Nonirradiated samples showed a slight increase in their phagocytic powers after storing. Heating for 15 min. at 65° did not destroy the opsonins and agglutinins brought out by small-dose x-ray irradiations of blood and plasma. Softer ray seemed to be more potent in producing such thermostable substances. Diluting the x-ray dose optimal for phagocytosis does not cause a proportional decrease in the phagocytic power. (CA)

548

Sarian, Jirair N. **IRRADIATED HUMAN PLASMA AND PHAGOCYTOSIS.** *Am. J. Roentgenol. Radium Therapy* **65**, 940-6 (1951).

In an attempt to understand the mechanism of the effects of roentgen rays on inflammations, the author briefly reviews the general theories and then describes his own experimental findings. Small doses of roentgen rays, 15 to 100 r, cause a significant rise in the opsonic indices of normal human blood. The injurious effect of 30 r on leucocytes, although small enough to fall within the range of experimental error, is yet demonstrable functionally. Irradiating plasma previously separated from normal human blood enhanced phagocytosis to a degree slightly less than that attained by using plasma derived from whole blood irradiated with the same dose. Comparison as to phagocytosis of *Escherichia coli* and *Staphylococcus aureus* indicates that irradiation either produces, or more probably

activates, the specific opsonins of the normal plasma. Thus convalescent or immune sera could be used (both therapeutically and prophylactically) more advantageously by irradiating them with optimal doses of roentgen rays. Such irradiated specific sera could be of particular value in the control of certain virus diseases, for example, neurotropic poliomyelitis. 55 references. (NSA)

549

Schwab, Louis, Frederick C. Moll, Thomas Hall, Henry Brean, Marjorie Kirk, Clinton Van Zandt Hawn, and Charles A. Janeway. **EXPERIMENTAL HYPERSENSITIVITY IN THE RABBIT.** *J. Exptl. Med.* **91**, 505-26 (1950).

The experiments described here involve the investigation of the inhibition of antibody formation by x-radiation, the relationship between complement and serologic sequences, and the relationship between complement, serologic sequence, and histologic changes. In the first experiments several rabbits were subjected to 150 to 400 r per dose of x-rays, delivered 5 to 8 times at interval of several days, both before and after the intravenous injection of whole bovine serum or bovine serum γ globulin. Tests for the presence of antigen and antibody were made 9 to 28 days later. Similar experiments were performed with nitrogen mustard instead of the x-radiations. Serum complement determinations, as well as tests for the presence of antigen and antibody, were made in subsequent experiments on rabbits. Other experiments are also described. It was found that x-radiation and nitrogen mustard inhibit the formation of precipitins for whole bovine serum and bovine serum γ globulin in the rabbit. Other data presented are interpreted as evidence in favor of the concept that the lesions seen are due to a reaction between antigen fixed in or on tissue cells and circulating antibody. The possible significance of serum complement in the pathogenesis of anaphylactic tissue lesions is discussed. 68 references. (NSA)

550

Shechmeister, I. L. and V. P. Bond. **THE RESPONSE OF MICE TO INOCULATION WITH CERTAIN AVIRULENT BACTERIA AFTER EXPOSURE TO SUBLETHAL TOTAL BODY X-IRRADIATION.** *Proc. Soc. Exptl. Biol. Med.* **77**, 77-80 (1951) (AD-233(B))

Mice exposed to sublethal doses of x irradiation and subsequently inoculated with live avirulent, or even dead, organisms generically different from the bacteria normally present in the intestines of these animals exhibited a high incidence of bacteremia and death. When avirulent live bacteria were injected, the organisms recovered by sacrifice and culture were either of the strain inoculated or were apparently autogenous bacteria. When heat-killed bacteria were introduced, the recovered organisms were of autogenous origin only. (NSA)

551

Shechmeister, I. L., V. P. Bond, and M. N. Swift. **THE SUSCEPTIBILITY OF IRRADIATED MICE TO INFECTION AS A FUNCTION OF POST-IRRADIATION TIME.** *Naval Radiological Defense Lab. Dec. 12, 1950. 22p.* (AD-279-(B))

The susceptibility of mice to airborne *Streptococcus zoo-epidemicus* was determined over a 50-day period following 350 r of whole-body x irradiation. Bacterial LD₅₀ values were determined for normal and irradiated mice on 12 different postirradiation days during this period, and the changes in susceptibility in each case were expressed as the ratio of the two. The resulting curve relating susceptibility to postirradiation time indicated that there was a linear increase in susceptibility over the first 15 days, which reached a peak five times that of controls. This was

followed by an exponential drop which approached the control level shortly after 30 days. The possible relationship of this phenomenon to other radiation effects is discussed. (NSA)

552

Taliaferro, William H. and Lucy Graves Taliaferro. **EFFECT OF X-IRRADIATION ON HEMOLYSIN DECLINE.** *J. Infectious Diseases* 87, No. 3, 201-9(1950).

X irradiation in 2 doses of 400 r to the entire body of rabbits during the decline of hemolysin 2 to 4 weeks after immunization with one or a series of intravenous injections of sheep red cells did not alter the downward trend of the titer as compared to controls not irradiated. Three intravenous injections of ovalbumin 9½, 11, and 12 weeks after immunization only elicited a possible heterologous anamnestic response to red cells in 1 of 7 rabbits. (NSA)

553

Taliaferro, William H. and Lucy Graves Taliaferro. **EFFECT OF X-RAYS ON IMMUNITY: A REVIEW.** *J. Immunol.* 66, 181-212(1951).

Small amounts of x rays, often administered locally, sometimes enhance antibody formation and the immunity of experimental laboratory animals to nonliving antigens and certain infections. This conclusion has also been reached with respect to a wide range of infections in man, but may not in all cases be justified because of inadequate controls. The mechanism involved in an enhanced immunity by x rays has been variously explained, but has not been adequately clarified. Large amounts of x rays have occasionally been reported to produce beneficial effects in the host, but further work on this aspect of the subject is needed. A well-established instance occurs in trichinosis. In this infection, treatment of the host with large doses of x rays directly inhibits early embryonic development of the worms. X rays approaching lethal amounts when administered to the entire body often decrease host immunity to specific infections and lower antibody formation. The mechanism whereby immunity is reduced needs further experimental analysis but is, in large part, reasonably explained by the pronounced radiosensitivity of lymphocytes (including various "blasts"). There is no evidence that x rays enhance the virulence of the parasites or affect their antigenicity. The differential effectiveness of the same dose of x rays in different infections and at different periods of the same infection may be partly correlated with the degree of immunity present at the time of radiation. 201 references. (NSA)

554

Taliaferro, William H., Lucy Graves Taliaferro, and E. L. Simmons. **INCREASED PARASITEMIA IN CHICKEN MALARIA (*PLASMODIUM GALLINACEUM* AND *PLASMODIUM LOPHURAE*) FOLLOWING X-IRRADIATION.** *J. Infectious Diseases* 77, 158-76(1945).

Chickens with sporozoite-or blood-induced infections of *P. gallinaceum* or with blood-induced infections of *P. lophurae* were irradiated with 500 or 600 r of x-rays at intervals beginning on the day of infection and with smaller doses (100-400 r) of x rays about 40 days after their initial infection. Irradiation induced increased parasitemia in both avian malaras but affected different periods of the two infections. Thus, in blood-or sporozoite-induced *P. gallinaceum* infections, irradiation on the day of infection produced a higher parasitemia and a statistically significant decrease in survival time of the host; during the acute rise and crisis of infections treated with quinine to reduce their severity, it was followed by acute fatal infections; and thereafter led to malarial relapses of varying degrees. On the other hand, in blood-induced *P. lophurae* infections, irradiation on the day of infection produced severe, often

fatal, infections and only slight relapses thereafter. The effectiveness of a given dose of x-rays varied with the age and susceptibility of the chicken, the species of parasite, the period of the malarial infection and the intensity of the infection prior to and at the time of irradiation, all of which modify or are expressions of immunity. Also, as far as tested during the developed infection of *P. gallinaceum*, single doses of from 300 to 600 r were increasingly effective with those of 100 or 200 r being practically ineffective. In general, two doses totaling 500 r or more within about a week of each other had a cumulative effect, but in general, were not equal to single doses of the same magnitude. The foregoing results of x-irradiation are discussed in relation to natural and acquired immunity and to the destruction of lymphocytes which would not only deplete an important mesenchymal reserve from which macrophages are mobilized but also, possibly, one source of antibodies. (Authors)

555

Wald, B. and V. Varteresz. **EXPERIMENTS RELATING THE ANTIPHLOGISTS EFFECT OF X-RAYS.** *Radiol. Clin.* 17, 348-62(1948).

In the experiments described, sodium chloride swellings were produced in humans irradiated with doses of 100 to 6,650 r in order to determine the functional changes brought about in the capillary endothelium by x-radiations. It was found that the anti-inflammation effect of x-rays was due to a reversible temporary paralysis of the capillary endothelium, thereby preventing exudation. X-ray therapy of most allergic inflammations and of some cases of acute nonallergic inflammations is suggested; the irradiation technique in such cases should consist of irradiation at 5- to 6-day intervals, since the x-ray effects on the endothelium recede in about that length of time. (NSA)

Injurious Effects of Radiation Therapy

556

Amory, Harold I. and Irving B. Brick. **IRRADIATION DAMAGE OF THE INTESTINES FOLLOWING 1,000-KV. ROENTGEN THERAPY. EVALUATION OF TOLERANCE DOSE.** *Radiology* 56, 49-57(1951).

A study of the effects of 1000-kv irradiation on the small and large intestine in a group of 20 patients is reported. As contrasted to previous similar reports, the present study is unique in that the patients were male, the disease for which they were being treated (testicular tumor with or without retroperitoneal lymph-node metastases) does not affect the intestine, and only external 1000-kv radiation was used. Damage of varying degree to the small and large intestine occurred in some patients receiving large doses of such radiation into the abdomen. Correlation of roentgenologic findings and autopsy results is presented. Though great individual variation is shown in a study of the cases, it is believed that the small and large intestine of the adult male can tolerate 4500 r of 1000-kv irradiation administered in 54 days without deleterious results. (NSA)

557

Bassett, R. C. and K. Lowenberg-Scharenberg. **AMYLOID DEGENERATION OF THE HUMAN BRAIN FOLLOWING X-RAY THERAPY.** *J. Neuropathol. Exptl. Neurol.* 9, 93-102(1950).

Two cases of the degeneration of the normal human brain following an overdose of X-rays are presented. The first patient received a total dose of 6,000 r delivered to the left temple region in 10 treatments within 12 days, 600 r being applied daily at 150 kv without filtration; the size of the field was 57 x 41 mm. Twenty-two months later she received a second course of radiation therapy, consisting of a total dose of 3,600 r delivered at 180 kv in 24 sessions of

150 r/treatment; field size and filtration are not reported. Approximately, 71 months after the first course the patient became nervous, complained of general malaise and headaches and experienced speech difficulties and impaired vision. Upon operation, the skull and dura showed no significant changes, but in a region including the area of Broca, the brain tissue was purple-gray; upon excision an unequivocal recovery was made. About 40 months following irradiation of the right parietal region with about 3,500 r at 130 kv without a filter and 110 kv with a filter, the second patient suffered convulsive seizures and upon operation a similar brain lesion was discovered. The dominant histological finding in the two cases was the formation of the amorphous substance in the areas of the brain exposed to excessive irradiation. It is concluded that the degeneration noted in these areas is similar to that observed in the spleen and is termed "amyloid" in nature. (NSA)

558

Bruce, Karl W. and Edward C. Stafne. **THE EFFECT OF IRRADIATION ON THE DENTAL SYSTEM AS DEMONSTRATED BY THE ROENTGENOGRAM.** *J. Am. Dental Assoc.* **41**, 684-9(1950).

Five cases in which irradiation affected the dental system are reported. Each patient received irradiation therapy in infancy for a pathologic process occurring in proximity to the developing dentition. Either x ray, surface radium packs, or radon seed implantation were used as the source of irradiation. Dental examination and roentgenograms were made at a time when the complaints of the patient centered attention on the dentition. From the evidence revealed by the roentgenograms, it is assumed that irradiation (1) can injure a tooth germ to the extent that a tooth will not form, (2) causes dwarfing of permanent teeth, (3) effects dwarfing of the roots of permanent teeth that are undergoing development during irradiation, (4) effects premature completion of calcification of permanent teeth, and (5) may cause early eruption of permanent teeth. (NSA)

559

Cathie, I. A. B. **ULCERATION OF THE SMALL INTESTINE FOLLOWING IRRADIATION OF THE PELVIS. REPORT OF TWO CASES.** *Am. J. Roentgenol. Radium Therapy* **39**, 895-8(1938).

In a series of nearly 400 cases treated for carcinoma of cervix uteri, two patients developed intractable diarrhea and died, although the roentgen dosage was well within the limits of normal tolerance. Since the lesions in the intestine were practically limited to the small intestine beyond the irradiated areas, the author believes that the changes produced were an example of severe radiation sickness. He emphasizes the fact that all transient diarrheas should be regarded with the gravest concern. (R)

560

Cogan, David G. **LESIONS OF THE EYE FROM RADIANT ENERGY.** *J. Am. Med. Assoc.* **142**, 145-51(1950).

This report discusses the sources and types of radiation, the transmission and absorption of radiant energy in the ocular media and the clinical characteristics of the lesions of the eye caused by radiant energy. Radiant energy is divided into two broad types: the electromagnetic type represented as waves of energy, the range of which covers the spectrum and includes roentgen rays, grenz rays, radio-waves and light waves; the second type consists of corpuscular radiation consisting of subatomic particles, such as electrons and neutrons. With the potentials commonly employed in roentgen treatment (100-200 kv), 90% of the energy incident on the anterior surface of the cornea may be expected to reach the retina; keratitis of the cornea may occur from irradiation with 4,000-6,000 r in several weeks' time, and cataracts are known to be caused by doses of

500-800 r at 100-200 kv; roentgen rays are tentatively classed as inactive on the retina. Radiation burns, their characteristics and treatment are also discussed. (NSA)

561

Dean, A. L. and D. P. Slaughter. **BLADDER INJURY SUBSEQUENT TO IRRADIATION OF THE UTERUS.** *J. Urol.* **46**, 917-24(1941).

The bladder not infrequently is injured by irradiation applied to the uterus. While uterine diseases commonly are treated with several types of irradiation the greatest bladder damage follows radium applications. Interstitial fibrosis occurs in the bladder wall and obliterative endarteritis occludes nutrient arteries. Because these changes usually are slow, patients are likely to have no bladder distress for a number of years after the uterus has been treated. For this reason these bladder injuries occur almost exclusively in patients cured of the primary uterine disease. The onset of symptoms is sudden. The patients suffer acutely with frequency, dysuria and hematuria. Cystoscopic examinations usually reveal single areas of ulceration surrounded by acute inflammation. Both the mode of onset and the cystoscopic picture suggest carcinoma. The authors have found that drugs of the sulfonamide group, appropriately chosen on the basis of cultures of the bladder urine, give prompt relief. This is in marked contrast to the unsatisfactory results of previous therapy. It has been interesting to note that the symptoms subside as infection is eliminated. Women with sterile urine can feel quite comfortable even though ulcerated areas of considerable size persist. (S.V.S.)

562

Drescher, H. **CONCERNING LOCAL INJURIES THROUGH IRRADIATION AS A CONSEQUENCE OF THE TREATMENT OF COLLUM CARCINOMA.** *Strahlentherapie* **80**, 99-106(1949).

Of 1,039 patients with collum carcinoma treated by radiation therapy, 26 (2.5%) developed injuries of the bladder and of the rectum; three of these patients showed injuries of both areas; four more patients developed radiogenous rectovaginal fistulae of the bladder. No systematic connection between dosage and injury could be established. After the usually tolerated dosage of 7,000 r for the bladder was increased to 8,500 r in order to obtain higher healing effects, neither X-ray ulcers nor carcinoma, nor spontaneous fractures of the femur neck were observed. Radiogenous shrinkages in the parametrium and subsequent stenosis of the urethra are mentioned. (NSA)

563

Engelstad, R. B. **THE RADIATION REACTION IN THE LUNGS OF THE HUMAN.** *Acta Radiol.* **18**, 32-44(1937).

After a short review of experimental pulmonary changes produced in rabbits by roentgen radiation, the author discusses 36 cases of pulmonary lesions in man: 21 cases of cancer of the breast, 10 cases of cancer of the esophagus, 4 cases of pulmonary metastasis of extra-pulmonary tumors and one case of cancer of the lung. The frequency of the radiation reaction in the lungs was 5.4% in cancer of the breast and 20.4% in cancer of the esophagus. Very large doses of roentgen or radium rays had been used in almost all cases where a radiation reaction was demonstrated in the lungs. When an epidermicidal dose is given in radiation of the thorax and particularly when several fields are irradiated, there is a possibility that the lungs may be injured. The radiosensitivity of the human lung seems to correspond rather well with that of the rabbit. The histological findings also seem to be similar to those in rabbits. The subjective, physical, and roentgenological symptoms are very little characteristic and a prolonged period of observation is necessary in order to make the

diagnosis. Fatal lung injuries due to radiation have not been observed. (Author's Summary)

564

Engelstad, R. B. PULMONARY LESIONS AFTER ROENTGEN AND RADIUM IRRADIATION. *Am. J. Roentgenol. Radium Therapy* 43, 676-81(1940).

Author reports having found 36 cases of pulmonary lesions due to roentgen or radium irradiations. Cites five case histories demonstrating lung reactions. (S.V.S.)

565

Friedmann, A. B. SPONTANEOUS RIB FRACTURES FOLLOWING IRRADIATION FOR CANCER OF THE BREAST. *Am. J. Roentgenol. Radium Therapy* 50, 797-800(1943).

A case of adenocarcinoma of the breast with axillary and supraclavicular and local skin metastases has been heavily irradiated and the disease has remained arrested over a 7-year period. As a sequel to the irradiation there are late degenerative changes in the brachial plexus, ribs, and skin with benign pathological fractures of six ribs and motor and sensory disturbances of the arm. (Author's Summary)

566

Gauwerky, Friedrich. COMPLICATIONS DUE TO RADIUM TREATMENT OF COLLUM CARCINOMA AND THEIR SIGNIFICANCE FOR SUCCESSFUL TREATMENT. *Strahlentherapie* 80, 51-70(1949).

A total of 590 cases of collum carcinoma were analyzed for complications which might have developed as a result of radium treatment. It was found that 378 cases (64%) were free from complications; 87 patients (14.8%) had developed such radiological complications as erosive proctitis, radiological ulcers of the rectum and radiological lesions and fistulae; 125 cases (21.2%) had developed such inflammatory complications as cystitis, pyelitis, parametritis, peritonitis, etc. Many cases from the literature and the author's own series were analyzed, particularly for injuries of the rectum and of the bladder and for formation of fistulae as a result of an overdose of radium. Where inflammatory processes developed, the chances for successful treatment were greatly reduced, even in otherwise mild cases. (NSA)

567

Gratzek, F. R., E. G. Holmstrom, and L. G. Rigler. POST-IRRADIATION BONE CHANGES. *Am. J. Roentgenol. Radium Therapy* 53, 62-76(1945).

Therapeutic administration of X-rays in infancy or childhood may result in retardation of bone growth. In adults, it may be followed by spontaneous fracture or aseptic necrosis. These changes occur in a very small percentage of all cases treated; these are not always the ones that have received the heaviest doses of radiation. Dietary deficiency and other factors are discussed but no satisfactory explanation is reached as to why a few patients develop these changes while the majority do not. (BA)

568

Greenfield, Maurice M. and Frederick M. Stark. POST-IRRADIATION NEUROPATHY. *Am. J. Roentgenol. Radium Therapy* 60, 617-22(1948).

In a series of 180 cases of carcinoma of the testis treated by intensive million volt X-ray therapy, three patients developed a peculiar neurologic disturbance. The principal feature in each case was a flaccid paralysis of the lower extremities without sensory loss. The authors have called this syndrome "post-hyphenate irradiation neuropathy" and, to their knowledge, it has not been previously described. The chief site of nerve injury was believed to be the anterior horn cells in the lumbosacral segments of the spinal cord. The three case reports are given. (NSA)

569

Hatcher, C. H. DEVELOPMENT OF SARCOMA IN BONE SUBJECTED TO ROENTGEN OR RADIUM IRRADIATION. *J. Bone and Joint Surg.* 27, 179-95(1945).

The experimental background of bone sarcoma following irradiation and the clinical literature are reviewed. Reports of 24 cases of bone sarcoma following irradiation were found. Curiously, in 17 of these cases roentgen therapy had been given for tuberculous arthritis, and in one for acute arthritis. The remaining six patients were exposed to radium; evidently these patients ingested or received injections of radioactive elements. Three case reports are presented. Case I is that of a male with a diagnosis of giant-cell tumor of the proximal epiphysis of the tibia, which was excised, with extensive post-operative X-ray therapy. The microscopic diagnosis was benign chondroblastoma. Six years later a mass in the same location was diagnosed as primary sarcoma in the proximal fibula and on amputation was found to be chondrosarcoma. Case II is that of a female who had received an unknown amount of radium and X-ray treatment for a giant cell tumor of the distal right radius, followed in three years by surgical removal of the distal radius and operative correction of the deformity, seven years after the original diagnosis. No evidence of malignancy was found. Eleven years after the original diagnosis the distal ulna showed a growth which was excised and found to be a fibrosarcoma with tumor cartilage. In case III a mass developed at the anterior end of the right 7th rib, 12 years after a right mastectomy followed by irradiation. Excision proved the mass to be a chondrosarcoma. In discussing the cases, the author admits the possibility of recurrence or metastasis, but is firmly convinced that the malignant changes were attributable to irradiation. Surgery is absorbed, although it also was used in all cases. (Much can be said against the possibility of irradiation as the cause of the malignant change in all these cases. (R)

570

Helmke, Roderich. CONCERNING INDIVIDUAL DIFFERENCES IN THE X-RAY SENSITIVITY OF HUMAN SKIN, EXAMINED BY THE APPEARANCE OF AN ERYTHEMA. *Strahlentherapie* 80, 585-90(1949).

Fifty men and fifty women were treated through 10 fields on the back with X-ray dosages from 200-400 r, increasing by 25 r from field to field. Special attention was paid to the appearance of the early X-ray erythema and the main X-ray erythema. The early erythema field was the one which, while showing a well-defined red field, had received the smallest r-dose. The main erythema field was determined 15 days after irradiation. For the appearance of the early erythema there was an individual variation range of 100 r in men and women; for the main erythema, the variation range was 50 r in men and 75 r in women. (NSA)

571

Hills, T. H. and R. W. Stanford. THE PROBLEM OF EXCESSIVE RADIATION DURING ROUTINE INVESTIGATIONS OF THE HEART. *Brit. Heart J.* 12, 45-53(1950).

An account of the types of measurements made during routine cases of angiocardiology and cardiac catheterization is given. Details are provided concerning the possible amounts of excess radiation to which the patient and the technical personnel may be exposed during the routine investigations; suggestions are made as to means whereby the excess exposure to radiations can be avoided or reduced to a safe level. Distance, lead and rubber aprons and gloves, and other protective devices and measures are discussed as close proximity to the patient. Accurate monitoring and calculation of the radiation exposure experienced by the patient are also mentioned as safeguards. (NSA)

572

Hobbs, Arthur A., Jr. **FETAL TOLERANCE TO ROENTGEN RAYS. A CASE REPORT.** *Radiology* **54**, 242-6(1950).

A pregnant woman, found to have adenocarcinoma of the breast, and operated upon, was later shown to have an osteolytic lesion in the sacrum and right ilium. Upon refusal to allow surgical interruption of the pregnancy, she was irradiated with a total dose of 1,500 r measured in air, the beams being directed dorsoventrally and ventrodorsally, so as to produce a calculated dose of 900 r at the midpelvic region; additional radiation was later directed to the dorsal field, adding 375 r to the dose at the center of the pelvis. Pregnancy was terminated with delivery a month later and soon thereafter the osteolytic lesion healed, but the patient died about six months later of liver metastases. The child has appeared to be normal ever since birth. It is stated that the circumstances and irradiation factors in this case parallel the requirements listed by Harris and Mayer for the accomplishment of spontaneous abortion, and no adequate explanation can be offered for the noneffectiveness of the x-irradiation, but it is concluded that the fetal age was apparently a modifying factor. (NSA)

573

Hubert, Walther. **ON DELAYED RADIATION REACTIONS IN THE BLADDER AND RECTUM AND THEIR TREATMENT.** *Strahlentherapie* **79**, 113-26(1949).

Gynecological radiation therapy often produces harmful after-effects in the bladder and rectum, especially in patients of advanced ages. It was found that these effects could be successfully treated with cod liver oil, 20 to 50 cm. of which was injected daily into the bladder, and every second day into the rectum, alternating with an injection of camomile tea. In five tables the following information derived from the treatment of 27 patients is summarized: distribution of harmful after-effects according to their location and the kind of irradiated uterine or portio carcinoma; age distribution of the patients suffering from various after-effects; time of first occurrence of the after-effects; and the results of the cod liver oil treatment. (NSA)

574

Jones, Arthur. **CLINICAL REACTIONS AND INJURIES IN SUPERVOLTAGE THERAPY.** *Proc. Roy. Soc. Med.* **41**, 703-9(1948).

This brief account of the clinical effects of supervoltage radiation and of the injuries which have resulted during the treatment of malignant disease with the million-volt apparatus includes the following: (1) injuries to the skin and subcutaneous tissue, (2) injuries to connective tissue, (3) effects on respiratory tract, esophagus, bladder, bone, eye, and liver, and (4) occurrence of muscle fibrosis. (NSA)

575

Leach, J. E. **ABNORMAL PULMONARY PHYSIOLOGY AS A RESULT OF CHRONIC IRRADIATION PLEUROPULMONITIS.** *Am. J. Roentgenol. Radium Therapy* **50**, 772-8(1943).

The purpose of this report is to point out some of the striking deviations from the normal pulmonary physiology that may occur in patients who sustain pulmonary fibrosis following deep roentgen therapy to tumors on or within the thorax. The most disabling feature of irradiation fibrosis of the lung is the marked dyspnea that may occur as a result of ordinary exercise. It is pointed out that chronic irradiation pleuropulmonitis is not merely a pleuropulmonary disorder, but also includes changes in the thoracic parietes, as well as the diaphragm and mediastinum. (S.V.S.)

576

Lukens, R. M. **COMPLICATIONS FOLLOWING IRRADIATION OF THE THYROID GLAND.** *Ann. Otol. Rhinol. and Laryngol.* **57**, 633-42(1948).

Although X-ray irradiation of the thyroid gland for exophthalmic goiter, hyperthyroidism, etc. is considered to be definitely indicated, the five case histories presented in this paper show the damage that can be caused to the blood vessels, overlying tissues, and underlying larynx and trachea when such irradiation is indiscriminate or excessive. The symptoms appearing in these cases were: hoarseness, sensation of lump in the throat, inspiratory dyspnea, wheezing, dysphagia, cough, expectoration, loss of weight, and chest pain. The physical findings were: congestion of the laryngeal mucosa, telangiectasis and scarring of the neck, stenosis of the larynx and trachea, inflammation of the laryngeal mucosa, telangiectasis of the vocal cords, granulomatous lesions in the tracheal walls, and destruction of the ciliary action of the epithelium resulting in viscid adherent tracheal secretions and crusting. The time between termination of irradiation and appearance of the first symptoms was from one to seven years and the patients have been under continuous treatment for relief one year (1 case), three years (1 case), nine years (1 case), ten years (1 case), and eleven years (1 case). Tracheotomy was required in three cases. (NSA)

577

Maas, Jerome M. **INTESTINAL EFFECTS OF PELVIC IRRADIATION.** *Modern Med.* **16**, 47-8(1948).

It is estimated that from 50% to 75% of all women treated by gynecologic radiation have permanent rectal sequelae though perhaps unrecognizable. They include extensive scarring, fistula, hemorrhage, or complete occlusion. Radium implants have been found more harmful than X-rays, and injury was greatest when they were combined for cervical or fundal tumor. The treatment of resulting conditions of proctitis, stenosis, bleeding, and rectovaginal fistula is discussed. (NSA)

578

Nadal, R. and J. Piequet. **POST-RADIOTHERAPEUTIC ESOPHAGEAL STENOSES.** *J. Radiol. Electrol.* **29**, 296-7(1948).

Three cases of stenosis occurring after x-irradiation which included the esophageal region as a part of the field are presented in detail. Irradiation was delivered at 180 to 200 kv, through a 1 mm Cu and 2-3 mm Al filter, at a focal distance of 40 to 50 cm., giving single doses of 200 to 250 r at varying intervals, with a total dose between 3,000 r and 12,000 r. The stenoses, involving skin area fibroid formation, developed progressively after variable periods; in these cases all other causes of the reaction are eliminated. (NSA)

579

Pennybacker, Joe and Dorothy S. Russell. **NECROSIS OF THE BRAIN DUE TO RADIATION THERAPY.** *J. Neurol. Neurosurg. Psychiat.* **11**, 183-98(1948).

The authors report the clinical and pathological features of five cases of necrosis of the brain following radiation therapy by accepted techniques and dosages. The clinical effects may come on suddenly, progress to a point, and become arrested; or they may come on gradually and lead to death. In each case there was a latent period between the radiation treatment and the onset clinical signs of necrosis. The shortest interval was nine months, the longest five years. The pathology of the necrosis appears to be related to reactions in the smaller blood vessels in which collagenous thickening, fibrinous necrosis, and thrombosis are con-

spicuous. As it seems impossible to predict in which cases necrosis will occur, it is suggested that radiation should be reserved for inoperable tumors and those cases in which no further surgical procedures are contemplated. (NSA)

580

Quimby, Edith H. and W. S. MacComb. **FURTHER STUDIES ON THE RATE OF RECOVERY OF HUMAN SKIN FROM THE EFFECTS OF ROENTGEN OR GAMMA-RAY IRRADIATION.** *Radiology* **29**, 305-12(1937).

The authors present curves and a table from which the accumulated dose in the skin can be calculated for any day during the period of treatment. If the total dose and total treatment time are the same within certain limits, the number of fractions into which the radiation is divided is not particularly important. But this refers only to the skin, and the clinical applicability of this information can be determined only by observing the tumor regression, systemic effect, etc. in a series of cases treated by each scheme. Within certain limits it appears that if the total dose and total treatment period are the same, the rate at which the radiation is administered within that period is not important; it may be continuous or fractionated at will. The term "saturation method" applied to the administration of a fairly large dose followed by a number of small ones, assuming a constant rate of recovery and a constant rate of making up for this, is not accurate. Since the amount of recovery decreases from day to day, it is necessary to know the correct recovery factor for each day. A method is outlined for calculating a true saturation scheme of irradiation. (YBR)

581

Quimby, Edith H. and Sidney C. Werner. **LATE RADIATION EFFECTS IN ROENTGEN THERAPY FOR HYPERTHYROIDISM; THEIR POSSIBLE BEARING ON THE USE OF RADIOACTIVE IODINE.** *J. Am. Med. Assoc.* **140**, 1046-7(1949).

Long-term follow-ups on patients receiving I^{131} for hyperthyroid conditions are necessary before it can be definitely stated whether or not this form of therapy may result in late degenerative malignancy in treated areas. Three definite cases out of 10 cases of further malignancy were found in records of 101 radiologists and thyroid experts; these had all received heavy radiation doses. Since the dose of X-ray is 3,000 to 3,500 r delivered to the whole gland, and the dose of I^{131} is 5,000 to 6,000 equivalent r delivered to the whole gland, but concentrated in such a way in specific parts that it is thought that the dose in some parts may be as high as 30,000 r, the possibility of subsequent malignancy is probably far greater with I^{131} than with X-ray therapy. (NSA)

582

Ricketts, William E., Joseph B. Kirsner, Eleanor M. Humphreys, and Walter Lincoln Palmer. *Gastroenterology* **11**, 818-32(1948).

Moderate roentgen irradiation (1100 to 2500 r, applied in divided doses) of the fundus and body of the stomach in man produces an acute transitory symptomless gastritis that is characterized gastroscopically by hyperemia, hemorrhage, edema, and adherent exudate, and histologically by degenerative changes in the epithelial cells and lymph follicles, increased cellular infiltration, and relatively minor changes in the blood vessels. Atrophy of the gastric mucosa often ensues; it is uniformly present in patients with prolonged post-radiation anacidity. (NSA)

583

Sarasin, R., G. Voluter, and J. Garcia-Calderon. **A CONTRIBUTION TO THE STUDY OF TRANSIENT PLEURO-PULMONARY MODIFICATIONS OCCURRING AFTER**

RADIOTHERAPY OF BREAST CARCINOMA. *J. Radiol. Electrol.* **29**, 445-52(1948).

Nine case histories of pulmonary complications developing after the use of radiation up to 12,000 r on breast cancer are given with radiographs of the affected area. Exudation with atelectasis is always a part of the symptomological picture; irritation of various types is reported and the histopathology of the mechanisms is discussed. These phenomena may be accompanied by a fibroid formation but are always transient in nature, appearing at times some months after irradiation and regressing after variable periods of time. It is mentioned that the radiological picture may resemble a pulmonary tumor. (NSA)

584

Scheie, Harold G., Richard H. Dennis, Richard C. Ripple, Larry L. Calkins, and John A. Buesseler. **THE EFFECT OF LOW-VOLTAGE ROENTGEN RAYS ON THE NORMAL AND VASCULARIZED CORNEA OF THE RABBIT. A PRELIMINARY REPORT ON THE PHILIPS MACHINE.** *Am. J. Ophthalmol.* **33**, 549-71(1950).

In order to determine the beneficial and injurious effects of low-voltage x-rays when applied to the eye under controlled conditions and to determine whether or not x-rays might be a satisfactory substitute for β irradiation, the studies described were performed. A Philips contact ray machine was operated at 44 kv and delivered varying total doses either to the normal rabbit eye or the rabbit cornea. It was found that exposure of the rabbit eye of up to 2,000 r weekly for as long as 5 weeks could be performed without apparent damage to the cornea or lens during the following 3.5 months. Exposures as small as 500 r and limited to the cornea, when given weekly for 21 weeks, resulted in transient corneal opacity. Dosages of 5,000 r, given in the same manner, caused permanent corneal opacity and irradiation cataract, first observed 14 months following the first exposure. Vascularization induced by an intracorneal sodium hydroxide injection could be markedly inhibited by the low-voltage x-rays; daily exposure was more effective in inhibiting corneal vascularization than exposures given at longer intervals, and small dosages of 300 r were as effective as larger ones up to 1,000 r. Exposures of 400 r and 500 r repeated 3 and 4 times at approximately 4-week intervals were used clinically in several hundred patients without evidence of cataract formation; these patients have been observed for as long as 2.5 years following treatment. (NSA)

585

Schneider, W. **SARCOMA AND CARCINOMA INTER-RELATIONSHIP IN X-RAY TREATED LUPUS VULGARIS.** *Strahlentherapie* **80**, 335-66(1949).

Nine cases of sarcoma occurring after X-ray therapy of lupus vulgaris are clinically and histologically described in detail. Though in all cases a carcinoma developed first, the co-existence of a sarcoma which had developed after the application of high X-ray dosages was histologically established in six cases. The sarcomas originated from the chronic granulation tissue, not through metaplasia of epithelial cell elements, and were the collision tumor-type, not the carcino-type. The fact that high X-ray dosages were applied and that the sites of the tumors were places of sharply expressed X-ray atrophy leads to the conclusion that these tumors, particularly the sarcoma, originated from severe X-ray injuries. (NSA)

586

Teloh, H. A., M. L. Mason, and M. C. Wheelock. **A HISTOPATHOLOGIC STUDY OF RADIATION INJURIES OF THE SKIN.** *Surg. Gynecol. Obstet.* **90**, 335-48(1950).

The history of irradiation injuries of the skin is briefly

summarized and clinical aspects of irradiation dermatitis, acute and chronic, are reviewed. Of 121 patients with radiation dermatitis, as a result of the use of X-rays, radium, and radon, 28.1% showed definite evidence of carcinoma, usually localized by the stromal barrier. Such epidermal changes as atrophy of epithelium with the consequent loss of rete pegs, alternating with focal areas of hypertrophy, characterized by marked acanthosis, hyperkeratosis, and rarely parakeratosis, were seen. The vascular picture consisted of marked endothelial proliferation with narrowing or occlusion of the lumen of the artery, fibrosis and hyalinization of the media, fibrosis of the adventitia and occasionally perivascular edema and lymphocytic infiltration. Stromal changes, and changes in hair follicles, sebaceous glands and sweat glands are also described. It is noted that in the 121 cases studied vascular changes were the most constant, the earliest and the most pronounced of the changes observed in the skin. Evidence is presented on the direct carcinogenic effect of irradiation on the epidermal portion of the skin. It is concluded that the therapy of a benign cutaneous or subcutaneous lesion by means of irradiation, with the potential production of a much more severe irradiation dermatitis, is not justified unless it can be carried out by a roentgenologist trained in the limitations and potentialities of such therapy. (NSA)

587

Vogt, Alfred. DELAYED INJURIES OF THE CRANIUM AFTER X-RAY THERAPY OF INTRACEREBRAL TUMORS. *Strahlentherapie* 80, 165-74(1949).

Two cases are described where injuries of the cranium occurred five and six years after X-ray treatment. One patient with a tumor of the hypophysis, and the other with acromegaly had been treated with large dosages of deep X-rays (10,500 to 13,200 r), delivered in doses of 300 r, to three fields over a period of two months to about two years; the radiations were administered by a 185 kv machine, with a filter of 0.5 mm Cu and at a target distance of 40 cm. At three or four places in the cranium, radiogenous fibroses developed. The author warns that fibroses resulting from pressure through growing intracranial tumors and other factors have to be carefully distinguished from radiogenous fibrosis in the interest of further treatment of a patient. Since both patients showed relief from their symptoms and could work, the possibility of producing fibrosis should not be a contraindication to radiation therapy of the brain where it is otherwise indicated. (NSA)

588

Walter, J. EPITHELIOMA AND PAPILLOMA ARISING ON RECENTLY IRRADIATED SKIN; REPORT OF THREE CASES. *Brit. Med. J.* 4648, 273-4(1950).

A series of three cases of epithelioma and papilloma developing a few months after X-ray reactions of only moderate severity is presented and the cases are discussed in detail. In the first case, the total treatment time was 31 days and the estimated tumor dose was 4,600 r; the skin reaction proceeded to a deep erythema with dry desquamation and a few small and moist patches. Healing was rapid and uneventful but about 14 weeks after the end of the treatments, a nodule developed on the irradiation site which was excised and concluded to be a papilloma; the patient is well to date. About 11 weeks after the delivery of a skin dose of 3,900 r to the second patient, with consequent erythema of moderate depth, a nodule identified as squamous epithelioma developed and one year after excision the patient died from the effects of the primary lesion (carcinoma of the hypopharynx). A total dose of about 3,500 r was delivered to the third patient over a period of 23 days with a moderate erythema developing; seven weeks after the end

of the treatments a nodule developed in the irradiation site which was identified as being squamous epithelioma; irradiation for a total of 3,500 r was then delivered in 23 days, and the patient is well to date. Several explanations of the occurrence of these secondary lesions are presented. (NSA)

589

Windholz, F. LATE CHANGES IN MUCOUS MEMBRANE OF THE IRRADIATED LARYNX. *Radiology* 48, 274-81 (1947).

Microscopic study of the mucous membrane of the cancerous larynx after protracted fractionated irradiation reveals that the primary effect of irradiation is cell destruction. At the time fibrinous reaction occurs, the mucous membrane is entirely destroyed. Later, regeneration of epithelium takes place. The regenerated epithelial structures which often replace the columnar epithelium are also metaplastic, revealing excessive cornification. This metaplasia has also been produced by irradiation in animal experiments. The structure of the regenerated epithelium varies according to the post-irradiation condition of the subepithelial connective tissue. In two cases out of ten the subepithelial connective tissue of the larynx was transferred into hyaline sclerotic tissue with large amounts of interstitial collagen, few cells, and obliteration of blood vessels. In these two cases, the epithelium was markedly atrophic and the tumor of the larynx has disappeared. Clinically, strong fibrin reaction was observed. In two other cases, displaying large residual or recurrent tumors, the superficial epithelium exhibited definite tendencies toward atypical growth after irradiation. The connective tissues were remarkably well preserved in these cases and clinically no fibrin reaction was observed. These studies indicate that, while the primary epithelical radiation effects are fading out, the changing generations of metaplastic epithelium adapt the growth and differentiation properties of their structures to the post-irradiation condition of the subepithelial connective tissue. In cases in which the tumor has disappeared, advanced diffuse atrophy (fibrosclerosis) of the connective tissue and epithelium is observed. (R)

590

Woodburne, Arthur R. and Osgood S. Philpott. RADIATION EFFECTS ON THE SKIN AND THEIR TREATMENT. *J. Michigan State Med. Soc.* 48, 461-79(1949).

A detailed review of studies on 100 patients showing evidence of skin damage due to irradiation is given. Such general effects as erythema, edema, hyperpigmentation, and dry atrophic, and depigmented skin are observed. Severe cases involving large areas of vessels in an obliterative vasculitis and consequent ulceration are cited. Dosages of 5,000-6,000 r over areas of 10 cm. diameter or more produce these serious results. Smaller doses of 1,000-3,000 r produce milder symptoms. The pathological changes, involving the vessel walls, collagen bundles, and nuclei are described in detail. Surgery is urged as soon as feasible in order to relieve suffering, permit rehabilitation, and prevent carcinoma. (NSA)

Effects on Blood

591

Brown, Crawford S., Esther Hardenbergh, and John L. Tullis. THE BIOCHEMICAL, CELLULAR, AND BACTERIOLOGIC CHANGES IN THORACIC DUCT LYMPH OF DOGS EXPOSED TO TOTAL BODY IRRADIATION. *Am. J. Physiol.* 163, 668-75(1950). (NP-1762)

A study of the biochemical, cellular, and bacteriologic changes in lymph produced by 500 r of total-body irradiation.

tion in dogs was undertaken in order to compare them with changes which have been found to occur in blood. Forty dogs were divided into 9 groups, each group representing a different time interval through 132 hr after irradiation. Dogs were anesthetized with nembutal, the thoracic ducts were cannulated with siliconed glass tubing, and the lymph fistulae allowed to drain for 6 to 10 hr. Lymph samples were taken every 1 to 2 hr. Blood samples were taken at longer intervals. Changes, with time after irradiation, of protein level, creatine, uric acid, sugar, and other components are discussed. (NSA)

592

Chanutin, Alfred and Stephan Ludewig. EFFECT OF WHOLE BODY X-IRRADIATION ON SERUM IRON CONCENTRATION OF RATS. *Am. J. Physiol.* **166**, 380-3 (1951).

Serum iron concentrations were determined in male and female rats exposed to total body irradiation with x-rays in doses varying from 10 to 1500 r. The average values are significantly increased in both groups during the first day following irradiation with doses of 100 r or greater. Subsequently, the serum iron concentrations remained elevated for about a week in the 500- and 600-r groups. Male animals appeared to be more sensitive to irradiation as judged by the increased values for serum iron. (auth) (NSA)

593

Gjessing, Erland C. and Alfred Chanutin. STUDIES ON THE PROTEINS AND LIPIDES OF PLASMA FRACTIONS OF X-RAY-IRRADIATED RATS. *Arch. Biochem.* **27**, 191-7(1950).

The nitrogen and lipid contents of 4 plasma fractions are presented for rats exposed to nonlethal and lethal doses of x-rays. Pronounced increases in the nitrogen contents of the α_1 -globulin-rich Fraction IV-4 and decreases in the albumin-rich Fraction V are seen. The most pronounced changes in the total lipid and cholesterol content are noted in Fraction IV-4. The percentage distribution of the components of the electrophoretic patterns of the 4 fractions do not deviate significantly from the controls except in the case of Fraction II + III. The γ -globulin content of this fraction is consistently diminished. (auth) (NSA)

594

Goldschmidt, Leontine, Robert L. Rosenthal, Victor P. Bond, and Maurice C. Fishler. ALTERATIONS IN THERMAL FRAGILITY OF RAT ERYTHROCYTES FOLLOWING TOTAL BODY X-IRRADIATION. *Naval Radiological Defense Lab.* Feb. 14, 1950. 12p. (AD-199(B))

A review of the literature has revealed indirect evidence that radiation affects the integrity of the circulating red cell, but that no direct change has been demonstrated. A spectrophotometric method for the quantitative measurement of red cell hemolysis produced by an elevated temperature (53°C) has been developed. By this method, a definite increase in red cell fragility was demonstrated in rats within 4 to 12 hours following their exposure to total body x-irradiation at 500 and 600 r. The possible mechanism of these red cell changes and their significance in radiation sickness are discussed. (NSA)

595

Halberstaedter, L. and J. Leibowitz. HEMOLYSIS AND FIXATION OF ERYTHROCYTES BY X-RAYS. *Biochem. J.* **41**, 235-9(1947).

Suspensions of erythrocytes down to a concentration of about 0.5% respond to irradiation with an effective x-ray dose by hemolysis independently of the nature of the medium in which they are suspended. At cell concentrations below 0.5%, the response of erythrocytes to irradiation depends on the medium in which they are suspended: (a) In

isotonic glucose, KH_2PO_4 , Na_2NPHO_4 , NaHCO_3 and glycine, the response to an effective x-ray dose is hemolysis. (b) In isotonic NaCl , KCl , CaCl_2 , NaNO_3 , $(\text{NH}_4)_2\text{SO}_4$, MgSO_4 and glycerol, the effect of an x-ray dose of 2×10^5 r and more is not hemolysis but cell fixation, the total loss of the ability to hemolyze. Addition to media listed in 2 (b) of serum, phosphate, or bicarbonate prevents cell fixation. The fixation-opposing activity of phosphate is considerably below that of serum or bicarbonate. The bicarbonate content of serum accounts for its high activity in preventing fixation. The relevance of the nature of the medium and of the cell concentration of the erythrocyte suspension for the occurrence of the fixation effect points to some "indirect action" mechanism of the irradiation. (BA)

596

Hennessy, Thomas G. and Rex L. Huff. DEPRESSION OF TRACER ION UPTAKE CURVE IN RAT ERYTHROCYTES FOLLOWING TOTAL BODY X-IRRADIATION. *Proc. Soc. Exptl. Biol. Med.* **73**, 436-9(1950).

Groups consisting of five adult female Curtis Dunning rats weighing approximately 200 g. were given total-body x-irradiation, delivered by a 180-kv machine through a 0.5 mm Cu and 3 mm Al filtration; the animals were individually irradiated in lucite containers. Four series were irradiated: series A and B consisted of four groups which received 5, 25, 125, and 250 r of the whole-body irradiation; series C consisted of three groups that received 5, 10, and 25 r; there was also a control series. Each animal received intravenously by tail vein a labeling dose of Fe^{59} in 0.5 cc. of FeCl_3 solution containing 2γ total iron and approximately $0.07 \mu\text{c}$ of Fe^{59} . In series A the labeling dose was given two days after the x-irradiation, in series B one day after, and in series C within four hours after the irradiation. Following the administration of the labeling dose of Fe^{59} , 0.5 cc. samples of blood were drawn by means of cardiac puncture, heparinized and centrifuged. The hematocrit was recorded, and the samples were tested for radioactivity. Graphs of the red cell Fe^{59} uptake curve in the rats at the various dosage levels of total-body x-irradiation are given. The results obtained in these studies show that the radioactive iron red cell uptake curve is a sensitive indicator of x-irradiation damage to the bone marrow; the histological evidence of the sensitivity of erythroid tissue to x-irradiation also was confirmed. (NSA)

597

Kocholaty, Walter, William W. Ellis, and Hans F. Jensen. EFFECT OF TOTAL BODY X-IRRADIATION ON THE PLASMIN INHIBITOR TITER IN THE BLOOD OF RATS. *Army Medical Research Lab.* Dec. 15, 1951. 6p. (AMRL-71)

Exposure of rats to 1000 r total body x irradiation produced a fall in the plasmin inhibitor titer of plasma, beginning at the second day after irradiation and then gradually increasing. Since starvation was found to exert a similar effect, no definite conclusions can be made as to whether irradiation per se caused a lowering in the titer. Total body x irradiation (1000 r) and starvation caused a weight loss of nearly identical magnitude. (NSA)

598

Kohn, H. I. CHANGES IN COMPOSITION OF BLOOD PLASMA OF THE RAT DURING ACUTE RADIATION SYNDROME, AND THEIR PARTIAL MITIGATION BY DIBENAMINE AND CORTIN. *Am. J. Physiol.* **165**, 27-42 (1951).

Adult rats were given a single total body exposure to 250 peak-kilovoltage x-rays, and the changes in the plasma followed for about 30 days. The changes in the plasma occurred in 2 phases, unaffected by sex, but somewhat dependent on the strain of rat. The magnitude of the changes varied with the x-ray dose (125 r, 350 r, 650 r), but the

timing and sequence did not. The changes in Cl and cholesterol were prevented by the daily administration of desoxycorticosterone acetate or lipoadrenal extract. Dibenamine or 2-dibenzylaminoethanol prevented the change in cholesterol alone. Injection of sheep erythrocytes 1 wk. before irradiation prevented the rise in albumin-globulin ratio. The greatest rate of change in the composition of the plasma occurred during days 3 and 4, the days on which the 1st deaths occur following a lethal exposure. It is proposed that radiation effects be classified as primary when occurring within the cells directly injured, and secondary when occurring in other cells. 55 references. (CA)

599

Lindemann, Bruno. RADIATION HEMOLYSIS, A CONTRIBUTION TO OUR KNOWLEDGE OF BIOLOGICAL EFFECTS OF IONIZING RADIATION. *Fortschr. Gebiete Röntgenstrahlen* **75**, 523-59(1951).

Electron-optical analyses were made of the structure of x-irradiated erythrocytes. Numerous illustrations of normal erythrocytes and erythrocytes in the process of hemolysis are given and the mechanism of the effect of x radiation causing hemolysis of erythrocytes is discussed. It is concluded that x radiation caused osmotic hemolysis of erythrocytes by alteration of the permeability of the erythrocyte membrane due to primary denaturation. Three factors of speed regulate the process of x-ray hemolysis, the reaction between hemolyticum and cell membrane, the penetration of the salt, and the disintegration of the cellular contents into a diffusible mass, the latter playing a decisive part. Morphologically analogous alterations of the membrane are caused by acid and x-ray denaturation. Degree of hemolysis depends on presence and amount of blood plasma in the suspension; it seems, therefore, that denaturation of the erythrocyte membrane is caused by indirect effects of x rays. The age of the individual erythrocytes and a protective effect by aggregation of cells influence the physiological degree of scatter in the reaction by an irradiated suspension of erythrocytes. (NSA)

600

Meyniel, Gaston and Suzanne Bazin. CHANGES IN THE ELECTRIC CHARGE OF ERYTHROCYTES OBSERVED IN IRRADIATED ANIMALS. *Compt. rend soc. biol.* **144**, 1463-5(1950).

The effect of ionizing radiations on the electric charge of blood corpuscles was examined by totally irradiating guinea pigs with doses of x rays slightly inferior to the threshold lethal dose. An electrophoretic study of erythrocytes showed a 25% diminution of their surface charge, appearing on the 7th day after the irradiation. Since the phenomenon is observed only in the presence of the serum of the animals; it is concluded that it is directly correlated with alterations in the proteinic fraction of the blood serum. (NSA)

601

Neve, R. A. and Cecil Entenman. CHANGES IN THE PLASMA PHOSPHOLIPIDS IN RATS FOLLOWING WHOLE BODY X-IRRADIATION. *Naval Radiological Defense Lab. Apr. 10, 1951. 17p. (AD-307(B))*

Changes in the plasma phospholipid phosphorus (PLP³¹) of fasted female rats have been determined following whole-body, 250-kv, x-irradiation, with doses ranging from 750 to 5000 r. Irradiation causes marked increases in the plasma level of PLP³¹. After 750 r the plasma level of PLP³¹ reaches a maximum at the second to third post-irradiation day. The plasma level of PLP³¹ after doses of 750, 1500, 2500, 3500 and 5000 r was, respectively, 6.47, 7.10, 7.78, 8.63, and 9.92 mg %, 2 days after irradiation. Plasma protein levels remained constant over two days after irradiation. Plasma volume, determined in some of the experi-

ments, showed little or no change over an interval of 5 days after irradiation. (auth) (NSA)

602

Sheppard, C. W. and Gertrude E. Beyl. CATION EXCHANGE IN MAMMALIAN ERYTHROCYTES. III. THE PROLYTIC EFFECT OF X-RAYS ON HUMAN CELLS. *J. Gen. Physiol.* **34**, 691-704(1951).

Freshly drawn heparinized human whole blood was exposed to x rays in amounts up to 54,000 r in vitro and then equilibrated under a controlled atmosphere at 24 or 38°C. For as long as 26 hr following exposure K was progressively lost from the cells and quantitatively replaced with Na with little, if any, osmotic disturbance. The mean rate of loss at 20,000 r and 24°C is about 0.4% of the initial cell K per hr and approximately doubles for a 20,000 r increase. It is accentuated if blood is stored at low temperature (5°C) following radiation exposure. Isotope experiments show that the rate of entrance of K into the cells is practically unaltered, the principal effect being an acceleration of the rate from cells to plasma. This suggests that radiation may have interfered with a mechanism of selective K accumulation based on preferential retention of the element. The Na which enters the cells following irradiation contributes to the rapidly changing portion of the cellular Na, suggesting that this fraction is ionic Na. (NSA)

603

Sheppard, C. W. and M. Stewart. LACK OF AN OXYGEN EFFECT IN THE DISTURBANCE BY X-RAYS OF SELECTIVE POTASSIUM ACCUMULATION IN HUMAN ERYTHROCYTES IN VITRO. *Federation Proc.* **10**, 125(1951).

Abstract reproduced here in its entirety.

When heparinized human whole blood is exposed to X-rays (30,000 r) and subsequently equilibrated in vivo under quasiphysiological conditions, potassium progressively leaves the cell and sodium penetrates in essentially equimolar amounts (Sheppard, *Biol. Bull.* **93**, 310). Experiments were performed in which blood was equilibrated with an atmosphere containing 5% CO₂ and 95% He or O₂. The completeness of the reduction on oxygenation of the blood was checked by spectrophotometry of the hemoglobin. After x-ray exposure the potassium leakage rate was determined by serial flame spectrophotometry of plasma samples. No difference could be detected between the leakage rate in samples irradiated under He or under O₂. This finding is in distinct contrast to the widespread depression of x-ray effects in many other tissues when irradiated under reduced oxygen tension.

604

Storey, R. H., L. Wish, and J. Furth. CHANGES IN CELL AND PLASMA VOLUMES PRODUCED BY TOTAL BODY X-RADIATION. *Proc. Soc. Exptl. Biol. Med.* **74**, 242-4 (1950) (ORNL-687)

Following irradiation of rabbits by 1000 r of x-rays there was a large drop in erythrocyte volume as measured by P³²-tagged cells beginning with the 3rd day and reaching a depth at about the 17th day after irradiation, followed by a slow recovery. There was at first a slight concomitant plasma-volume drop followed by a rise on about the 10th day that elevated the lowered total volume but did not bring it up to normal in 23 days. Similar changes occurred in mice that were exposed to 575 r. 11 references. (NSA)

605

Supplee, Helen, James D. Hauschildt, and Cecil Entenman. PLASMA PROTEINS AND PLASMA VOLUMES IN RATS FOLLOWING TOTAL BODY X-IRRADIATION. *Naval Radiological Defense Lab. May 17, 1951. 21p. (AD-318(B))*

The effects of alterations in plasma volume on the plasma protein concentration after x irradiation were studied. Simultaneous measurements were made of plasma protein concentrations, plasma volumes, and total blood volume in rats for as long as 20 days after exposure to 400, 600, and 750 r total-body x radiation. In rats that received 750 r, plasma volumes decreased to values 20% below the control by the 3rd day; no significant decrease occurred in animals exposed to 400 or 600 r. Beginning with the 4th day after all exposures, an increase in the plasma volume was apparent and persisted throughout the experimental period. Plasma protein concentration was depressed by the 3rd or 4th day in all groups although the decrease was not statistically significant after exposure to 400 r. Recovery was incomplete even after the 20th post irradiation day. Comparison with starved control animals indicated that the initial loss of plasma protein after irradiation could be attributed only partially to impaired food intake. (2 tables, 4 charts) (NSA)

606

Ting, T. P. and Raymond E. Zirkle. **THE NATURE AND CAUSE OF THE HEMOLYSIS PRODUCED BY X-RAYS.** *J. Cellular Comp. Physiol.* **16**, 189-95(1940).

In defibrinated beef or human blood, exposed to 33,000 r of x-rays, radiation hemolysis sets in about 15 or 20 hrs. after irradiation. It is preceded by a swelling of the red cells which can be demonstrated by the hematocrit method. If this swelling be prevented by adding 1 vol. of isotonic sucrose to 9 vol. of blood, no hemolysis occurs before the end of 36 hrs. Swelling is therefore the chief cause of the radiation hemolysis. Since irradiated cells swell as fast in control serum as in irradiated serum, the effect of the radiation is on the cells themselves. Vapor pressure measurements show that the osmotic pressure of the cell contents is slightly raised, but this effect can account for only a few % of the swelling observed. The membrane is accordingly the more probable site of the important changes. The cations of Na and K readily penetrate red cells suspended in appropriate isosmotic salt solns. This, along with the fact that swelling in serum is prevented by suitable addition of isotonic non-electrolyte soln. (sucrose), indicates that the swelling, and therefore the radiation hemolysis, is due to an increased permeability to salts. (BA)

607

Volkin, Elliot and Henry I. Kohn. **A FACTOR IN THE PLASMA OF THE IRRADIATED RAT WHICH CHANGES THE A/G RATIO.** *Arch. Biochem.* **30**, 326-32(1951). (ORNL-734)

Total-body x-irradiation (250 kvp) of the rat caused a rise in the serum or plasma albumin-globulin (A/G) ratio. The effect was maximal 4 days after exposure to about 700 r. The rise was found when the A/G ratio was determined by sodium sulfate fractionation or by the analytical ultracentrifuge, but not by electrophoresis. Ether extraction of the plasma just prior to analysis returned the elevated value of A/G to normal. A substance was obtained from alcohol-ether extracts of plasma or serum which raised the A/G ratio of normal rat serum or plasma *in vitro*. 12 references. (NSA)

608

Zacek, Jan, Ul. Klimecky, and D. Motacek. **THE PROBLEM OF RADIOTOXINS. II.** *Spisy Lekarske Fak. Masaryk. Univ.* **22**, 8(1948).

Rat erythrocytes were irradiated with 6,030 r and then were injected subcutaneously into healthy animals as 5 cc. suspensions, in order to determine the severity and nature of radiotoxic effects; the leucopenic effects were checked at 24 hour intervals. It was found that the radiochemical changes could not be traced to any particular chemical constituent of the cells; radiotoxins were formed only in the

intact, live erythrocytes, probably by complex chain reactions. Hemolysis of the cells prior to irradiation prevented the formation of toxins, while hemolysis immediately after the irradiation stopped the chain reactions and minimized the concentration of toxic material. (NSA)

609

Zacek, Jan and R. Rosenberg. **THE ACTION OF X-RAYS ON THE MEMBRANE OF RED CORPUSCLES.** *Compt. rend. soc. biol.* **144**, 462-4(1950).

Blood, drawn by venous puncture, received an x-ray dose of 24,000 r at 80 kv after which it was hemolyzed and dried, and then examined under an electron microscope. The size and shape of the cell membrane did not change (as compared with nonirradiated cells). However, the ordinary granular surface was replaced in some spots by a fine fibrous protein-like structure. The authors believe this change is due to the chemical decomposition of the lipoprotein following the x-radiation. The lipoids form an interstitial network which diffuse out during hemolysis and washing. (NSA)

Hemopoiesis—Humans

610

Bourret, J. **THE BLOOD CHANGES IN ROENTGEN PERSONNEL.** *Deut. med. Wochschr.* **74**, 447(1949).

For six years at the Civil Hospital at Lyon, a semi-annual blood checkup has been pursued in order to determine the amount of radiation exposure the roentgen personnel have suffered from roentgen rays and radioactive materials. Furthermore, a clever device, such as that worn by American Atomic workers is worn by the personnel, a film badge which indicates an exposure to the rays. However, it has been found that the weekly exposure of the personnel is between $\frac{1}{4}$ and $\frac{1}{100}$ r, well within the 1 r weekly tolerance limit. Workers specializing in roentgen diagnosis of the digestive tract encountered the largest amount of exposure. Even here, the systematic blood control system showed no serious damage from ray exposure. (NSA)

611

Browning, Ethel. **BLOOD CHANGES IN LUMINIZERS USING RADIOACTIVE MATERIAL.** *Brit. Med. J.* **1**, 428-31(1949).

In a 7-year study of 2,737 workers who used radioactive material (and 100 control workers), complete blood analyses were done while they were working, and, of these, 366 were followed up. Exposure was limited to small amounts by various precautionary methods and occurred from external irradiation by α particles, β and γ rays, radon inhalation, ingestion from hand contamination, and inhalation of radioactive dust. Transient lymphocytosis, the presence of Turk cells, premyelocytes, and premature large mononuclear cells were found, as well as a rare occurrence of anemia. The author discusses the findings and concludes that the blood changes are due to a slight temporary hyperstimulation of the reticuloendothelial system. (NSA)

612

Cantril, S. T., L. Jacobson, and J. J. Nickson. **THE EFFECTS OF IRRADIATION ON THE BLOOD AND BLOOD FORMING TISSUES.** *Argonne National Lab. Jan. 11, 1943. Decl. Apr. 6, 1946. 33p. (MDDC-991)*

A review is given of the effects of external whole body and local irradiation in man and experimental animals. Internal irradiation by radioactive substances in man and experimental animals is considered. The lymphocyte and its predecessors are the most sensitive cells in the blood system. The characteristic response is a diminution in the number of circulating cells or an increase in the number of

lymphocytes. The red blood cells are relatively insensitive to the effects of irradiation except for long continued exposure. Platelets are a fairly sensitive index of irradiation damage to the blood system in the acute exposure of whole body irradiation. Monocytes are of importance only in evaluating the more extreme degrees of irradiation change. When complete monocytosis occurs radiation damage is severe. (ADD)

- 613 Cronkite, Eugene P. IONIZING RADIATION INJURY. *J. Am. Med. Assoc.* **139**, 366-9(1949).
A single excessive serious exposure to ionization radiation is evidenced by marked lymphocytopenia followed by a characteristic sequence of events in the other leukocyte members. The diagnosis of repeated exposures to lesser amounts of ionizing radiation requires blood studies and differential counts of radiation in urine, fecal, and nasal secretions. The principal protection from ionizing radiation is physical control of radiation intensities by establishing monitoring procedures and prevention of contamination of personnel by radioactive materials. (N)
- 614 Denstad, T. THE RADIOSENSITIVITY OF THE BONE MARROW. *Acta Radiol.* **22**, 347-59(1941).
The erythropoietic as well as the myelopoietic cells of bone marrow are very sensitive to the action of rays, especially the first mentioned ones. The immature forms are the first to disappear. The regeneration capacity, however, is good, even if large doses are administered. It is assumed that granulocytopenia (and most likely also lymphopenia) following radiotherapy are both due to a long distance action of the rays, an inhibiting action on myelopoiesis (and lymphopoiesis). The conclusions which might be drawn from this supposition with regard to the action of radiotherapy on leukemia and polycytosis are discussed. (auth)
- 615 Dickie, A. and L. H. Hemplemann. MORPHOLOGIC CHANGES IN THE LYMPHOCYTES OF PERSONS EXPOSED TO IONIZING RADIATION. *J. Lab. Clin. Med.* **32**, 1045-59(1947).
Persons chronically exposed to ionizing radiation and toxic chemicals showed a significant decrease in total leukocyte counts, while no significant change in the absolute number or in the percentage of lymphocytes in the differential count was found. Morphologic study of supravital preparations of blood cells of persons chronically and acutely exposed to ionizing radiation or in persons working with toxic chemicals showed a striking increase in the number of refractive neutral red bodies in the cytoplasm of the circulating lymphocytes. These neutral red bodies have high density and are considered to be granules. They were not identified in fixed preparations. (GA)
- 616 Diethelm, Lothar and Wolfgang Hilscher. DANGER FROM RADIATION AND THE BLOOD PICTURE. *Roentgen Blätt.* **2**, 145-63(1949).
An extensive statistical treatment was given to blood data on average people and on radiologists subject to radiation exposure of up to 10 years, confirming previous findings. Leucocytes, reticulocytes, and hemoglobin were sensitive but eosinophils, monocytes, and erythrocytes were not affected. The normal daily fluctuation of reticulocytes was found to reach a minimum at night and was correlated with the action of sleep. (NSA)
- 617 Gunz, F. W. CULTURE OF HUMAN LEUKAEMIC BLOOD CELLS IN VITRO; SOME EFFECTS OF X-RAYS. *Brit. J. Cancer* **3**, 330-44(1949).
This paper presents the results of two groups of experiments on the action of x-rays on human leukemic blood cells; in the first group of experiments, the leucocytes were directly irradiated in vitro; in the second, they are explanted after the therapeutic irradiation of the patient. Samples of the venous blood of eight patients with chronic myeloid leukemia were incubated in a culture for 15 min, then irradiated with either 10, 50, 100, 1,000, or 10,000 r by a 220-kv apparatus at a target distance of either 21 or 81 cm and at a dosage rate of 622 or 62 r/min, respectively. It was found that mitosis was temporarily inhibited by a dose of 100 r, and apparently permanently inhibited by 1,000 r; as a result the number of immature leucocytes declined in the cultures. No increase in mitotic abnormalities occurred except when special arrangements were made, in which case a large number of abnormal, degenerating cells appeared, probably derived from breaking-down prophase. There was no sign that the x-rays acted by direct destruction of the resting cells. In the second series of experiments the leukemic leucocytes taken and cultured after the therapeutic irradiation of the patients showed a diminished proliferative activity in vitro. (NSA)
- 618 Helde, Matts. THE CONNECTION BETWEEN ROENTGEN RAY RISKS FOR WORKERS AND CHANGES IN THEIR BLOOD PICTURES. *Acta Radiol.* **27**, 308-15 (1946).
This is an investigation of various blood changes as related to probable amount of exposure to roentgen rays. Hypersegmentation, granulocytopenia, pathologic lymphocytes, and shift to the left appear to be well correlated with amount of exposure. Anemia, leukocytopenia, granulocytosis, leukocytosis and basophilia are not well correlated with exposure. (GPR)
- 619 Ingram, M. THE OCCURRENCE OF LYMPHOCYTES WITH BILOBED NUCLEI IN CYCLOTRON PERSONNEL, p.59-64 of QUARTERLY TECHNICAL REPORT, OCTOBER 1, 1950 THRU DECEMBER 31, 1950. Atomic Energy Project, Univ. of Rochester. Feb. 1, 1951. 6p. (UR-152(p.59-64))
The incidence of lymphocytes with bilobed nuclei in the blood of cyclotron workers is reviewed for the period extending from July 1948 through October 1950. An increase in the incidence of the unusual lymphocytes in the group as a whole occurred during the early periods of cyclotron operation. The construction of a protective earth and concrete dike between the cyclotron building and the cyclotron laboratory was followed by a return of the incidence of lymphocytes with bilobed nuclei to approximately normal levels. The significance of the relationship between an increased incidence of lymphocytes with bilobed nuclei and exposure to very small doses of radiation from the cyclotron is discussed briefly. (NSA)
- 620 Ingram, M. and S. W. Barnes. OBSERVATIONS OF THE BLOOD OF CYCLOTRON WORKERS. *Physiol. Rev.* **175**, 1765-6(1949).
This document is reproduced below in its entirety. Attention is called to the finding of two types of unusual cells in the blood of personnel of the 130 in. cyclotron at Rochester, New York. These are, respectively, very early mononuclear cells and cells which appear to be lymphocytes with bilobed or double nuclei. These cells, particularly the latter, occur in very small numbers, and it has been necessary to inspect several thousand leukocytes from each person in order to be assured of the finding. The "early mononuclear cells" are large, peroxidase negative, have deeply

basophilic cytoplasm and no nucleoli. The "lymphocytes with bilobed nuclei" tend to be somewhat larger than typical large lymphocytes. The nuclei stain slightly lighter than the nuclei of the other lymphocytes but are similar in consistency and have no nucleoli. The cytoplasm is clear, basophilic, peroxidase negative, and commonly contains a few typical azurophilic granules. Both kinds of cells have been found in individuals not associated with the cyclotron who have abnormal blood smears due to infections, specifically in several cases of infectious mononucleosis and in one case of acute pharyngitis due to Hemolytic H. Influenza. There is, however, no indication that the findings in cyclotron personnel are due to infections. Early mononuclear cells are occasionally found in routine films of "normal blood," however, lymphocytes with bilobed nuclei have not, to our knowledge, been described previously, and it is felt that they represent a true departure from the usual or normal blood picture. Although it is not possible to draw any conclusions relative to the significance of these cells as indicators of radiation damage, the findings may conceivably have such significance, and are presented at this time so that they may come to the attention of responsible individuals associated with cyclotrons in other institutions. (NSA)

621

Ingram, M. and S. W. Barnes. **EXPERIMENTAL CONFIRMATION OF A PREVIOUSLY REPORTED UNUSUAL FINDING IN THE BLOOD OF CYCLOTRON WORKERS.** *Science* 113, 32-4(1951) (UR-137)

The relationships between the increased incidence of lymphocytes with bilobed nuclei and exposure to radiation from the cyclotron has been confirmed experimentally. Three dogs were exposed on three different occasions to doses of radiation which were believed to be well below the tolerance dose. After each exposure there was a marked increase in the incidence of blood smears containing one or more of the abnormal lymphocytes. The frequency of occurrence of such smears was maximal during an approximately two-week period after each exposure. (NSA)

622

Jacobson, Leon O. and Edna K. Marks. **THE HEMATOLOGICAL EFFECTS OF IONIZING RADIATIONS IN THE TOLERANCE RANGE.** *Radiology* 49, 286-96(1947).

Lymphocyte reduction in the peripheral blood is the most sensitive indicator of acute or subacute exposure to externally originating or internally deposited radioisotopes. No hematological change is detected in mice, rabbits, or guinea pigs with a daily wholebody exposure to 0.1 r of γ radiation extending over three years. Changes may be observed for doses above 1.1 r per day, with guinea pigs most sensitive, followed by mice and rabbits. Human being subjected to wholebody x-ray exposure totaling 300 r given in divided daily doses of 5 to 20 r showed a degree of sensitivity of the hemopoietic system roughly comparable to that of the guinea pig and the dog. (CA)

623

Kikuchi, T., et al. **HEMATOLOGICAL OBSERVATION IN THE ATOM BOMB SUFFERERS IN HIROSHIMA CITY ONE YEAR AFTER THE BOMBING (2ND REPORT).** *Kyoto Imperial University.* [nd] 11p. (NP-305)

Hematological observations were made of atomic bomb sufferers (510 cases) one year after the bombing and of healthy Japanese (173 cases) as controls in Hiroshima city, with results as follows: Red blood cell counts were less than 4 million in 71.7% of the sufferers and in 61.8% of the controls. Color index over 1.21 was found in 50.6% of the sufferers and in 8.8% of the controls. In white blood cell count, there was no case under 3,000 in 1 cmm of blood in the controls; and the counts under 4,000 were found in 14.2% of the sufferers (counts under 3,000 in 2.1%) and in 3.5% of

the controls. In differential count of leukocytes (eosinophils, neutrophils, lymphocytes, monocytes, and plasma cells) and Sugiyama's mean nuclear lobes of neutrophil leukocytes, there were no remarkable differences in both cases; but the curve of neutrophil leukocyte count in the sufferers shifted to lower percentage than that of controls and in the curve of lymphocyte count, this relation was contrary. Blood platelet count was under 90,000 in 28.9% of the sufferers and in 14.9% of the controls. Bleeding time was almost normal in both cases, but the cases with bleeding time over five minutes were found in 4.9% of the sufferers and in 5.2% of the controls. The data are tabulated. (NSA)

624

Knowlton, Norman P., Jr. **THE VALUE OF BLOOD COUNTS IN INDIVIDUALS EXPOSED TO IONIZING RADIATION.** Los Alamos Scientific Lab. [nd] 25p. (AECU-397; LADC-682)

A study of the blood counts of 10 men exposed to about 0.2 r of γ rays per week for 117 weeks showed a small but significant decrease in the white blood cell, absolute neutrophil, and absolute lymphocyte counts. A control group of 117 individuals showed no such change while a group of 46 people exposed to 0.01 to 0.1 r per week showed a slight but not very significant decrease in these blood elements. It was concluded that, although the routine blood count is a poor detector of radiation injury, it is the best clinical test available. (NSA)

625

Knowlton, Norman P., Jr. **THE CHANGES IN THE BLOOD OF HUMANS CHRONICALLY EXPOSED TO LOW LEVEL GAMMA RADIATION.** [nd] Decl. Dec. 21, 1948. 16p. (AECU-1021; LADC-587; LAMS-816(Rev.) (p.76-92))

A group of 10 individuals exposed to 0.2 r of gamma radiation per week showed a significant fall in the total white blood count and the absolute neutrophil and lymphocyte counts during a 77-week period. The degree of fall would not have been predicted from experimental irradiation in animals, and other unknown factors might also have been causal agents. It is suggested that hematological and exposure data in other laboratories be analyzed statistically to confirm or disprove the effects of such low dosages of ionizing radiation on humans. (NSA)

626

Low-Beer, B. V. A. and Paul M. Aggeler. **HEMATOLOGICAL EFFECTS OF IONIZING RADIATIONS. VII. PROGRESS REPORT APRIL 1, 1949-FEBRUARY 28, 1950.** Radiation Laboratory, Univ. of Calif. [nd] 87p. (UCRL-862)

The progress made in the study of hematological effects of total-body irradiation during the period from Apr. 1, 1949, to Feb. 28, 1950 is reported. The purpose of this investigation is the observation of morphological changes which become evident in the peripheral blood of patients following exposure to therapeutic doses of ionizing radiations. Patients who have been followed hematologically include one group treated with 100-, 200-, or 1000-kv x-rays who had been exposed to total accumulated body doses of 100 to 390 r as measured on the skin; a group treated with radiophosphorus, P^{32} , for advanced generalized arthritis who had received intravenously total doses of 3600 to 8000 μ c; and a group who had been orally administered radioiodine, I^{131} , in amounts varying from a few hundred to 100,000 μ c for Grave's disease. Dose-effect relations are analyzed. (NSA)

627

Marks, Edna K. **EFFECTS OF RADIATION EXPOSURE ON THE CELLS OF THE PERIPHERAL BLOOD.** Argonne National Lab. Mar. 1947. Decl. Mar. 10, 1947. 3p. (MDDC-912)

A reduction in the erythrocyte values may be expected following acute and chronic total body irradiation. The anemia following chronic total body irradiation may be normocytic, hyperchromic, or macrocytic depending upon the size of dose and the sensitivity of the subject. The total number of reticulated erythrocytes is reduced following radiation exposure, but no changes have been found in the morphological character of the reticulum. Along with the reduction of platelet values after irradiation, giant thrombocytes are frequently found, occasionally larger than normocytes. The hyalomere is extremely abundant and the granules in the chromomere are usually prominent and large. The most sensitive cellular constituent of the peripheral blood appears to be the lymphocyte, and the reduction in its values closely parallels that of the total number of leukocytes. With increasing amounts of radiation exposure, the number of lymphocytes with abnormal morphological characteristics increases. (ADD)

628

Marks, Edna K., George Sacher, and Leon O. Jacobson. **EFFECT OF EXERCISE ON LEUCOPENIA; A STATISTICAL ANALYSIS**, p.456-66 of **INDUSTRIAL MEDICINE ON THE PLUTONIUM PROJECT**, Robert S. Stone, ed. New York, McGraw-Hill Book Company, Inc. 1951. (National Nuclear Energy Series, Division IV, Volume 20, Part B, Paper 6) (AECD-2133; ANL-HDY-466)

Leucocyte and differential leucocyte counts were made on 35 subjects immediately before, immediately after, and 15 minutes after the subjects performed the "standing running exercise." These individuals were male and female employees of the Metallurgical Laboratory. One group was selected from those who worked in that part of the laboratory where exposure to ionizing radiations up to the tolerance amount was possible, and the other had no known exposure to significant amounts of such radiations. Certain individuals in the exposed group had leucopenias; radiation exposure was suspected in the etiology of these leucopenias. The effect of exercise on the leucocyte response of the leucopenic and non-leucopenic individuals in the exposure group was compared to the response of the control unexposed group. Upon analysis no difference in response of these two groups was noted; all responded with an increase in leucocyte values immediately after completion of the exercise. The increase was comparable in the exposed and non-exposed individuals. Furthermore, no change in the stage of maturation of the polymorphonuclear neutrophils or morphological change in the lymphocytes was noted in either group. The evidence suggests that the response to the exercise test is due to a transient alteration of the distribution of mature cells in the vascular system and lymphatics as a result of increased blood flow. The test could thus be of little value in detecting a decreased response potentiality of the leucoprotic tissues as a result of exposure to radiations. (NSA)

629

Moses, Campbell and Madeline Platt. **CHANGES IN THE TOTAL CIRCULATING EOSINOPHILE COUNT IN CYCLOTRON WORKERS**. *Science* **113**, 676(1951).

Eosinophile counts were made on three workers who received an indeterminate exposure while sanding the Cu dees of a cyclotron. Two of the three workers demonstrated a marked increase in the number of total circulating eosinophiles over a period of 12 weeks. All counts have since returned to normal and have remained normal for 6 months. It is suggested that the total circulating eosinophile count may be a useful indication of exposure to radiation in individuals employed in x-ray, cyclotron, and other laboratories with radiation hazards. (NSA)

630

Moshman, Jack. **MEDICAL RECORDS PILOT STUDY**. Office of Research and Medicine, ORE, AEC. [nd] 44p. (ORO-13)

A pilot study has been completed of the medical records of operating contractors of the AEC in which it was designed to indicate any statistically significant changes in an individual's laboratory and clinical examination which might be due to chronic exposure to low-level irradiation. 1050 individual cases are considered from both the medical and statistical aspects. The study consisted of a detailed investigation of five specific hematological factors, namely, the red blood cell count, hemoglobin, white blood cell count, percentage of lymphocytes, and the percentage of polymorphonuclear neutrophils. (NSA)

631

Mossberg, Harry. **RADIATION THROMBOCYTOPENIA**. *Acta Radiol.* **28**, 110-14(1947).

The author has recently published in the same journal an article entitled "Two cases of allergy-like reaction with hemorrhagic diathesis following roentgen treatment." Both cases died of a hemorrhagic diathesis following relatively big doses. It occurred to the author that there might exist a similar though perhaps less pronounced effect with "ordinary" roentgen treatment. He therefore investigated 40 patients, in two-thirds of whom he found a definite reduction in the number of platelets. Five patients showed not only thrombocytopenia but also clinical manifestations of hemorrhagic diathesis. Thrombocytopenia is especially liable to occur when radiation is applied over the thorax, particularly over the sternum. The importance of following the thrombocyte count during and after roentgen treatment is referred to. (EM)

632

Mossberg, Harry. **THE BEHAVIOR OF THE THROMBOCYTES DURING AND AFTER LOCAL RADIOTHERAPY**. *Acta Radiol.* **29**, 277(1948).

The aim of this investigation was to give a contribution to the knowledge of the number of thrombocytes in the circulating blood during and after local radiotherapy, with doses of a size generally used in, for instance, treatment of malignant tumors. The literature on radiation effects on the hemopoietic system is reviewed selectively beginning 1903. Different theories concerning the radiation effect on the blood and the cells of the bone marrow are quoted and discussed.

633

Mossberg, Harry. **PLATELET VALUES IN PERSONNEL ENGAGED IN ROENTGEN DIAGNOSTIC WORK**. *Acta Radiol.* **34**, 186-92(1950).

Among personnel occupied in roentgen diagnostic work the author has found a definite decrease in the platelet count in about one-third of the cases. On account of these findings the author is of the opinion that the platelet count should be used as an integral part of the routine blood control of personnel engaged in radiologic work. (NSA)

634

Nickson, J. J. **BLOOD CHANGES IN HUMAN BEINGS FOLLOWING TOTAL-BODY IRRADIATION**, p.308-37 of **INDUSTRIAL MEDICINE ON THE PLUTONIUM PROJECT**, Robert S. Stone, ed. New York, McGraw-Hill Publishing Company, Inc. 1951. 511p. (National Nuclear Energy Series, Division IV, Volume 20, Part B, Paper 2) (AECD-2432; CH-3868)

Results of examinations of elements of the peripheral blood in 14 individuals following exposure to total body radiation are presented. The individuals are divided into three groups: Group I consists of eight individuals who

were irradiated with X-rays at one sitting; Group II consists of three individuals who were irradiated with X-rays in divided doses; and Group III consists of three normal individuals who were irradiated with X-rays by three doses of 7 r each. In Group I the most persistent abnormality noted was a diminution in the number of lymphocytes shortly after the completion of the treatment. In Group II depression in the lymphocytic count was also the most marked single change. In Group III no alterations were noted in the elements of the peripheral blood which were studied. (NSA)

635

Nordenson, Nils G. **BLOOD CHANGES IN RADIOLOGIC WORK.** *Acta Radiol.* 27, 416-32(1946).

Material obtained from blood investigations on 1,566 individuals working with roentgen rays or radium is presented in comparison with similar studies on 450 individuals not so engaged. Blood changes, including leukopenia, granulocytopenia, increased "shift to the left," hypersegmentation and pathologic lymphocytes, eosinophilia and basophilia, tendency toward leukocytosis, polycythemia, and anemia occurred in 52% of the radiologic personnel. Correlation between the degree of protection and the incidence of blood changes was good when the variation in individual resistance was considered. Significant injuries were observed in about 6% of the group. These the author designates as persistent granulocytopenia and leukopenia, combined and pronounced changes in an individual study, hemoglobin of less than 62%, a red cell count of less than three million, a white count of less than 3,000, and a lymphocytosis of more than 60%. No serious case of anemia was seen. (R)

636

Parcher, F. and B. Kane. **REACTIONS OF THE HEMOPOIETIC SYSTEM TO AGENTS USED IN THE TREATMENT OF DERMATOSES. EFFECTS OF LOW VOLTAGE ROENTGEN RAY THERAPY.** *Arch. Dermatol. and Syphilol.* 53, 1-5(1946).

This study was made over a period of four years. Eight patients with generalized dermatoses of various types were selected. Low voltage roentgen rays were administered. As a rule, three treatments were given each week for a maximum of eight weeks, and approximately six fields were exposed at the time of each treatment. Seventy-five unfiltered rays were administered to each irradiated field at a focus-skin distance of 16 cm $\times$ m.a. $\times$ 100 kv for 30 seconds. Filtered rays were given at a focus-skin distance of 25 cm. $\times$ 5 m.a. $\times$ 137 kv for 30 seconds filtered through 1 or 3 mm of aluminum. Blood counts were made before treatment was started, repeated at intervals during the course and again after therapy was discontinued. This low voltage irradiated was followed by leukopenia or by leukopenia and hypochromia anemia -- quantitative changes similar to those following high voltage irradiation. It is believed that individual variations in radiosensitivity and dosage are the primary factors in the development of these changes. (BA)

637

Price, C. H. G. **OBSERVATIONS UPON THE LYMPHOPENIA OF X-RAY IRRADIATION.** *Brit. J. Radiol.* 21, 481-93(1948).

Observations made upon 16 women treated for carcinoma with deep X-ray irradiation by a formal technique show that the reaction of the lymphocyte count follows a characteristic pattern. The major change in the total lymphocyte count appears to take place during the early part of a course of treatment, and is mainly shown in the lymphocyte/integral dose curves by the values of component B (an indirect effect, which for small doses may be due to the effect of substances elaborated in the suprarenal cortex and having a regressive effect upon lymphoid tissue). It is suggested

that this component may represent the result of the direct action of the radiation (component A), and the drop in the total lymphocyte count due to this is large and relatively rapid. The further drop in the total lymphocyte count which takes place in addition to component A may then be due to the indirect action of the radiation, which effect tends to diminish as the dose of radiation increases. Eventually, a stage is reached at which further irradiation, at the rates of dosage here considered, causes only a very small change in the total lymphocyte count. (NSA)

638

Schwartz, S., et al. **STUDIES OF THE HEMOLYTIC EFFECT OF RADIATION.** *Univ. of Chicago Metallurgical Lab.* July 10, 1946. 51p. (MDDC-1342)

Evidence is presented indicating that both acute and chronic radiation anemia are due in part to a hemolytic reaction, and not solely to an inhibition of erythropoietic activity as has been assumed by most investigators. The hemolytic concept is based on the following evidence taken from a survey of the literature as well as from the authors' experimental studies. (1) The red cell count in human and animal subjects may fall at a rate that is faster than can be accounted for by assuming even 100% inhibition of erythropoiesis. (2) The red cell count may decline at a time when the reticulocyte count is actually elevated. (3) Histological evidence of increased red cell destruction has been demonstrated repeatedly. (4) The bone marrow of humans that have anemia due to chronic radium poisoning is typically hyperplastic, not aplastic. (5) Increased bile pigment excretion has been shown to occur following administration of large doses of P^{32} or total body X-ray. Excessive irradiation appears to destroy both mature and immature cells in increased amounts. More studies of human subjects are required to evaluate the importance of this hemolytic factor. Special attention in these studies should be given to bile pigment excretion and reticulocyte measurements. A bibliography of 65 references is included. (ADD)

639

Snell, Fred M., James V. Neel, and K. Ishibashi. **HEMATOLOGIC STUDIES IN HIROSHIMA AND A CONTROL CITY TWO YEARS AFTER THE ATOMIC BOMBING.** *Arch. intern. med. exp.* 84, 569-604(1949).

Nine hundred and twenty-four relatively heavily irradiated subjects were examined in Hiroshima to determine their peripheral hematological condition 20-33 months after irradiation; they were chosen on the basis of degree of epilation. The results of erythrocyte and leukocyte counts, differential blood counts, hemoglobin concentrations, hematocrit readings, plasma readings, and reticulocyte counts were compared with those of a normal group of subjects from another city. It was observed that: the erythrocyte counts, hemoglobin concentrations and hematocrit readings were slightly, but significantly, depressed for the irradiation subjects; the irradiation subjects showed a slight relative depression of lymphocytes and a slight elevation of eosinophils; plasma protein values possibly were higher in the Hiroshima subjects; and, there was a significantly greater variability in the results in Hiroshima than in the normal group, which cannot be attributed to a differential response on the part of any particular age or sex group. The individual subjects who absorbed greater amounts of radiation tended to show the most pronounced depression in the erythrocyte and lymphocyte counts and the greatest elevation in the eosinophil counts. The authors advise against attributing the slight differences observed here entirely to atomic radiation. (NSA)

640

Tripodo Cesare and Giuseppe del Buono. **HEMOPOIETIC FUNCTION AND IRRADIATION OF THE PYLORIC-**

DUODENAL TRACT. PART I. BEHAVIOR OF ERYTHROPENIA AND OF DIGESTIVE LEUCOCYTOSIS IN NORMAL PERSONS SUBJECTED TO IRRADIATION OF THE PYLORIC-DUODENAL TRACT. *Haematologica* **31**, 693-710 (1948).

A total of 11 normal persons was irradiated in the region of the pyloric-duodenal tract with three doses of 200 r, delivered by a 160-kv x-ray machine at a target distance of 30 cm and through an aluminum filter. The irradiation was spaced at intervals of 3 days for a total dose of 600 r. No distinct changes in the number of erythrocytes, in the leucocyte picture, in the number of platelets, in the sedimentation rate of the erythrocytes, or in the behavior of the leucocyte digestive reaction to the administration of a meat diet were noted; a decrease in the normal erythropenic digestive reaction, however, was noted. Confirmation that digestive erythropenia represents the initial mechanism that in normal conditions determines and regulates physiological erythropoiesis has been obtained. (NSA)

641

Warren, S. BLOOD FINDINGS IN CYCLOTRON WORKERS. *Radiology* **39**, 194-9(1942).

The blood counts and hemoglobin levels of 85 persons more or less exposed to slight radiation from cyclotrons and temporarily radioactive isotopes have been followed for periods varying from 3 to 30 months. Most persons under these conditions show no significant changes that are not explained by intercurrent disease. Four showed minor variations in white cell count. As with exposure to x-ray or radium radiation, transient depression in white cell count is followed by elevation. This change occurs more rapidly in lymphocytes than in granulocytes. Some persons have an unstable bone marrow as shown by marked fluctuations in white cell counts when subjected to only minor exposure to radiation. Such persons should not work where they are exposed to radiation. The precautions for the safety of these two groups of cyclotron workers appear adequate. (auth)

642

Whitby, Lionel. THE EFFECTS OF ATOMIC ENERGY ON THE BLOOD. *Prensa med. argent.* (1947).

The deleterious effects upon the blood of atomic energy and high voltage x-ray brings up the necessity for a thorough study of the problems and of the more practical method of immunization. The penetrating and pernicious effects of the radiations are similar to those produced by the gamma rays of radium. There are three such effects; (1) those produced by a sudden and intense irradiation, as observed among the victims of atomic bomb explosion; (2) those produced by repeated small, well-tolerated doses, as observed in workers with radioactive substances and in investigators of nuclear physics; and (3) the effects secondary to continuous internal irradiation given off by radioactive substances accumulated in the marrow. The inhabitants of Hiroshima and Nagasaki subjected to intense and penetrating acute irradiation, showed, first a latent period; then granulocytopenia, which occurred during the first three weeks; three to five weeks later, thrombocytopenia, with hemorrhagic diathesis, made its appearance; and from five to seven weeks after the explosion, cases of aplastic anemia developed. The sternal marrow in these cases, was found aplastic, physiologically if not always anatomically. Bones absorb radium thorium, and radioactive calcium and strontium. The bone marrow is subjected to a continuous bombardment of destructive alpha rays, as observed in workers in the manufacture of luminous watches. Aplastic anemia with an aplastic marrow, or with a hyperplastic impotent marrow, develops as a result of this internal irradiation, and the hematologic picture is similar to that observed in the victims of atomic bomb explosion. (GPR)

643

Zimmer, E. A. CHANGES PRODUCED BY X-RAYS IN BLOOD CORPUSCLES. PART 4. *Strahlentherapie* **82**, 261-80(1950).

Results are discussed of an experimental investigation of typical changes produced in the numbers of blood corpuscles by x-irradiations of various organs. Small doses on the bone marrow reduce the number of erythrocytes, while large doses increase it (consequently, the known failures in the radiotherapy of polycythemia are due to excessive doses); small doses on the spleen increase the erythrocyte count. The number of thrombocytes increases when bone marrow is irradiated with 400 r; it decreases when the spleen is treated with small doses. The leucocyte count decreases after a small-dose irradiation of the liver, or after a large-dose irradiation of the bone marrow; it increases when small doses are applied on the bone marrow. Other observations dealt with irradiations of cancerous patients (atypical blood changes), of patients with hyperthyreosis, of splenectomized persons (atypical changes), and with irradiations of the skull (decrease of the erythrocyte count). (Extensive bibliography.) (NSA)

Hemopoiesis—Animals

644

Adams, W. S. and J. S. Lawrence. THE PRODUCTION OF LEUKOPENIA BY CHRONIC IRRADIATION OF THE ABDOMINAL VISCERA OF THE CAT. *Univ. of Rochester.* Apr. 30, 1948. Decl. May 24, 1948. 14p. (AECD-2006)

Eight normal cats were irradiated in the following manner: daily doses (except Sundays) of 100 r each were delivered to the abdomen, the remainder of the cat being protected by a lead shield. A total dose of 3,200 r was given. There was a uniform drop in the leucocyte count, polymorphonuclear leukocytes and lymphocytes (a fall of 64, 57 and 76 per cent, respectively). This depression may be explained on the basis of any one, or a combination of the following factors: (1) radiation of a larger segment of the bone marrow than had been suspected, (ionization chamber tests for "scatter" radiation showed that only very small amounts were affecting the part of the cat beneath the lead shield). (2) alterations occurring in the liver and spleen which increased the rate of utilization, destruction, or production of leukocytes. (3) alterations occurring in the intestinal wall which resulted in leukopenia possibly because of (a) increased demands for leukocytes, (b) increased loss of leukocytes through the damaged epithelial surface and/or (c) decreased production of white blood cells because of failure to absorb or elaborate certain substances necessary for normal hemopoiesis. (4) damage to an area rich in lymphoid tissue thereby producing lymphopenia. The authors believe that factors 3 and 4 are probably the most important in the production of the observed leukopenia. (ADD)

645

Allen, Bennet M., Ole Arne Schjeide, and Ronald Piccirillo. THE INFLUENCE OF ANOXIA UPON DESTRUCTION AND MITOSIS OF THE HEMATOPOIETIC CELLS OF X-IRRADIATED TADPOLES. *Atomic Energy Project*, Univ. of Calif., at Los Angeles. Aug. 14, 1951. 13p. (UCLA-149)

The influence of anoxia on the initial (24-hr) effect of 500 r of x irradiation of 10 μ y of colchicine upon the hematopoietic cells of tadpoles of the bullfrog, *Rana catesbeiana*, has been determined. Anoxia markedly reduces the cell destruction resulting from the x irradiation and in like percentage reduces the colchicine effect—pynosis and arrested mitosis—during this period. Anoxia applied after either of these treatments gave almost as great a "protec-

tion" against these effects. It is probable that this "protection" observed at the end of 24 hr is wholly or in part to be interpreted as a delay of mitosis. Four equally spaced 1-hr exposures to anoxia proved much more effective than two, but there was marked destruction in spite of either amount of anoxia. The closely comparable degree of "protective" effect of anoxia upon both the x-irradiated and colchicine-treated groups and the fact that colchicine is an inhibitor of mitosis add further support to the view that destruction of hematopoietic cells takes place at or near mitosis. (NSA)

646

Anderson, Elizabeth. **CHANGES IN PERIPHERAL BLOOD AFTER SINGLE DOSES OF EXTERNAL BETA RADIATION**, p.185-92 of **EFFECTS OF EXTERNAL BETA RADIATION**, Raymond E. Zirkle, ed. New York, McGraw-Hill Book Company, Inc. 1951. 242p. (National Nuclear Energy Series Division IV, Volume 22E, Paper II) (MDDC-534)

In an effort to discover whether beta ray burns can be correlated with thermal burns, a series of measurements of hematocrit and specific gravity of blood plasma were taken on two rats which had received total body irradiation with 7,500 rep of β ray. Techniques were selected which gave accurate readings with small samples of blood. The copper sulfate method was used for measuring specific gravity of the plasma. No significant change in the hematocrit was recorded, but specific gravity readings were below the normal range for rats on the 12th, 14th, and 17th days after exposure. These results suggest (1) that the plasma lost due to the β ray burns is lost at such a low rate that the blood volume remains unchanged but (2) that the lost plasma proteins cannot be replaced quite fast enough to keep their concentration normal. Since death attributed to thermal burns is primarily due to a fall of blood volume, it would appear that the physiological changes taking place are quite different for the two types of burns. (ADD)

647

Arvy, Lucie, Jacques-Andre Boiffard, and Manfred Gabe. **INCREASE IN THE NUMBER OF LABROCYTES IN THE HEMATOPOIETIC TISSUES OF MICE FOLLOWING X IRRADIATION**. *Compt. rend. soc. biol.* **232**, 1022-4(1951).

The important increase in the number of labrocytes (heparinocytes, tissular basophils) found in the medulla of lymphatic ganglia and bone marrow of male white mice following whole-body exposure to 2000 r of x radiation is detailed. The thymic medulla, normally deprived of labrocytes, contains a large number following irradiation. Relation of this phenomenon to the general adaptation syndrome is discussed. (NSA)

648

Barnes, W. A. and O. B. Furth. **STUDIES ON THE INDIRECT EFFECT OF ROENTGEN RAYS IN SINGLE AND PARABIOTIC MICE**. *Am. J. Roentgenol. Radium Therapy* **49**, 662-81(1943).

In addition to direct effects of x-rays on living tissue, there has been much discussion of indirect local and general effects, based on little definite experimental evidence. In the experiments reported, 2 of 4 mice in each group were joined in parabiosis. Two to four weeks later, one single mouse and one twin were irradiated over the entire body with 800-6,000 r of 200 kv lightly filtered x-rays; the other twin and the other single mouse being completely shielded. Slight leukopenia occurred in the shielded parabiont after exposure of its twin to 800-1,000 r. In the irradiated parabiont the leukopenia was less severe than in the irradiated single animal. It is suggested that one or both of the following occur: (a) Following the fall in number of leukocytes in the irradiated twin, leukocytes migrate from the non-irra-

diated to the irradiated animal, resulting in the mild leukopenia of the former. (b) The blood of the irradiated animal is so altered that when it passes to its twin it depressed the leukocyte level of the latter, but being diluted in the blood of the non-irradiated animal, the effect produced is small. (BA)

649

Betz, H. and J. Lecomte. **HEMATOPOIETIC REACTIONS FOLLOWING REMOTE IRRADIATION OF RABBITS**. *Compt. rend. soc. biol.* **144**, 303-5(1950).

The rear paws of 12 rabbits were exposed to 200 r, the remainder of the body being protected by a lead shield. The animals were sacrificed from 3 hr to 14 days following irradiation. Blood and histologic (spleen, cervical ganglions, bone marrow) changes are described. (NSA)

650

Block, M. H., Leon O. Jacobson, Edna K. Marks, and E. Gaston. **THE EFFECT OF TOTAL-BODY X-IRRADIATION ON A PRE-EXISTING INDUCED ANEMIA IN RABBITS. III. HISTOPATHOLOGICAL STUDIES**. Univ. of Chicago Metallurgical Lab. June 1946. 45p. (AECU-229; CH-3890)

Exposure of normal rabbits to 800 r total-body x-radiation produces an intense destruction and atrophy of lymphatic and myeloid tissue that is manifested in the peripheral blood by a leucopenia, thrombocytopenia, and anemia. In rabbits with an anemia, reticulocytosis, and with a hyperplasia and left shift in erythrocytopoiesis in the spleen and bone marrow, exposure to 800 r total-body x-radiation results in: (a) the usual destructive and atrophic sequelae in the hematopoietic tissues but with significantly less destruction of erythroblasts and significantly less inhibition of mitotic proliferation of erythroblasts so that comparatively large numbers of immature erythroblasts survive in the marrow and spleen; (b) a continued reticulocytosis which is derived from these islands of viable erythroblasts during what should, in normal animals, be a much more atrophic period; and (c) a marked reticulocytosis in the regenerative period which is in part explained by a quicker regeneration of normal erythrocytopoiesis in the spleen. These results challenge the commonly held belief that cells that are more immature and rapidly dividing are more susceptible to irradiation. (NSA)

651

Bloom, M. A. and W. Bloom. **THE RADIOSENSITIVITY OF ERYTHROBLASTS**. *J. Lab. Clin Med.* **32**, 654-9 (1947).

Mammalian bone marrow exposed to total-body irradiation with x-ray and fast and slow neutrons revealed severely depressed hematopoiesis. The degree of injury varies with the dose. Changes in marrow cells after radioactive isotope injection are much the same. The erythropoietic are more susceptible than myelocytopoietic cells and the erythropoietic in turn more susceptible than megakaryocytes. Similar findings were demonstrated in chickens. Degenerating erythroblasts are not to be compared with degenerating lymphocytes. (BA)

652

Bloom, W. and Leon O. Jacobson. **SOME HEMATOLOGIC EFFECTS OF IRRADIATION**. *Blood* **30**, 586-92(1948).

Studies with acute and chronic application of externally originating ionizing radiations and internally deposited radioisotopes fail to reveal evidence in the blood forming tissues and peripheral blood of a primary stimulation of hematopoiesis. Leukocytosis during the first 24 hr after acute exposure is considered to be a reaction to injury. (BA)

653

Boffil, J. and O. Miletsky. **EXPERIMENTAL INVESTIGATIONS ON THE DAMAGE PRODUCED BY X-RAYS IN THE BONE MARROW**. *Ann. méd.* **47**, 220-44(1946).

The authors have applied total irradiation to dogs and guinea pigs, subtotal (with protected sternum in dogs, and protected foot or head in guinea pigs), or local radiation, followed by the removal of marrow by puncture or biopsy. Radiation with an apparatus of constant tension, 180 or 200 kv; filter 0.5 Cu, DF = 1 m 50 for the dogs, 0.50 m for the guinea pigs. Dose of 400, 500, or 500 r in one sitting. Eleven experiments: three on dogs, eight on guinea pigs. (EM)

654

Brecher, G. and E. P. Cronkite. POST-RADIATION PARABIOSIS AND SURVIVAL IN RATS. *Proc. Soc. Exptl. Biol. Med.* **77**, 292-4(1951).

Rats can survive an otherwise fatal dose of radiation if joined after radiation to nonirradiated litter mates. Such rats show accelerated bone marrow regeneration when compared with single controls. It is suggested that post-radiation parabiosis is primarily of benefit because it accelerates recovery of myelopoiesis by the transfer of some cellular or non-cellular material from the non-irradiated partner. (auth) (NSA)

655

Brecher, G., K. M. Endicott, H. Gump, and H. P. Brawner. EFFECTS OF X-RAY ON LYMPHOID AND HEMOPOI-ETIC TISSUES OF ALBINO MICE. *Blood* **3**, 1259-74 (1948).

In order to gather details of the selectivity of radiation injury produced by whole body irradiation of 400 r (186 kv 20 milliamperes, at 50 cm with 0.25 mm copper and 0.55 mm aluminum filters, 6.24 minutes), quantitative myelograms, peripheral blood counts, and the histologic appearance of lymphoid tissues were studied in albino mice of the CFW strain during a period of four weeks. Measurements were made of the initial damage to all blood forming tissues and the reticuloendothelial system, the extent and duration of the suppression of their activity, and the rate of their recovery. Nucleated red blood cells disappeared almost completely from the marrow within 24 hours after irradiation. Regeneration of the erythroid series began about the 7th day. Only mild to moderate anemia developed, presumably due to the longevity of red blood cells. Suppression of mitotic activity and diminution of the myeloid marrow were marked during the first week after irradiation. Granulocytopenia in the peripheral blood was severe for a very short period only. In contrast, early damage to the lymphoid tissue was more pronounced and lymphopenia was of longer duration than granulocytopenia in spite of early regeneration of the lymphoid tissues. Differences in the relative amount of damage to lymphoid and myeloid tissues and in their rates of regeneration were not of sufficient magnitude to indicate a truly selective damage to the lymphoid tissues under the conditions of the experiments. No morphologic evidence of damage to the reticulo-endothelial system was found. The possible use of irradiated animals for functional studies of the lymphoid apparatus is discussed. (NSA)

656

Brues, Austin M. and Leola Reitz. ACUTE HEMATO-LOGIC RADIATION RESPONSE OF THE GUINEA PIG AS A FUNCTION OF LETHALITY, p.183-7 of BIOLOGICAL AND MEDICAL DIVISIONS; QUARTERLY REPORT, AUGUST, SEPTEMBER, OCTOBER, 1948. Argonne National Lab. Nov. 1, 1948. 5p. (ANL-4227-(p.183-7))

Three groups of guinea pigs were used: four were irradiated with 150 r; four were irradiated with 200 r total body x-ray; and four were non-irradiated controls. The lymphocytes respond similarly to those of various other species given equivalent dosages, whereas the response of the

heterophils is greater than in any other species on which data are available. Both marked leucopenia and terminal anemia are prominent in the guinea pig after 200 r. Lymphocyte response is a function of x-ray dosage, whereas the effect of x-ray on the absolute heterophil count appears to be closely related to the LD-50. (S.V.S.)

657

Cronkite, E. P., F. W. Ullrich, D. C. Eltzholtz, C. R. Sipe, and P. K. Schork. THE RESPONSE OF THE PERIPHERAL BLOOD OF SWINE TO WHOLE BODY X-RAY RADIATION IN THE LETHAL RANGE. Naval Medical Research Institute. Apr. 7, 1949. 23p. (NP-1411; NM-007-039; NM-006-012.08.26)

Four groups of swine containing 4, 4, 12, and 4 animals were exposed to 200, 300, 400, and 600 r, respectively, delivered bilaterally from a 1000 kv industrial x-ray tube. The mortality in the groups was as follows: 200 r, 12.5%; 300 r, 87.5%; 400 r, 100.0%; 600 r, 100.0%. The expected leukopenia appeared with cell levels of the order of 1 to 3000/cmm after six to seven days, the initial levels being about 17,000/cmm. The response of the peripheral leukocytes in the 200 r group showed a less rapid downward trend than that of the other groups. A reticulocytosis, in general, preceded recovery and could be used as a fair but not invariable sign of recovery. (NSA)

658

Davis, R. Wendell, N. Dole, M. J. Izzo, and L. E. Young. HEMOLYTIC EFFECT OF RADIATION. *J. Lab. Clin. Med.* **35**, 528-37(1950).

Four renal bile fistula dogs were exposed to total-body radiation in single doses of 150 r (one dog) and 250 r (3 dogs). The excretion of bilirubin in the urine by each of the 4 dogs increased significantly during the first or second week following exposure. Possible sources of the increments in bilirubin output are discussed and it is considered that accelerated destruction of mature erythrocytes could be neither established nor disproved by these experiments. It is considered that some bilirubin is derived from destruction of partly hemoglobinized normoblasts in the marrow. It is also suggested that somewhat more than the normal portion of the total bilirubin excretion might stem from hemoglobin precursors if such molecules should be less successfully incorporated into erythroid cells after radiation. The morphology of the red cells did not appear to be altered in any of the radiated dogs and serial measurement of osmotic and mechanical fragility of the erythrocyte revealed no significant alterations after radiation in the 2 dogs tested. Reticulocytosis and erythrophagocytosis could not be detected in smears of venous blood prepared after exposure. (auth)

659

De Bruyn, P. P. H. THE EFFECT OF X-RAYS ON THE LYMPHATIC NODULE, WITH REFERENCE TO THE DOSE AND RELATIVE SENSITIVITIES OF DIFFERENT SPECIES. *Anat. Record* **101**, 373-405(1948).

Guinea pigs, rabbits, and rats were irradiated with x-rays, 200 kvp, filtered with 0.5 mm of copper and 1.0 mm of aluminum in order to study the relationship between changes in the lymphatic nodules and dose of administration, and to learn whether there is a relationship between the histologic effects of radiation with x-rays and their lethal action. The dose rate varied from 11 r/min. to 16 r/min. The amount of x-rays which killed 50% of the animals with 30 days (LD-50/30 days) (used as the measure of lethal sensitivity) is 800 r for rabbits, 600 r for rats, and 175 r for guinea pigs. The animals were killed in pairs after irradiation at intervals ranging from 30 minutes to 4 months. The mesenteric lymph nodes, patches of Peyer,

and in the rabbit, the appendix also were used after being fixed in Zenkerformol, embedded in celloidin, and stained with hematoxylin-eosinazure II. Doses of 800 r and 600 r destroyed completely the great majority of the lymph nodules in rabbits. The nodules began to regenerate 21 days and 14 days, respectively, after treatment. A majority of nodules were only partially destroyed after 400 r. These regenerated rapidly and were normal in appearance after five days. A dose of 100 r did not produce a marked change in the majority of the nodules, and 50 r was the lowest dose producing histologically detectable changes. Six hundred roentgens and 400 r doses in rats produced changes identical to those in rabbits. However, doses of 175 r in guinea pigs produced changes comparable to those in rabbits and rats after irradiation with 400 r or lower. This suggests, considering the LD-50/30 days value of the three animals, that the intensity of damage to the lymph node is related to absolute dosage and is independent at the LD-50/30 days of these species. (NSA)

660

De Bruyn, P. P. H. and R. C. Robertson. EFFECTS OF X-RAY AND NITROGEN MUSTARD ON LYMPHATIC NODULE OF THE RABBIT. *Proc. Soc. Exptl. Biol. Med.* **72**, 717-18(1949).

The histological effects on the lymphatic nodules of the rabbit of x-rays and the nitrogen mustard methyl bis (B-chloroethyl)amine hydrochloride are presented; the LD-50 (50% lethal) dose of these is 800 r for the x-rays and 2 mg./kg for the nitrogen mustard; it was found that there is no quantitative histological difference in the response of the lymphatic nodules in rabbits to the LD-50 doses of these two agents. The difference is minor in the mesenteric lymph node, where there is a slightly earlier regeneration after nitrogen mustard; the difference is greater in the appendix, since the histologic changes after nitrogen mustard administration at the LD-50 level are comparable to those changes observed after half of the LD-50 dose of x-rays. (NSA)

661

Dixon, Frank J. RADIATION-INDUCED HEMORRHAGIC DISEASE IN CHICKENS. *Proc. Soc. Exptl. Biol. Med.* **68**, 505-7(1948).

Young chicks were given repeated subcutaneous injections of P^{32} in order to produce severe radiation injury for a study of hemorrhagic disease resulting from radiation. The red blood cell, granulocyte, and platelet counts and blood coagulation time were charted during a 17-day observation period in which 25% of the birds died. Thrombocytopenia and agranulocytosis developed quickly. Although the character of the blood clot changed markedly, there was no significant increase in the coagulation time as reported for animals (Allen and Jacobson, *Science*, **105**, 388, 1947), and the hemorrhage was much less severe than in animals. There was no increase in the number of mast cells such as occurs in people injured by atomic bomb radiation. The chicken appears relatively resistant to radiation when compared with mammals studied (Warren and Whipple, *Journal of Experimental Medicine*, **38**, 741, 1923). (NSA)

662

Dougherty, T. F. and A. White. PITUITARY-ADRENAL CORTICAL CONTROL OF LYMPHOCYTE STRUCTURE AND FUNCTION AS REVEALED BY EXPERIMENTAL X-RADIATION. *Endocrinology* **39**, 370(1946).

CBA mice, 60 to 80 days old, received total body x-radiation. A large dose of x-rays, 200 r, produced within three hours a lymphopenia, tissue lymphocyte degeneration, and total serum protein and gamma globulin increases. These changes also occurred in one day postoperative adrenal-

ectomized mice receiving 200 r. This dose gave an anamnestic response in previously immunized mice in the absence of the adrenals. It has been demonstrated that 10 r produced the same physiological alterations, including the anamnestic response, in normal, but not in adrenalectomized, mice. Therefore, 10 r influenced lymphoid tissue function by augmenting pituitary-adrenal cortical secretion. Large doses of x-radiation may produce lymphocyte degeneration without adrenal mediation and thus increase circulating gamma globulin and antibodies. This is further proof that adrenal cortical steroids produce hyperglobulinemia by their degenerative effects on lymphocytes, an end cell of adrenal cortical hormone action. It is suggested that x-rays exert both a direct and an indirect effect on lymphocytes. The direct action may be manifested even in the absence of the pituitary or adrenals, whereas the indirect action of x-radiation on lymphocytes is mediated via the pituitary-adrenal cortical mechanism. (auth)

663

Downey, Hal. CYTOLOGY OF RABBIT THYMUS AND REGENERATION OF ITS THYMOCYTES AFTER IRRADIATION; WITH SOME NOTES ON THE HUMAN THYMUS. *Blood* **3**, 1315-41(1948).

Newly born rabbits and young normal rabbits, four to five months of age, were irradiated for this study of regeneration of lymphocytes in the thymus. A detailed study of the lymphocytes and of cells from the epithelial and mesenchymatous reticulum, and of the granulocytes was made on non-irradiated animals. The following conclusions were reached. Thymocytes are genuine lymphocytes. The largest lymphocytes of lymph nodes do not occur in the thymus; the smallest ones with pycchromatic nuclei and scanty cytoplasm are more numerous in the thymus. Some lymphoblasts similar to myeloblasts occur in the rabbit thymus. All three types of granulocytes develop from lymphocytes and to some extent from the mesenchymatous reticulum in the rabbit. In the rabbit the heterophil and eosinophil granules are acidophilic when first formed, while in the human thymus many have a basophilic quota as in the marrow. The reticulum is largely of epithelial origin and retains its epithelial characteristics in cytoplasm and nucleus. In the rabbit some mesenchymatous tissue is blended with the reticulum and may give origin to lymphocytes and granulocytes. The epithelium may form macrophages but does not differentiate to lymphocytes and other types of cells. In imprints from the rabbit the epithelial cells usually can be distinguished from those of the mesenchymatous reticulum. During regeneration following irradiation the latter tissue can be seen to form some lymphocytes locally; other lymphocytes enter the organ through the lymph vessels. Imprints stained with May-Grunwald and Giemsa are of great value for detailed cytology of the thymus and for determining cell relationships. Sections of thymus fixed in Helly's fluid, stained with methyl green and pyronin and dehydrated in dioxan are excellent for lymphocytes and the transitional stages resulting from their development from fixed mesenchymatous tissue during regeneration of the organ following exposure to X-rays. (NSA)

664

Ducuing, J., P. Marques, and O. Miletsky. ACTION OF X-RAYS UPON THE BLOOD AND THE HEMATOPOIETIC ORGANS AFTER REPEATED TOTAL-BODY IRRADIATIONS (EXPERIMENTAL STUDY). *J. radiol. élec.* **31**, 666-71(1950).

Total body irradiation was given to one dog (25 r each time, 775 r per series; 4 series with one year's interval between 2 series) and to 3 guinea pigs: no. 1, 2 x 400 r with 52 days' interval; no. 2, 300 r and 25 r after 90 days; no. 3,

2 x 500 r with 80 days' interval). There was always a sudden fall in leucocytes, platelets and erythrocytes after each series, as well as a prolonged bleeding time. Recovery followed, which each successive time was progressively less complete. After the 4th series the dog died, while the 3 guinea pigs died rapidly after their second series (no. 2 after a 2nd series of only 25 r). The clinical aspect of these deaths was that of acute leukaemia, the bone marrow of the dog and guinea pigs no. 1 and 2 showed signs of true aplasia (lack of all formation of any blood cells), while in the bone marrow of no. 3 the red blood cells totally failed to appear and the few white blood cells seen consisted only of immature or pathological forms (medullary aplasia). (EM)

665

Furth, Jacob, G. A. Andrews, R. H. Storey, and Leon Wish. THE EFFECT OF X IRRADIATION ON ERYTHROGENESIS, PLASMA, AND CELL VOLUMES. *Southern Med. J.* 44, 85-92(1951) (ORNL-878)

The complex pathophysiological disturbances causing postirradiation anemia cannot be investigated by using methods commonly practiced to evaluate the red-cell picture, since simultaneous changes in plasma volume mask the magnitude of drop in erythrocyte mass. The investigations on blood tissues of dogs, rabbits, and mice after massive irradiation reported here include determinations of red-cell and plasma volumes, reticulocyte count, number of newly formed erythrocytes (those that had taken up intravenously injected radioactive Fe), disappearance of various labeled substances from the blood and location of their retention in the body. These lead to the following conclusions: After massive irradiation, erythropoiesis ceases almost immediately and is not resumed until after 7 to 14 days. The plasma volume at first drops, and later rises. Heightened permeability of capillaries permits escape of blood cells and other substances from circulation. Phagocytic reticuloendothelial function is not markedly altered. The hypothesis is advanced that continuous leakage of erythrocytes through damaged endothelium to tissue spaces and lymph channels is a major factor in the causation of post irradiation shock and anemia. (NSA)

666

Gaston, Evelyn O., Edna K. Marks, and Leon O. Jacobson. EFFECT OF X-IRRADIATION ON THE MATURATION OF THE CIRCULATING RETICULOCYTE. *Univ. of Chicago Metallurgical Lab.* May 10, 1948. Decl. July 22, 1948. 37p. (AECD-2132; CH-3870)

The time required for the disappearance of the reticulocytes from the blood of normal and x-irradiated rabbits with and without phenylhydrazine or bleeding-induced anemia was studied *in vivo* and *in vitro*. *In vitro* studies were also made on the rate of disappearance of the normal human reticulocyte and the reticulocyte of humans with various diseases. When studied *in vitro*, reticulocytes in blood drawn from normal rabbits disappear over a period of 24-48 hours. Reticulocytes from normal rabbits and from rabbits with phenylhydrazine or bleeding-induced anemia have a comparable maturation rate. A dose of 800 r total-body x-radiation does not alter the rate of maturation in samples of blood drawn three hours after treatment; the rate is delayed in samples drawn 24 hours after irradiation. Blood from rabbits having induced anemia gives comparable results. *In vivo* studies also show comparable results. The reticulocyte maturation time in the blood of normal human subjects ranges between 24-48 hours when studied *in vitro*. Nitrogen mustard does not alter the maturation rate in patients having polycythemia vera. (This study was made one day after the administration of nitrogen mustard.) (NSA)

667

Henshaw, P. S., J. W. Thompson, and H. L. Meyer. EXPERIMENTAL ROENTGEN INJURY. V. EFFECTS ON HEMATOPOIETIC RESERVES AND REGENERATIVE CAPACITY. *J. Natl. Cancer Inst.* 5, 233-47(1945)

Experiments were carried out to determine the additive effects of doses of x-rays (controls) 12½, 25, 50, 100, 200, 400 r applied to the whole bodies of C₃H mice; 4,000 lymphocytes per cu mm of whole blood as the lower limit of normal. Histologic examination showed mild injury in the hematopoietic organs after repeated small exposures and acute extensive destruction after the large doses. Remarkable regenerative capacities were observed. Similar experiments were made with guinea pigs, by using 25, 50, and 100 r doses, and 3,500 lymphocytes per cu mm of whole blood as the lower limit of normal. Generally the same effects were seen as in mice although the guinea pigs showed a greater general susceptibility to radiation. Only mild changes in erythrocyte level were observed in either type of animal at any time. The fact that small doses, that singly elicit no detectable change in lymphocyte level, produce leucopenia after repeated application indicates that subliminal effects are produced and are additive; the destruction of lymphocytes occurs with each small dose and the rate of destruction must go beyond the reserve of lymphocytes—acellularity in the hematopoietic organs was noticeable in the animals that received the larger doses. The persisting lymphopenia might be regarded as the beginning of a state of exhaustion. (BA)

668

Hsu, C. L. and W. C. Ma. DIRECT AND INDIRECT EFFECTS OF ROENTGEN RADIATION ON THE BLOOD-FORMING ORGANS OF RATS. *Am. J. Cancer* 39, 319-33 (1940).

Normal albino male rats, 6 to 9 months, 350-450 g. weight received daily doses of 125 r in 10 minutes on the skin of the posterior surface of the right hind leg to maxima of 1,000, 2,500, and 5,000 units, the factors being 100 kv, 4 ma through 4 mm Al, at 30 cm, and were killed by ether ca. 24 hours after completing treatment, for examination of the spleen, submaxillary lymph nodes, the femoral marrow. Results were: decrease of bone marrow cells in proportion to dosage in both femurs, and of lymphoid cells in the lymph nodes and spleen. (BA)

669

Ingram, M. and W. B. Mason. THE EFFECTS OF CHRONIC EXPOSURE TO ROENTGEN RADIATION ON THE PERIPHERAL BLOOD OF EXPERIMENTAL ANIMALS. Atomic Energy Project, Univ. of Rochester. July 17, 1950. 23p. (UR-121)

Routine hematological examinations have been done repeatedly on dogs, rabbits, rats, and monkeys which have been exposed to daily doses of whole-body roentgen radiation in amounts near the tolerance range, i.e., doses varying from 0.1 to 10.0 r/day. These dosages have been administered for a continuous period of not more than 2 yr. Both 250- and 1000-kvp machines were used. During the experiments the rats and monkeys acquired extraneous pathology of such a degree that it was necessary to exclude these animals. In dogs and rabbits, changes in the hemograms which followed chronic exposure were detected only by statistical methods. It would seem unlikely that routine hematological examination would provide a reliable means of detecting minimal radiation damage in any one animal. Lymphocytes appear to be the most sensitive hematological indicators of the damage which results from chronic exposure to roentgen radiation. The least sensitive element in the peripheral blood appears to be the mature erythrocyte.

The effectiveness of small daily doses of roentgen radiation in producing hematological changes is dependent, in part, on the duration of such exposure. In some instances, changes were first noted during the second year of daily exposure. The data demonstrate a marked difference in the hematological responses of dogs and rabbits exposed daily to the same doses of radiation. The reticulocyte depression, relative to that of the lymphocyte, is less pronounced in the present experiments than in the case of exposure to single large doses of whole-body roentgen radiation. Chronic exposure did not elicit the marked reticulocytosis which characterized the recovery response to acute exposure. No consistent difference was observed in the hematological changes which followed exposure to like quantities of roentgen radiation from the 250- and the 1000-kvp machines. (NSA)

670

Ingram, M. and W. B. Mason. **THE EFFECTS OF ACUTE EXPOSURE TO ROENTGEN RADIATION ON THE PERIPHERAL BLOOD OF EXPERIMENTAL ANIMALS.** Atomic Energy Project, Univ. of Rochester. July 17, 1950. 36p. (UR-122)

Rats, dogs, and monkeys have been exposed to single whole-body doses of roentgen radiation. The dosage for rats varied from 5 to 1500 r and that for monkeys from 300 to 2000 r. Dogs received 300 r, a dose approximating LD₅₀. Hemograms of all animals were determined at regular intervals for 25 to 60 days following irradiation. Bone marrow examinations were included in the studies utilizing doses approximating LD₅₀. The data pertaining to monkeys have been excluded from the present report because of extraneous infections which invalidate attempts to relate the observed changes to the radiation received. The major findings may be summarized as follows: (1) Results of the present experiments indicate that routine hematological examinations are inadequate for detecting slight radiation damage in any one individual. Changes which occur following exposure to small doses can be demonstrated only by statistical methods. (2) The results of routine hematological examinations appear to be unreliable as criteria for determining the prognosis following isolated instances of whole-body exposure to roentgen radiation. No consistent or convincing difference between leukocyte counts of survivors and nonsurvivors could be demonstrated in the various experiments. (3) Lymphocytes and reticulocytes are similar with regard to the promptness and magnitude of their depression following single exposures to whole-body radiation. In general, depression of these cells is more marked and occurs earlier than that of other elements of the peripheral blood. (4) The depression of neutrophils occurs slightly later than that of lymphocytes and reticulocytes. (5) Significant depression of erythrocytes and hemoglobin is the last to occur following exposure, and the dosage required to produce such depression is much larger than that required to produce other changes. The recovery phase of the erythrocyte trends is characteristically preceded by a marked reticulocytosis. (6) With routine techniques, examination of bone marrow appears to offer no particular advantage in indicating radiation damage since changes are equally prompt in both marrow and peripheral blood cells. (7) In general, the magnitude of peripheral blood cell changes is roughly proportional to the dose for exposures up to approximately LD₅₀. Doses greater than LD₅₀ tend to induce the maximum response and, if sufficiently large, prove fatal in a relatively short time. (NSA)

671

Jacobson, L. O., et al. **THE EFFECT OF TOTAL BODY X-IRRADIATION AND P³² ON THE PERIPHERAL BLOOD**

OF NORMAL RATS AND RATS WITH COBALT-INDUCED POLYCYTHEMIA. Argonne National Lab. Mar. 1948. Decl. Apr. 20, 1948. 2p. (AECD-2014)

A polycythemia was produced in Sprague-Dawley rats by the subcutaneous injection of cobaltous chloride five times weekly. The polycythemia was fully established in 90 days. The effect of X-irradiation or P³² on the blood and blood-forming tissue of normal animals and those with induced polycythemia was studied. Six groups of seven rats each were treated in the following manner: Group I. Control—No treatment was given this group. Group II. Control-cobalt—The animals were injected with cobaltous chloride five times weekly. Group III. X-Ray + cobalt—The animals were injected with cobaltous chloride five times weekly. When polycythemia was fully established, 300 r whole-body X-ray was administered in a single dose. The cobalt injections were continued after x-irradiation. Group IV. P³² + cobalt—The animals were injected with cobaltous chloride five times weekly. When polycythemia was fully established a dose of radiophosphorus (1 µc/g. body weight) was administered intraperitoneally. The cobalt injections were continued following the administration of P³². Group V. X-ray—Normal animals were given one single exposure of 300 r whole-body X-radiation. Group VI. P³²—Normal animals were given one single injection of radiophosphorus (1 µc/g. body weight). A comparable depression of the leucocytes of the peripheral blood was produced in normal and polycythemic animals after radiophosphorus injection. The dosage of radiophosphorus (1.0 µc/g.), used in this experiment, produced no significant effect on hemoglobin, erythrocyte or hematocrit values in normal or polycythemic animals. A comparable reduction in hemoglobin, erythrocyte, hematocrit and leucocyte values of the peripheral blood occurred in normal and polycythemic animals exposed to 300 r whole-body x-radiation. Recovery was essentially the same in the two groups. Histological studies of appropriately sacrificed animals in these various groups have not been completed. On the basis of these data no apparent difference in the sensitivity of the hemopoietic system to a single dose of P³² (1.0 µc/g) or to x-irradiation (300 r) is evident between normal and polycythemic rats as judged by the pattern of response of certain hematologic constituents of the peripheral blood. (ADD)

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Jacobson, Leon O., Edna K. Marks, E. O. Gaston, E. L. Simmons, and M. H. Block. **STUDIES ON RADIO-SENSITIVITY OF CELLS.** Science 107, 248-50(1948).

The effect of 800 r whole body x-radiation upon animals with a previously induced regenerative anemia was compared with the effect of the same dose on normal comparable animals. Determinations were made of the erythrocytes and reticulocytes/cu mm and Hb in g/100 ml. Normal irradiated animals developed an anemia that reached the maximum in 14 days. Animals with a regenerative anemia prior to irradiation developed no further anemia. The recovery time was similar for both groups. The mean reticulocyte value of a group of phenylhydrazine-injected x-rayed animals was decreased below the normal control value on the 6th postirradiation day only. A phlebotomized group of animals responded to irradiation in a manner comparable to the phenylhydrazine-treated group. Histologic studies showed that erythropoietic tissue in bone marrow and spleen were wholly destroyed in three days in normal animals receiving 800 roentgens. A slow recovery began on the 7th to 9th day. The erythropoietic tissue was only partially destroyed in animals irradiated with 800 r after treatment with phenylhydrazine or phlebotomy. The data

indicate that erythroblast vulnerability to irradiation injury is not increased by increased mitotic activity and proliferation. (BA)

673

Jacobson, L. O., E. K. Marks, and E. Lorenz. **THE HEMATOLOGICAL EFFECTS OF IONIZING RADIATIONS.** *Radiology* 52, 371-95(1949) (AECD-2085; CH-3864)

The objectives of the Health Division of the Plutonium Project were essentially: (1) to study the fundamental and comparative biological action of external radiations and internally administered radioactive materials, (2) to apply the findings toward the protection of individuals who worked in the Project, and (3) to use the findings generally for the protection of the public which was potentially in danger of exposure to these physical hazards. The hematologic studies conducted were divided into four main categories: (1) the effects of acute whole body exposure to externally administered penetrating radiations, (2) the effects of chronic whole body exposure to externally administered penetrating radiations, (3) acute toxicity of parenterally and enterally administered radioactive elements, and (4) chronic toxicity of parenterally and enterally administered radioactive isotopes. In order properly to correlate studies on the peripheral blood effects with those occurring in the hemopoietic tissue, the animals in the same or parallel experiments were sacrificed at appropriate intervals for histological study. All experiments included an adequate number of controls, and the frequency of sampling depended upon the chronic nature of the experiment. (NSA)

674

Jacobson, Leon O., Edna K. Marks, and E. L. Simmons. **THE EFFECT OF TOTAL BODY X-IRRADIATION ON A PRE-EXISTING INDUCED ANEMIA.** *J. Lab. Clin. Med.* 32, 341(1947).

A regenerative anemia was produced in rabbits by the subcutaneous administration of phenylhydrazine hydrochloride. The hematologic effects of 800 r total body x-irradiation on such anemic animals were compared to effects on animals given only phenylhydrazine and allowed to recover spontaneously and to a group of animals given 800 r alone. A group of normal untreated animals was studied simultaneously. The characteristic rise and subsequent reduction in heterophils and immediate precipitous fall in the lymphocyte values followed the administration of 800 r in the group in which a regenerative anemia had been produced with phenylhydrazine as well as in normal control animals. The time of recovery of those elements to normal limits in the two groups was likewise comparable. An "abortive rise" in the leucocyte values of both of these groups was noted between the fifth and eleventh days after the irradiation. The group of animals which received x-irradiation alone developed an anemia with its maximum at 14 days and with recovery by 23 days. The animals in which a regenerative anemia was produced by phenylhydrazine and which were irradiated at or near the point of maximum anemia developed no further anemia, values returning to normal limits by 23 days. The erythrocyte and hemoglobin values of the group in which an anemia was produced by phenylhydrazine and which were allowed to recover spontaneously, however, returned to normal within 14 days. The reticulocyte values of animals which had received phenylhydrazine had reached approximately 21 per cent when the x-irradiation was given and were reduced to a minimum value of 1.0 per cent within two days after the x irradiation. Recovery to normal limits occurred by 9 days in this group. The reticulocyte values of normal control animals which were given 800 r fell maximally within two days, reached a minimum of less than 0.1 per cent, and recovered slowly but completely by 23 days.

The failure of 800 r total body x-irradiation to produce further anemia in animals with a previously induced regenerative anemia or to materially interfere with recovery is dependent in part on the number of surviving erythroblasts in the erythropoietic tissue. Histologic studies made on animals prepared in a comparable manner and sacrificed at varying appropriate intervals indicate that erythropoietic tissue was completely destroyed by 72 hours in the normal rabbits which received 800 r and recovery proceeded slowly. On the other hand, although massive destruction of erythropoietic tissue occurred after exposure to 800 r in animals in whom a regenerative anemia had been produced with phenylhydrazine, this destruction was delayed beyond 72 hours. This appears to indicate that a latency to x-ray effect was produced in erythropoietic tissue which had previously been stimulated.

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Jacobson, Leon O., Edna K. Marks, E. L. Simmons, C. W. Hagen, and Raymond E. Zirkle. **EFFECTS OF X-RAYS ON RABBITS. PART II. THE HEMATOLOGICAL EFFECTS OF TOTAL BODY X-IRRADIATION IN THE RABBIT.** *Univ. of Chicago Metallurgical Lab.* July 1946. Decl. July 31, 1947. 11p. (MDDC-1174; CH-3798)

The hematological constituents of the peripheral blood have been studied in Swift snuffle-free rabbits before and after the administration of acute total body x-irradiation. Doses of 25 r to 800 r were administered and studies made through 96 days in many experiments. From the observations made, the conclusions derived are: A significant normochromic anemia develops in groups of rabbits exposed to 500 and 800 r. A significant anemia develops only in individual animals within a group with doses below 500 r. Reticulocyte reduction is significant with doses of 100 r and above. An initial leucocytosis, significantly greater than controls, occurs within the first 24 hours after doses of 500 r. After 500 r and 800 r, a sharp rise in leucocytes occurs by 12 hours, followed by a decline and another peak of leucocytes at 24 hours. The leucocytosis during this period is due exclusively to an increase in heterophils. Lymphocytes decrease significantly within 24 hours after exposure to 25 r and above. Reduction is apparent three hours after irradiation with 100 r and above, with a minimum value at from 24 to 48 hours. Recovery proceeds slowly. Supravital staining (Janus green and neutral red) reveals an increase in neutral red granules after 200 r and above. Mitochondrial changes are variable. Monocytes decrease initially but return to normal limits or are increased by four to six days after 200 r and above. Heterophil values increase initially after 500 and above. No significant reduction was observed with doses of 300 r and below. Doses of 500 r to 800 r inclusive produce a significant depression within 96 hours, with recovery by 23 days or less. Platelet values are reduced in a manner paralleling the granulocytes. An "abortive rise" in lymphocytes and heterophils between the 4th and 11th day after x-irradiation characteristically precedes recovery with doses of 200 r and above, respectively. Morphological changes in erythrocytes, leucocytes, and platelets occur after doses of 100 r and above. The lymphocyte values of the peripheral blood are the most sensitive known indicator of effect of acute total body x-irradiation. A bibliography of 59 references is included. (ADD

676

Langendorff, H. **THE SUPPRESSION OF THE RETICULOCYTE COUNTS OF THE WHITE MOUSE AFTER ROENTGEN RADIATION. III. COMMUNICATION (G).** *Strahlentherapie* 62, 304-14(1938).

The effects of single doses and protracted fractional doses were compared. The intensity was 0.5-8 r/min. for the

single dose and 1 r/min. for the second method. The total dose applied varied from 100-1,000 r. The effect of the fractional method without protraction was much more pronounced both on the reticulocytes as well as on the organism as a whole than for the protracted fractional dose. The reaction following "long time" irradiation took a longer course in most instances than for the other method; likewise the same total dose was tolerated better with the protracted fractional dose than with simple fractionation. (BA)

677

Latta, J. S. and O. C. Ehlers. THE EFFECTS ON THE BLOOD AND HEMOPOIETIC ORGANS OF REPEATED SHORT EXPOSURES TO X-RAYS. *Am. J. Anat.* **47**, 447-74(1931).

Twelve albino rats were subjected to a series of short X-ray exposures, in most cases totaling 4-1/3 hours; three were sacrificed during this treatment, six at or near the end of the experiment and three after different periods of recovery. After complete exposure, a very pronounced leukopenia (less than 1,000 leucocytes) and anemia (slightly over 2,000,000 erythrocytes) were invariably present. The hemopoietic organs were correspondingly aplastic, with pictures of extreme degeneration. Recovery as evidenced by blood counts and histological conditions in the hemopoietic organs was variable, rapid, but not complete at the end of 28 days. A study is presented of the changing conditions of the hemopoietic organs, particularly in aplastic and regenerating conditions. Evidence is presented pointing to extravascular erythropoiesis, with the absence of inter-sinusoidal capillaries, hemoblasts serving as the cells of origin. (BA)

678

Lawrence, John S., Andrew H. Dowdy, and William N. Valentine. EFFECTS OF RADIATION ON HEMOPOIESIS. *Radiology* **51**, 400-13(1948).

The types of radiant energy under discussion are either electromagnetic energy waves, such as roentgen and γ rays, or particulate matter having mass, such as α and β particles, protons, and neutrons. The effects following radiation administered as: (1) single dose to the body as a whole, (2) repeated small doses to the body as a whole, (3) single or repeated doses to one area, and (4) internal radiation (probably β and γ mostly) were considered. The greater part of the observations referring to the irradiation with a single dose to the body as a whole have been performed on animals. The hemopoietic picture is decidedly affected in any post-irradiation period for the duration of the life and by the speed of utilization of the different morphological elements in the blood. For example, after a dose of 500 r, the rapid decrease in lymphocytes reflects their short life span, for the first decrease was observed in 15 minutes. The granulocytes did not decrease appreciably in numbers until the end of 24 to 36 hours. The platelets began to disappear at the end of 72 to 120 hours, and the erythrocytes between 120 and 168 hours. After doses of 200 r or less very few or no changes in the erythrocytes or platelets were observed. When the dose was less than 100 r, no large reductions in the reticulocytes were noted. However, a dose of 25 r caused a decrease in the formation of lymphocytes at the end of 24 hours. The results were less well defined in studies of the effect of small repeated doses; but in all the animals studied, distinguishable changes in some of the hemopoietic elements were observed after a year of daily exposure to 10 r. In spite of the fact that changes could not always be demonstrated following small repeated doses, no doses were so small that they did not affect the average survival of large groups of animals. From this it is apparent that the total dose is important and that the

small daily exposures to x-rays are cumulative. The incidence of leukemia clearly increased in the animals exposed repeatedly to small doses. Experiments demonstrated clearly that local irradiation does not produce direct effects upon the hemopoietic tissues that are not directly in the exposed region. Since the larger part of human exposure probably take the form of small repeated doses, the most important deductions from these studies are concerned with the cumulative effect and the total dose in the production of pathological changes. There is the possibility of leukemia and related illnesses to be considered whenever there is exposure to a considerable quantity of x-rays. And finally an apparent recovery from radiation effects may be followed by the sudden appearance of severe anemia or other blood dyscrasies. (NSA)

679

Lawrence, John S., William N. Valentine, and Andrew H. Dowdy. THE EFFECT OF RADIATION ON HEMOPOIESIS; IS THERE ANY INDIRECT EFFECT. *Blood* **3**, 593-609(1948).

The general aim of the investigations has been to obtain evidence for or against "indirect" radiation effects. To this end, 26 successful cross circulation experiments (carotid to carotid anastomosis) have been performed between normal cats and radiated cats. Cross circulation was established in most instances at some specified time interval after the radiation of one partner. All intervals up to 82 hours after radiation of one partner were covered. In seven experiments cross circulation was established and then one animal radiated while the other was shielded. These were considered the most critical experiments of the group. Detailed data on leukocyte and lymphocyte counts in the normal animals obtained during an approximately 28 day period of follow-up are presented. These data are not considered to support the thesis of indirect effects peculiar to radiation. A trend toward slightly lowered absolute lymphocyte counts in normal animals after cross circulation was not considered significant, and in no instance did leukopenia develop in the normal animal. The literature is reviewed and discussed. (NSA)

680

Lorenz, Egon. RECOVERY PATTERN OF THE BLOOD PICTURE IN GUINEA PIGS FOLLOWING A LIMITED TOTAL BODY EXPOSURE TO CHRONIC GAMMA RADIATION. *J. chim. phys.* **48**, 264-74(1951).

The recovery pattern of chronically γ -radiation exposed guinea pigs is presented in detail. Inbred guinea pigs were given 8.8 r daily until the number of erythrocytes in the peripheral blood decreased to approximately 2.8 million cells per mm (normal 5.7 ± 1.2 million). Data on guinea pigs indicate a sensitivity of the hematopoietic system comparable to that of man. Complete data on the blood picture and bone marrow studies are presented. (NSA)

681

Lutwak-Mann, C. and F. W. Gunz. EFFECT OF BODY EXPOSURE TO X-RAYS UPON BONE MARROW. *Biochem. J.* **44**, III of Proc. Biochem. Soc. (1949).

Rabbits irradiated with a single 1,000 r X-ray dose, and rats irradiated with a single 500 r dose were observed for two weeks following irradiation. Weight of the animals, gross and histological changes in bone marrow, bone marrow glycolysis and respiration, adenosine triphosphate, nucleic acid P determinations, and bone marrow mitotic figures were followed. Partial recovery was observed in hemoglobin content, mitotic figures, glycolysis, respiration and nucleic acid P. (NSA)

682

Pearce, M. L., M. A. Greenfield, and W. N. Valentine.

STUDIES ON THE RADIOSENSITIVITY OF BONE MARROW; III. THE DYNAMICS OF ERYTHROCYTE REGENERATION AFTER HEMORRHAGE AND IRRADIATION. Atomic Energy Project, Univ. of California, Los Angeles. Apr. 19, 1951. 15p. (UCLA-125)

A method for the calculation of "birth rate" of erythrocytes in the face of a changing blood count is presented in terms of life-span data. By setting up the dynamics of erythrocyte regeneration in terms of a two-compartment system, an equation is derived to predict expected red-cell count at any time after hemorrhage. The regeneration of erythrocytes after hemorrhage in irradiated and nonirradiated cats is compared with predicted values. (NSA)

683

Price, C. H. G. OBSERVATIONS UPON THE LYMPHOPENIA OF X-RAY IRRADIATION; PART II. Brit. J. Radiol. 24, 556-67(1951).

In experiments in which three groups of albino rats were exposed to fractional doses of 95 kv X rays it has been confirmed that the total lymphocyte count is related to the total dose of radiation administered. It has also been confirmed that the lymphocyte survival/dose curve is of a double exponential form. On comparison of the mean total lymphocyte survival/dose curves of the three groups of animals it could be shown: (a) That the degree of the biological change was more readily affected by an alteration in the volume of tissue irradiated than by a change in the rate of dosage of radiation. (b) That with suitable arrangement the regenerative effect of formative tissues could be demonstrated. (c) That on analysis of the total lymphocyte survival/dose curves into two separate components, the major effect was best explained as the direct result of the ionizing radiation, which effect can be regarded as a single hit target phenomenon. On a group basis there was evidence to show that the integral dose and concomitant change could be correlated with the observed group tolerance of the animals. This was not, however, apparent on consideration of the individual animal. (NSA)

684

Rekers, P., P. Salisbury, J. Miller, N. Marti, and N. Papageorge's, Jr. CROSS CIRCULATION STUDIES ON THE IRRADIATED DOG. Atomic Energy Project, Univ. of Rochester. Mar. 30, 1950. 12p. (UR-159)

Cross-circulation studies between dogs that had received a single x-radiation dose of 450 K, LD₉₅, 6 to 10 days previously and normal dogs have been carried out by use of direct carotid to carotid artery anastomosis and a cross-transfusion apparatus. With each technique elevation of the leukocyte and erythrocyte levels was noted during the period of cross circulation. At the termination of the carotid type of cross circulation, there was a drop in the leukocyte count to pre-circulation levels within 20 hr, while with the cross-transfusion apparatus the leukocyte count continued to rise for 8 hr or more after cross circulation and returned to the marked leukopenic level 48 hr after the termination of the cross-circulation procedure. Data on thrombocyte deflections are not sufficiently definite. (NSA)

685

Roberts, E., L. E. Card, and G. L. Clark. EFFECTS OF X-RAYS ON THE BLOOD CELLS OF THE CHICK. Biodynamica 6, 165-76(1948).

This work was begun in an investigation of the effect of X-ray treatment on the resistance of chicks to pullorum disease caused by *Salmonella pullorum*. Because the disease is a septicemia, the effects of the x-rays on all the types of blood cells of the classification were studied. This set of data is "apparently the first complete account to be published on this subject." Day-old White Leghorn chicks were irradiated with a total dosage of 360 r units over

periods of 120 minutes or 30 minutes. Another series were given a dosage of 720 r units over periods of 120, 30, or 6 minutes. Counts were made on all the blood cells (erythrocytes, heterophils, lymphocytes, monocytes, eosinophils, and basophils) at intervals after treatment ranging from 150 minutes to 48 hours. The lymphocytes were considerably reduced following irradiation. This was followed by an immediate decrease in the resistance of the baby chicks to the pullorum disease. There was also a slight reduction in the number of basophils, but the effects on the other cells did not appear significant. In both series of experiments the reduction in number of lymphocytes increased as the exposure time increased although the dosage remained constant. (NSA)

686

Rosenthal, R. L., B. I. Pickering, and L. Goldschmidt. A SEMI-QUANTITATIVE STUDY OF BONE MARROW IN RATS FOLLOWING TOTAL BODY X-IRRADIATION. Blood 6, 600-13(1951).

A method is presented for the quantitative enumeration of the bone marrow cells by adjusting the differential count for the degree of cellularity, which is derived from imprint preparations of femoral marrow. This method has been employed in a study of bone marrow changes at various intervals following 700 r of total body x-irradiation in the rat. The findings have been correlated with the peripheral blood counts. The erythroid cells of the bone marrow show rapid decreases in number because of their marked destruction. The myeloid cells chiefly undergo accelerated maturation. The decreases in megakaryocytes, mast cells and lymphocytes appear to be related to their life spans and the absence of further production. The reticulum cells and plasma cells show neither an absolute increase nor decrease. Formation of new cells, except possibly for plasma cells, from the reticulum cells is completely inhibited for the first nine days following total body irradiation of rats with 700 r. Regeneration is first apparent at 12 days after x-ray as evidenced by areas of erythropoiesis, and, to a lesser extent, Myelopoiesis. Megakaryocytes reappear in small numbers at 15 days. Although this regeneration is apparent in only 50% of the animals studied at 12 and 15 days following irradiation, all these animals showed evidence of transition of reticulum cells to mast cells. (NSA)

687

Schack, J. A. and R. C. MacDyffee. INCREASED RADIO-RESISTANCE OF RED BONE MARROW AFTER ANOXIA. Science 110, 259-60(1949).

One hundred and forty female mice were randomly distributed into two groups, one maintained at sea level as a control unit and the other exposed to a simulated altitude of 15,000 feet for 10-14 hours a day. Both groups were kept at 25-30°C.; animals were sacrificed frequently and the marrow from the femurs was examined for erythroblasts and normoblasts which were counted together as an erythroid percentage of the total marrow cells; this percentage was 10.6% in the normal animals and 18.6% in the anoxic animals. Both groups were then exposed to 500 r of total-body x-irradiation from a 200-kv machine and maintained at sea level; the erythroid percentage was rapidly reduced in the first two days, followed by a rise from the fourth to the sixth day, and a fall until the ninth day for normal animals; the experimental animals were identical in their reaction except for the absence of the last stage. It is indicated that the hyperplasia of the red marrow produced by exposure to low oxygen tension increases the resistance of the erythroid elements of the mouse to subsequent exposure to x-radiations. (NSA)

688

Selling, Lawrence and Edwin E. Osgood. THE ACTION

OF BENZOL, ROENTGEN RAYS, AND RADIOACTIVE SUBSTANCES ON THE BLOOD AND BLOOD-FORMING TISSUES, p.2689-802 of HANDBOOK OF HEMATOLOGY H. Downey, ed., Chapter 39, Volume IV. New York, Paul B. Hoeber, Inc. 3136p. 1938.

A general review of the action of radioactive substances and roentgen rays on body tissues. Includes sections on the effects of α , β , and γ radiation on the blood and tissues in vitro; γ ray effects; α ray effects; and a bibliography. (S.V.S.)

689

Sima, I. THE ACTION OF BLOOD AFTER EXPOSURE TO X-RAYS OR ULTRAVIOLET LIGHT. Jap. J. Med. Sci. IV. Pharmacol. 12, 157-65(1940).

Injected into the lymph sac, blood from pigs but not from cattle, rabbits, or toads increased the thickness of pigment layers. After exposure to x-rays or ultraviolet light, the action of pig blood was increased; cattle and rabbit blood showed a positive response, but not toad blood. This action was attributed to decomposition of erythrocytes, with the liberation of histamine which acted on the adrenals of the injected frogs, to increase adrenaline liberation into the circulation. Irradiation in the presence of trypanflavine, methylene blue or erythrosin did not alter the nature of action of the blood specimens tested. (CA)

690

Stearner, S. P. THE EFFECT OF A SECOND ACUTE X-RAY EXPOSURE ON THE RECOVERY OF THE CIRCULATING ERYTHROCYTES IN IRRADIATED RATS. Argonne National Lab. Aug. 1, 1947. 19p. (AECD-2024-D)

Experiments on the rat exposed to acute doses of x-rays showed that although recovery was largely complete at 35 days, a small but significant difference in the erythrocyte count (between control and irradiated groups) persisted for about three months. It was expected that a second exposure to the same dose at this interval would produce more severe damage than did the first exposure. White rats, about 2 months old at the start of the experiment were given 600 r at 0 and at 35 days or 600 r at 35 days only. The data suggest that the anemia following a second irradiation may be more severe than that following the first. Although the red count did not fall lower after the second exposure than after the first, the control count was higher during the latter half of the experiment. In addition those irradiated at 35 days only, showed an anemia that was less severe than that which developed in the group irradiated twice. However, recovery did not appear to be more retarded after the second acute exposure, but in all instances was not complete at 35 days. Comparison of erythrocyte and hemoglobin values of the irradiated groups showed that the recovery of the number of circulating erythrocytes was less rapid than the recovery of the hemoglobin values. This was especially apparent in the first group, but was seen only to a small extent in the group irradiated at 35 days only. This may be accounted for by the macrocytosis that was present at the last sampling (70 days). The mean erythrocyte diameters were: Control -6.85 μ ; group 600 r at 0 and 35 days -7.25 μ ; and group 600 r at 35 days only -8.17 μ . (NSA)

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Stearner, S. Phyllis, E. L. Simmons, and Leon O. Jacobson. THE EFFECTS OF TOTAL BODY X-IRRADIATION ON THE PERIPHERAL BLOOD AND BLOOD-FORMING TISSUES OF THE RAT. Argonne National Lab. Apr. 7, 1947. 42p. (ANL-4001; MDDC-1319)

Following exposure to single doses of 300 r and 600 r, a maximum anemia developed after 14-16 days. Recovery was complete at 30 days following 300 r, but a significant difference persisted until 94 days between control animals

and those exposed to 600 r. Detailed histologic study of the bone marrow and blood elements was continued for 35 days after irradiation. Exposure to daily x-ray doses of 33.5 r resulted in a total of 3,080 r and a maximum survival of 3 months. This dose rate produced only a slight depression in hemoglobin and erythrocyte values and a small decrease in number of circulating heterophils. However, lymphocytes were reduced after 1 week of treatment and fell continually until the death of the animals. A dose rate of 7.7 r per day was not shown to shorten the life span of the rats and had a doubtful effect on the circulating erythrocytes. The number of circulating heterophils was not decreased, but lymphocytes were reduced after 1 month of daily exposure and remained at a low level. Exposure to 7.7 r for over 8 months could not be shown to have produced any change in the blood forming organs. The response of the peripheral blood cells to daily doses of x-rays indicated that the effects upon lymphopoietic tissue were much greater than upon the elements formed in the bone marrow. Response of rats and rabbits were very similar. (TIS)

692

Stearner, S. P., E. L. Simmons, and Leon O. Jacobson. THE EFFECTS OF X-IRRADIATION ON THE PERIPHERAL BLOOD AND BLOOD-FORMING TISSUES OF SPLENECTOMIZED RATS. Argonne National Lab. Oct. 1, 1947. Decl. Apr. 23, 1948. 18p. (AECD-2022; ANL-4100)

White rats were splenectomized and after five days, exposed to 600 r and 100 r x-radiation. Although a leucocytosis was frequently seen after splenectomy, in some cases no significant change in the peripheral leucocyte count was observed. The lymphopenia and granulopenia that followed exposure to radiation were as severe in splenectomized rats as in intact rats. Histological studies indicated that splenectomy did not produce a significant hyperplasia of lymphopoietic or granulopoietic tissue in the rat. Therefore, there was no opportunity to compare the effects of radiations on normal and hyperplastic leucocyte-forming tissues. The functions of the spleen are not clearly understood, but appear to be complex. It is possible that splenectomy may produce numerous physiological changes which complicate the interpretation of radium effects on the blood-forming organs. Although the reason is not clear, the results make it apparent that splenectomy is not a satisfactory technique for producing a hyperplasia of lymphopoietic or granulopoietic tissue. In Bartonella-infected rats, splenectomy resulted in a severe anemia. In animals that survived, irradiation with 600 r did not cause a more severe anemia, but markedly retarded the recovery. The bone marrow of these animals was shown to contain a hyperplasia of erythroblastic elements. A small percentage of erythroblasts persisted during the early stages following irradiation of splenectomized rats, although none were seen at this time in intact irradiated animals. Later, however, damage appeared to be equally severe in both irradiated groups. (ADD)

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Stearner, S. Phyllis, E. L. Simmons, and Leon O. Jacobson. THE EFFECTS OF SINGLE DOSE TOTAL-BODY X-IRRADIATION ON THE PERIPHERAL BLOOD OF THE RAT. Anat. Record 99, 576-7(1947).

Following exposure to single doses of 300 and 600 r, a maximum anemia developed after 14-16 days. Recovery was complete at 30 days following 300 r, but a significant difference persisted until 94 days between control animals and those exposed to 600 r. The relatively long life of the red cell (20-30 days) may explain the delayed appearance of the effects of irradiation on the circulating erythrocytes. A macrocytic anemia was demonstrated by the presence of an

increased mean corpuscular volume and mean erythrocyte diameter. The white blood elements showed a maximum depression three days after x-irradiation. Recovery began 10 days after exposure to 300 and 600 r, and was essentially complete at 30 days. After 25 r there was a very small decrease in number of circulating leucocytes and recovery was complete after 14 days. Exposure to 300 and 600 r produced drastic effects on heterophils as well as lymphocytes. A comparison of the effects of x-irradiation on the peripheral blood of rats and rabbits showed that the pattern of response was similar in the two species and that only minor differences were present. Recovery of the lymphocyte count to control values was more rapid in the rat than in the rabbit following exposure to median lethal doses to both groups. The heterophil count fell to a lower level in the rat, but recovered at about the same time as did that of the rabbit. (AR)

694

Suter, G. M. RESPONSE OF HEMATOPOIETIC SYSTEM TO X-RAYS. University of Rochester. Mar. 22, 1947. Decl. Apr. 7, 1947. 8p. (MDDC-824)

The peripheral blood, constantly replenishing itself from its bone marrow and lymphopoietic precursors, is very sensitive to both gamma and neutron radiation. In the study of peripheral blood, numerous laboratory animals were used. Studies of the effects on the peripheral blood can be divided into two types: that of animals acutely exposed and chronically exposed to whole body radiation. Attempts were made to compare species sensitivity of the various laboratory animals on various bases in order that some conclusions could be made about the effects on humans. On the basis of mortality studies the most sensitive species studied appeared to be the dog, with monkey, rat, and rabbit correspondingly less sensitive. It was found difficult to draw such conclusions from the study of the blood of these animals. The site of injury with x-radiation and neutron radiation appeared to be directly in the blood-forming organs, the bone marrow, lymph nodes, and spleen. The peripheral blood showed only slight changes when isolated and radiated directly. Chronic studies were made for purposes of establishing tolerance both to X-ray and neutron radiation. Experimental results are summarized in ten graphs and two tables. (ADD)

695

T'Ang, Y. H. THE EXPERIMENTAL BASES OF TOTAL AND SUBTOTAL RADIOTHERAPY. J. belge radiol. 28, 207-99(1939).

We have attempted through animal experimentation to establish the scientific bases for total and subtotal radiotherapy. As to hematology, we have studied very carefully the blood changes following total or subtotal irradiation over a wide range of doses. We have also studied various other hematologic tests. We can conclude that doses of 100 to 150 r administered to the whole body of the animal at the rate of 10-25 r/day are without danger. This dose increases leucocytosis and stimulates red cell formation. Only when doses of 200 r or more are reached, can the beginning of a mild leucopenia be seen. The dangerous dose is about 500 r at one time or 5000 to 6000 r at the rate of 10-25 r/day in whole-body irradiation. The observation of reticulocytosis is not an adequate test in radiotherapy; we believe that a distinct leucopenia with a slight state of anemia constitutes an absolute indication for the cessation of treatment. Vitamin C appears to decrease the radiosensitivity of an organ to a lethal dose of radiation. The peroxide of diformaldehyde increases this radiosensitivity. Vitamins B₁, B₂, and B₆ are without effect. Some schedules of treatment by subtotal radiation in human therapy are given, as well as some re-

sults by way of example. The domain of application of this therapy is very large, not only in anti-neoplastic therapy, but above all in the domain of inflammatory, endocrine, allergic and tonic radiotherapy. (auth)

696

Valentine, W. N., C. G. Craddock, and J. S. Lawrence. THE EFFECT OF ROENTGEN RADIATION ON THE PRODUCTION OF THORACIC DUCT LYMPHOCYTES. Univ. of Rochester. Mar. 3, 1948. Decl. Apr. 23, 1948. 5p. (AECD-2023)

A study was made of the effect of 1,500 r whole body irradiation on the numbers of thoracic duct lymphocytes and rate of flow of thoracic duct lymph in cats. Since the procedure of thoracic duct cannulation itself results in some reduction in lymphocyte numbers and lymph flow, it was necessary to compare irradiated animals with an untreated control group. Nine control animals were employed while 11 animals were used in the irradiated group. In each animal lymph was collected in hourly or two-hourly volumes and studies were made to ascertain the volume, total lymphocytes, and lymphocytes per cu mm of each specimen. In each case the values for the first two hours flow were expressed as 100% and the values of each subsequent specimen computed as a percentage of this baseline. Animals were irradiated after a normal baseline was obtained. The total number of lymphocytes in thoracic duct lymph falls rapidly after heavy whole body irradiation as does the lymphocyte count per cu mm of lymph. There is only slight difference in rate of lymph flow in control and irradiated groups. Data are presented on these points. The data suggest that from the time irradiation was begun the total production potential of the lymphoid tissues drained by the thoracic duct did not exceed about four hours normal supply. In terms of the peripheral blood, this amounts to ability to replace via thoracic duct lymph about 50-60% of the circulating lymphocytes before total exhaustion ensues. (ADD)

697

Valentine, William N. and Morton Lee Pearce. STUDIES ON THE RADIOSENSITIVITY OF BONE MARROW. I. THE RELATIVE SENSITIVITY OF ERYTHROID AND MYELOID ELEMENTS. Univ. of Calif., Los Angeles. Apr. 4, 1951. 29p. (UCLA-123)

A comparison has been made of (a) the regenerative capacity of erythroid tissue in irradiated and nonirradiated cats, and (b) the relative regenerative capacity of myelopoietic and erythropoietic tissue in the same animals after the same irradiation injury, by irradiating animals immediately after a large acute hemorrhage of 40% of the circulating red cell mass. Dosage employed was 200 r to the whole body. Recovery from standard anemia was only slightly slower in the irradiated than in the control group. However, myelopoiesis was severely depressed for more than 30 days. These data suggest that on the basis of functional impairment, erythropoietic tissue is significantly less sensitive to radiation injury than is the myelopoietic tissue of the same animal. (NSA)

698

Valentine, William N., Morton Lee Pearce, and John S. Lawrence. STUDIES ON THE RADIOSENSITIVITY OF BONE MARROW; II. THE EFFECT OF LARGE, REPEATED WHOLE BODY IRRADIATION EXPOSURE ON HEMATOPOIESIS. Univ. of Calif., Los Angeles. Apr. 16, 1951. 15p. (UCLA-124)

Six cats were subjected to four whole-body irradiation exposures over a period of 1½ yr. Irradiation dosage was 200 r to the whole body. Irradiation in each case was immediately preceded by a large phlebotomy, so that functional impairment of erythropoiesis resulting from irradiation could

be assessed in terms of a defective regeneration of erythrocytes. Little evidence of permanent functional damage to erythropoietic tissue by repeated exposures under the conditions of this experiment were observed. Hemoglobin regeneration was slightly slower after the fourth and last irradiation. Whether this represents encroachment on marrow reserve by multiple irradiations or whether it was an artifact resulting from iron deficiency cannot be said with certainty. Multiple exposures exerted little apparent effect on the leukocyte regeneration curves. (NSA)

699

Van Dyke, D. C. and R. L. Huff. LIFE SPAN OF WHITE BLOOD CELLS AS MEASURED IN IRRADIATED PARABIOTIC RATS. *Am. J. Physiol.* **165**, 341-7(1951).

Inbred female rats of the Slonaker strain were used to form the parabiotic pairs. Littermates were united at 20-30 days of age, and 2 months later one member of each pair was irradiated. Controls were single rats of the same sex and weight which had received the same treatment. 950 r of 200 kv x-rays was delivered to one member, the so-called non-irradiated members receiving 28 r. Total white cell counts were made daily on the pairs and on controls. As the leucopoietic tissues of the irradiated members were destroyed, the white cell count was a measure of the leucocytes introduced into the circulation from the circulation of the normal member. The relationship between the number of leucocytes introduced into the circulation and the level maintained in the circulation allows calculation of the average life span of the leucocyte. These studies indicated the life span of the mononuclear lymphocytes in the blood of the irradiated rat to be 170 minutes, and that of the polymorphonuclear leucocytes to be 23 minutes. (V.E.)

Clotting Mechanisms—Humans

700

Amaniera, G. and B. Bertiglia. PROTHROMBIN STUDY IN RADIOTHERAPY-TREATED PATIENTS WITH NEOPLASMS. *Giorn. clin. med. (Parma)* **31**, 312-24 (1950).

A noticeable increase, no variation, and a slight decrease in prothrombin content was found in 75, 21, and 4%, respectively, of the cases. (CA)

701

Beller, F. K., Jr. ON THE POSSIBILITY OF DEMONSTRATING X-RAY AND Ra DAMAGE IN PERSONNEL BY OBSERVATION OF THE PROTHROMBIN LEVEL IN THE BLOOD. *Fortschr. Gebiete Roentgenstrahlen* **75**, 95-8(1951).

Through observations on the personnel of a radiological institute, it is established that slight radiation injuries cannot be demonstrated by the decrease of the prothrombin level. It appears that, in a general way, x rays do not affect the clotting potential of the blood. This conclusion is confirmed by the fact that various authors give discordant information on changes produced by radiations in the differential blood picture and in the coagulation time. (NSA)

702

Kaufmann, J. THE COAGULOGRAM AS A CRITICAL INDICATOR OF IRRADIATION EFFECT. *Am. J. Roentgenol. Radium Therapy* **55**, 464-72(1946).

Complete blood studies were made repeatedly on the employed personnel of the department of radiology of a large general hospital. These are analyzed as erythrogram, leukogram, and coagulogram. The latter, consisting of platelet count, bleeding time, clot retraction, prothrombin time, fibrin time, and complete coagulation, appears to be most important in revealing early changes due to irradiation.

Fibrin, prothrombin and coagulation times are all lengthened before changes appear in red or white cell count. The lengthening of prothrombin time from a maximum normal of 30 seconds—45 seconds warrants a caution to the individual should be temporarily removed from any exposure area, and the deficiency neutralized by every possible means including vitamin K therapy. If the condition does not improve, the individual should seek other occupation, away from the possibility of exposure to radiation. (BA)

703

Masini, Vincenzo. EFFECT OF IRRADIATION ON THE COAGULATION TIME OF THE BLOOD IN NORMAL INDIVIDUALS. *Radiologia (Buenos Aires)* **2**, 393-403(1945).

The author reports the effect of 200 r administered over the spleen, liver, lower abdomen or buttocks of normal individuals upon the coagulation time of the blood. As compared with the coagulation time taken before irradiation, such treatment produces a decrease in the coagulation time with little variation in the fibrinogen and in the platelets. (R)

704

Ostro, M. and D. I. Macht. A PHARMACOLOGICAL AND RADIOLOGICAL STUDY OF HEMOPHILIA. *South-eastern Med. J.* **39**, 860-7(1946).

Evidence is presented to show that upon exposure of blood samples of normal animals and humans, including hemophiliac subjects to therapeutic doses of x-rays, a definite shortening in clotting time will occur. The effect, in vitro, is best evident when the dosage ranges from 63-105 r. The same thromboplastic effects of x-rays can be obtained by exposing the subjects themselves to small doses of deeply penetrating x-rays. Irradiation in the region of the spleen of two hemophiliacs produced a shortening of the clotting time which was evident several days after initial exposure. On the basis of these findings the authors propose a radiologic approach to the therapeutic treatment of hemophilia. (BA)

705

Segre, Mario. CHANGES OF COAGULATION TIME, BLEEDING TIME, AND MORPHOLOGICAL BLOOD COMPOSITION AFTER IRRADIATION WITH X-RAYS OF THE SPLEEN AND HYPOPHYSIS. *Arch. sci. med.* **65**, 255-302(1938).

The coagulation time and bleeding time were shortened in both cases, bleeding time more in spleen irradiation. The thrombocytes decreased in number, the spleen having a larger effect. An erythropenia after 6 to 12 hours amounted to 20% in irradiation of the spleen, to 9% in irradiation of the pituitary. The later effect on erythrocytes was variable. Spleen treatment caused a sustained increase of leucocytes for 15 days; treatment of the pituitary showed a temporary decrease. Details of the various blood elements are discussed. (CA)

706

Soykova-Pachnerova, E. and O. Soyka. CHANGES IN THE PROTHROMBIN LEVEL IN WOMEN WITH CANCER TREATED BY IRRADIATION. *Časopis Lékárů Českých* **88**, 169-71(1949).

Checking up on reports in the literature of prothrombin-level changes after x-ray and radium therapy, the authors examined 65 women with ovarian and uterine cancer by the Quick test at the first treatment, three months after it, and at the second treatment. They found the prothrombin-level to be less affected by the treatment than by the patients' general condition. A prothrombin-level which does not change during treatment is claimed to be indicative of a favorable prognosis, whereas in cases where there is a change, the bigger the change the worse the prognosis;

whether the change is upward or downward is claimed to be unimportant. (NSA)

Clotting Mechanisms—Animals

707

Adams, W. **BEHAVIOR OF THE PROTHROMBIN LEVEL OF FEMALE RABBITS BEFORE AND AFTER ROENTGEN IRRADIATION.** *Strahlentherapie* **71**, 114-20(1942).

One or repeated doses of 60 up to 600 r caused no essential change in the prothrombin content. Only if the coagulation times before irradiation were relatively prolonged, did there appear after irradiation a reduction in the clotting time which corresponded to a prothrombin increase. The known effect of roentgen rays on the clotting time can, therefore, not be explained by changes in the prothrombin picture. (CA)

708

Allen, J. Garrott, Burton J. Grossman, Richard M. Elghammer, Peter V. Moulder, Charles L. McKeen, Leon O. Jacobson, Mila Pierce, Taylor R. Smith, and James M. Crosbie. **ABNORMAL BLEEDING.** *J. Am. Med. Assoc.* **139**, 1251-4(1949).

Data on six cases of hemorrhage (one due to irradiation by P³²) include reports on clotting time, protamine titration, erythrocyte, leucocyte and thrombocyte counts, prothrombin activity and clot retraction, and fibrinolysin. Protamine sulfate and toluidine blue were given with good results in all cases. When the bleeding was uncomplicated, protamine sulfate (50 mg in 5 cc of water intramuscularly every 4 to 6 hours, and 150 mg in saline slowly intravenously) is preferred to toluidine blue; isotonic saline solutions of 6 to 8 mg./kg. body weight are given slowly intravenously once a day for three days and then half of this dose for three following days. The authors conclude that abnormal bleeding may result from the presence of heparinoid substances in the blood accompanied by increased protamine titration, frequently a prolonged clotting time and in some cases severe thrombopenia; the bleeding was controlled by toluidine blue and/or protamine sulfate, either of which is capable of reacting with several endogenous substances both like and unlike heparin; thrombopenia did not respond to either, and in cases where it was accompanied by an increased protamine titration, the response was insufficient to eliminate splenectomy, since the two conditions are probably independent; it is concluded that the random use of the two compounds will lead to random results. (NSA)

709

Allen, J. Garrott and Leon O. Jacobson. **HYPERHEPARINEMIA: CAUSE OF THE HEMORRHAGIC SYNDROME ASSOCIATED WITH TOTAL BODY EXPOSURE TO IONIZING RADIATION.** *Science* **105**, 388-9(1947).

The hemorrhagic disease, characterized by a thrombocytopenia, prolonged bleeding and clotting times, and impaired clot retraction, has been thought to result from the associated thrombocytopenia, but the researches of the authors have lead them to the conclusion that increased free heparin in the blood is of the greatest significance, the thrombocytopenia playing only a secondary role. Evidence for this viewpoint is cited. (V.E.)

710

Allen, J. Garrott, Katherine Lathrop, and Margaret M. Sanderson. **FURTHER STUDIES ON THE CLOTTING DISTURBANCE IN THE DOG EXPOSED TO 450 r X-RADIATION.** Argonne National Lab. [nd] 12p. (AECU-496; UAC-56)

This report is primarily concerned with the disturbance in the clotting time (plasma factors) incident to a radiation exposure. It has been previously reported that an antico-

agulant similar to heparin can be demonstrated in the blood of dogs after lethal x-irradiation. Although the chemical identity of this material is not known, it is characterized by certain reactions which suggest that its nature is heparinoid. These studies have been extended, and data are presented which further suggest the possible heparinoid nature of the anticoagulant found in the blood after irradiation. Other nonheparin anticoagulants may be liberated, but thus far none has been found in the irradiated dog. Thrombocytopenia and capillary damage are also present and may contribute to the hemorrhagic state. (NSA)

711

Allen, J. Garrott, Peter V. Moulder, D. M. Enerson, K. A. Lathrop, and M. H. Sanderson. **SUMMARY OF IRRADIATION EFFECTS OF THE BLOOD COAGULATION MECHANISM, p.148-67 of PROGRESS REPORT; ABNORMAL BLEEDING.** Argonne National Lab. Mar. 1950. 20p. (ANL-4474(p.148-67))

The hemostatic mechanism is more complicated than can currently be explained, and the damages produced by total-body x irradiation are so far-reaching that most, if not all, of the clotting mechanism may be directly or indirectly affected. In addition, there is evidence of widespread vascular damage about which little is known. However, certain features of the pathogenesis of this syndrome are established and limited therapeutic aid is available. A summary discussion on certain of the phenomena described in the previous parts is presented in this section. Some recent data are included to augment the discussion. The whole-blood clotting time, a clotting inhibitor, thrombocytopenia, and capillary injury are discussed. 15 references. (NSA)

712

Allen, J. Garrott, M. Sanderson, and Leon O. Jacobson. **HYPERHEPARINEMIA - THE CAUSE OF THE HEMORRHAGIC DISEASE PRODUCED BY TOTAL BODY EXPOSURE TO IONIZING RADIATIONS.** *Science* **105**, 388(1947). (MDDC-836)

The hemorrhage disease in dogs given a single lethal total body exposure to x-ray (450 r) is characterized by a prolonged clotting time. No defeat of the known elements of clotting was demonstrable except for a reduction in the platelet number and the appearance of an anticoagulant not normally present in detectable quantities. The thrombocytopenia per se does not appear to be the important factor responsible for the hemorrhagic disease because the bleeding may occur before the platelets are reduced and transfusions of fresh citrated whole blood did not prevent or stop hemorrhage. Moreover, the factors that specifically inhibit the anticoagulant, restored the clotting time to normal, but did not prevent thrombocytopenia or elevate the platelet count. The anticoagulant reacts like heparin in all respects tested. Its activity was destroyed by specific antiheparin substances such as protamine, toluidine blue and other dyes of the thionin series. Toluidine blue prevented hemorrhage in dogs after x-ray exposure and stopped hemorrhage once it appeared. It was possible to isolate from the blood of dogs in the state of hemorrhage an anticoagulant, which on the basis of unit potency per mg. of weight, was as active as the standard sodium acid salt of heparin. The administration of large quantities of vitamin K and vitamin C were ineffective in preventing or stopping hemorrhage. Toluidine blue was ineffective in preventing or curing the hemorrhagic disease produced in normal dogs given dicumarol. Thrombocytopenia, neutropenia, and anemia were produced in normal dogs by the administration of a nitrogen mustard. The whole blood clotting time was not prolonged and hemorrhage did not occur. The hemorrhagic disease associated with over exposure to x-ray was closely correlated with infec-

tion. This suggestion was made that the anticoagulant was bound to the immune proteins and was released when the antibodies were exhausted or destroyed. The administration of high titre anti-sera and antitoxins prevented hemorrhage and prolonged the lives of the two dogs in which they were used. (ADD)

713

Allen, J. Garrott, M. Sanderson, M. Milham, A. Kirschon, and Leon O. Jacobson. **HEPARINEMIA: AN ANTICOAGULANT IN THE BLOOD OF DOGS WITH HEMORRHAGIC TENDENCY AFTER TOTAL BODY EXPOSURE TO ROENTGEN RAYS.** *J. Exptl. Med.* **87**, 71-85(1948).

In 25 dogs irradiated with 240 r over the whole body the clotting time became prolonged about the sixth day, hemorrhages occurred towards the end of the second week, and the dogs died two or three days later. The blood calcium level was unchanged, the prothrombin time fell only terminally, and the fall in the platelets was unrelated to the bleeding or the prolonged clotting time. The clotting time was not shortened by the addition of thromboplastin but was shortened when trypsin or thrombin was added. By addition of the plasma to plasma from a normal dog, anticoagulant was demonstrated in the abnormal plasma. As heparin can be inactivated by some basic dyes and proteins, toluidine blue and protamine sulfate were added and found to neutralize the anticoagulant both *in vitro* and *in vivo*, although they did not shorten the bleeding time. Vitamin K did not prevent hemorrhages in these dogs, and toluidine blue did not arrest the hemorrhages due to dicoumarol. A heparin-like substance was isolated from the abnormal blood. (AWM)

714

Allen, J. Garrott, L. J. Savage, Peter V. Moulder, and D. M. Enerson. **CLOTTING TIME CHANGES AFTER TOTAL-BODY X IRRADIATION, p.19-23 of PROGRESS REPORT; ABNORMAL BLEEDING.** Argonne National Lab. Mar. 1950. 5p. (ANL-4474(p.19-23))

This report is an analysis of the clotting times of 79 irradiated dogs studied consecutively from July 1, 1948 to February 1, 1950. The clotting time measurements were made by the same personnel, and the data obtained are illustrated. The platelet counts made daily on this same series of animals are also presented. It is indicated beyond doubt that the evidence pointing to increased clotting time after irradiation is not attributable to chance alone. (NSA)

715

Ambrosi, F. **ACTION OF X-RAYS ON BLOOD PROTHROMBIN CONTENT.** *Boll. Soc. ital. biol. sper.* **16**, 478-80(1941).

Irradiation of blood *in vitro* with moderate doses of x-rays did not alter the prothrombin content as determined by Quick's method. (CA)

716

Barnes, W. A. **PROTHROMBIN FORMATION FOLLOWING INJURY OF BONE MARROW BY ROENTGEN RAYS.** *Am. J. Roentgenol. Radium Therapy* **46**, 356-61(1941).

Mice, rats, rabbits, and a dog were subjected to large doses (up to 6,400 r) of 200 kv x-rays and the course of the prothrombin level was followed. No significant alteration was found during periods of 1-6 days after single large doses, although the bone marrows became almost aplastic. After long-continued irradiation, the numbers of platelets and the leucocyte counts were conspicuously lowered, but no change in the prothrombin level was found. (CA)

717

Cohn, Stanton H. **EFFECTS OF TOTAL BODY X-IRRADIATION ON BLOOD COAGULATION IN THE RAT.** *Naval Radiological Defense Lab.* Mar. 2, 1951. 23p. (AD-298(B))

The hemorrhagic syndrome following exposure of rats to 400 r of x irradiation was studied, and a blood coagulation defect was found. Although the Lee-White clotting time was determined to be normal following irradiation, the clotting defect was quantitatively reflected by an increased heparin clotting time and by alterations in blood resistance measurements. The thrombocytopenia following exposure of rats to radiation appears to be a major factor in the defective clotting and consequent hemorrhage. The heparin clotting time measurements and electrical resistance measurements presented in this paper provide quantitative baselines for the clotting reactions of normal and irradiated animals. These values may be used as standards in evaluation of various methods of prevention and treatment of the spontaneous bleeding. (NSA)

718

Cronkite, E. P., B. Halpern, D. P. Jackson, and George V. LeRoy. **A STUDY OF THE HEMORRHAGIC STATE IN DOGS AFTER A LETHAL DOSE OF TWO MILLION VOLT X-RAYS.** *J. Lab. Clin. Med.* **36**, 814(1950).

Ten dogs were given a single dose of 600 r (300 r to each side) of 2,000,000-volt x rays. The following studies of blood clotting were performed serially: platelet count; clotting time of whole blood; clot retraction and lysis; one-stage prothrombin time; protamine-heparin titration of whole blood (Allen); test for circulating anticoagulants (Conley); heparin-protamine titration of oxalated plasma (LeRoy); and determination of fibrin N. All animals died between the 8th and 13th day after irradiation. There was visible evidence of spontaneous hemorrhage in every one for at least 48 hr before death. The occurrence of purpura bore a very close relation to the onset of elevation of temperature. Diffuse, extensive hemorrhage was found in every animal at autopsy. During the performance of the autopsies the blood clotted firmly. The mean clotting time of whole blood was significantly prolonged after the 6th day. The mean platelet count was less than 50,000 after the 8th day. There was no evidence that heparinemia was responsible for either the prolonged clotting time or the hemorrhagic state. In every dog whose clotting time was longer than 1 hr it was possible, at some time, to reduce it to less than 1 hr when protamine sulfate was added in the course of the protamine-heparin titration (Allen). In every animal the one-stage prothrombin time was within normal limits. Conley's test for circulating anticoagulants was positive in two dogs, and was questionably positive in four dogs at some time after irradiation. However, in every animal Conley's test was negative at some time after irradiation when the clotting time of whole blood was longer than 1 hr. Fibrinogen was present in increased amounts in all dogs from the 7th day after irradiation. It appears that the hemorrhagic state that occurs in animals that have received lethal doses of x rays is not identical with any of the hemorrhagic diseases encountered in clinical practice. In addition to the thrombocytopenia, there is reason to suspect the occurrence of a circulating anticoagulant, the nature of which is not known. (NSA)

719

Dixon, Frank J. **RADIATION-INDUCED HEMORRHAGIC DISEASE IN CHICKENS.** *Proc. Soc. Exptl. Biol. Med.* **68**, 505-7(1948).

In order to study the hemorrhagic disease resulting from radiation, severe radiation injury was produced by repeated subcutaneous injections of P^{32} into young chicks. Agranulocytosis and thrombocytopenia developed rapidly. Blood coagulation time was not altered but the blood clots were jelly-like and completely devoid of ability to retract. The hemorrhagic disease which developed was much less se-

vere than that seen in mammals. The increased number of mast cells associated with atomic bomb radiation injury in human subjects was not seen in the chickens. (CA)

720

Enerson, D. M., B. J. Grossman, and J. G. Allen. **PLASMA ANTITHROMBIN IN IRRADIATED AND HEPARINIZED DOGS; A PRELIMINARY STUDY**, p.88-98 of **PROGRESS REPORT; ABNORMAL BLEEDING**. Argonne National Lab. Mar. 1950. 11p. (ANL-4474(P.88-98))

The blood of 4 normal dogs given intravenous injections of heparin (0.5 mg/kg of body weight) displayed a pronounced increase in the whole-blood clotting time with only a slight increase in antithrombin titer. Fifteen of 17 dogs given total-body x irradiation developed mild to moderate increases in the whole-blood clotting times with pronounced increases in the antithrombin titer. 11 references. (NSA)

721

Galluzzi, N. J., D. M. Enerson, D. J. Glotzer, P. V. Moulder, and J. Garrott Allen. **PHYSICAL PHENOMENA IN BLOOD COAGULATION**, p.99-111 of **PROGRESS REPORT; ABNORMAL BLEEDING**. Argonne National Lab. Mar. 1950. 13p. (ANL-4474(p.99-111))

An increase in plasma surface tension has been observed following total-body x irradiation in the dog. This increase can be explained in part on the basis of changes in both the concentration and the state of particulate aggregation of plasma proteins. The in vivo changes are greatly out of proportion to the measurable in vitro changes of surface tension with variations in protein concentration. (NSA)

722

Held, A. and H. Hulbach. **THE FIBRINOGEN CONTENT OF THE BLOOD UNDER THE INFLUENCE OF ROENTGEN IRRADIATION AND THE PRIMARY EFFECT OF RADIATION**. *Strahlentherapie* 51, 664(1934).

It has been known that the coagulation time of the blood has decreased following exposure to roentgen rays. The authors found in their experiments that this is probably due to an increase of the fibrinogen. The reticulo-endothelial system is undoubtedly involved in the reaction. The drop in the fibrinogen content of the blood which follows immediately after the exposure to roentgen rays is explained as a direct effect of radiation. (R)

723

Holden, William D., Jack W. Cole, A. F. Portmann, and J. P. Storaasli. **HYPOTHROMBOPLASTINEMIA FOLLOWING TOTAL BODY IRRADIATION**. *Proc. Soc. Exptl. Biol. Med.* 70, 553-6(1949).

Determinations of the hemoglobin, erythrocyte count, leucocyte count, platelet count (blood smears, 2.5% sodium citrate), clotting time, protamine titration where indicated, and thromboplastin assay of dogs subjected to total body irradiation were made prior to, and on successive days following, irradiation. Healthy mongrel dogs were irradiated with 450 r (LD-100%) from a 220 kvp machine at 15 ma through a 0.5 mm copper filter and a 1.0 mm aluminum filter, at a rate of 6-7 r per minute. The results obtained are given in tabular and graph form. A hemorrhagic syndrome was produced which was manifested by multiple areas of hemorrhage in the pulmonary, gastrointestinal, and urinary systems, anemia, leucopenia, thrombocytopenia, prolongation of clot retraction, and hypothyromboplastinemia. (NSA)

724

Jackson, D. P., E. P. Cronkite, G. J. Jacobs, and C. F. Behrens. **PROTHROMBIN UTILIZATION IN FATAL RADIATION INJURY**. Naval Medical Research Institute. June 26, 1951. (NM-006-012.04.36)

Eight dogs were given 600 r, 2,000 K.V.P., 1.5 ma., H.V.L. 4.3 mm. Pb, 15.0 (± 0.15) r per minute, whole body radiation by the bilateral exposure technique. The follow-

ing studies were performed serially: hematocrit, white blood cell count, platelet count, prothrombin concentration (Ware and Seegers), whole blood clotting time, and prothrombin utilization (Buckwalter, Blythe, and Brinkhous). All eight dogs died between the ninth and fifteenth post-irradiation day. Clinically and at autopsy, all of the dogs exhibited evidence of extensive diffuse hemorrhage. The typical pancytopenia was demonstrated in all eight dogs. A slight terminal decrease in the concentration of prothrombin occurred in four of the dogs. The results indicate that prothrombin utilization after this amount of radiation approaches zero from the ninth post-irradiation day to death. The whole blood clotting time became prolonged only after the utilization of prothrombin approached zero and the platelet level had fallen below 50,000 per mm³. At autopsy, the blood clotted promptly after the vessels were cut, and the blood was allowed to escape into the tissues. In the opinion of the authors, it does not seem necessary to introduce the concept of the presence of an anticoagulant in order to explain the hemorrhagic syndrome of radiation injury. The occurrence of a profound pancytopenia, severe infections, increased capillary fragility with possibly other vascular factors, and the changes attributable to these conditions would appear adequate to explain this syndrome. However, the results do not rule out the existence of a weak and, as yet, uncharacterized anticoagulant. (auth)

725

Jacobson, L. O., E. K. Marks, E. Gaston, J. G. Allen, and M. H. Block. **THE EFFECT OF NITROGEN MUSTARD AND X-IRRADIATION ON BLOOD COAGULATION**. *J. Lab. Clin. Med.* 33, 1566-77(1948).

A prolonged clotting time occurs in rabbits after a 3 mg/kg intravenous dose of nitrogen mustard within 24 hours after administration and persists for approximately 12 days. Spontaneous recovery occurs in surviving animals by the 12th to 14th day. A maximum reduction in blood platelets occurs by the 4th day in rabbits receiving 3 mg/kg nitrogen mustard, with recovery by the 12th to 14th day. Thus, the clotting time is prolonged prior to significant platelet reduction. However, the period of platelet reduction (4th through 12th day after nitrogen mustard administration) roughly parallels the period in which maximum increase in the clotting time exists. Spontaneous recovery of the clotting defect and the return of platelet values to normal levels in the peripheral blood occur at a comparable time (circa 14 days). Animals which developed a prolonged clotting time had normal calcium and prothrombin values. The prolonged clotting time and decreased "heparin tolerance" are reversible with antiheparin substances. The anticoagulant present in the blood is probably heparin or a heparin-like substance. The clotting defect produced by nitrogen mustard resembles that produced by whole-body x-irradiation (800 r) in rabbits and is also reversible with antiheparin substances. It is suggested that the potentially serious clotting defect may be produced by other agents producing toxic effects directly or indirectly on the blood-forming tissue. This should be borne in mind since a method of treatment is available (antiheparin substances) which may make it possible to pass the critical period of potential hemorrhage until spontaneous recovery ensues. (NSA)

726

Lathrop, Katherine and J. Garrott Allen. **STUDIES ON ULTRA-VIOLET ABSORPTION OF DOG PLASMA**, p.130-5 of **BIOLOGICAL AND MEDICAL DIVISIONS; QUARTERLY REPORT, AUGUST, SEPTEMBER, OCTOBER, 1948**. Argonne National Lab. Nov. 1, 1948. 5p. (ANL-4227(p.130-5))

Authors report on an investigation of the ultra-violet absorption of plasma from dogs under various experimental

conditions to determine if any information can be obtained to further clarify the nature of changes taking place which alter the clotting mechanism. Determinations were made of the ultra-violet absorption curve of oxalated plasma from (1) normal dogs, (2) irradiated dogs (450 r total-body x-irradiation), and (3) normal plasma plus heparin *in vitro*. Data are presented which may indicate that changes in the ultra-violet absorption pattern in dog plasma following total-body x-irradiation are due to heparin-like compounds.

(S.V.S.)

727

Lathrop, K. A., R. F. Gilmore, and J. G. Allen. *IN VIVO* CHANGES IN THE ULTRAVIOLET ABSORPTION SPECTRUM OF DOG PLASMA FOLLOWING EXPOSURE TO X IRRADIATION, p.123-7 of *PROGRESS REPORT; ABNORMAL BLEEDING*. Argonne National Lab. Mar. 1950. 5p. (ANL-4474 (p.123-7))

A study was undertaken of the ultraviolet absorption spectrum of plasma of dogs following exposure to 450 r total-body x irradiation. Simultaneous plasma protein and albumin-globulin assays have been made on a large number of the animals studied. The ultraviolet absorption at 278 mμ closely parallels the protein level, irrespective of quantitative changes in the albumins and globulins. (NSA)

728

Moulder, P. V., K. A. Lathrop, B. J. Grossman, N. J. Galluzzi, M. H. Sanderson, E. M. Burnham, and J. G. Allen. *CORRELATED STUDIES ON THE IRRADIATED DOG*, p.128-47 of *PROGRESS REPORT; ABNORMAL BLEEDING*. Argonne National Lab. Mar. 1950. 20p. (ANL-4474(p.128-47))

A number of blood and plasma abnormalities in the irradiated dog have been presented in previous sections. In an attempt to correlate these abnormalities, three dogs were given 450 r total-body x irradiation and the following studies were made: (1) complete hemocytology; (2) coagulation survey; (3) plasma proteins; (4) surface tension and viscosity measurements; (5) plasma ultraviolet light absorption; and (6) protein and protease sulfhydryl polarographic curves. Data were collected from the three animals, and large quantities of blood had to be drawn each day. The results, however, correspond with the findings in other irradiated dogs in which the effect of exposure upon each of these analyses was made. One of the reasons why these studies were made was the hope that some of these functions might serve as an index of the severity of x-ray exposure. No group of changes could be demonstrated shortly after irradiation that could be used to indicate the lethality of the dose. (NSA)

729

Penick, G. D., E. P. Cronkite, I. D. Godwin, and K. M. Brinkhaus. *PLASMA ANTIHEMOPHILIC ACTIVITY FOLLOWING TOTAL BODY IRRADIATION*. *Proc. Soc. Exptl. Biol. Med.* 78, 732(1951).

Plasma antihemophilic activity of dogs subjected to total body irradiation remained at normal levels. Whole hemophilic blood with a full complement of platelets accelerated the clotting of irradiated dogs blood, while platelet-poor hemophilic plasma did not. (auth)

730

Rosenthal, Robert L. and Agnes L. Benedek. *BLOOD COAGULATION AND HEMORRHAGE FOLLOWING TOTAL BODY X-IRRADIATION IN THE RABBIT*. *Am. J. Physiol.* 161, 505-14(1950).

Rabbits exposed to single doses of total body x-irradiation from 200-1000 r showed a blood coagulation impairment characterized by a thrombocytopenia, diminished clot retraction, increased clotting time of recalcified plasma, and increased anticoagulant effect of both added heparin and

toluidine blue on the clotting time. These changes can be attributed to the diminished platelet count and function following x-irradiation. No free excess heparin was demonstrated in the blood following radiation. The rabbit, in contrast to man, dog, and guinea pig, shows an inconspicuous hemorrhagic response following x-ray exposure. (CA)

731

Scheraga, H. A. and L. F. Nims. *THE EFFECT OF X-RAYS ON FIBRINOGEN*. Cornell University and Brookhaven National Lab. [nd] 1p. (AECU-968)

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High doses of two-million-volt x rays produce a marked increase in the viscosity of solutions of bovine fibrinogen. Examination of these solutions in the ultracentrifuge indicates the presence of significant amounts of an additional component of higher sedimentation constant than that of the original material. Simultaneous studies of the thrombin-induced clottability of these solutions seems to indicate that the clotting activity is not significantly decreased even though there are these changes in the structure of the native fibrinogen. The character of the clots does change, however, the clots formed from solutions irradiated with the higher doses compacting and breaking up upon slight mechanical disturbance; those clots formed from the original material and also those from solutions irradiated with the smaller doses exhibit normal synergetic properties at the pH studied. (NSA)

732

Scheraga, H. A. and L. F. Nims. *THE ACTION OF X-RAYS ON FIBRINOGEN SOLUTIONS*. Brookhaven National Lab. [nd] 21p. (AECU-1628)

Irradiation of fibrinogen solutions leads to fragmentation as well as polymerization of the original fibrinogen molecule. Irradiated solutions exhibit increased viscosity and, at doses greater than 300 kr, gel spontaneously. The magnitude of the changes can be decreased by the addition of protecting agents. The kinetics of the irradiation reactions are in accord with the hypothesis that the action of the x rays involves free radicals resulting from the ionization of water molecules. Despite the marked changes in the structure of fibrinogen produced by x rays, all of the material is recoverable as fibrin upon addition of thrombin even when only 10% of the native fibrinogen is left. It seems evident, therefore, that the split fragments resulting from the x irradiation contain the groups necessary for the clotting reaction and that these are not those easily oxidized by OH radicals. (NSA)

733

Stański, Feliks and Roman Kordecki. *IRRADIATIONS BY ROENTGEN RAYS AND HEPARINEMIA AND LEUKERGY*. *Med. Weterynar.* (Poland) 6, 453-5(1950).

Experiments were conducted on dogs divided into two groups. In the first group, the dogs were irradiated with roentgen rays in various doses, and leukergy and coagulation time were examined. In the second group, the experimental dogs received heparin intravenously in various doses, and leukergy and coagulation time were examined. The results of the experiments in the first group are listed. It appears that small doses of roentgen rays cause a slow prolongation of the coagulation time, and the leukergy phenomenon appears only when the coagulation time is considerably prolonged (5x). The results of irradiations by larger doses of roentgen rays over a period of one month are also listed. The marked prolongation of the coagulation time was accompanied by a marked positive leukergy reaction. Post-mortem and histological findings are reported as follows: local depilation of skin on the irradiated area, parenchymatous (cloudy swelling) degeneration of the liver, small focal hemorrhages and perivascular small-round-cell in-

filtrations in the kidneys, and proliferation of the histiocytary cells, especially in the liver. The results of experiments with heparin injected intravenously (vena saphena externa) in an 8-mg dose are shown. The coagulation time increased slowly, and leukergy appeared after 2 hr, culminating in 8 hr, when the coagulation time dropped almost to normal. The results of the influence of a large dose of heparin (12 mg) on the coagulation time and leukergy are shown. The coagulation time was very prolonged, and leukergy appeared after 2 hr, reaching its highest peak after 3 hr. Postmortem and histological findings were negative. It may be concluded that roentgen rays, causing an increase of heparin in the blood, produce thus a positive leukergy reaction. (NSA)

734

Sutherland, J. M. and J. G. Allen. FURTHER STUDIES ON THE ISOLATION OF HEPARIN FROM BLOOD OF IRRADIATED DOGS, p.112-22 of PROGRESS REPORT; ABNORMAL BLEEDING. Argonne National Lab. Mar. 1950. 11p. (ANL-4474(p.112-22))

A method is presented for the extraction of heparin from blood by which crystals of the barium salt of heparin can be prepared and identified from blood to which heparin has been added in amounts of 10 mg % or larger. The amount of heparin necessary to cause prolonged clotting time in irradiated dogs is 4 to 28 μg %, or less than 5% of the least amount detectable by the method employed. By this procedure, no anticoagulant could be extracted from the blood of irradiated dogs. 17 references. (NSA)

Miscellaneous

735

Blair, Henry A. RADIUM TOXICITY AND EXTERNAL RADIATION - BIOLOGICAL EFFECTS, p.6-45 of QUARTERLY TECHNICAL REPORT JULY 1, 1951, THRU SEPTEMBER 30, 1951. University of Rochester. Oct. 25, 1951. 40p. (UR-189(p.6-45))

Radium analysis of municipal water supplies of 33 cities, comprising about 20% of the population of the United States, is presented in tabular form. Results of a study of the differential leukocyte count of an Indian elephant presented in table form and discussed briefly. Serum, sodium, potassium, chloride, and carbon dioxide content were determined serially on dogs receiving single massive whole-body exposures to x rays. Sodium, potassium, and chloride were also studied by a balance technique. Results give rise to preliminary conclusions that the slight, but probably real, electrolyte changes in dogs following single massive whole-body exposures to x rays are in keeping with changes known to occur as a result of dehydration and starvation and are probably attributable to these factors. Preliminary observations of the effects of radiation on the metabolic process in baker's yeast confirm previously published data showing complete inhibition of colony formation without inhibition of over-all metabolism following irradiation with 20,000-r 250-kv x rays. Using 90,000-r air dose, of 250-kv x rays, a small but constant stimulation of both oxygen uptake and anaerobic CO_2 production was observed. Rate of uptake of glucose by the cells was not slowed up by an x-ray dose almost five times that sufficient to produce complete inhibition of colony formation. Results are presented by graphs and tables, accompanied by a brief discussion. A feasible method for the degradation of porphyrins of the protoporphyrin IX type is described. Urinary and serum fibrinolytic activity was measured in dogs after 450 to 700 r of whole-body radiation. Three or four days before death both the urine and serum fibrinolytic activity increased significantly, reaching maximum values just before death. The relation between the enhanced fibrinolytic enzyme activity and the hemorrhagic lesions noted at autopsy is discussed. (NSA)

736

Bless, A. A. BIOELECTRIC POTENTIALS AS A MEASURE OF RADIATION INJURY. Proc. Natl. Acad. Sci. U. S. 36, 617-23(1950).

Potentials measured from the tip of the coleoptile to the seed coat have been compared with coleoptile length in wheat seedlings irradiated with up to 6000 r of x irradiation at various ages. Coleoptile lengths in a given group are more homogeneous in value than the corresponding potential measurements. On the other hand, bioelectric potentials are very sensitive to temporary changes in the condition or environment of the organism. It is reasonably safe to say that the average value of the potential of specimens is as good a measure of radiation injury as any other parameter, provided an adequate number of specimens are used. It is possible that a series of readings on one specimen may give as good an indication of radiation injury as a single reading of many specimens. (NSA)

737

BIOLOGY AND MEDICINE, p.131-62 of QUARTERLY PROGRESS REPORT; JULY 1 - SEPTEMBER 30, 1951. Brookhaven National Lab. [nd] 32p. (BNL-132(p.131-62))

Progress is reported on a number of biological problems. Preliminary observations of cytological and morphological changes induced in plants by chronic γ irradiation are reported for plants grown in the 200-curie γ field. Data on weight changes and water consumption and metabolism of rats following x irradiation, histological changes in the pituitary of rats following irradiation, and the kinetics of phosphate interchange in tissues are included. Studies of uptake and distribution of Ba, La, Cu, and P by *Drosophila* are reported. Further studies of the effects of radiation upon nucleic acids in plants and animals and metabolism of nucleic acids are discussed. A decontamination unit for use in event of heavy contamination of personnel is described. Cl^{38} was found to reduce ascites in three patients with metastatic growths in the peritoneal cavity. The mechanism of this reaction is under investigation. Effects of radiation upon antibody production are being studied and preliminary data are included. (NSA)

738

Brues, Austin M. RADIATION EFFECTS, p.21-40, 56, 58-9, 91-8, 164-70, 177-86, 192 of BIOLOGICAL AND MEDICAL DIVISIONS, QUARTERLY REPORT, FEBRUARY, MARCH, APRIL, 1951. Argonne National Lab. [nd] 44p. (ANL-4625(p.21-40, 56, 58-9, 91-8, 164-70, 177-86, 192))

Survival data are presented for two strains of mice, C_3Hb (without the milk agent) and the hairless strain, given a single whole-body 400-r x irradiation within 12 hr after birth or chronic γ irradiation of 4.4 or 8.8 r (8 hr) beginning at age 1 month. Survival data on mice (progeny of crosses between C_3H and C-57 black strains) exposed 6 to 12 hr after birth to x irradiation of the head alone indicate a 20 day LD_{50} of 1000 to 1100 r; observations on rate of hair growth, age at which eyes opened, and formation of cataracts are reported; examination of the eyes by ophthalmoscope is recommended for early recognition and study of cataracts. Some preliminary data on the plasma electrolyte balance in dogs receiving a single total-body x-ray exposure of 450 r are given. The binding of organic ions by bovine serum albumin x radiated with 1000 to 120,000 r has been investigated; the binding energy decreases with increasing x-ray dosage above 10,000 r. The dosage rate required to reduce mitotic frequency below 50% in regenerating rat liver and Hall mouse carcinoma is given as a function of distance from 2 to 200 μC Sr^{90} - Y^{90} beads; effects of the β radiation on tumor cells are illustrated. Incidence and microscopic appearance of tumors induced in female Sprague-Dawley rats by radiation on the dorsal skin from point and diffuse sources of Sr^{90} are shown. The comparative and additive

physiological and genetic effects of x radiation and nitrogen mustards on *Paramecium aurelia*, and the action of infrared, visible, ultraviolet, and x rays on the mating reaction in *Paramecium bursaria*, are being investigated. Some data are given on the effect of x rays on the metabolism of haploid and diploid yeasts, and on the oxidation of dihydrodiphosphopyridine nucleotide (DPNH₂) by x rays. (NSA)

739

Brues, Austin M., ed. CHRONIC EXTERNAL IRRADIATION; NEUTRON TOXICITY, AND HEMATOLOGY, p.9-47 of DIVISION OF BIOLOGICAL AND MEDICAL RESEARCH; QUARTERLY REPORT; AUGUST, SEPTEMBER, OCTOBER, 1951. Argonne National Lab. [nd] 39p. (ANL-4713(p.9-47))

Data on the effects of homologous and heterologous bone marrow injections on survival in mice following x irradiation are presented in tabular form. The addition of 0.025M K citrate to distilled water suspensions of *Rous sarcoma* virus gave a high degree of protection against an x-ray dose of 75,000 r. Studies on the mechanism of citrate protection are in progress. Data on the pattern of loss and recovery of weight of the testes of mice exposed to a single dose of x radiation and a single intravenous injection of Rn in equilibrium with its short-lived decay products are presented in tabular form. Results indicate that the α particle does not manifest as high a factor of biological effectiveness relative to x radiation as has been assumed. A summary is included of visible lens opacities 6 to 7 months after various doses of x radiation to the head of newborn mice. Histologic examination showed progressive destruction of the cells of the retina following 1000 r x irradiation, with obvious signs within 3 hr after irradiation. The effects of shielding of liver, intestine, or spleen, and of spleen shielding followed by splenectomy at 5 min and at 24 hr upon the hematocrit values, reticulocyte and leukocyte counts of mice exposed to 1025 r x irradiation are presented graphically. Data indicate that cysteine injected up to 4 days before sacrifice does not significantly alter the 24-hr uptake of P³² by rat and mouse tissues. Studies of the effects of spleen shielding and subsequent splenectomy upon antibody formation in rats receiving total-body x irradiation confirm previous observations concerning the protective effects of spleen shielding on antibody formation. (NSA)

740

Brues, Austin M., ed. PHYSIOLOGY, RADIUM TOXICITY, HISTOPATHOLOGY, AND RADIOCHEMISTRY, p.48-73 of DIVISION OF BIOLOGICAL AND MEDICAL RESEARCH; QUARTERLY REPORT, AUGUST, SEPTEMBER, OCTOBER, 1951. Argonne National Lab. [nd] 26p. (ANL-4713(p.48-73))

Data from a study of the effects of cysteine and hypoxia on the survival of rabbit thymocytes irradiated in vitro with 200-r x rays, and data on the effects of chilling on the protection afforded x-irradiated thymic cells by cysteine are presented in tabular form. From results of the study it is concluded that the effect of cysteine on irradiated thymic-cell-serum suspensions can not be ascribed to a direct competition for the short-lived free radicals presumably formed in the aqueous phase, and also that the protection is not due simply to the removal of O and consequent decrease in the toxic breakdown products of water. Preliminary results suggest that cysteine binds O rapidly in the presence of thymic cells suspended in serum, and the effect of chilling suggests that other events, presumably related to the binding of O, must take place. Further work on this problem is in progress. Changes in body weight, food intake, and water intake were found to be related to x-ray dosage in rats, and cysteine pretreatment and a force-fed, semi-liquid diet greatly decreased the characteristic postirradiation drop in body weight. A method of measurement of the γ

activity in humans due to the nonemanating fraction of Ra present in the body is reported and comparison is made of counting results in patients whose Ra burden was established by the absolute method of measurement, and with Rn exhaled in the breath by these patients. In the clinical study of persons exposed to radium, one 68-year-old male given radium chloride intramuscularly 25 years ago was found to have an estimated total-body radium of 13.9 μ g, however, complete radiography indicates only minimal skeletal changes. A dosage of 800-r x radiation delivered to the tenotomized legs of rats did not appear to greatly disturb tendon regeneration although the regenerative process took a longer time in irradiated than in control rats. (NSA)

741

Brues, Austin M., ed. SPECIAL PROBLEMS, p.74-86 of BIOLOGICAL AND MEDICAL DIVISIONS, QUARTERLY REPORT, AUGUST, SEPTEMBER, OCTOBER, 1951. Argonne National Lab. [nd] 12p. (ANL-4713(p.74-86))

A method is described whereby data on tumor incidences may be put into such a form that comparison can be made according to standard statistical procedures for handling rare discrete events. In a study of the effects of pile-irradiated cholesterol on mice it was concluded that ionizing radiation does not produce appreciable carcinogenic activity in cholesterol and that direct action of ionizing radiation on cholesterol is not responsible for radiation carcinogenesis. Data on the mortality of cysteine-treated chicks following x irradiation are presented in tabular form. Preliminary data indicate that larger cysteine doses are required to protect against radiation toxicity in newly-hatched than in older chicks. Dog plasma was found to afford protection against radiation injuries to mice when administered intravenously just prior to exposure to 800-r x radiation. The toxicity of normal dog plasma to mice was found to be lost after 5 hr incubation or perfusion through the dog spleen. White's medium, a synthetic nutrient containing salts, amino acids, and vitamins, did not afford protection to mice after perfusion through dog spleen, but did give active protection if given intravenously after perfusion through the spleen that had been lead-protected during irradiation of the dog. Neither agent was protective when administered before x irradiation. (NSA)

742

Brues, Austin M., ed. INVERTEBRATE ZOOLOGY, PHYTORADIOBIOLOGY, AND MICROBIOLOGY, p.87-100 of DIVISION OF BIOLOGICAL AND MEDICAL RESEARCH; QUARTERLY REPORT, AUGUST, SEPTEMBER, OCTOBER, 1951. Argonne National Lab. [nd] 14p. (ANL-4713(p.87-100))

With the grasshopper egg as a test object, a study was made of the effect of x irradiation on enzymogenesis. Data on the effect of x irradiation on the acetylcholine content of postdiapause grasshopper eggs are presented graphically. Preliminary experiments on the radiosensitivity of the native enzyme complex involved in the conversion of tryptophan to auxin in bean seedlings are summarized. In an attempt to correlate knowledge concerning the degradation of nitrogen mustards in solution with loss of biological effect with time, groups of *P. aurelia* were exposed for 1 hr to the solution at various times after its preparation. Results indicate that the mean half life of the initially active mustard component was about 20 min. *Paramecia* were irradiated in the lettuce medium in which they were grown, in salt solution into which they had been put just prior to exposure, in salt solution into which they had been put 14 hr prior to exposure, and in a fresh salt solution after having remained in a salt solution 14 hr prior to exposure. Suppression of fission and preautogamous death were markedly increased immediately in animals that were placed in the salt solution

just before irradiation. Further investigations of the radio-sensitivity of the mating reaction of *P. bursaria* has resulted in the hypothesis that release of the mating substance is increased by illumination while its production is inhibited by illumination. It is thought that a flavin acts as the initial photoreceptor in the early reactivity period. (NSA)

743

Coon, Julius M. QUARTERLY PROGRESS REPORT ON RADIOBIOLOGY, REPORT NO. 4. Toxicity Lab., Univ. of Chicago. Jan. 15, 1950. 88p. (TID-364)

This report is composed of sections entitled as follows: Continuous Exposure of Animals to γ Radiation; The Toxicity of γ Radiation to Mice Exposed at Varying Dose Rates; Changes in the Distribution of Phosphorus in Irradiated Rabbit Bone Marrow; Studies on the Metabolism and Toxicity of Radioactive Metals; Studies on the Mechanism of Acute Beryllium Poisoning. III-The Effects of Beryllium on Phosphatases and on Intermediary Carbohydrate Metabolism; Studies on the Carbohydrate Metabolism of the Rabbit Ileum; The Effects of Beryllium Chloride in Locke-Ringer Solution upon the Isolated Rabbit Ileum and Heart; Effect of X-Radiation on Intestinal Cathepsins; Effect of Vitamin B 12 on X-Ray Toxicity to Mice; Further Studies on the Action of Beryllium Chloride; Some Notes on the Sampling of Aerosols by Impaction Methods. (NSA)

744

Goldhaber, G. and B. Feldman-Muhsam. IMMEDIATE EFFECT OF X-RAYS ON THE MOVEMENTS OF LARVAE AND PUPAE OF MOSQUITOES. *Nature* 153, 528(1944).

Experiment is described which demonstrates the acceleration of the movements of larvae and pupae of the mosquito *Aedes aegypti* immediately after the onset of irradiation. When the irradiation is interrupted, they return at once to normal behavior. (S.V.S.)

745

Jones, M. W., B. Kivel, and A. A. Bless. THE BIOELECTRIC POTENTIAL OF SEEDS AS A FUNCTION OF GROWTH AND OF X-RAY DOSAGE. *Plant Physiol.* 26, 19-29(1951).

It was found that x rays, in general, decrease the bioelectric potential of plant seeds and lower their vitality. High-yielding seeds were found to have higher potentials than those of low-yielding varieties. The bioelectric potential is not a function of the weight of the seed; it is zero at dormancy and rises slowly during the first few hours in a humid environment, then it rises much more rapidly as coleoptile elongation begins. (NSA)

746

Larkin, J. C. AN ERYTHEMATOUS SKIN REACTION PRODUCED BY AN ALPHA-PARTICLE BEAM. *Am. J. Roentgenol. Radium Therapy* 45, 109(1941).

While working with the cyclotron, a graduate student inadvertently put his hand in a beam of 32,000,000 volt alpha particles. He described the sensation as one of extreme heat and withdrew his hand as rapidly as possible so that the time of exposure was estimated at about one second. In four hours, the area was erythematous, two small blisters appeared, but the original sensation of pain did not persist. The next day the area became painful and remained so for four days during which the erythema regressed. By the 10th day there was desquamation of the stratum corneum, marked thickening of the skin, and the area was insensitive to touch. On the next day, the area was again becoming erythematous, quite swollen and very sore. After 18 days the erythema began to regress, but the thickening and roughening of the skin continued to progress even after four months. Even after four months there was some

thickening of the dermis. This is the first case of a visible erythematous reaction caused by a beam of alpha particles. (BA)

747

QUARTERLY PROGRESS AND WORK ACCOMPLISHMENT REPORT FOR QUARTER ENDING SEPTEMBER 30, 1951. Tennessee Univ. [nd] 33p. (ORO-54)

Progress is reported in the study of the fission-products metabolism in domestic animals and the dependence of their behavior upon normal mineral metabolism. Blood-volume values for swine were determined using the P^{32} -labeled red-cell method. Swine with average body weight of 10 lb were found to average 7.4 ml of blood per 100 g body weight, while those averaging 344-lb body weight had 4.6 ml of blood per 100 g body weight. Values for intermediate body-weight groups are also included. Blood values for the southwestern burro (*Equus asinus asinus*) were determined and are presented in tabular form. The multicurie irradiation field for large animals was loaded, calibrated, and placed in operation. Normal blood values for the healthy burro have been established to serve as a basis for following the changes caused by irradiation. Particular attention is invited to the results of a preliminary experiment on the effects of whole-body irradiation upon the subsequent fertility of the male rabbit. These data emphasize the fact that observations on the sperm themselves or even on the initial fertilization do not suffice to give a true measure of irradiation effects on fertility; it is necessary, therefore, to use the number of viable young produced as the criterion. As an indication of results, it was shown that while control rabbits in 34 matings produced an average of 6.56 viable young per mating, the values for males exposed to 100, 200, and 300 r were 3.4 in 15 matings, 4.5 in 26 matings, and 3.2 in 16 matings, respectively. (NSA)

III EFFECTS OF INTERNAL RADIATION AND METABOLISM AND TOXICOLOGY OF INTERNALLY DEPOSITED RADIO-ELEMENTS

General Dosage Studies

748

Abrams, R. PRODUCTION AND ANALYSIS OF RADIOACTIVE AEROSOLS. [Univ. of Chicago Metallurgical Lab.] July 2, 1946. Decl. Mar. 11, 1947. 80p. (MDDC-795; CH-3629)

The biological program calling for exposure of animals to air-borne radioactive materials made it necessary to develop procedures for producing aerosols, exposing animals to the aerosols, and measuring particle size and concentration. Since carrier-free materials were used, techniques were devised for the remote control handling of material with negligible weights, but with high radioactivity so as to obtain maximum deposition in the lungs of the experimental animals. Of a number of methods of producing aerosols that were investigated, three were extensively used. Atomization of aqueous solutions in a right angle jet atomizer was useful for tracer. But because of the great dilution with air it was not possible to obtain high efficiency. Burning a salt in a D.C. carbon arc was adequate for obtaining high intensity fission product smokes, but failed with Pu where it was necessary to use larger masses of material. High concentration Pu smokes were obtained by wrapping Pu metal in thin aluminum foil and discharging a high energy condenser (1000 joules) through the foil. To maximize lung deposition and to avoid skin contamination and ingestion anesthetized rats which

breathed from a small chamber through glass cannulae were used. This chamber consisted of a 2.8 liter brass cylinder from which 32 rats breathed while lying on a surrounding bakelite superstructure. In the case of the exploding foil it was necessary to use a 4.1 liter cylinder with a partition which protected the rats from the violence of the explosion. A number of methods were investigated for collecting smoke samples for analysis. The most satisfactory was the thermal precipitator which makes use of the dust-free zone around hot bodies to precipitate all the particles in a sample of air on to a Parlodion-coated microscope cover slip. Concentrations were estimated by doing direct γ and β counts on these cover slips. Later the Parlodion film was stripped off the glass and mounted for particle size observation in the electron microscope. Mean particle size with the methods used in the experiments averaged 0.1 to 0.2 μ . (ADD)

749

AMERICAN ASSOCIATION OF ANATOMISTS, SIXTY-SECOND ANNUAL SESSION AT TEMPLE UNIV., PHILADELPHIA, PA., APRIL 1949. *Anat. Record* **103**, 417-595(1949).

Papers reviewed are the following: Deposition of radioactive strontium and the rare earth promethium in the skeletal tissues of the rat, C. W. Asling, D. A. Heller, D. H. Copp, and J. G. Hamilton. Detection of the entry of radiophosphate in bones with the help of a new technique, the "inverted autograph," Leonard F. Belanger. Deposition of C^{14} in the metaphysis of long bones of young rats, William Bloom. The effect of x-ray irradiation upon the lumbo-sacral region of the axolotl (*Siredon mexicanum*), V. V. Brunst. Effects of P^{32} on regenerating amphibian tissues, J. N. Dent. Steady state of the iodine in the thyroid gland of the male rat, J. Dougherty. The use of radioactive phosphorus in studies of fetal circulation, Newton Everett and Robert J. Johnson. The development of roentgenographic methods to determine depth of penetration of liquid jets into living human subjects, Frank H. J. Figge. The localization of physiological amounts of thyroxine labeled with radioiodine in the tissues of the rat, J. Gross. Radioautographic reactions in tissues other than bones and teeth after injection of radio-phosphorus, C. E. Stevens. The following papers were read by title: A radioautographic study of the localization of radioactive europium in certain soft tissues of the rat, C. D. Van Cleave. Studies on the effects of x-radiation on morphogenesis of *Amblystoma punctatum*, S. W. Hanford. The effect of intraperitoneally injected radium chloride upon the peripheral blood of albino male rats, Paul G. Roofe and Frank E. Hoecker. Roentgenology as a means of instruction in anatomy in North American medical schools, Wayne A. Simril, A. Jack Stacy, and Sydney F. Thomas. Detection of radio-elements by various radio-autographic techniques, C. P. Leblond, L. F. Belanger, R. Bogoroch, C. E. Stevens, J. Gross, and G. Wilkinson. Abstracts of the papers are presented. (NSA)

750

Brues, Austin M. BIOLOGICAL HAZARDS AND TOXICITY OF RADIOACTIVE ISOTOPES. *J. Clin. Invest.* **28**, 1286-96(1949).

There is no evidence that radiation dosages corresponding to standard permissive dosages will result in increased incidence of malignant disease detectable in a population of moderate size. 32 references. (CA)

751

Brues, Austin M., ed. TOXICITY, p.55, 72-84, 99-124, 142-51, 187-91, 193-4, 209-21 of QUARTERLY REPORT, FEBRUARY, MARCH, APRIL, 1951; DIVISION OF BIOLOGICAL AND MEDICAL RESEARCH. Argonne National

Lab. [nd] 70p. (ANL-4625(p.55, 72-84, 99-124, 142-51, 187-91, 193-4, 209-21))

Radioautographic studies of the distribution of Ra in trabecular and cortical bone of the tibia and fibula of a human 25 yr following Ra ingestion, distribution of Ca^{248} in rat bone, and distribution of Ra and Pu^{239} in dog bone are presented. Studies of the fate of C^{14} absorbed by mice and rats during a 30- to 60-min period of exposure to $C^{14}O_2$ have been made. The calculated rates of passage of alveolar CO_2 into the blood were 23 μ moles/min in the mouse and 160 μ moles/min in the rat. Uptake of C^{14} was essentially unaffected by the CO_2 concentration of inhaled air. Passage of C^{14} from the bicarbonate compartments into inner compartments proceeded at a somewhat slower rate. Rates of uptake of C^{14} from $C^{14}O_2$ by the livers of adult and newborn mice are compared, and the bone carbonate turnovers of adult mice and rats are discussed. The toxicity ratio between Ra and Pu has been evaluated from the data of a large number of experiments. The best available Ra/Pu ratios, in terms of injected μ c/kg are: acute toxicity to small animals, 15; chronic survival, 10; formation of bone tumors in rats and mice, 15; formation of bone tumors in rabbits, 8; and bone fractures in rats and rabbits, about 10. A maximum permissible retained dose of 0.04 μ c of Pu in man is the best value available from present biological information. The median lethal dosage to rats of H^3O_2 administered continuously over a 2-month period corresponds to between 57 and 77 rep/day on the basis of dosage rate in body water. The mean accumulated dosages to death are between 3000 and 3700 rep, being consistently higher at 77 than at 96 rep/day. The effectiveness in protecting against Be poisoning of various dyestuffs having structural similarity to aurin tricarboxylic acid was tested with negative results. The acute toxicities of members of the mesothorium chain (Ra^{224} , Th^{228} , Ra^{228} - Ra^{226} , Po^{210} equilibrium mixture, and Ra^{224} - Th^{228} equilibrium mixture) have been studied in CF-1 female mice. The 20- to 30-day LD_{50} 's for all the elements except Ra^{226} fall between 36 and 58 μ c/kg. The Ra^{226} values range from 830 to 1100 μ c/kg. (NSA)

752

Brues, Austin M., ed. ON ESTIMATION OF TOTAL RADIATION DOSAGE FROM THE METABOLIZED OR COMPARTMENTALIZED ISOTOPE, p.85-90 of BIOLOGICAL AND MEDICAL DIVISIONS, QUARTERLY REPORT, FEBRUARY, MARCH, AND APRIL, 1951. Argonne National Lab. [nd] 6p. (ANL-4625(p.85-90))

Despite the complexity of time-retention curves in a steady-state system of many homogeneous compartments, the integrated dosage from an isotope entering such a system under known external conditions is wholly predictable. It can be computed on the assumption that all the exchangeable isotope in any volume maintains a specific activity $\times$ time equal to that in the external compartment. A deviation from this indicates the presence of an irreversible process or deviation from the steady state, or possibly a situation where a diffusion gradient is important. To the extent that a metabolic system satisfies the requirements indicated, the use of "mean retention time" is valid. (NSA)

753

Brues, Austin M. COMPARATIVE CHRONIC TOXICITIES OF RADIUM AND PLUTONIUM. Argonne National Lab. Apr. 1951. 20p. (ANL-4799)

A preliminary quantitative survey is presented of the survival and gross pathologic changes in animals given Ra and Pu, and a discussion of the significance of the findings and their relation to the human toxicity problem is outlined. The toxicity ratio between Ra and Pu is evaluated from the data of a large number of experiments. (NSA)

754

Buchanan, Donald L. AN INTERRELATIONSHIP BETWEEN TIME-RETENTION CURVES IN SHORT VS. PROLONGED ISOTOPE EXPOSURES. Argonne National Lab. Nov. 1950. 13p. (AECU-1183; UAC-329)

A concept is presented which relates isotopic retention of an isotope in animals subjected to a "single dose" to the level of retention found experimentally after prolonged constant intake of the same isotopic compound. The mean retention time, which is easily obtained from experiments of the latter type, specifies the integral of the time-retention curve obtained in experiments of the former type and by so doing rigorously sets an upper limit to the total radiation dose that the animal may receive from the intake of a known amount of a given isotopic compound. The concept is extended to allow calculation in localized arbitrary volumes of tissue. (NSA)

755

Bush, F. THE INTEGRAL DOSE RECEIVED FROM A UNIFORMLY DISTRIBUTED RADIOACTIVE ISOTOPE. Brit. J. Radiol. 22, 96-105(1949).

Methods of calculation of the integral dose received in simple geometrical bodies containing a uniformly distributed γ -ray emitting radioactive isotope are described, and a general relation between this dose and the volume, and the elongation of the body, deduced. These calculations have been extended to the case of a "patient," composed of cylinders and elliptical cylinders. A table is given, showing the integral dosage-rates in patients of different heights and weights from a uniformly distributed γ -ray emitter. The effect of variation in the quantum energy of the emitted radiation on the integral dose is examined. An expression is found which gives the fraction of the energy due to β -particle emission which is lost from the surface of the patient or animal. This loss may be important in the case of small animals. (NSA)

756

Waldo, Cohn E. TOXICITY OF INHALED OR INGESTED RADIOACTIVE PRODUCTS. Nucleonics 3, 21-6(1948) July

A general formulation is presented which relates the concentration of a radiosubstance in air, water, or food to the total dose or daily intensity of radiation received by a given tissue as a result of the type and extent of intake of the polluted source. This relation is expressed in terms of biological constants (degree of absorption, deposition pattern, excretion rate) and physical constants (half-life, radiation energy) of the contaminating substance. Use of the derived formula is demonstrated by a number of examples. (CA)

757

Copp, D. H., D. J. Axelrod, and J. G. Hamilton. THE DEPOSITION OF RADIOACTIVE METALS IN BONE AS A POTENTIAL HEALTH HAZARD. Am. J. Roentgenol. Radium Therapy 58, 10-16(1947).

Radio-Sr follows the path of Ca metabolism and is deposited only in the bone salts, whereas radioactive Pu, Y, and Ce are laid down in the uncalcified organic matrix of bone in contrast to the accepted view with regard to behavior of other heavy metals which deposit in the skeleton. Radio-Sr is eliminated more readily with a biological half life of three to four months. The other elements mentioned are excreted very slowly with a biological half life of one to three years. (CA)

758

Craver, B. N. RADIOACTIVE EMANATIONS: THEIR NATURE, MECHANISM OF ACTION, BIOLOGICAL EFFECTS AND TOLERANCE LIMITS. J. Ind. Hyg. and Toxicol. 29, 196-200(1947).

The characteristics of the various common types of radiation produced by atomic disruption have been described. The nature of the biological changes that they produce have been discussed as well as the mechanism of their production. The curie and the roentgen have been defined and human tolerance-limits in terms of those units. (Author's Summary)

759

Evans, R. D. TISSUE DOSAGE IN RADIO-ISOTOPE THERAPY. Am. J. Roentgenol. Radium Therapy 58, 754-6(1947).

The biological action of roentgen rays is due to the effects on living cells of high-speed secondary electrons produced by the primary roentgen rays. The beta rays from a radioactive isotope are also high speed electrons. These beta rays can therefore be expected to produce tissue effects similar to those produced by roentgen rays. The beta rays have a maximum range of only a few millimeters of tissue actually containing the radioactive isotope, and the dosage rate at any time is proportional to the concentration of the isotope in the tissue. It might be desirable to express the radiation doses produced by the beta rays in some fundamental energy units, such as ergs per gram of tissue. Ordinarily, however, the doses are converted into equivalent roentgens, with air as the standard substance. A discussion is given of dosage rate and total dosage delivered by radioactive isotopes. (GPR)

760

Herd, K. E. DEPOSITION OF RADIOACTIVITY IN RATS DRINKING PILE EFFLUENT WATER. Hanford Works. Jan. 24, 1951. 13p. (HW-20102)

Two groups of rats drank *ad libitum* only effluent nuclear reactor cooling water adjusted to activity density levels of approximately 3×10^{-4} and 3×10^{-6} $\mu\text{c}/\text{ml}$ for periods of 200 to 500 days. Growth rate of the experimental rats was not affected by the radioactivity, and no histological changes were observed. Both effluent-drinking groups showed β radiation levels significantly higher than the controls. In the group receiving the greater concentration, blood and kidneys usually had the highest activity density with an accumulation of Na^{24} and P^{32} approximating 2×10^{-6} $\mu\text{c}/\text{g}$. This study suggests that the hazard to mammals drinking Columbia River water containing greatly diluted effluent is negligible if the diet provides all the essential elements. (NSA)

761

Lanz, H., K. G. Scott, J. Growley, and J. G. Hamilton. THE METABOLISM OF THORIUM, PROTACTINIUM, AND NEPTUNIUM IN THE RAT. [Radiation Lab. Univ. of Calif.] Aug. 23, 1946. 18p. (MDDC-648)

The distribution of carrier-free thorium, protactinium and neptunium in the rat following intramuscular and oral administration has been studied. Oral absorption for all three is negligible. Following parenteral administration, the skeleton is the organ showing the highest degree of prolonged and selective localization. (ADD)

762

Lisco, Hermann. DOSAGE LEVELS IN ADMINISTRATION OF ISOTOPES TO ANIMALS AND MAN. U. S. Naval Med. Bull. Supplement, 48, 161-3(1948).

Radioactive isotopes have injurious effects upon animals and man. These effects are functions of a number of factors, two of which are the half-life and the distribution of the isotope in the body. Since the distribution varies from isotope to isotope, depending upon metabolic function, turnover, and excretion rates, different manifestations of radiotoxicity can be expected. Laboratory studies have provided information on the ranges of dose levels in animals at which acute and chronic injurious effects can be

expected. Isotope studies include Sr^{89} , Y^{91} , Ra , Ce^{144} , Pu^{239} . Although this list does not include isotopes commonly used for tracer studies, certain conclusions may be drawn from the data which have been obtained. Studies of P^{32} and C^{14} are now being carried out. Virtually nothing is known at present about the distribution of C^{14} in the mammalian body and its retention in and toxicity to the organism. Some preliminary data suggest, however, that some retention does occur in bone and this fact should be borne in mind by investigators using C^{14} . There is information on dose levels of P^{32} and I^{131} presently used in man for treatment of disease, and the blood picture (lymphocytes, platelets) is a fairly accurate and reliable indicator of incipient radiation damage. However, it will be exceedingly difficult to detect minute quantities of radioactive isotopes lodged in discrete areas in the body and producing localized irradiation over a long period of time without concomitant damage to the bone marrow. It has been tacitly assumed that tracer levels of radioactive isotopes have no effects upon the systems under investigation. Although this is probably true in most instances, it might be worth considering a number of *ad hoc* experiments, so that definite information may become available on tolerance-levels as applied to animal experiments of this type. (NSA)

763

Marinelli, L. D. DOSAGE DETERMINATION WITH RADIOACTIVE ISOTOPES. *Am. J. Roentgenol. Radium Therapy* **47**, 210-6(1942).

With the increasing employment of radioactive isotopes in chem., biol., and phys. research, it becomes increasingly important to have an accurate method of dosimetry. By the use of a suitable method of specifying energy absorption, the question can be closely related to x-ray and radium dosimetry. On this basis, the radiation from these substances can be specified in "equivalent roentgens." Formulas are derived which permit the estim. of the radiation delivered when the concn. of the isotope in the material is known. In biol. or clinical use of the substances, the dosage in addn. to initial tissue uptake, depends also upon elimination; the importance of this depends partly on the half life of the particular isotope. The main difficulties in this dosimetry are of biol. nature; accurate detn. of isotope concn. in different tissues requires either actual radioactive measurements on tissue fragments obtained from living individuals, or on calcns. based on thorough quant. knowledge of tissue metabolism which is not available at present. (CA)

764

Marinelli, L. D. DOSAGE DETERMINATION IN THE USE OF RADIOACTIVE ISOTOPES. *J. Clin. Invest.* **28**, 1271-80(1949).

In this extensive paper, formulas expressing the relationship between radiation dose and isotope concentrations are presented and their clinical applications are discussed by the use of tables containing a considerable amount of information. Examples of the application of the formulas to such specific isotopes as P^{32} , Sr^{89} , Ca^{45} , Na^{24} , Na^{22} , K^{42} , I^{131} , I^{130} are included along with definite problems. In the two specific tables presented, for β and γ rays, respectively, the half-life, radiation average energy, fraction disintegrating per day, and specific dosage data are contained. References for those isotopes which are not included in the body of the article or for supplementary information are presented in a special section in the bibliography. (NSA)

765

Marinelli, L. D., E. H. Quimby and G. H. Hine. DOSAGE DETERMINATIONS WITH RADIOACTIVE ISOTOPES. II. PRACTICAL CONSIDERATIONS IN THERAPY AND PRO-

TECTION. *Am. J. Roentgenol. Radium Therapy* **59**, 260-78(1948).

When radioactive isotopes are employed either as tracers or in therapy, it is important to be able to determine the radiation dosage. This cannot in general, be measured, but when the half life, radiation energy, and biological uptake and excretion are known, it can be calculated. The paper is divided into two parts, based on clinical and physical aspects of the problem. In the physical part (Part II) are given mathematical developments of formulae for dosage rates and total doses for beta and gamma-ray emitting isotopes, together with subsidiary formulae for safe concentration, weight per mc, etc. In the clinical part (Part I) these formulae are accepted, and doses considered for specific cases, for a number of isotopes of common interest. Particular consideration is given to the determination of safe tracer doses. Two extensive tables are presented, for beta and gamma rays respectively, giving half life, radiation average energy, fraction disintegrating per day, and specific dosage data, including the safe tracer concentration, for some 38 isotope elements. An extensive bibliography is included. (GPR)

766

Maynoerd, W. V., J. H. Martin, and D. A. Layne. PRODUCTION OF RADIOACTIVITY IN ANIMAL TISSUES BY HIGH-ENERGY X-RAYS. *Nature* **164**, 728-30(1949).

Based on the fact that photo-disintegration of atomic nuclei by high-energy x-rays occurs, induced activity in tissues is observed when rat tissues are exposed to beams of x-rays. The decay curves, plotted semilogarithmically, reveal two half-lives of 2.1 and 20 min, respectively, agreeing with the known half-lives of oxygen¹⁶ and carbon¹¹. Decay curves for ice and water coincide with the 2.1 min curves of the tissues. Calculation of the rate of energy absorption from the x-ray beam results in a value of 0.93 ergs/g sec, whereas the rate of absorption of energy due to the disintegration from O_2 , by assuming a mean energy per disintegration of 0.7 mev, is 0.4×10^{-4} ergs/cc sec. Even if C disintegration is included, the rate of absorption of energy during irradiation due to the activation is only of the order of 0.01% of that due to the more usual mechanisms of absorption, namely, electron recoil and pair absorption. (CA)

767

Morgan, K. Z. TOLERANCE CONCENTRATIONS OF RADIOACTIVE SUBSTANCES. *J. Phys. and Colloid Chem.* **51**, 984-1003(1947).

Reviews some of the elementary equations and procedures involved in determining tolerance concentrations of radioactive substances when taken into the human system. (GPR)

768

Morgan, K. Z. SYMPOSIUM ON PREPARATION AND MEASUREMENT OF ISOTOPES FOR USE IN BIOCHEMISTRY. HAZARDS PRESENTED BY RADIOACTIVE MATERIALS AND HOW TO COPE WITH THEM. *U. S. Naval Med. Bull. Supplement*, **48**, 142-60(1948).

Equations are given for calculating the tolerance concns. of radioactive material in the body. The tolerance values of some of the radioactive elements are summarized. (CA)

769

Norris, William P. and Walter Kisielleski. COMPARATIVE METABOLISM OF RADIUM, STRONTIUM, AND CALCIUM. *Cold Spring Harbor Symposia Quant. Biol.* **13**, 164-72(1948).

Sprague-Dawley rats, kept on a constant diet, received Ca^{45} or $\text{Sr}^{89,90}$ intravenously, 40 μC of Ca, 115 μC of Sr, and 25 μC of Ra were included in the injections, respectively. Time determinations on the blood, feces, urine and skeletal levels of the elements were then performed; the results of which are tabulated and discussed. Other similar experimental courses were run, 0.02–0.91 $\mu\text{C}/\text{g}$ of body weight of radium per animal being administered intraperitoneally to 100 Sprague-Dawley rats; the retention was measured as before. 38 references. (NSA)

770

Oddie, T. H. DOSAGE FROM RADIOISOTOPES UNIFORMLY DISTRIBUTED WITHIN A SPHERE. *Brit. J. Radiology* 24, 333–6(1951).

Formulas are developed for a geometric factor to allow for variations of dosage rate at points in tissue both inside and outside a sphere containing a uniformly distributed radioactive material. Values of this factor are tabulated. The results are applied to find the order of variations of dosage rate that are to be expected with a spotty distribution of I^{131} in a thyroid gland. It is shown that the dosage rate may quite easily change by a factor of more than 100 in different parts of the tissue mass. (NSA)

771

Pearson, I. A., J. M. Hammer, K. E. Corrigan, and H. S. Hayden. STUDIES ON THE BEHAVIOR OF FUNGI IN THE PRESENCE OF RADIOACTIVE ISOTOPES. *J. Bacteriol.* 56, 397–402(1948).

The behavior of 43 pathogenic and nonpathogenic fungi in the presence of radioactive phosphorus, iodine, and high voltage x-ray was studied, and a technique for handling cultures containing radioactive substances was developed. The amounts of P^{32} , I^{131} , and x-ray were not lethal, and exposure to them did not cause any marked changes in the morphology or pathogenicity of numerous fungi studied. It was found that solutions of radioactive phosphorus and iodine have no self-sterilizing properties. Autoradiographs of fungi were made showing that the fungi themselves were radioactive. It was impossible to obtain autoradiographs of single spores or mycelia since considerable scattering was present; the technique is being studied further and developed. (NSA)

772

Posin, Daniel Q. INVESTIGATIONS WITH RADIOACTIVE SR, P, AND FE. *Proc. Montana Acad. Sci.* 3 and 4, 10–15(1942–43).

Four days before giving birth to young, a pregnant rat was given an injection of radioactive p. One of the young, less than a day old, showed considerable body and skeleton radiation. After about two months the radioactive p was about equally distributed in density in the young and the mother. A hen injected with radioactive Sr laid eight radioactive eggs. The first egg was boiled for 20 minutes and it was found that some activity was present in the white, practically none in the yolk, and the shell was very active. When the hen stopped producing Sr-radioactive eggs, radioactive Fe was injected and the eggs laid for several days thereafter were found to be radioactive. The activity was exclusively in the yolk. Saline washings of *E. coli* grown on a medium containing radioactive p were radioactive. This activity was most marked in the first washing and was almost negligible in the fourth. The sedimented mass was very radioactive. When a suspension of this mass was injected in a rat the bacteria hovered principally near the point of injection. A radioautograph of a rat injected with Sr^{89} showed the leg-bone to be more active than the marrow and the skull more active than the brain. The relative distribution of radioactive p and Sr in rats is shown by other radioautographs. (CA)

773

Prosser, C. Ladd, C. W. Hagen, Jr., and W. Grundhauser. THE LETHAL ACTION OF X-RADIATION, STABLE ISOTOPES OF FISSION ELEMENTS, Sr^{89} , AND (BA - LA)¹⁴⁰ UPON GOLDFISH. Argonne National Lab. July 1947. 21p. (MDDC-1480; ANL-4017)

Solutions of stable barium at 1 ppm killed 50% of goldfish within 30 days. Cerium was toxic at 10 ppm, and bromine, at 1,000 ppm. Solutions of strontium and iodine were non-toxic, at least up to 1,000 ppm. Single doses of 850 r x-radiation killed 50% of goldfish within 30 days. Half a group of goldfish receiving 100 r daily were dead at 26 days; half a group at 50 r daily were dead at 33 days; whereas half the controls and those receiving 25 r daily were dead at 40 days. Calculations of radiation dosage show that in solutions containing fission products at 1 $\mu\text{C}/\text{ml}$, the dose due to external radiation is a small fraction in comparison with that due to internal radiation. In solutions of Sr^{89} at an initial concentration of 0.1 $\mu\text{C}/\text{ml}$, deaths were no more frequent than among controls. At an initial concentration of 0.4 $\mu\text{C}/\text{ml}$, however, a significant number of deaths occurred. On the basis of measurements of accumulated Sr^{89} , the median total accumulated dose of internal beta radiation varied from 1,580 to 27,550 rep at daily (24 hour) rates of 50 to 680 rep. Lethal doses for goldfish in aquaria in which Sr^{89} was replenished monthly were similar to those given in a single dosage. This similarity was also observed for lethal doses in single experiment with (Ba-La)¹⁴⁰. (ADD)

774

Prosser, C. Ladd, William Pervinsek, J. Arnold, G. Svihla, and P. C. Tompkins. ACCUMULATION AND DISTRIBUTION OF RADIOACTIVE STRONTIUM, BARIUM-LANTHANUM, FISSION MIXTURE AND SODIUM IN GOLDFISH. Univ. of Chicago Metallurgical Lab. Feb. 15, 1945. Decl. Nov. 18, 1946. 40p. (MDDC-496)

Small non-feeding goldfish accumulated radioactive strontium, barium-lanthanum, fission mixture elements and sodium from solution in which they were immersed. Accumulation was rapid initially and continued at a rate greater than the loss of radioactivity in the medium by decay and adsorption. Hence, the ratio of the concentration of active material in the fish to that in the solution increased with time. After a few days this concentration ratio was usually between 10 and 100. The concentration ratio was independent of dose over the range investigated (0.01 μC to 1.0 $\mu\text{C}/\text{ml}$). Calcareous tissues, such as skeleton and scales, accumulated about 75% of the radio-strontium and radio-barium in the whole fish. Lanthanum and a mixture of cerium, yttrium and zirconium-columbium appeared to be accumulated in visceral tissues, especially the intestine, and to be more actively adsorbed on feces and glass than were the alkaline earths. The comparable distribution, particularly of bone-seekers, on immersion and injection indicated that these elements were taken up through gill and oral membranes and were distributed by the blood. Radio-sodium was present in greater proportion in the gills at six hours than later. Fission mixtures shifted in abundance from soft parts to bony portions of the gills during the first few days. Injection experiments indicated that there was no fecal excretion of strontium but that there was a small amount of fecal excretion of Ba^{140} - La^{140} and of fission mixture. Some fission mixture components appeared to be taken out of the medium, either from feces or water, and precipitated along the intestinal folds. The yolk of eggs in ripe ovaries accumulated some components of fission mixture but not strontium or barium. Young growing or regenerating bone accumulated more radio-

active material than did older bone; cartilage accumulated none of the bone-seekers. Large mature goldfish accumulated radioactive material more slowly than did small fish. This may have been in part related to their calcium turnover. Uptake of strontium⁹⁰ and uptake of fission mixture were shown to be greater when the surrounding pond water was low in calcium (1.8 p.p.m.) than when it was high in calcium (36 p.p.m.). Inactive strontium also retarded the uptake of radio-strontium. When the fish were transferred from active to inactive pond water they lost some Ba-La and fission mixture radioactivity from soft tissues during the first few hours but they did not lose the major part of their radioactivity any faster than by decay alone. The rate of loss of radio-strontium appeared to be unaffected by the calcium content of the water. Goldfish were unable to desorb any appreciable quantities of fission elements from suspended clay. (ADD)

775

Richards, Paul I. and Benjamin A. Rubin. IRRADIATION OF SMALL VOLUMES BY CONTAINED RADIOISOTOPES. *Nucleonics* 6, No. 6, 42-9(1950).

This paper treats the problem of radiation dosage where the average path length of the emitted β particle is a significant fraction of the dimensions of the volume being internally irradiated. A calculation of this type is particularly useful when considering the decay of radioactive substances within small organisms. The fraction of ionizing energy escaping from a slab is calculated for low-energy radiation (nonuniform energy loss in slab) and for very energetic radiation (uniform energy loss) and is plotted as a function of S/R , where S is the slab thickness and R the range. Other special cases are considered, i.e., strips long compared to R with width $b < R$ and $S < b$; the correction to this for smaller strips; thin circular disk of thickness $S < (\text{radius}) r < R$; the case where one dimension of the body is large compared to R but the other two are R or less; the case where all dimensions are small, but the deviations from sphericity is an elongation rather than a flattening. 11 references. (NSA)

776

Rossi, Harald H. and R. Hobart Ellis. DISTRIBUTED BETA SOURCES IN UNIFORMLY ABSORBING MEDIA. I. *Nucleonics* 7, No. 1, 18-25(1950).

Values of dose and flux may be estimated if a beta-emitting isotope is uniformly distributed in a limited region of a biological medium, and if such a "distributed source" has one of a number of simple geometric shapes. In this introduction to the subject, theoretical consideration is given to doses and flux received from point sources, half spaces, slabs, planes, and spheres. The concluding portion of this article, Part II, in *Nucleonics* (1950) Aug. will be devoted to practical applications of the method. (NSA)

777

Salerno, Paul R., H. L. Friedell, James H. Christie, and Marvin Berg. THE SYNERGISTIC LETHAL ACTION OF CERTAIN RADIOISOTOPES IN RATS. Western Reserve Univ. School of Medicine. Oct. 22, 1951. 15p. (NYO-1624)

Synergistic lethal action has been clearly established with a number of internally distributed radioactive isotopes. The synergism appears to be a function of the simultaneous radiation injury of two separate systems. It would appear that the reticulo-endothelial system and the hematopoietic systems are closely related and the effects are much more profound when both are injured, than when the injury is confined to either one. An attempt to clarify the relationship between these two systems will be made by further experiments. It is to be noted also that when two

different isotopes are restricted to the same organ system by virtue of their distribution, the effects appear to be due to simple summation. (Authors)

778

Schubert, Jack. ESTIMATING RADIOELEMENTS IN EXPOSED INDIVIDUALS--II. RADIATION DOSAGE AND PERMISSIBLE LEVELS. *Nucleonics* 8, No. 3, 66-78 (1951).

The practical side of judging the amounts and fates of radioactive substances that enter a worker's body involves consideration of arbitrary standards. These standards interrelate physiological data on "standard man" and the properties of the radioelements most harmful to him. 38 references. (NSA)

779

Wahlberg, T. A METHOD FOR THE DETERMINATION OF THE RADIATION DOSE PRODUCED BY ARTIFICIAL RADIOACTIVE SUBSTANCES IN TISSUE. *Acta Radiol.* 30, 291(1948).

A method is described for the determination of the radiation dose and activity by means of ionization measurements when radioactive substances are distributed in the body. The relationship of equivalent r and mc units expressed in the equation $1 mc/g = 7.1 \times 10^{-7} V_{\beta} e.r./sec$, where V_{β} is the mean energy of the β -particle in ev , and $e.r.$ is the equivalent roentgen defined as the energy absorbed per gram of air irradiated with a radiation quantity of one r , can be directly measured and tested by this apparatus. The radiation dose at a point within the body is measured by the ionization of an air-filled cavity around the point. The ionization is in turn defined in terms of electrostatic units/cm. The method of measurement is based on definitions and facts included in the article. Measurements show that the magnitude of the dose, within a margin of error, is the same whether the radioactive substance is distributed in water, soft tissue, or bone tissue. (NSA)

Arsenic

780

Ducoff, Howard. PROGRESS REPORT: PRODUCTION OF ARSENIC 76 AND IN VITRO METABOLISM OF ARSENIC, p.162-8 of BIOLOGICAL AND MEDICAL DIVISIONS QUARTERLY REPORT, NOVEMBER 1948 TO FEBRUARY 1949. Argonne National Lab. Feb. 1, 1949. 6p. (ANL-4253(p.162-8))

The rate of entry of As^{76} as arsenite into rabbit erythrocytes in whole blood, in suspension in plasma, and in suspension in saline was measured at 37° and at 5° . The concentration of radioarsenic within the cell fluid was found to exceed that in the suspension medium; the effect was more marked at 5° than at 37° . Decline of activity in As^{76} -tagged rabbit erythrocytes resuspended in plasma and in saline was measured at 37° . The substitution of arsenate for phosphate in some steps of the glycolytic cycle is discussed as a possible factor influencing uptake of As . (ACD)

781

Ducoff, Howard S., William B. Neal, Robert L. Straube, Leon O. Jacobson and Austin M. Brues. BIOLOGICAL STUDIES WITH ARSENIC⁷⁶. II. EXCRETION AND TISSUE LOCALIZATION. *Proc. Soc. Exptl. Biol. Med.* 69, 548-54(1948).

Arsenic excretion was studied in man, rats, and rabbits. Less than 10% of the excreted arsenic is found in feces in any of these species; rats have by far the slowest rate of excretion. Data are given for arsenic distribution in various organs in man, the rat, the rabbit, and 2 strains of mouse. The degree of individual variation within each

species was very great; in contrast to man and to other animals studied, the rat retains most of the injected dose in the blood for a considerable length of time. The ratio of arsenic concentration in kidney, liver, and spleen of healthy inbred mice was found to be fairly constant for a given time after administration, and this ratio is suggested as a criterion for effects of various types of treatment. Using this ratio as criterion, it was found that arsenic distribution is altered by the presence of transplanted tumors. Factors changing arsenic distribution are discussed in relation to effects on levels of sulfhydryl-containing substances. (NSA)

782

Lanz, Henry, Jr., Patricia C. Wallace, and Joseph G. Hamilton. METABOLISM OF ARSENIC IN LABORATORY ANIMALS USING ARSENIC 74 AS A TRACER. Univ. Calif. (Berkeley) Publ. Pharmacol. 2, 263-82(1949).

The metabolism of As was studied following intramuscular injection of $\text{Na}_3\text{As}^{74}\text{O}_4$ into rats, dogs and other animals. (R.D.B.)

Barium-Lanthanum

783

Finkle, R. D., R. H. Snyder, and Walter E. Kisielecki. ACUTE RADIOTOXICITY OF (BA-LA)¹⁴⁰ IN RATS AND MICE. PART IV. LETHAL ACTION AND CLINICAL SYMPTOMS. Univ. of Chicago Metallurgical Lab. [nd] Decl. Aug. 12, 1947. 6p. (MDDC-1207; CH-3825)

In the (Ba-La)¹⁴⁰ experiments, rats and mice were injected intraperitoneally with toxic doses of radiobarium. The dose of (Ba-La)¹⁴⁰ necessary to kill 50% of the injected mice in one month was about 3 to 5 $\mu\text{c/g}$. The dose required to kill half of the injected rats in 90 days was about 4 $\mu\text{c/g}$. The mice that died and some of those that recovered showed outward symptoms of injury. They were lethargic, and there was usually some loss of hair. Before death, the eyes became watery and the lids encrusted, and finally, the eyes were sunken and nearly closed. The eye symptoms and lethargy noticed in the mice were also apparent in the rats. The animals were usually nervous and irritable when disturbed. Large quantities of inert barium chloride were injected subcutaneously into mice. A similar experiment with inert lanthanum was performed. The experiment designed to test chemical toxicity of barium and to test another route of administration was unsatisfactory. (ADD)

784

Snyder, R. H., George A. Sacher, and J. D. Toresi. ACUTE RADIOTOXICITY OF (BA-LA)¹⁴⁰ FOR RATS AND MICE. PART III. EFFECTS ON WEIGHT AND FOOD INTAKE OF ANIMALS TREATED WITH (BA-LA)¹⁴⁰. Univ. of Chicago Metallurgical Lab. June 24, 1947. Decl. Sept. 15, 1947. 23p. (MDDC-1343; CH-3832)

In the (Ba-La)¹⁴⁰ experiments mice and rats were injected intraperitoneally with toxic doses of radiobarium. The weight curves indicate that there was definite retardation of growth in mice at 2.25 $\mu\text{c/g}$ and in rats at 1.96 $\mu\text{c/g}$. The threshold for weight loss was, therefore, about half of the midlethal dose for each species. There was a permanent, roughly constant deficit of growth after injection, which increased in magnitude with the size of the dose at a rate of 2.72 ± 0.25 per cent per $\mu\text{c/g}$. Graphs and charts are included. (ADD)

785

Snyder, R. H., W. E. Kisielecki, D. S. Anthony, and R. D. Finkle. ACUTE RADIOTOXICITY OF (BA-LA)¹⁴⁰ IN RATS AND MICE. PART II. METABOLISM OF (BA-LA)¹⁴⁰.

Univ. of Chicago Metallurgical Lab. June 1946. 17p. (MDDC-1279; CH-3826)

In these experiments mice and rats were injected intraperitoneally with toxic doses of (Ba-La)¹⁴⁰. Absorption was relatively rapid and excretion was considerable during the first day. Mice usually excreted 25% of the injected dose by 12 hours, and rats excreted a comparable amount by 50 hours. This excretion rate was comparable to that reported by Hamilton who found for rats a total excretion, in four days, of about 46% Ba^{133} and 25% Ba^{140} . Excretion declined rapidly so that after six days, mice excreted 0.4% and rats excreted 0.5% of the injected dose per day. In rats, a little more than twice as much Ba^{140} was excreted in the feces as in the urine. In mice, about 45% of the injected dose of Ba^{140} was deposited in bone, and in rats, about 60% of the dose was deposited there. In both species, these values represent practically all of the retained Ba^{140} . Absorption and decay curves on soft tissues, however, show that most of the injected La^{140} was present in the spleen, liver, and kidney immediately after injection. Limited data indicated that practically none of the La^{140} formed in bone by Ba^{140} decay left the bone for the soft tissues. It can be concluded that the excretion and distribution of radiobarium, and the distribution of radiolanthanum at the toxic levels are comparable to those at the tracer levels. No significant variations of barium metabolism with the size of dose were noted in mice. With rats, however, large (lethal) doses were retained more completely by the skeleton than were the lower doses. It is likely that this effect of dose represents a "flooding" of the excretion apparatus and, therefore, is dependent on the amount of inactive barium injected with the Ba^{140} . The authors did not have the opportunity to confirm both the observation and explanation with a larger number of animals. (ADD)

Beryllium

786

Crowley, Josephine F., Joseph G. Hamilton, and Kenneth G. Scott. THE METABOLISM OF CARRIER-FREE Be^7 IN THE RAT. J. Biol. Chem. 177, 975-84(1949) (AECD-2254; UCRL-148)

Recent studies have shown that the soluble Be compounds are toxic, and the toxicity is a function of both Be and the anionic part of the molecule. Acute beryllium poisoning manifests itself in at least three organ systems of the body, midzonal necrosis of the liver, necrosis of the distal third of the proximal convoluted tubule of the kidney, and poisoning of the hemopoietic system leading to anemia and leucocytosis. Owing to the necessity of using at least micrograms of material when studies are made with stable isotopes of beryllium, it is difficult to measure the normal metabolism of beryllium because of its toxicity. When a radioactive isotope of this element is used the actual number of beryllium atoms which can be traced is reduced by a factor of at least 10^5 . For this reason it is possible to ascertain the manner in which the normal animal handles extremely minute amounts of beryllium which are far below the possible levels of chemical toxicity. The metabolism of beryllium in the rat has been investigated with tracer amounts of carrier-free Be^7 . About one half microcurie of Be^7 in an ionic solution was administered to each rat via intramuscular injection. Within 24 hours 40% of the Be^7 had been absorbed from the injection site and 53% of the absorbed Be^7 had been eliminated from the body, mainly in the urine. By the 64th day after injection, a total of 80% had been absorbed from the injection site and 70% had been eliminated from the body. Of the absorbed Be^7 which re-

mained in the body, the major portion was taken up by bone. Within 24 hours after injection, the bone had accumulated 29.4% of the absorbed Be^7 and maintained this level to the 64th day, when the bone contained 26.9% of the absorbed material. Many of the soft tissues of the body demonstrated a small initial uptake followed by a ten fold decrease in Be^7 content by the 64th day. The radio-beryllium content of the spleen and muscle remained relatively constant throughout the interval of the experiments. Less than 0.1% of the Be^7 administered orally was absorbed from the intestinal tract. (NSA)

787

Scott, J. K., W. F. Neuman, and Roberta Allen. EFFECT OF ADDED CARRIER ON THE DISTRIBUTION AND EXCRETION OF SOLUBLE BERYLLIUM 7. J. Biol. Chem. **182**, 291-8(1950).

When Be^7 only (9.3×10^{-11} g/kg for rats, 4.4×10^{-11} g/kg for rabbits) was injected intravenously, most of the Be^7 was excreted in the urine and deposited in the bone. When carrier plus Be^7 was injected, Be was found in the liver, spleen and bone marrow also. The clearance of Be from the blood was much faster when Be^7 only was injected than when Be plus Be^7 was injected. Significant amounts of Be were excreted in feces of rats when Be plus Be^7 was injected. (CA)

Calcium

788

Copp, D. Harold, Joseph G. Hamilton, D. C. Jones, D. M. Thomson, and C. Cramer. THE EFFECT OF AGE AND LOW PHOSPHORUS RICKETS ON CALCIFICATION AND THE DEPOSITION OF CERTAIN RADIOACTIVE METALS IN BONE. Radiation Lab., Univ. of Calif. Sept. 1951. 31p. (UCRL-1464)

The effect of age and low-P rickets on the retention of Ca^{45} , $\text{Sr}^{89,90}$, Ba^{140} , Y^{88} , and Ce^{144} in bone was investigated. The radioactive metals were injected into young growing rats in which there was active growth of new bone, young rats with low-P rickets in which new osteoid matrix was forming but deposition of bone salt did not take place, and mature adult rats in which bone growth had practically ceased. Urine and feces were collected separately and the animals were sacrificed after 8 days. Excreta and tissues were analyzed for radioisotope and radiographs prepared from thin undecalcified sections of bone. Data indicate the metabolism of Ca, Sr, and Ba was markedly affected by age and low-P rickets, while metabolism of other heavy metals such as Y and Ce was not affected. Radioautographs of rachitic femur show that $\text{Sr}^{89,90}$ and Ca^{45} were deposited only in the presence of bone salt, while Y^{88} and Ce^{144} and other heavy metals were also laid down in uncalcified osteoid matrix. Kinetic studies of skeletal uptake and excretion of radiocalcium and radiostrontium showed considerable mineral exchange, even in adult rats. Skeletal uptake was more rapid and greater in growing animals, and the radioactive isotopes remained fixed in the new bone salt. In rachitic rats the initial uptake by bone was rapid, but Ca^{45} or $\text{Sr}^{89,90}$ was then rapidly lost from the skeleton and excreted in urine. When normal animals were injected with Ca^{45} or $\text{Sr}^{89,90}$, and then fed a diet low in P, the excretion of the radioactive isotopes in urine was increased, and removal from the skeleton was accelerated. (NSA)

789

Dudley, R. A. and B. M. Dobyns. THE USE OF AUTORADIOGRAPHS IN THE QUANTITATIVE DETERMINATION OF RADIATION DOSAGES FROM CA 45 IN BONE. Science **109**, 327-8(1949).

An autoradiographic technique capable of quantitatively measuring local dosage rates in tissue, currently being applied to the study of radioactive Ca^{45} dosages in bone, is described. The technique is similar to that described by Axelrod and Hamilton (Am. J. Path., **23**: 389(1947)) in their radioactive sulfur and arsenic studies of mustard gas and lewisite concentration in the skin and eye tissues. It consists of making an autoradiograph of the tissue being studied, producing calibration exposures from radioactive sources of known activity on the same film, developing the tissue and calibration exposures simultaneously, and comparing their blackening microphotometrically. The application of the technique to studies on the Ca^{45} bone-uptake in the dog is discussed and autoradiographs and a microphotometer record obtained in such experiments are given. It is noted that, if the same dilution that exists in dogs also exists in humans, the maximum local dosage rate would be a permissible 0.034 reps/day. (NSA)

790

Falkenheim, Marlene, Elizabeth E. Underwood, and Harold C. Hodge. CALCIUM EXCHANGE AS THE MECHANISM FOR ADSORPTION OF THE RADIOACTIVE ISOTOPE BY BONE. J. Biol. Chem. **188**, 805-17(1951) (AECU-95; UR-53)

The exchangeable bone calcium represents at the most less than 20% of the total bone calcium; this fraction is of the same order of magnitude as that previously reported for the exchangeable bone phosphate. This reaction is reversible to the same "quasi equilibrium" point. (Author's abstract)

791

L'Heureux, Maurice V., Wilbur R. Tweedy, and Elinor M. Zorn. EXCRETION OF CALCIUM⁴⁵ BY NORMAL RATS. Proc. Soc. Exptl. Biol. Med. **71**, 729-32(1949).

Graded amounts of labeled Ca (0.07 - 14.0 mg) were injected subcutaneously and the relative proportions excreted in the urine and feces were determined. (CA)

792

Lienke, R. I., George Cullen, and Wallace D. Armstrong. STUDIES ON THE EXCRETION AND DISTRIBUTION OF RADIOACTIVE CALCIUM. Trans. Conf. Metabolic Inter-relat., 1st Conf. 73-6(1949).

The fate of Ca^{45} was followed during and after the continuous intraperitoneal injection of $\text{Ca}^{45}\text{Cl}_2$ in rats. Absorption from the peritoneal cavity was incomplete. Significant amounts of Ca^{45} was excreted in the feces. Of the tissues, the skeleton retained by far the largest amount of Ca^{45} . (CA)

793

Norris, William P. METABOLISM OF BONE-SEEKING ELEMENTS, p.78-9 of CONFERENCE ON BIOLOGICAL APPLICATIONS OF NUCLEAR PHYSICS. Brookhaven National Lab. 1948. 1p. (BNL-C-4(p.78-9))

Discussion of the metabolism of bone-seeking elements: Ca^{45} , Sr^{89} , or Ra in rats; intravenous injections. (S.V.S.)

794

Norris, William P. and Walter Kisielleski. THE METABOLISM OF INTRAVENOUSLY INJECTED CALCIUM⁴⁵, p.134-9 of MEDICAL AND BIOLOGICAL DIVISIONS, QUARTERLY REPORT, NOVEMBER, DECEMBER, JANUARY, 1948-1949. Argonne National Lab. Feb. 1, 1949. 5p. (ANL-4253(p.134-9))

As part of a study of the metabolism of the alkaline earths, rats were injected intravenously with calcium 45 (1.5 mg. Ca and 45 μc calcium 45 per rat) and its metabolism was studied. The animals were sacrificed at intervals of 1, 5, and 20 minutes at 1, 6, 24, and 72 hours, and at 10, 30, 70, 124, and 200 days after injection. Excreta samples

were collected and each rat was analyzed in 16 parts that included several of the soft tissues, bone, blood, pelt, muscle, and residual carcass. The metabolism of intravenously-injected calcium was found to proceed in a fashion that was qualitatively similar to that reported for Sr and Ra. The bones were observed to take Ca from the blood at a rapid rate with the retention at 10 days being 90% of the injected dose and the maximum content being reached at about 400 minutes. The biological half-time in bone was approximated to be in the order of 50 to 500 years. Ca in the soft tissues was found to be in rapid equilibrium with blood Ca. Within six hours after injection the specific activity (per cent injected dose per mg. Ca^{40}) in the blood, soft tissues (kidneys, lungs, liver, gastrointestinal tract, testes, muscle, pelt), urine, and feces became almost identical and continued so for the duration of the experiment. (ACD)

795

Singer, Leon and W. D. Armstrong. RETENTION AND TURNOVER OF RADIOCALCIUM BY THE SKELETON OF LARGE RATS. *Proc. Soc. Exptl. Biol. Med.* **76**, 229-33 (1951).

The Ca specific activities of the femoral epiphyses, femoral diaphyses, humeri, lumbar vertebrae, and the remainder of the skeleton of large rats differ soon after administration of Ca^{45} but decrease to a common value after 52 days, following which the specific activities decline at equal but much reduced rates. The retained fraction of the dose of Ca^{45} declines to 42-45% on the 52nd day, after which excretion is slow. These results indicate the existence in large rats of two kinds of skeletal Ca which differ markedly in their rate of turnover and in the length of time over which they fix injected Ca. Some data on the Ca^{45} activity of the urine and teeth are also given. (CA)

Carbon

796

Armstrong, Wallace D. and S. H. Zbarsky. EXCRETION AND DISTRIBUTION OF CARBON 14 DURING AND FOLLOWING CONTINUOUS INTRAPERITONEAL INJECTION OF CARBON 14 AS SODIUM CARBONATE. *Trans. Conf. Metabolic Interrelat. 1st Conf.* 67-71(1949).

The distribution of carbon 14 in continuous injection is similar to that after a single intraperitoneal injection, although a somewhat larger fraction is taken up by the tissues. The device used for continuous injection of rats is described briefly. (CA)

797

Bloom, William. DEPOSITION OF C^{14} IN THE METAPHYSIS OF LONG BONES OF YOUNG RATS. *Anat. Record* **103**, 425(1949).

The following is an abstract and is reproduced here in its entirety.

In 1947, Bloom, Curtis and McLean reported that in rats examined three days to 4 months after injections of $\text{NaHC}^{14}\text{O}_3$ little or none of the isotope was demonstrable in autoradiographs of the metaphysis of long bones. The study of more animals and earlier intervals has shown that the above statement is true but that it is not correct for the first two days after injection. Seven newly weaned rats were examined within two days after intraperitoneal injection of $2 \mu\text{C}$ of C^{14} per gram. Autoradiographs show that the isotope is deposited immediately in large amounts in the metaphysis. However, the relatively weak beta particles emitted apparently do not interfere with the growth of the bone, for by 48 hours the "old" metaphysis with C^{14} has been almost entirely resorbed. The "new" metaphysis

which has formed is devoid of radioactivity except for the tips of the trabeculae of the secondary spongiosa. This is in contrast to those bone-seeking isotopes emitting alpha or strong beta particles which, in the dosages we used previously, interfere with growth at the metaphysis.

798

Bloom, W., H. J. Curtis, and F. C. McLean. A NOTE ON THE DEPOSITION OF C^{14} IN BONE. *Science* **105**, 45 (MDDC-516)

The autoradiographs of the bones of rats injected with carbon 14 show a markedly different picture from those of the strontium 89 rats. Those from rats killed three days after injection of carbon 14 show the shaft of the bones as black lines. The bone in the epiphysis is a faint grey, while the metaphysis of the growing end of the bone is negative or practically so, leaving a gap of about 2 mm between epiphysis and diaphysis. The non-growing end of the bone is completely outlined in grey. The marrow cavity is so pale that it is probably negative. The autoradiographs of the 2, 4, 8, and 16 week specimens show essentially the same picture as those after three days, except that the bones have grown in length and width. With the growth in length, the unblackened zone at the metaphysis increased to 3-4 mm at two weeks, 4 mm at four weeks, 10 mm at eight weeks and 12-17 mm at 16 weeks. Since the blackened lines representing the lateral extent of the diaphysis at the time of injection are still present after 16 weeks, it would seem that the marrow cavity did not increase much in diameter at the site of deposition of radioactive carbon. However, new bone was deposited externally so that the bone as a whole increased in thickness. Sections of the liver and kidney gave fairly intense autoradiographs at the 3-day and 2-week stages, but were negative after the longer intervals. Since the films were exposed for the same length of time, it would appear that there was approximately as much carbon 14 in the bones after 16 weeks as after three days, while there was a great decrease in the carbon 14 content of the soft tissues. From the autoradiographs of bones of these few rats it is concluded that carbon 14 injected as carbonate appears primarily in those areas occupied by pre-existing bone. It does not appear in appreciable quantities in the areas of most recently deposited bone salt. This observation demands further study on the carbon metabolism of bone. Since the carbon 14 content of the bones did not decrease appreciably in four months, it is believed that the health hazards involved in working with this isotope must be studied. Particular attention should be paid to the possible development of bone tumors. (ADD)

799

Brues, Austin M. and Agnes N. Stroud. RETENTION OF C^{14} ADMINISTERED AS BICARBONATE TO ADULT AND EMBRYONIC MICE. *Argonne National Lab. Nov.* 1950. 19p. (AECU-1091; UAC-326)

Mice were exposed to $\text{Na}_2\text{C}^{14}\text{O}_3$ by injection, followed by a 10-hr period of rebreathing their expired air. Observations have been made on tissue C^{14} concentration to 10 months after exposure in adults and 20 months in mice exposed as embryos. Eventual loss rates in exposed embryos were parallel to those in exposed adults. The retention in various organs follows roughly a logarithmic function with concentration decreasing as the square root of time. This relationship holds, within a factor of 2, from 1 day to 10 months after exposure. It is possible that this curve may represent a series of exponential decay rates, and certainly no conclusions can be drawn as to the fate of C^{14} beyond the period of investigation. Bone carbonate C^{14} disappears somewhat more slowly than organic C^{14} . Consideration is given to the further data required to determine

safe human exposure values to $C^{14}O_2$ and $Na_2C^{14}O_3$. It is obvious that present values are much more conservative than necessary. 12 references. (NSA)

800

Buchanan, Donald L. ELIMINATION OF INTRAVENOUS CARBON¹⁴ BICARBONATE BY MAN. *J. Clin. Invest.* **30**, 630-1(1951) (AECU-1262; UAC-359)

A body of data has been obtained concerning the excretion rates and tissue retention of inorganic C^{14} administered to rats and mice. The present study compares the human excretion of injected $NaHC^{14}O_3$ to rates observed in smaller animals in order to provide a basis for the computation of permissible human doses of this isotopic compound. In this work 10 μ c of material was injected intravenously into healthy human volunteers and all expired CO_2 was collected in fractions during the following 3 hr. With the subject at rest, approximately 75% of the radioactivity is exhaled as CO_2 during the 1st hour; 90% is gone in 2 hr; and 95% has been blown off at the end of the 3rd hr. Within the error of the methods used the rate of isotope excretion by different-sized animals is proportional to the metabolic rate per unit mass of animal. When published data of others are included, this relation seems valid for animals as large as the cow (Kleiber) and as small as the mouse. On this basis the extrapolation to man of information obtained in long-term experiments with rats and mice indicates that an intravenous injection of 20 to 40 mc of $NaHC^{14}O_3$ or the inhalation of a comparable amount of $C^{14}O_2$ would be required to give a 70-kg man a total radiation dose of 1 roentgen equivalent over his entire life span. (NSA)

801

Buchanan, Donald L. UPTAKE AND RETENTION OF FIXED CARBON IN ADULT MICE. *J. Gen. Physiol.* **34**, 737-59(1951).

Mice were continuously exposed to air containing $C^{14}O_2$. The specific radioactivities of urea C, total fecal C, and numerous components of tissue C were compared as a function of the duration of exposure with the radioactivity of the air CO_2 . The data indicate that the total CO_2 fixed from the air is proportional to its concentration in the air. The rates of uptake at the beginning of the exposure and the rates of loss at the termination of the exposure differed strikingly among the tissues studied. However, the ultimate ratio of fixed air- CO_2 C to total C in these tissues seemed to be approaching limiting values which would not vary by more than a factor of 3 from one another. It appears that of the total organic C in an adult mouse, approximately 0.01% may originate directly from the CO_2 of the air when the animal respire in air having a CO_2 concentration of 0.03%, and that 1.8% or more of the total C may originate from CO_2 within the animal. Data are presented which indicate the life span of the mouse erythrocyte to be 49 days. The continuous permissible level for mice is given as 31 μ c/m³. 28 references. (NSA)

802

Govaerts, J. RATE OF ELIMINATION OF C^{14} ADMINISTERED AS $BAC^{14}O_3$. *Science* **111**, 467-9(1950).

After a brief review of previous work, experiments are described in which nine mice received intravenous injections of a fine suspension of $BAC^{14}O_3$ in isotonic glucose in order to deposit the barium carbonate in the lungs in a time determined by preliminary experiments. The animals were placed in metabolic cages for the duration of the experiments. Expired CO_2 , urine, and feces were collected and analyzed for counts. After the animals were sacrificed, the lungs, kidney, liver, and spleen were removed and prepared for assay using the Van Slyke-Foche method. The data are presented graphically and discussed; the author

concludes that most of the C^{14} absorbed by the organism as barium carbonate is expired by the lung as $C^{14}O_2$, and that the dangers to those who work with C^{14} are not so great as expected. (NSA)

803

Skipper, Howard E., Martelia J. Bell, and Juanita B. Chapman. THE HAZARD INVOLVED IN THE USE OF CARBON 14. II. THE EFFECT OF A SINGLE DOSE OF CARBON 14 LABELED SODIUM BICARBONATE ON THE PATTERN OF DEATHS FROM SPONTANEOUS LEUKEMIA IN AKM MICE. *Cancer Research* **10**, 362-3(1950).

As a portion of a study of the danger involved in research with C^{14} , the effect was studied of this isotope, as $C^{14}O_2$, on a neoplastic disease (leukemia) known to be influenced by radiation. Injection of $NaHC^{14}O_3$ at the rate of 18 μ c/mouse had no effect on the pattern of deaths from spontaneous leukemia in a leukemia-susceptible strain of mice. (CA)

804

Skipper, Howard E., Constance Nolan, and Linda Simpson. STUDIES OF THE HAZARD INVOLVED IN USE OF C^{14} ; III. LONG TERM RETENTION IN BONE. *J. Biol. Chem.* **189**, 159-66(1951).

As judged from autoradiographs made from long bones of mice injected with $NaHC^{14}O_3$, the rate of turnover of carbonate carbon by various areas in the bone cross section may be listed as follows: marrow and epiphyseal cartilage metaphysis of the growing end · epiphysis and the non-growing end · bone shaft (diaphysis). After a period of 4 months the greatest part of the injected C^{14} can be found in the bone. The approximate per cent of the injected dose retained in the skeleton was 0.25 at the end of 24 hr, 0.03 at the end of 1 month, 0.02 at the end of 6 months, and 0.01 at the end of 1 yr. The average skeletal radiation received by mice injected with 18 μ c of $NaHC^{14}O_3$ was calculated to be approximately 0.07 rep/day for the period 0 to 24 hr, 0.008 between 2 and 4 weeks, about 0.003 from 5 to 6 months, and 0.002 for the interval 10.8 to 12.7 months. The "active" volume of the bone shaft (as estimated from autoradiographs) was receiving approximately 0.16 rep/day from 1 to 2 weeks after injection of 18 μ c of $NaHC^{14}O_3$ and about 0.04 rep/day at from 5 to 6 months. A single injection of 18 μ c $NaHC^{14}O_3$ (a 50-mc man-equivalent) has resulted in radiation to certain bone-shaft cells ("active" volume) of mice which is greater than the maximum allowable radiation to tissue for man (0.04 rep/day). 5 figures. (NSA)

805

Skipper, Howard E., Locke White, Jr., and Carl E. Bryan. BODY RETENTION OF CARBON 14 FROM LABELED SODIUM BICARBONATE. *Science* **110**, 306-7(1949).

Twelve mice were injected intraperitoneally with a solution containing 2.5 mg of $NaHC^{14}O_2$ and a total activity of 18 μ c. The expired CO_2 from all animals was collected over varying intervals and two mice were sacrificed for organ and tissue analysis at 24 hr, 48 hr, 1, 2, 4, and 12-week periods. Procedures used in determining expired CO_2 and excreta have been reported. No outstanding selective accumulation of C^{14} from a gross anatomical standpoint was observed. The rate of uptake and loss by the jejunum was significantly greater than for other tissues studied. Similar doses would be considerably lower than human tolerance limits. Studies on long-term C^{14} retention from insoluble carbonates and organic substance are necessary before any final C^{14} hazard conclusions can be drawn. Data are given. (CA)

806

Skipper, Howard E., Locke White, Jr., and Carl E. Bryan. STUDIES ON THE HAZARD INVOLVED IN USE OF C^{14} .

I. RETENTION OF CARBON FROM LABELED SODIUM BICARBONATE. *J. Biol. Chem.* **180**, 1187-95(1949).

Following injn. of $\text{NaHC}^{14}\text{O}_3$ in mice, greater than 90% of the total activity injected was lost through the respiratory route in one hour. After one day most of the blood C^{14} was fixed in a noncarbonate form. No profound localization of C^{14} was observed although uptake and turnover were more rapid in the jejunum. Expts. with pregnant mice indicated that the embryos were able to fix C^{14} more rapidly than the parent tissue. Data are given on the retention of C^{14} in 9 tissues, bone, and the total body of mice at various intervals after intraperiton. injns. (BA)

Cerium

807

Anthony, D. S. and K. A. Lathrop. **ACUTE RADIOTOXICITY OF INJECTED CERIU¹⁴⁴ IN THE RAT.** Argonne National Lab. June 26, 1947. Decl. Sept. 19, 1947. 25p. (MDDC-1326; CH-3824)

Groups of 10 or more rats were given doses of 10, 7, 5, 3, and 2 μC of $(\text{Ce-Pr})^{144}$ per gram of body weight by intravenous injection. The metabolism of the Ce was studied and the effect of this radioactive material on the general clinical condition, survival time, and weight was observed. At no time was the excretion of cerium rapid, and in fact, it required approximately 35 days for the rats to excrete half of the injected dose. The rate of excretion of Ce^{144} in the urine fell continuously with time, while the rate of excretion in the feces rose to a maximum at about one week and then dropped with time. The ratio of the amount excreted in the urine to that in the feces fell continuously with time. The early retention of Ce^{144} was largely in the liver but this dropped rapidly with time. Apparently, some of the radiocerium released by the liver was taken up by the skeleton since the activity of the bones rose to a maximum during the period when the liver was rapidly losing its cerium. As the liver became exhausted of Ce, the activity in the skeleton dropped with time. The rats that died within the first 30 to 40 days showed an almost complete lack of gross lesions which are usually noted in radiotoxicity studies. In 4 of the 6 animals that died between 70 and 120 days after injection, there was abundant visible evidence of radiation injury to the liver. In a few animals dying at still later times, osteogenic sarcomas were found. The 30-day LD-50 for intravenously injected Ce^{144} in the rat was found to be about 3 $\mu\text{C/g}$ of body weight. By 120 days, the LD-50 was down to between 2 and 3 $\mu\text{C/g}$. At all dose levels there was a diminution of the growth rate as measured by increase in body weight. (ADD)

808

Overstreet, R., L. Jacobson, K. Scott, and H. Fisher. **RADIO CERIU¹⁴⁰** (CE^{>140}) Argonne National Lab. [nd] 1p. (MDDC-1142-B; CH-554; A-678)

Preparation without Carrier—Radio cerium has been prepared from a uranium fission mixture without the use of Ce carrier. Thorium was used as a carrier and the thorium and cerium finally separated from one another by iodate precipitation. The identity of the purified radio cerium without carrier was demonstrated by the following procedure: (1) Chemical identification with the use of inert Ce as a carrier upon an aliquot fraction of the final purified solution. (2) Confirmation of the presence of short-lived praseodymium daughter which was described by Spedding. (3) Beta-ray absorption curves were found to be comparable to those published in various reports of the chemistry group. **Tracer Studies**—A large group of animals have

been injected with $\text{Ce}^{>140}$ (including some unknown activities) by intraperitoneal and intramuscular injection without carrier. A sufficient number have been injected so that they may be sacrificed in groups of three extending from one day period to the 64 day period. In addition some animals have received $\text{Ce}^{>140}$ by stomach tube. Preliminary results, which include, the one, four, eight, and sixteen day period, reveal that $\text{Ce}^{>140}$ is handled in a manner very similar to that observed with La^{140} . No significant absorption occurs by way of the digestive tract. Considerable retention by the lungs was noted when the radio cerium was administered directly into this organ. A full report will follow. (ADD)

809

Seibert, H. C. and R. Abrams. **ACUTE TOXICITY OF INHALED 275-DAY CE¹⁴⁴.** Argonne National Lab. July 25, 1946. Decl. Sept. 6, 1946. 26p. (MDDC-329; CH-3539)

In an attempt to estimate the acute toxicity of insoluble, radioactive material in the lungs, rats were exposed to smokes containing 275-day Ce^{144} . Groups of 200-g rats received the following doses: 3.2, 14, 39, 50, and 200 $\mu\text{C/rat}$. Weight loss was significant only in those exposed to 200 μC . These had a median survival time of 39 days and were all dead within 120 days. The 39 μC rats had a median survival time of 282 days, while 90% of the 14 μC animals were still alive after 300 days. As has been demonstrated in tracer experiments, absorption from the lungs was slow, and liver and skeleton were the primary sites of deposition of the absorbed material. It was not possible to show any definite effect of dose on distribution. Radiation doses to the various tissues were calculated, but, in general, it was not possible to correlate death with the dose to any single tissue. Preliminary histological examination revealed some tendency for the bronchial epithelium to undergo a squamous proliferation. (ADD)

Cobalt

810

Braude, R. **THE DISTRIBUTION OF RADIOACTIVE COBALT IN PIGS.** *Brit. J. Nutrition* **3**, 789-92(1949).

Two female pigs were fed diets containing a mixture of Co^{56} , Co^{57} , and Co^{58} , for 43 days. The relative amounts of radioactive Co found (values tabulated) in most organs were similar to those found by Comar and Davis, except that the values for the pancreas, liver, and bile were lower, and those for cartilage and long bones were higher. (CA)

811

Comar, C. L. and George K. Davis. **COBALT METABOLISM STUDIES. IV. TISSUE DISTRIBUTION OF RADIOACTIVE COBALT ADMINISTERED TO RABBITS, SWINE, AND YOUNG CALVES.** *J. Biol. Chem.* **170**, 377-89(1947).

The tissue distribution of radioactive Co when given either by vein or orally was determined and the concentrations in most tissues were tabulated for rabbits, swine, and young calves. No species difference of Co metabolism or distribution was noted. Young calves absorbed more from the intestinal tract than did older animals but distribution was the same. About 95% of intravenous Co was removed from the blood in a few minutes, that which remained being almost entirely in the plasma. About 65% is ultimately excreted in the urine and about 30% in the feces. After 17 hours the blood contained 0.035 γ and the liver 3.56 $\gamma/100$ g. The Co concentration in the pancreas was about $\frac{1}{4}$ that in the liver and twice that in the spleen. The concentration in red bone marrow was about $\frac{1}{2}$ that in the spleen and 3 times that of white bone marrow. (CA)

812

Comar, C. L. and George K. Davis. COBALT METABOLISM STUDIES. III. EXCRETION AND TISSUE DISTRIBUTION OF RADIOACTIVE COBALT AS ADMINISTERED TO CATTLE. *Arch. Biochem.* **12**, 257-66(1947).

A dipping type of Geiger-Müller counter was used for the determination of radioactive Co in cattle tissue and excreta. Approx. 18% of the orally administered Co appeared in the feces, but only traces in the urine. When Co was injected, about 62% appeared in the urine and about 33% in the feces. Significant quantities of Co were found in the urine 40 min. after injection. The estimated amount of Co eliminated by daily biliary secretion was 5-15% of the injected Co. Co injected into animals which were deficient in Co was distributed in practically every tissue and organ of the animal with the higher concentrations of Co in the glandular tissues, particularly the adrenals, thyroid, liver, thymus, intestinal lymph glands, and the pancreas. Co accumulation in muscle tissue was small, and there was no particular accumulation in the spleen or red bone marrow. Significant quantities of Co are transmitted from the dam to the fetus. (CA)

813

Comar, C. L., George K. Davis, and Ruth F. Taylor. COBALT METABOLISM STUDIES. I. RADIOACTIVE COBALT PROCEDURES WITH RATS AND CATTLE. *Arch. Biochem.* **9**, 149-58(1946).

A procedure is described for the determination of Co in metabolism studies. Radioactive Co is administered orally or intraperitoneally to the experimental animal, and the Co in the HCl solution of the ash from the tissue being examined is recovered by an electroplating operation in an alkaline solution (6×10^{-10} g of Co can be detected). It was concluded from the results obtained with the piebald rat that the requirement of the rat for Co, if there is such, must be very small. With the rat, only the liver showed a small accumulation of Co, but it was not retained. Eighty per cent of Co is excreted in the feces and 10% in the urine in 24 hrs. Only 0.25% of the orally administered Co was retained by Co-deficient cattle, but 5% of the intravenously administered Co was retained with the bulk of the Co being retained in the adrenal glands. A significant amount of the injected Co was found in the abomasum contents. (CA)

814

Comar, C. L., George K. Davis, Ruth F. Taylor, C. F. Huffman, and Ray E. Ely. COBALT METABOLISM STUDIES. II. PARTITION OF RADIOACTIVE COBALT BY A RUMEN FISTULA COW. *J. Nutrition* **32**, 61-8(1946).

When 174γ labeled Co was injected into the jugular vein of a rumen fistula cow about 6% of the dose was present in the blood after several hours with the value falling to 1% or less after 10-15 days. None was found in the rumen contents, about 7% appeared in the feces, and about 65% was found in the urine with large amounts being rapidly eliminated by this path. Very small amounts were found in the milk and saliva. When 174γ labeled Co was introduced directly into the rumen, none was detected in the blood. About 82% of the dose was present in the rumen contents after 4 hrs with the amount decreasing regularly to less than 1% after 7 days. Over 65% was accounted for in the feces and only extremely small amounts in the urine. No Co was detected in the milk or saliva. (CA)

815

Culbertson, W. F. J., Audrey A. Free, and Doreen M. Thornton. DISTRIBUTION OF RADIOACTIVE COBALT IN THE RAT. *Brit. J. Nutrition* **4**, 42-8(1950).

When a diet containing 0.01-0.06 p.p.m. Co^{60} was fed to rats for 14 days 5-7% was retained. The concentrations of

Co^{60} in the organs of the rats maintained on low Co^{60} diets for 14-90 days are given. The highest concentrations were found in the liver, kidneys, spleen, and pancreas. (CA)

Europium

816

Van Cleave, C. D. A RADIOAUTOGRAPHIC STUDY OF THE LOCALIZATION OF RADIOACTIVE EUROPIUM IN CERTAIN SOFT TISSUES OF THE RAT. *Anat. Record* **103**, 514-15(1949).

The rare earth europium is one of the many fission products whose metabolism is being studied under the direction of Dr. J. G. Hamilton at Crocker Radiation Laboratory, University of California, where the work here reported was done in collaboration with Dr. Dorothy Heller. One series of rats was given an intravenous injection of 50 μc of europium per animal; another series, the same amount intramuscularly. The animals were sacrificed after 1, 4, and 16 days and samples of liver, kidney and spleen fixed in alcohol and prepared as usual for paraffin sectioning. Radioautographs were prepared using x-ray film; the tissue sections were later stained. Camera lucida drawings of the stained section, mag. $30\times$, were made; the radioautograph substituted and oriented to conform with the landmarks of the original tracing; areas of activity indicated in the autograph were marked in the tracings. Preliminary examination of the material seems consistent with the interpretation that following intravenous injection, radioeuropium is rapidly removed from the blood by the reticulo-endothelial system and at the same time excreted by the kidneys. Activity in the liver is strongest in central and hepatic collecting veins; absent in portal canal structures. Pick-up from sites of intramuscular injections is too scanty to produce autographs in spleen and kidney but not in liver. Activity in bone was not investigated.

Fission Products and Heavy Metals

817

Abrams, R., H. C. Seibert, A. M. Potts, W. Lohr, and S. Postel. METABOLISM OF INHALED FISSION PRODUCT AEROSOLS. *Univ. of Chicago Metallurgical Lab.* Apr. 16, 1946. Decl. Aug. 28, 1946. 114p. (MDDC-248; CH-3485)

This paper deals with the metabolism, in rats, of airborne fission products. Four different isotopes were used, selected for their long lives and as representatives of the various chemical species occurring in fission. There were Sr^{90} (55 days), Zr^{95} (65 days), Y^{91} (57 days), and Ce^{144} (275 days). Aerosols of these materials were produced by atomizing aqueous solutions and by burning dried residues in a carbon arc. Strontium differs from the other elements investigated in the ease with which it is absorbed from the lungs. Over 50% left the lungs within a matter of minutes, and 95% was gone within one hour. Of the Sr^{90} originally in the lung, 60% was deposited in the skeleton in less than four hours, and after 12 hours the total radiation dose to the skeleton exceeded that to the lungs. These results indicated that inhalation was as effective a means of administration as intravenous injection, and that lung damage as a result of inhalation of Sr^{90} would be of less importance than bone marrow damage. The other three elements, Y, Zr, and Ce, may be grouped together insofar as they differ from Sr. They were all eliminated from the lung much more slowly than was Sr. Thus the times required for 90% elimination were: Y^{91} , 12 days; Zr^{95} , 25 days; and Ce^{144} , 45 days. In all cases the skeleton was the major site of deposition

and eventually contained between 15 and 30% of the initial lung deposit. In no case, in periods ranging up to 200 days, did the total radiation dose to the bone exceed that to the lung, as it did within 12 hours with Sr. With all three elements the probability of radiation damage to the lung is great. Very little deposition occurred in the soft tissues. The kidney contained about 0.5% of the dose with all the elements. Concentration in the liver was lower than in the kidney with all isotopes except Ce^{140} . This element showed a very high initial liver deposition, but this was gradually eliminated so that after two months the liver concentration fell below that in the kidney. (ADD)

818

Cochran, Kenneth W., John Doull, Marcella Mazur, and Kenneth P. DuBois. ACUTE TOXICITY OF ZIRCONIUM, COLUMBIUM, STRONTIUM, LANTHANUM, CESIUM, TANTALUM, AND YTTRIUM. Arch. Ind. Hyg. and Occupational Med. 1, 637-50(1950).

Aqueous solutions or suspensions of compounds of Zr, Cb, Sr, La, Cs, Ta, and Y were administered in single doses by intraperitoneal injection or orally by stomach tube to male and female rats. Observation was made for 10 days, since the animals either recovered or succumbed during this period. The LD_{50} values are given for the various compounds used. Differences in these values are pointed out for the several compounds of each element studied, and the dependence of these values on the route of administration (oral or injection) is discussed. 28 references. (NSA)

819

Greenberg, D. M. PROPOSED PROCEDURE FOR STUDY OF REMOVAL OF LONG LIFE FISSION PRODUCTS FROM THE BODY. Argonne National Lab. [nd] 35p. (MDDC-1143-E)

A group of proposed procedures for the study of removal of long life fission products from the body has been compiled. Measures which have been tried and have a considerable measure of success are: acid or alkali administration associated with a low calcium diet; parathyroid hormone administration; high potency vitamin D; citric acid administration; displacement with non-radioactive isotopes. (ADD)

820

Hamilton, J. G. METABOLISM OF FISSION PRODUCTS. Univ. of Chicago Metallurgical Lab. Aug. 9, 1943. Decl. May 19, 1947. 30p. (MDDC-1000; CH-848)

Ce^{140} was prepared without carrier from uranium fission material. The identity and purity was confirmed by suitable chemical and physical studies which included isolation and identification of the 18 minute Radio-Praseodymium daughter. A large group of animals received a solution of Ce^{140} as CeCl_3 by different routes of administration. Its metabolic behavior in most respects qualitatively resembles those of yttrium and lanthanum although it is more poorly mobilized when administered parenterally or directly into the lungs. In this respect it more closely resembles zirconium than the rare earths. Radio-strontium without carrier was found to be chiefly deposited in the skeleton whether given either orally or by intraperitoneal injection. Approximately 15% was absorbed when given by mouth and 70% retained when injected. The rate of elimination of the assimilated strontium is slow and is less than the rate of radioactive decay of Sr^{90} . The simultaneous administration of inert Sr with Sr^{90} diminishes the skeletal deposition by as much as 50% following intraperitoneal injection. Other measures, which included the administration of NH_4Cl , sodium citrate, the parathyroid hormone, and massive doses of vitamin D were without significant effect. (ADD)

821

Hamilton, J. G. TECHNICAL PROGRESS REPORT ON THE METABOLIC STUDIES OF FISSION PRODUCTS. Argonne National Lab. May 2, 1944. Decl. June 25, 1947. 2p. (MDDC-1061; CH-1572; A-2240)

Incomplete tracer studies with plutonium indicate that less than 0.05% of this element is absorbed from the digestive tract in any of the three valence states. The behavior of plus 4 plutonium following intramuscular and intrapulmonary administration is very similar to that of zirconium. The metabolic properties of plus 3 and plus 6 plutonium are very similar to those of yttrium and plus 3 uranium. (ADD)

822

Hamilton, J. G. METABOLISM OF FISSION PRODUCTS. Argonne National Lab. Apr. 22, 1944. Decl. May 14, 1947. 27p. (MDDC-1001; CH-1659; A-2270)

A progress report emphasizing the following: (a) preparation of carrier-free Zr^{93} , (b) tracer studies with Zr^{93} and Zr^{93} , (c) intramuscular and intrapulmonary tracer studies with carrier-free Y^{88} , (d) intramuscular and intrapulmonary tracer studies with carrier-free Ce^{140} , (e) decontamination studies of radio-strontium, radio-yttrium, and radio-cerium. (ADD)

823

Hamilton, J. G. TRACER STUDIES ON FISSION PRODUCT METABOLISM. Radiation Lab., Univ. of Calif. Feb. 2, 1945. Decl. June 24, 1947. 8p. (MDDC-1062; CH-2673)

Radioactive isotopes, free from inert carrier, of Sr, Y, Zr, Cb, Ru, Te, Cs, Ba, La, Pr, Ce, and Np were administered to rats as chlorides in isotonic solutions of NaCl at pH ranging from 2.3 to 3.5. Iodine was given as NaI, and Xe was given by inhalation in an oxygen-gas mixture. Unseparated fission products, free from inert carrier and uranium, after 90 days cooling were administered in an isotonic solution of NaCl at pH 2.5. Adult rats received the various radioactive preparations in solution by oral, parenteral, and intrapulmonary administration. In the earlier experiments the parenteral administration was by way of the intraperitoneal route. Due to the difficulty of absorption of some of the radioactive isotopes, considerable retention of activity on the surfaces of the intra-abdominal organs took place. In order to gain a more accurate picture of the true deposition of these radioactive isotopes in the intraabdominal organs it became necessary to employ the intramuscular route of administration. The animals were sacrificed in groups of three for each route of administration and at varying intervals ranging from 1 to 64 days. Sixteen to 18 representative tissues were removed from each animal and their activities individually measured. The most significant conclusions that can be derived in the survey of all of the work done with the long life fission products can be summarized in the following manner: the alkaline earths, rare earths, Zr, Np, and Cb when introduced into the body are deposited primarily in the skeleton, where the average degree of retention of the absorbed radioelement is approximately 50% of the initial absorbed quantity. The retained fractions of these radioelements are eliminated at rates which are less than their rates of radioactive decay with the exception of the 340 day Ce and possibly Sr^{90} . The remaining five long-lived radioelements, Ru, Te, Xe, I, Cs do not show any significant degree of localization in the skeleton and in addition there is no very striking deposition in any other of the tissues with the exception of deposition of I in the thyroid. The rates of elimination for all of these four radioelements are much greater than their rates of radioactive decay, with the exception of I accumulated in the thyroid. In this particular

case the release of accumulated I in the thyroid is many times slower than its rate of radioactive decay. The members of the long-lived fission product group which are absorbed by way of the digestive tract include the alkaline earths, tellurium, iodine, and cesium. A high degree of retention by the lungs has been observed following direct intrapulmonary administration of the rare earths, Zr, Cb, Ru, and Np. The pulmonary retention observed for the alkaline earths, Te, I, and Cs is negligible under the conditions of the experiment. (ADD)

824

Hamilton, J. G. THE HEAVIEST ELEMENTS AND FISSION PRODUCTS. Radiation Lab., Univ. of Calif. [nd] Decl. Nov. 18, 1946. 2p. (MDDC-490)

A study has been made of the metabolism in the rat of the heaviest elements and of fission products. The heavy elements studied include thorium, protactinium, neptunium, plutonium, and americium, and the fission products investigated were radioactive isotopes of Sr, Y, Zr, Cb, Ru, Te, I, Xe, Cs, Ba, La, Ce, and Pr. In addition, a rather detailed investigation of the metabolism of an unseparated mixture of uranium fission products was undertaken. The result of these studies indicated that these heavy elements are absorbed to a very small degree by way of the digestive tract, deposited primarily in the skeleton following parenteral administration, and eliminated very slowly. The metabolism of plutonium in two human subjects was investigated and found to be comparable to the behavior of this radio-element in the rat. The most significant conclusions that can be derived in the survey of the work done with the long-lived fission products can be summarized in the following manner: Sr, Ba, Y, La, Ce, Pr, Zr, and Cb, when introduced into the body, are deposited primarily in the skeleton where the average degree of retention of the absorbed radio-elements is approximately 50% of the initially absorbed quantity. The retained fractions of these radio-elements are eliminated at rates which are less than their rates of radioactive decay with the exception of the 340-day Ce and possibly Sr⁹⁰. The remaining five long-lived radio-elements, Ru, Te, Xe, I, and Cs do not show any significant degree of localization in the skeleton and in addition, there is no very striking deposition in any other of the tissues, with the exception of the deposition of iodine in the thyroid. The rates of elimination for all of these five radio-elements are much greater than their rates of radioactive decay, with the exception of iodine accumulated in the thyroid. In this particular case, the release of accumulated iodine in the thyroid is many times slower than its rate of radioactive decay. The members of the long-lived fission product group which are absorbed by way of the digestive tract include strontium, barium, tellurium, iodine, and cesium. Radioautographic studies of the deposition of Y, Zr, Ce, U, Pu, and Am in bone indicate that these materials are selectively accumulated in the osteoid matrix. (ADD)

825

Hamilton, J. G. SUMMARY OF METABOLISM OF CARRIER-FREE FISSION PRODUCTS IN THE RAT. Radiation Lab., Univ. of Calif. May 14, 1947. 3p. (MDDC-1002; CH-775)

The following carrier-free fission products were studied to determine their effect upon the metabolism of the rat: Sr⁸⁵, Y⁸⁸, Zr⁸⁹, Cb⁹³, Ru⁹⁶, I¹³¹, Xe¹²⁷, Ba¹³³, La¹⁴⁰, Ce¹⁴⁰, and a raw fission mixture. The results are presented in chart form. (ADD)

826

Hamilton, J. G. THE METABOLISM OF THE FISSION PRODUCTS AND THE HEAVIEST ELEMENTS (PLUTO-

NIUM PROJECT SYMPOSIUM). Radiology 49, 325-43 (1947).

All radioactive elements that accumulate in bone with the exception of Sr are not deposited in the mineral structure of bone, but are localized in and adjacent to the osteoid matrix. The large fraction of La, Ce, Pr, 61, Am, and Cm, deposited in the liver was an unexpected finding, and it may be predicted that the same will be true for Nd, Sm, and Eu. (CA)

827

Hamilton, J. G. THE METABOLIC PROPERTIES OF THE FISSION PRODUCTS AND ACTINIDE ELEMENTS. Revs. Mod. Phys. 20, 718-28(1948).

An investigation of the assimilation, distribution, retention, and excretion of the fission products and actinide elements in the rat administered by mouth and by injection has been conducted. The fission products studied included the carrier-free radioactive isotopes of Sr, Y, Zr, Nb, Ru, Te, I, Xe, Cs, Ba, La, Ce, Pr, and Pm. The actinides studied were Ac, Th, Pa, U, Np, Pu, Am, and Cu. The fission products Sr, Ba, Y, La, Ce, Pr, Pm, Zr, and Nb and all of the actinides are absorbed to a very small degree by way of the digestive tract, deposited primarily in the skeleton following parenteral administration, and eliminated very slowly from that organ. From 25% to 70% of the material absorbed following parenteral injection is laid down in the skeleton and is eliminated from that organ at rates less than the rates of radioactive decay, with the exception of Cb⁹⁵, Ce¹⁴⁴, Pm¹⁴⁷, and possibly Sr⁹⁰. There is no significant degree of localization of the remaining 5 elements in the skeleton or in any other tissue with the exception of the accumulation of I in the thyroid gland. The rate of elimination for all of these 5 radioelements is much greater than their rate of radioactive decay with the exception of I, the release of which accumulated in the thyroid is much slower than its rate of radioactive decay. The members of the long-lived fission product group which are absorbed by way of the digestive tract include Sr, Ba, Te, I, and Cs. With the exception of U, elimination from bone occurred very slowly. Radioautographic studies indicated that Sr, and presumably Ba, are deposited primarily in the mineral structure of the bone. The other fission products deposited in this organ are laid down in the region of the inner and outer coverings of the bone and about the trabeculae, but do not apparently enter into the mineral structure of this organ to a degree comparable to Sr. In the case of the actinide elements, a similar accumulation in the region of the non-mineralized portion of the bone has been observed with Ac, Th, Pu, Am, and Cu. The curious property of the members of the fission products and the majority of the actinide elements to be laid down in this portion of the skeleton and to be retained there for prolonged intervals, renders them of considerable concern from the point of view of the possible medical hazards to be encountered should these materials be accidentally introduced into the body. (TIS)

828

Hamilton, J. G. PART I. PROGRESS REPORTED ON TRACER STUDIES CONCERNED WITH METABOLISM OF ND¹⁴⁷, PR¹⁴³, SR¹³⁵, AND GA⁶⁷. PART II. BIOLOGICAL STUDIES OF RADIATION EFFECTS, MEDICAL AND HEALTH DIVISIONS QUARTERLY REPORT, JANUARY, FEBRUARY, MARCH 1949. Radiation Lab., Univ. of Calif. [nd] 88p. (UCRL-332)

Results of tissue distribution studies are tabulated for Nd¹⁴⁷, Sn¹¹³, and Ga⁶⁷, as well as data on metabolic effects of Zr⁸⁵ and bone uptake of Sr^{85,90}. An extensive study on blood coagulation is reported. The heparin clotting time

test and the clot retraction rate test, a quantitative measure of clot retraction obtained by electric resistance measurements were taken on numerous human subjects and on patients with chronic leukemia, polycythemia and other hematopoietic diseases. Coagulation defects found in patients with these diseases are reported in greater detail and the possible relations of platelets and heparin to various hemorrhagic and thrombotic conditions is discussed. Preliminary observations indicate that radioactive isotope therapy in leukemia and polycythemia has beneficial effects upon altered blood coagulation. 104 references. Preliminary reports are included on hematological effects of total body irradiation and I^{31} therapy. (TIS)

829

Hamilton, Joseph G. THE METABOLISM OF THE RADIOACTIVE ELEMENTS CREATED BY NUCLEAR FISSION. New Engl. J. Med. 240, 863-70(1949).

A review is made of part of the medical research activities within the atomic-energy program and covering the biological properties and metabolism of the radioactive elements created by nuclear fission. A summary of the metabolism of the principal members of the long-lived fission products (also neptunium and plutonium), obtained after parenteral and oral administration in the rat, is contained in one table. Absorption of the products through the digestive tract and the lungs, and retention of the products in the skeletal system and other parts of the body are discussed. The length of retention of some of these products in the skeletal system creates a great radiation hazard. Practical progress in studies developing methods of releasing these products from the bone are discouraging. In conclusion, it is stated that there is no new major mystery surrounding the problem of protection against the radioactive products associated with the release of atomic energy. (NSA)

830

Hamilton, J. G., C. W. Asling, W. M. Garrison, K. G. Scott, and D. Axelrod-Heller. DESTRUCTIVE ACTION OF ASTATINE 211 (ELEMENT 85) ON THE THYROID GLAND OF THE RAT. Proc. Soc. Exptl. Biol. Med. 73, 51-3(1950).

Astatine 211, prepared by alpha-particle bombardment of Bi in the cyclotron, is radioactive with a half-life of 7.5 hr but unlike most artificial radioelements it emits alpha particles rather than electrons and gamma rays. It also emits X-rays of 80 e. Kv. The radiobiological importance of the emission of alpha particles is that each of these nuclear particles will dissipate an initial kinetic energy of 6 mev in about 50 μ of a soft tissue. The beta rays from the 8-day I^{31} possess a maximum energy of 0.6 mev with a range of nearly 2000 μ of tissue. When At²¹¹ chloride is injected into rats the At accumulates in the thyroid and produces an extreme degree of radiation injury of the thyroid tissue without apparent involvement of the adjoining parathyroids. (CA)

831

Kawin, Bergene, D. H. Copp, and J. G. Hamilton. STUDIES OF THE METABOLISM OF CERTAIN FISSION PRODUCTS AND PLUTONIUM. Radiation Lab., Univ. of Calif. Aug. 7, 1950. 120p. (UCRL-812)

The distribution and excretion of radioisotopes of cerium, niobium, plutonium, strontium, yttrium, and zirconium has been studied in adult female rats of the Long-Evans strain. The metabolism of Pu(VI) was unaltered by general treatment with the sulfhydryl compounds 2,3-dimercaptopropanol (BAL) and cysteine. This suggests that the metabolism of Pu is not related to that of sulfhydryl groups. These compounds do not appear to have use as therapeutic agents for plutonium poisoning. Cysteine ap-

peared to increase the amount of Pu retained at the site of intramuscular injection. Parathormone had no significant effects on the distribution and excretion of either Pu or Y. The resorption of bone by parathormone did not appear to labilize these bone-deposited elements, nor make them more susceptible to the positive effects of zirconium citrate. Massive doses of zirconium citrate appeared to have some positive effects on the distribution and excretion of Ce, Nb, Pu, and Y. Sodium citrate had relatively little effect on the metabolism of these elements, with the exception of Y. Both citrates were without significant effect on the metabolism of radiostrontium. Zirconium citrate may alter the metabolism of the several radioisotopes through a "carrier" action as a chelated radiocolloidal citrate complex. The possible influence of this complex on the uptake and excretion of the several radioisotopes during the first hour following their administration has been discussed. (NSA)

832

Lanz, H. C. and J. D. Teresi. THE METABOLISM OF SHORT-LIVED AIR-BORNE FISSION PRODUCTS. Argonne National Lab. May 1945. Decl. May 14, 1947. 39p. (MDDC-954; CH-2844)

A fission recoil apparatus has been constructed in which uranium foil is subjected to neutron bombardment in the pile. Gas passing over the foil picks up the fission recoil atoms and carries them to animal exposure chambers and measuring equipment located outside the pile shield. The time taken for an atom to go from the foil to the exposure chamber (hold-up time) varied from 1.8 to 30 seconds. A special ionization chamber was developed to measure the activity, which varied from 17 to 0.5 μ c/cc. It has been shown that this gas contains not only the noble gas fission products but also all fission products which normally exist in the solid state. Rats and mice exposed to this gas in an exposure chamber suffer damage and die, but no more so than would be expected from the amount of external gamma radiation which they received while in the exposure chamber. A special apparatus was constructed which would allow rats to breathe the gas without receiving external radiation. Rats receiving exposures of eight hours per day for five consecutive days received burns of the mouth and upper respiratory tract. Some of these animals lived but most of them died, apparently from starvation because of failure to eat. Metabolism experiments have shown that of the material that is inhaled, about 25% goes to the skeleton and is excreted very slowly; about 8% stays in the lungs and is excreted slowly; about 6% goes to the liver and is slowly excreted; and the remainder is excreted with moderate rapidity. The highest specific activity is found in the thyroid. A histological study of tissues of animals sacrificed at various times following exposure has shown that the most severe treatment possible with this apparatus has failed to produce any detectable tissue damage which could be attributed to internal deposition of radioactive materials. Radioautographs showed that the activity was deposited uniformly over the bronchial and alveolar surfaces. It was concluded that for short-lived air-borne fission products the hazard is very much greater from external radiations than from internally deposited radioactive materials. (ADD)

833

Overstreet, R., L. Jacobson, H. Fisher, and K. Scott. PROGRESS REPORT ON METABOLISM OF FISSION PRODUCTS FOR PERIOD ENDING OCTOBER 15, 1943. Argonne National Lab. [nd] 49p. (MDDC-1011; A-1441; CH-1049)

Unseparated fission products have been isolated from 18 pounds of neutron bombarded $UO_2(NO_3)_2 \cdot 6H_2O$ free from carrier and containing less than 0.03 g of U/ μ c of activity.

The final solution was assayed for its content of Sr, Y, Pr, Zr, Nb, Ru, Te, Cs, Ba, Ce, and UX₁. Tracer studies were done on a large group of rats which received the prepared solution by intramuscular, intraperitoneal, intrapulmonary, and oral routes of administration. The time intervals ranged from 1 to 64 days. The skeleton was the chief point of deposition for the absorbed radioactive mixture for all 4 routes of administration. Considerable and prolonged retention occurred in the lungs following intrapulmonary administration. From 3 to 5% was absorbed from the digestive tract. Excretion was slow and the digestive tract was the chief channel of elimination. Approximately 50% of the activity was excreted over the 64 day period following intraperitoneal and intramuscular injection. Tissue distribution studies are reported to some detail for Ru¹⁰⁶ and Np^{238, 239}. Photomicrographs of representative lung sections and their corresponding radio-autographs are included in the report. No significant deposition was noted in the bronchi, lymphoid tissue, and blood vessels, while the radioactivity was distributed widely throughout the alveolar structure of the lungs. Frequently a tendency for the alveolar pattern of the section to be duplicated on the radio-autograph was observed. (TIS)

834

Overstreet, R., L. Jacobson, and K. Scott. **UNSEPARATED FISSION PRODUCTS**. Argonne National Lab. [nd] (MDDC-1143-C)

A procedure has been devised for the separation of raw fission products without carriers from neutron-irradiated uranyl nitrate. An analysis of the final separated material which had been completely freed from uranium gave a distribution which was quite similar to the values noted by Coryell and Seaborg. The intraperitoneal injection of this material in small group of rats sacrificed at 4 and 16 days after injection revealed the skeleton to be the single most important organ for retention of this material. At four days approximately one-third of the administered dose was in the bones and this value was found to be slightly higher at the end of 16 days. High values for retention were observed in the liver and spleen of the four day interval. By the 16th day, however, these levels fell considerably. The over all picture of excretion indicated that the rate of elimination was rather slow although somewhat more rapid than in the case of yttrium. Four days after oral administration only 1.6% of the administered dose was absorbed and almost all of this was found in the skeleton. This observation suggests the possibility that a very large proportion of the absorbed fission material was strontium. (ADD)

835

Scott, K. G., et al. **THE METABOLISM OF CARRIER-FREE FISSION PRODUCTS IN THE RAT**. Radiation Lab., Univ. of Calif. [nd] Decl. Aug. 26, 1947. 209p. (MDDC-1275)

The alkaline earths, rare earths, zirconium, and columbium when introduced into the body are deposited primarily in the skeleton, where the average degree of retention of the absorbed radioelements is approximately 50% of the initially absorbed quantity. The retained fractions of these radioelements are eliminated at rates which are less than their rates of radioactive decay with the exception of the 340 day cerium and possibly Sr⁹⁰. The remaining five long-lived radioelements, ruthenium, tellurium, xenon, iodine and cesium do not show any significant degree of localization in the skeleton and in addition, there is no very striking deposition in any other of the tissues with the exception of deposition of iodine in the thyroid. The rates of elimination for all of these four radioelements are much greater than their rates of radioactive decay, with the exception of iodine accumulated in the thyroid. In this particular case, the release of accumulated iodine in the thyroid is many

times slower than its rate of radioactive decay. The members of the long-lived fission product group which are absorbed by way of the digestive tract include the alkaline earths, tellurium, iodine, and cesium. (ADD)

836

Scott, K. G., et al. **STUDIES ON THE INHALATION OF FISSIONABLE MATERIALS AND FISSION PRODUCTS AND THEIR SUBSEQUENT FATE IN RATS AND MAN**. Argonne National Lab. Dec. 31, 1945. Decl. Aug. 28, 1947. 166p. (MDDC-1276; CH-3590)

The purpose of these experiments was to ascertain the possible hazard resulting from inhalation of fissionable materials and fission products. Aerosols of plutonium, uranium plus fission products, protactinium, and short-lived fission products obtained from the cyclotron and the Clinton Pile were administered to rats. A Zr⁹⁰ aerosol was administered to one human subject and to rats. Aerosols of the above elements were almost totally retained by the head and lungs immediately after exposure. After four days the lungs contained the largest percentage of these elements. The elements deposited in the head were quickly eliminated via the gastrointestinal tract. The same avenue of elimination was used by the lungs, but at a slower rate. The small percentage absorbed into the body was primarily deposited in the skeleton after conditions of equilibrium had been established. Radioautographic studies indicate that the site of deposition in the lungs of these materials is in the bronchial passage and the alveolar structures. They are rapidly removed from the bronchial tree, presumably by ciliary action and are very slowly released from the alveoli. No accumulation of any of the radioelements was observed in either blood vessels or lymph nodes. Charts, diagrams, and photographs are included, and a bibliography is appended. (ADD)

837

Scott, Kenneth G., D. Harold Copp, Dorothy J. Axelrod, and Joseph G. Hamilton. **THE METABOLISM OF AMERICIUM IN THE RAT**. J. Biol. Chem. **175**, 691-703 (1948).

An investigation of the metabolism of americium in the rat has been conducted, following its administration by intramuscular injection and by stomach tube. No appreciable absorption took place from the digestive tract. Within 24 hours after parenteral administration, 55% of the total amount of americium absorbed from the site of injection was deposited in the liver and 20% accumulated by the skeleton. Excretion occurred primarily by way of the digestive tract and most of the americium eliminated appeared to come from the liver. There was no significant change in the content of americium in the skeleton throughout the interval of the experiment. The distribution of americium in bone was studied by the radioautographic technique with thin, undecalcified sections of the femur. Americium was heavily deposited in the region of trabecular bone below the epiphysis, at the endosteal and periosteal surfaces of the shaft, and throughout the cortical bone in the region of small blood vessels. (NSA)

Gallium

838

Brucer, Marshall. **DISTRIBUTION OF GALLIUM IN MAN; AUTOPSY EVIDENCE**. J. Pharmacol. Exptl. Therap. **101**, 4-5(1951).

This paper is reproduced here in its entirety.

One 14-yr-old patient with osteogenic sarcoma (primary removed) metastatic to the lungs was given 50 mc of Ga⁷² in 375 mg of stable Ga as a gallium citrate complex. It was

administered intravenously in divided doses of 5 to 15 mc at 4-day intervals. At autopsy the distribution in 38 types of tissue was found relatively uniform. Only in kidney, liver, and bone was there increased retention of Ga^{72} . All metastatic nodules sampled showed greater activity per gram than did any normal organ. One 68-yr-old patient with multiple myeloma received intravenously 178 mc of Ga^{72} in 681 mg of stable Ga in the citrate complex. The doses of 4-day intervals ranged from 20 to 50 mc each. On autopsy, the marrow, cortical bone, liver, kidney, and spleen showed the greatest retention of Ga^{72} . There was no normal bone, but the greater relative distribution in areas of increasing myeloma activity was shown by autoradiograms. (NSA)

839

Dudley, H. C., G. W. Imirie, Jr., and J. T. Istock. **DEPOSITION OF RADIOGALLIUM (Ga^{72}) IN PROLIFERATING TISSUES.** *Radiology* **55**, 571-8(1950).

Radiogallium, Ga^{72} , has been shown to concentrate at areas of osteogenic activity, i.e., the epiphyseal junction and the callus of healing fractures in rabbits, and in osteogenic sarcoma of the mouse. In certain fibroadenomas, fibrosarcomas, and the mixed mammary tumor of animals, no significant localization of Ga^{72} occurred. Autoradiographic studies of the deposition of Ga^{72} in bone, by impregnation of bone sections with liquid photographic emulsion, has made possible more detailed localization of this element. It is suggested that radiogallium citrate is worthy of clinical trials in tracer amounts for diagnostic purposes and at higher levels for possible therapeutic effect. (NSA)

840

This abstract has been intentionally omitted.

841

Dudley, H. C. and G. E. Maddox. **DEPOSITION OF RADIO GALLIUM (Ga^{72}) IN SKELETAL TISSUES.** *J. Pharmacol. and Exptl. Therap.* **96**, 224-7(1949).

The results of a radioautographic study of the distribution of Ga in the skeletal tissues of the rabbit and dog following injections of non-toxic doses of radio-gallium (Ga^{72}) are presented. The radio-gallium was injected as the lactate or citrate into the animals at a dosage level of 0.5 mc/kg of body weight; the animals were sacrificed 12 hours after the injections, and the bones were removed, cleaned of adhering tissue, mounted in dental stone, sectioned, and placed on emulsion x-ray film. The radioautographs show that in young animals the Ga is selectively deposited in the areas of greatest osteogenic activity (the epiphyseal line); in adult animals there is also a deposition in this general area, but it takes place in a more diffuse manner throughout the trabecular bone. The most significant finding is the rapidity of deposition of the Ga. (NSA)

842

Dudley, H. C., J. L. Munn, and Katherine E. Henry. **STUDIES OF THE METABOLISM OF GALLIUM. II.** *J. Pharmacol. and Exptl. Therap.* **98**, 105-10(1950).

Radiogallium (Ga^{72}) with a specific activity of 0.11-0.12 mc/mg was injected subcutaneously as gallium citrate 20 mg amounts into a series of 12 rats in order to determine the distribution of the gallium. Similar experiments were performed with rabbits and dogs; in rabbits the excretion of the isotope was also investigated. It was found that in the rat, rabbit, and dog only bone and the kidneys receive large amounts of the element. Following the subcutaneous injection of the element as citrate, the rabbit excretes 30-55% of the total dose in the urine within 16 hours, while the osteoid structures absorb an additional 30-48% within this time. Definite amounts are also excreted into the stomach and intestines by the gastrointestinal mucosa; the

contents of the tract contain 1-2% of the subcutaneous dose within 12-18 hours after injection. (NSA)

843

English, J. A. and H. C. Dudley. **DISTRIBUTION OF RADIOACTIVE GALLIUM IN THE TEETH AND JAWS OF EXPERIMENTAL ANIMALS.** *Dental Research* **29**, 93-100(1950) 14p. (Naval Med. Research Inst. Report NM-008-009(Report 1))

Radiogallium in the form of soluble Ga lactate (pH 7.0-7.4) was injected subcutaneously into rats and rabbits. The dosage was 0.2 to 0.4 mc of Ga^{72} per kg of body weight (6 mg/kg), which is well below the toxic level. The animals were killed six hours after injection and thin sections (50-100 μ) were made of the bone and teeth by cutting with high speed abrasive discs and grinding to the desired thickness against an abrasive wheel. These thin sections were placed next to special x-ray film for 24 to 48 hours. The rays emanating from the radioactive isotope affected the film just as do the rays from an x-ray tube. The developed negatives were compared with transillumination photographs which were subsequently made from the ground sections. By this means it was determined that radiogallium is predominantly deposited in endosteum, periosteum, tooth pulp, and periodontium. There appears to be a moderate deposition in cancellous bone. Cortical bone and the dentin of the root portion of teeth take a barely perceptible amount of radiogallium, whereas coronal dentin and enamel give no indication that any radiogallium is deposited. The main advantages of the autoradiographic method over methods using the electroscope or Geiger counter for determining the radioactivity are that fractional portions of teeth and bone are not required, and the visual localization is rapid and effective. The relative distribution of the radioactive substance in each anatomic area is apparent, however, quantitative measurements were not attempted in this study. (NSA)

844

King, E. R., Jesse D. Perkinson, Jr., H. D. Bruner and Joe Gray. **EXCRETION OF GALLIUM BY THE RAT AND BY MAN.** *Science* **113**, 555-7(1951).

A detailed comparison is made between excretion of Ga in the rat following intravenous administration of $GaCl_3$, a rapidly ionizing salt, and the slowly ionizing complex gallium citrate. The rats received 200 to 300 μ c of Ga^{72} in 1.5 to 2 mg of stable Ga. About 73% of the Ga given as the citrate was excreted in the urine by the fourth day compared with 59% for the chloride salt. The fecal excretion of the $GaCl_3$ was about twice that of the citrate. At 96 hr the urine/feces ratio was ~8 for the chloride salt and 19.3 for the citrate complex. A second comparison is made between excretion by the rat and by man of tracer and larger intravenous doses of gallium citrate. In man the chief route of excretion is also the urinary tract. In the rat studies the effective half life at the dose level used was 8.33 hr. For the larger doses in man it was ~12.5 hr. (NSA)

Gold

845

Burstone, M. S. **STUDIES ON THE EFFECT OF RADIOACTIVE COLLOIDAL GOLD ON THE DEVELOPMENT OF THE ORAL STRUCTURES OF THE MOUSE.** *Arch. Pathol.* **50**, 419-26(1950).

The injection of colloidal radioactive gold, Au^{198} , adjacent to the jaw of the immature mouse will result in abnormalities of osteogenesis and odontogenesis, including failure of root formation. The changes are interpreted as being the result of local irradiation, since the side of the

head farther from the injected area exhibits relatively normal development of tooth and bone structure. These changes are similar to those observed in immature mice receiving systemic dosages of radioactive phosphorus. The serous-type glands manifest a greater radiosensitivity than the mucous type. The duct elements are relatively radio-resistant. (NSA)

846

Desaive, P. and J. Closon. RADIOACTIVE GOLD AU¹⁹⁸ AND ARTICULATIONS. *J. belge radiol.* **24**, 438-44(1951).

Colloidal Au¹⁹⁸ in 3- to 12.8-mc doses was injected intravenously, intraperitoneally, or intraarticularly into rabbits. Subsequent distribution and apparent radiation-induced changes in synovial and adjacent tissues are illustrated. (NSA)

847

Friedell, Hymer L. MONTHLY PROGRESS REPORT, NOVEMBER 1951. Atomic Energy Project, Western Reserve Univ. [nd] 6p. (NYO-1639)

Distribution studies in normal and sub-total hepatectomized rats injected intravenously with colloidal Au¹⁹⁸ showed a marked alteration of deposition and hematological response in the hepatectomized animals. These changes are discussed. Rats receiving colloidal Au¹⁹⁸ prior to x irradiation showed approximately one-third of the x-ray effect after receiving pretreatment with cysteine. (NSA)

848

Hahn, P. F., Marvin A. Jackson, and Horace Goldie. LIVER CIRRHOSIS WITH ASCITES, INDUCED IN DOGS BY CHRONIC MASSIVE HEPATIC IRRADIATION WITH RADIOACTIVE COLLOIDAL GOLD. *Science* **14**, 303-5 (1951).

A report is made of lesions in the liver of 7-week old dogs following the intravenous administration of from 59 to 102 mc of radioactive colloidal Au given in three doses over a period of approximately six weeks. Dosages were estimated at 67,000 and 65,000 equivalent β -roentgen to the liver. Approximately 6 weeks after the last injection of the colloid, increasing amounts of ascitic fluid accumulating in the abdominal cavity were noted. A marked retardation in growth and general appearance was also noted. Tracer quantities of radioactive Au colloid administered by vein showed a marked lag in the time of disappearance from the circulatory system, suggesting an impaired ability for phagocytosis by the reticuloendothelial system. Both dogs died from the severe damage induced by the radiation in the liver. At autopsy about 1,000 ml of clear, slightly yellow fluid was withdrawn from the peritoneal cavity of one dog and about 1,800 ml from another. The most obvious effects of irradiation in both dogs were disappearance of endothelium and marked increase in connective tissue surrounding the blood vessels of the liver. Pathological changes in the liver induced by the massive chronic irradiation resembled a combination of Chiaris syndrome (obliteration of the hepatic vein) and of central fibrosis. Considerable damage to both spleen and kidneys was also noted. (NSA)

849

Sheppard, C. W., J. P. G. Goodell, and P. F. Hahn. COLLOIDAL GOLD CONTAINING THE RADIOACTIVE ISOTOPE AU¹⁹⁸ IN THE SELECTIVE INTERNAL RADIATION THERAPY OF DISEASES OF THE LYMPHOID SYSTEM. *J. Lab. Clin. Med.* **32**, 1437-41(1947).

Colloidal gold containing Au¹⁹⁸ was obtained from the chain-reacting pile at Oak Ridge and used in therapy of lymphoid diseases. This isotope has an ideal half-life and good radioactive characteristics. Very stable colloids can

be prepared. It is easily administered and the cost of such therapy is low. (BA)

850

Wheeler, Brownell, Marvin A. Jackson, and Paul F. Hahn. HEMATOLOGY OF THE DOG FOLLOWING INTRAVENOUS ADMINISTRATION OF RADIOACTIVE COLLOIDAL GOLD. *Am. J. Physiol.* **166**, 323-7(1951).

Fourteen dogs were injected with 1 mc/kg of Au¹⁹⁸ by vein. All the dogs showed a definite decrease in white count, but only one was thrown into a marked leukopenia. In 12 out of 14 dogs sedimentation rate increased following radiation, although this response was not as clear cut as the decrease in white count. Hemoglobin and hematocrit decreased in a slow and progressive manner over a period of several weeks. Liver function tests failed to reveal any marked degree of hepatic impairment, but a few dogs showed changes indicative of mild liver damage. Some of the possible mechanisms for these changes are discussed briefly. The results show that intravenous administration of radioactive colloidal gold at dosage levels similar to those employed therapeutically in the treatment of leukemia and cancer is relatively well tolerated by normal dogs. It seems probable, therefore, that, insofar as hematological changes and liver functions are concerned, these dosage levels present little immediate danger to patients who receive them. (NSA)

Iodine

851

SYMPOSIUM ON RADIOIODINE. Brookhaven National Lab. July 28-30, 1948. 118p. (AECU-51; BNL-C-5)

The following papers were presented: Radioactive Iodine: Its Use in Studying Certain Functions of Thyroid Tumors, Rulon W. Rawson; The Biological Effect of Irradiation by Radioactive Iodine, Bengt N. Skanse; The Mechanism of Action of Anti-thyroid Drugs, Malcolm M. Stanley; Turnover Rates as Measured by Radioiodine, William T. Salter, MacAllister Johnston, and John Gemmel; Standardization of Radioactive Iodine, Sergei Feitelberg; Calculation of Dosage in Radioiodine Therapy, Edith H. Quimby; Uptake and Excretion Measurements and Their Significance, Eleanor Oshry and Charlotte Schmidt; The Radiation Treatment of Hyperthyroidism, F. M. Chapman; Graves' Disease. Treatment with Radioiodine I¹³¹, Mayo H. Soley, Earl R. Miller, and Nadine Foreman; Indicator of Thyroid Function in Man, Widney C. Werner, Edith H. Quimby, and Charlotte Schmidt; Histologic Types of Thyroid Carcinoma and Their Respective Abilities to Store Radioactive Iodine I¹³¹ as Demonstrated by Radioautograms, Patrick J. Fitzgerald; Radioautographs: Methods and Uses, Titus C. Evans; Studies on Dosage in Cancer Therapy, L. D. Marinelli and Ruth F. Hill; Clinical Methods and Results of Radioiodine Therapy in Metastatic Thyroid Cancer, S. M. Seidlin; I¹³¹ as a Therapeutic Agent in Cancer of the Thyroid, J. B. Trunneil. (NSA)

852

Chapman, E. M. TREATMENT OF GRAVES' DISEASE WITH RADIOACTIVE IODINE. *Western J. Surg. Obstet. Gynecol.* **56**, 1-64(1948).

Radioactive iodine is prepared by the nuclear bombardment of tellurium with deuterons in the cyclotron. The principal isotopes produced are I¹³⁰ (half-life of twelve hours) and I¹³¹ (half-life of eight days). From observations in treating 45 patients with diffuse goiters and hyperthyroidism, Chapman believes that radioactive iodine with a half-life of twelve hours is an effective single thera-

peutic agent. Like other methods of therapy it has certain limitations. Its possible late toxic effects will have to be observed with the passage of time. Contraindications to its use seem to be pregnancy beyond the first month, and disease of the kidneys. (NSA)

853

Feller, D. D., I. L. Chaikoff, Alvin Taurog, and Hardin B. Jones. THE CHANGES INDUCED IN IODINE METABOLISM OF THE RAT BY INTERNAL RADIATION OF ITS THYROID WITH IODINE 131. *Endocrinology* **45**, 464-79(1949).

Adult male rats were injected intraperitoneally with either 24, 30, 300, or 875 μ c. of carrier-free I^{131} and sacrificed at 1, 2, 3, 6, 8, or 10 days thereafter. A method for estimating the dose in rep is presented. Criteria used as indicators of metabolic changes in the thyroid gland were: (1) concentration of protein-bound I in plasma, (2) chemical iodine content of the gland, (3) retention of the initial I^{131} by the gland, and (4) capacity of the gland to concentrate a second injection of I^{131} . The earliest indicator was the concentration protein-bound I in plasma. After 875 μ c of I^{131} a triphasic curve of response was observed. At 24 hr post injection a decrease occurred followed by a sharp rise, with highest values on the third post-injection day. The plasma I then fell to thyroidectomy levels. Injection of 300 μ c of I^{131} decreased the concentration of protein-bound I in plasma, and was not followed by a rise. Changes in I^{127} of the thyroid gland appeared two days after 300 or 857 μ c of I^{131} and the gland was depleted by the 8th day. The percentage of initial I^{131} one day post-injection was the same regardless of dose, but at the end of 2 days the glands receiving larger doses of I^{131} were losing it rapidly. Rats treated with 300 μ c and given a second dose 3 days later collected only about $1/10$ as much as controls given an initial dose. Thyroid function did not appear disturbed in the rat up to 10 days after 24 or 30 μ c of I^{131} . (CA)

854

Findlay, D. and C. P. Leblond. PARTIAL DESTRUCTION OF RAT THYROID BY LARGE DOSES OF RADIOIODINE. *Am. J. Roentgenol. Radium Therapy* **59**, 387-95(1948).

Two adult female albino rats, kept on a low iodine diet for ten weeks, were given single doses of 78.5 and 60.8 microcuries of carrier-free radioiodine, I^{131} , respectively. Thyroid function was estimated by basal metabolic rate and heart rate determination. After six days the animals were sacrificed and the thyroid histology studied by means of stained sections and autographs. It was calculated that about 20,000 equivalent roentgens were received by the thyroid glands of the animals. Such doses of radio-iodine impair the function of the thyroid, as suggested by some decrease in oxygen consumption and heart rate of the animals. The histological study of the thyroid glands of these animals shows destructive lesions of the follicles especially in the central areas of the gland. Many peripheral follicles retain a normal appearance. Autographic studies show that only the normal looking follicles with smooth colloid have the ability to retain radioiodine. Although the thyroid gland is resistant to the action of radiations, it can be destroyed by the isotope I^{131} . The damage is favored by the retention of radioiodine inside the thyroid follicle until they are markedly damaged. (NSA)

855

Furth, J. and W. T. Burnett, Jr. HORMONE-SECRETING TRANSPLANTABLE NEOPLASMS OF THE PITUITARY INDUCED BY I^{131} . *Proc. Soc. Exptl. Biol. Med.* **78**, 222-4(1951).

Pituitary growths induced by thyroid destructive doses of I^{131} are readily transplantable in mice whose thyroid glands had been similarly destroyed, but not in normal mice. These growths discharge gonadotropic hormones which in turn stimulate the production of gonadal hormones. Discharge of thyrotropic hormones by these tumors is assumed but remains to be demonstrated. On the basis of observations made it is postulated that the growths of the pituitary induced by thyroid-destroying quantities of I^{131} are conditioned neoplasms formed by cells which are driven to proliferation through the stimulus created by the absence of TH; the same chromophobe pituitary cell can discharge both gonadotropic and thyrotropic hormones. (NSA)

856

Godwin, John T., B. J. Duffy, Jr., Patrick J. Fitzgerald, J. B. Trunnell, and Rulon W. Rawson. PATHOLOGICAL EFFECTS AND RADIOAUTOGRAPHIC LOCALIZATION OF I^{131} IN HUMANS. *Cancer* **4**, 936-51(1951).

Radioautographic localization and pathological findings in postmortem studies of nine patients who were given carrier-free I^{131} in varying doses and intervals prior to death are reported. Radioautographs were negative on all organs except the thyroid, neoplastic thyroid lesions, the corpora amylacea of the prostate in one case, and the submaxillary-gland ducts and spleen in another. The degree of I^{131} pickup and histological effects varied widely in lesions of similar histological pattern in which localization would be anticipated. No effects directly attributable to I^{131} were seen in tissues other than thyroid carcinoma, metastatic deposits, and marrow in one instance. (NSA)

857

Goldberg, R. C. and I. L. Chaikoff. THE CYTOLOGICAL CHANGES THAT OCCUR IN THE ANTERIOR PITUITARY GLANDS OF RATS INJECTED WITH VARIOUS DOSES OF I^{131} AND THEIR SIGNIFICANCE IN THE ESTIMATION OF THYROID FUNCTION. *Endocrinology* **46**, 91-104 (1950).

A cytological study of the pituitaries of rats injected with 18, 300, 525, and 875 μ c of I^{131} is presented. The injection of 18 μ c of I^{131} resulted in no cytological changes in the anterior pituitary and is concluded to be a safe tracer dose. Evidence is presented to show that the changes occurring in the anterior pituitaries of rats after the injection of large amounts of I^{131} are not the result of radiation damage to the pituitary itself but solely the consequence of thyroid destruction. The injection of 300 μ c of I^{131} resulted in considerable thyroid destruction, but 5 to 8 months later, normal glandular function was regained. From a study of the reaction in the anterior pituitary, it was shown that the atypical thyroids present 6 to 8 months after single injections of 525 μ c of I^{131} synthesize negligible amounts of thyroxine or none at all. The cytological changes occurring in the anterior pituitary after the injection of 875 μ c of I^{131} are concluded to be identical with those occurring after total surgical thyroidectomy. (NSA)

858

Goldberg, R. C. and I. L. Chaikoff. DEVELOPMENT OF THYROID NEOPLASMS IN THE RAT FOLLOWING A SINGLE INJECTION OF RADIOACTIVE IODINE. *Proc. Soc. Exptl. Biol. Med.* **76**, 563-6(1951).

Examination of 10 rats sacrificed 18 months after a single injection of 400 μ c of radioactive I revealed the following changes in the thyroid gland: (1) Hürthle-like elements (previously reported by the authors in thyroids of rats sacrificed 8 months after a single I^{131} injection) were

evident in the parenchyma of all glands. (2) Multiple adenomata, apparently benign in nature, were evident in the parenchyma of all glands. (2) Multiple adenomata, apparently benign in nature, were found in the thyroids of 2 rats. (3) Two types of anaplastic, nonencapsulated neoplasms, one of which was invading adjacent thyroid tissue, were also found in the thyroids of these 2 rats. (NSA)

859

Goldberg, R. C., I. L. Chaikoff, Stuart Lindsay, and D. D. Feller. HISTOPATHOLOGICAL CHANGES INDUCED IN THE NORMAL THYROID AND OTHER TISSUES OF THE RAT BY INTERNAL RADIATION WITH VARIOUS DOSES OF RADIOACTIVE IODINE. *Endocrinology* 46, 72-90(1950).

Rats of the Long-Evans strain were given single intraperitoneal injections of 18, 300, 525, or 875 μC of I^{131} . Autopsies were performed at intervals of three days, and 1, 5, 6, and 8 months after the injection. No evidence of damage to any tissue was observed as early as 12 to 24 hours after injection in the thyroid glands of animals receiving 300 or 525 μC of the isotope. The process consisted of five stages: degeneration and necrosis of epithelial cells with follicular disruption; vascular degeneration and thrombosis; acute and chronic inflammatory changes; fibrous organization; and, epithelial regeneration. The thyroids of rats subjected to 875 μC of the isotope responded in a similar fashion, except that no epithelial regeneration occurred; regeneration to normal thyroid structure was found in the animals which had received 300 μC of I^{131} , but atypical thyroid cells (resembling Hürthle cells) were present 5 to 8 months after the 525 μC administration. Viable-appearing parathyroid glands were demonstrated in all the injected animals, with some fibrosis appearing only in the higher isotope concentration groups. Evidence of tracheal damage, and slight reversible changes in the kidneys were noted; normal livers were demonstrated. (NSA)

860

Gorbman, Aubrey. EFFECTS OF RADIOTOXIC DOSAGES OF I^{131} UPON THYROID AND CONTIGUOUS TISSUES IN MICE. *Proc. Soc. Exptl. Biol. Med.* 66, 212-13(1947).

Radioactive I (I^{131} as NaI) was given in a single subcutaneous injection in doses ranging from 3-50 millicuries/kg. Higher doses produced complete thyroid destruction within a few days. Lower doses permitted survival of some thyroidal epithelium in the isthmus and cranial apex of the gland for as long as 120 days after injection. Lesions were noted in the tracheal epithelium with all doses, and in the recurrent laryngeal nerve with higher dosages. (BA)

861

Gorbman, Aubrey. TUMOROUS GROWTHS IN THE PITUITARY AND TRACHEA FOLLOWING RADIOTOXIC DOSAGES OF I^{131} . *Proc. Soc. Exptl. Biol. Med.* 71, 237-40(1949).

Following doses of radioactive iodine sufficient to cause destruction of most or all of the thyroid, tumorous enlargements were found in the pituitary glands and tracheas of mice. Hypophyseal growths as large as 240 mg (control, 2.1 mg) occurred. Less than 10% of animals sacrificed more than 250 days after I^{131} administration had pituitaries weighing less than 10 mg. Tracheal tumors of the fibrous tunica propria, obstructing the tracheal lumen, were of lower incidence (4%) but appeared earlier. Fibrous thickenings of the tunica propria and metaplastic regeneration of tracheal epithelium were more common. This study is based on 158 mice observed for a period of time sufficient to show the metaplastic and atypical growth changes, as well as 34 untreated controls. (R)

862

Gorbman, A. DEGENERATIVE AND REGENERATIVE CHANGES IN THE THYROID GLAND FOLLOWING HIGH DOSAGES OF RADIOACTIVE IODINE. *Trans. N. Y. Acad. Sci.* 2, 201-3(1949).

The results of experimental studies to determine the degree of thyroidal and other tissue injury per given amount of radioiodine are given. Mice of C57-CFW-strain, whose thyroid glands had an average weight of 5 mg, were used. They were injected subcutaneously with 100, 200, 400, or 1000 mc doses. The "biological half-life" of the iodine was 2 days. By calculation, it was decided that the doses delivered were 26,000 and 75,000 equivalent r. The mice were sacrificed at intervals of 2, 3, 7, 24, 120, and 300 or more days after the injections. The severity of injury to the thyroid after two or three days varied from minimal to complete destruction within the 100-1000 mc range of dosages. Under specified circumstances, 200 μC or more of I^{131} cause complete thyroidal destruction in mice. Doses of 100 μC permit survival of small bits of atypical thyroidal tissue, which even after 400 days show no tendency toward regeneration. (NSA)

863

Miller, Earl R. and Glenn E. Sheline. STUDIES WITH RADIOIODINE. III. PROBLEM OF DOSAGE IN THE TREATMENT OF HYPERTHYROIDISM. *Radiology* 57, 720-8(1951).

Attempts to predetermine radiation dose of radioiodine, expressed in roentgens of radiation to the thyroid gland, in the treatment of hyperthyroidism are reviewed. Discrepancies in data obtained from test and therapeutic doses are discussed. Results of treatment of hyperthyroid patients with I^{131} are presented in tabular form. (NSA)

864

Rugh, Roberts. THE EFFECT ON THE NURSING MOUSE OF THERAPEUTIC DOSES OF I^{131} p.168-9 of INTERNATIONAL CONGRESS OF RADIOLOGY, 6th Congress, London. 1950.

Eighty per cent of radioactive iodine I^{131} injected subcutaneously into the adult mouse, is excreted within 24 hours. Most of the remaining iodine is concentrated in the very small thyroid gland. If the mouse is nursing, the young begin to remove iodine in the milk within 8 minutes of the mother being injected, and at a rate such that within 4 hours the content of iodine in the litter may exceed that retained by the mother. This indicates that the milk functions as an accessory excretory channel, so that the thyroid of the nursing mouse receives relatively less iodine than does the thyroid of the non-nursing mouse. The ratio of iodine concentration in the major tissues of the nursing as opposed to the non-nursing mouse 4 hours after injection is approximately as follows: mammary 3/1; thyroid 1/7; stomach 1/8; and carcass 1/4. It is quite obvious therefore that the distribution of radio-iodine is drastically altered by the mere fact of lactation. Mouse thyroids examined histologically at intervals following a single injection in doses ranging from 3, 10 to 20 $\mu\text{C}/\text{gr}$. body weight, show no immediate damage. Within one month, however, the thyroids of both the mothers and the nursing young were severely damaged, though the irradiation damage to the thyroids of the young was somewhat less than that seen in the thyroid of the mother. This may be due to the lower concentration of the radio-iodine rather than to any differential radiosensitivity of the two age group thyroids. Controls consisted of mice treated with the same concentration of iodine which was not radio-active. Damage to the thyroid begins at the centre of the gland and progresses outward; the peripheral follicles are the least affected and the last to be damaged.

At the higher dose level a fibro-necrosis develops beginning in the centre of the gland, which involves particularly the interfollicular tissue but also damages the contiguous follicles. This differential effect is due to the fact that homogeneously distributed beta rays have an accumulative effect, causing maximum damage at the centre of the gland. The maximum range of the beta rays is 2 to 3 mm. and the concentration range is from 0.5 to 1.0 mm. in tissue, so that the mouse thyroid is particularly suited to demonstrate this beta ray effect since its thickness is only slightly greater than the effective beta range in tissue. The 0.1 mm. thick thyroid band which joins the two lobes posterior shows no such additional effect, since its thickness is much less than the beta ray concentration range. The parathyroid glands are not directly affected, but since the surrounding tissue becomes necrotic and the blood supply to the parathyroid is affected these paired glands are secondarily damaged. There is no radio-autographic evidence of any radio-iodine concentration in the parathyroids.

865

Rugh, Roberts. RADIOIODINE AND HISTOPATHOLOGICAL EFFECTS. *J. Morphol.* **89**, 457-99(1951).

Histopathological effects on the thyroid glands of nursing adult mice and their suckling young, following the injection into the mother of NaI^{131} in doses ranging from 3 to 20 μc per gram of total body weight, at a time when the litter young were but three days of age, are discussed in detail. The thyroid gland of the mothers and their young were studied histologically at two months and at 10 weeks, following a single treatment with I^{131} . 55 references. (NSA)

866

Watts, William E. and Don R. Matheson. STUDIES ON LYMPHOCYTES FROM PERSONS TREATED WITH RADIOACTIVE IODINE. *J. Lab. Clin. Med.* **35**, 885-9 (1950).

A study was made to determine whether the number and frequency of refractile cytoplasmic granules known to be present in 34% of the normal lymphocytes increase on exposure of the host to ionized radiation. Samples of blood were obtained from the capillaries of two patients with cancer of the thyroid and from eight patients with exophthalmic goiter before the administration of therapeutic doses of I^{131} and at varying intervals thereafter. Further control studies were made on blood from normal persons and from patients with other diseases. Samples were also taken from three technicians who had been exposed to irradiation for 8 to 27 years and from four patients who were receiving massive doses of x-rays in the treatment of malignant diseases. The number of refractile granules in each sample of blood were counted. A significant change in the number of frequency of the refractile granules in lymphocytes from persons exposed to ionized irradiation was not found. A search was made for other concise or specific qualitative cytologic effects of irradiation, but none was found. The refractile granules were found to be best studied in fresh, unstained preparations by phase microscopy. (NSA)

Iron

867

Stewart, W. B., R. T. Snowman, C. L. Yuile, and G. H. Whipple. RADIOIRON EXCRETION BY THE SKIN AND KIDNEY OF DOGS. *Proc. Soc. Exptl. Biol. Med.* **73**, 473-5(1950).

After intravenous or oral administration of single doses of Fe^{55} to dogs, little or no Fe^{55} could be washed from the skin and hair; this fact indicates that no significant amount

was excreted through the skin in 1-7 days. A small amount was found in the urine. (CA)

Lanthanum

868

Overstreet, R., L. Jacobson, K. Scott, and H. Fisher. RADIO LANTHANUM (La^{140}). Argonne National Lab. [nd] 12p. (MDDC-1142-A)

Preparation of Radio Lanthanum without Carrier—A satisfactory method for the preparation of La^{140} has been successfully developed. The twelve day Ba^{140} has been separated from fission products with the use of inert Ba as a carrier. Following the preparation and purification of the Ba^{140} the radio lanthanum was separated from the former using ferric hydroxide as carrier. The iron was subsequently removed by extraction with iso-propyl ether. Decay curves have been measured on La^{140} samples thus separated and the half-life found to be 40.9 hours. No detectable long-lived tail was observed in samples followed over as long an interval as seven half-lives. This indicates that there was present less than 1% of any long-life impurities such as radio barium or radioactive rare earths. The half value thickness for the beta-rays using Al absorbers was found to be 86 milligrams per square centimeter. Tracer Studies—The distribution of La^{140} following intraperitoneal and intramuscular injection was followed for a period of eight days. A significant proportion of the injected material remained unabsorbed by both routes of administration. The liver and skeleton were found to show the highest accumulation of this element. The uptake per gram of tissue in the liver was considerably higher than in the case of Y^{86} . The uptake by the bone per gram of weight was significantly less in the case of La^{140} . However, the La^{140} was accumulated in the bone and was firmly fixed in this organ. No significant absorption took place by way of the digestive tract. When La^{140} was introduced directly into the lungs it was found that a large proportion was firmly fixed in this structure. (ADD)

Phosphorus

869

Abels, J. C., J. M. Kenney, L. Craver, L. D. Marinelli, and C. P. Rhoads. POSTIRRADIATION CHANGES IN THE LEVELS OF ORGANIC PHOSPHORUS IN THE BLOOD OF PATIENTS WITH LEUKEMIA. *Cancer Research.* **1**, 771-5(1941).

The ingestion of a subtherapeutic dose of radioactive P (P^{32}) by 5 leukemic patients was in each instance followed by a rapid and marked change in the conc. of the organic acid soluble phosphorus of the leukocytes and erythrocytes. All detns. were made by the method of Fiske and Subbarrow. No such alterations were observed after the ingestion of a comparable amount of non-radioactive P (P^{31}). That these changes were due solely to the radiation delivered by the radioactive isotope was confirmed by observing similar changes in the organic acid soluble P fraction in the blood cells of these same patients after the adm. of either 3 r (air) whole-body x-ray, or 20 r (air) x-ray to the precordial area. These observations indicate that the radiation delivered by "tracer doses" of radioactive isotopes, used to study metabolism, may, in some instances, disturb normal cellular function, in which case the study would reflect radiation rather than normal metabolism. (BA)

870

Anthony, D. S. and R. H. Snyder. ACUTE RADIOTOXICITY OF INJECTED P^{32} IN MICE. PART I. METABO-

LISM AND SURVIVAL. Argonne National Lab. Feb. 11, 1947. 16p. (MDDC-881)

The results of pilot experiments on the metabolism and radiotoxicity of radioactive phosphorus are reported in the paper. Data were obtained on the toxicity of a well-known radioactive element in the same strains of animals and under the same experimental conditions as data obtained with less familiar radioactive elements. Determinations of the relative radiotoxicity of different isotopes could therefore be made without reference to work done under different conditions. Since the effects of radioactive phosphorus on man has been studied, comparison of these effects with those on laboratory animals provided a basis for extrapolation with other radioactive elements. The experiments with radioactive phosphorus greatly facilitated planning and interpretation of later experiments on the toxicity of other heretofore rare radioactive elements. (ADD)

871

Blume, James M., C. E. Hagen, and Ruth W. Mackie. RADIATION INJURY TO PLANTS GROWN IN NUTRIENT SOLUTIONS CONTAINING P^{32} . Soil Sci. 70, 415-26(1950).

Experiments are described in which young barley plants were grown in nutrient solutions containing various amounts of P^{32} . The lengths of leaves and the dry weights of tops and roots were used as the criteria of injury caused by the radioactive material. Meristematic regions of the plants were examined histologically, and photomicrographs of normal and of injured root tips and apical buds are shown. It was found that damage to the tops was more severe than damage to the roots, and that the injury was due primarily to radiation from the P^{32} accumulated within the plant, the P^{32} which remained in the nutrient solution having relatively little effect. There was no evidence of damage to cells other than those which were in zones of active division. Absorption of phosphate from solution was not affected by radiation injury. The lowest level at which damage was produced under the experimental conditions employed corresponds to 5.6 mc of P^{32} per gram of P_2O_5 . (NSA)

872

Bould, C., D. J. D. Nicholas, and W. D. E. Thomas. RADIATION EFFECTS IN PLANT NUTRITION EXPERIMENTS WITH PHOSPHORUS 32. Nature 167, 140-2 (1951).

Concentrations of P^{32} far greater than is normally used in tracer work and with much higher specific activities, i.e., ranging from 12 to 29,760 microcuries P^{32} /g. P^{32} produced very small radiation effects which are not of sufficient magnitude to preclude the use of P^{32} in plant nutrition experiments. (CA)

873

Burstone, M. S. STUDIES ON THE ALTERATION OF DEVELOPMENT OF THE TEETH AND ADJACENT STRUCTURES FOLLOWING LOCAL ADMINISTRATION OF CHROMIC PHOSPHATE CONTAINING PHOSPHORUS 32 . J. Am. Dental Assoc. 42, 418-21(1951).

The suspension of Cr phosphate had an approximate activity of 1 millicurie per cc; 0.05 cc. was injected subcutaneously into each of 30 mice, adjacent to the left mandible; examination was made 8-60 days later and revealed changes in both histodifferentiation and morphodifferentiation. The alterations in development included distinct hemiatrophy of the face on the injected side and occlusal imbalance of the incisors, and were also similar to those produced by systemic injection of solutions containing soluble radioactive P compounds. (CA)

874

Cornatzer, W. E., George T. Harrell, Jr., David Cayer, and Camillo Artom. SUBACUTE TOXICITY OF RADIOACTIVE PHOSPHORUS AS RELATED TO THE COMPOSITION OF THE DIET. Proc. Soc. Exptl. Biol. Med. 73, 492-5(1950).

In the present investigation the subacute toxicity of P^{32} given parenterally to mice (in one dose in the form of Na_2HPO_4) was studied in relation to the possibility that changes in the composition of the diet might modify the action. It was found that in mice maintained on a 10% casein, 32% fat diet, the LD_{50} dose at the 21st day was 4 to 6 μ c of P^{32} /g of body weight; neither the fatty infiltration of the liver or its prevention (by supplementing the diet with choline) changed the survival figures. The survival time of the mice was highest when they were maintained on a diet low in fat and protein and was significantly decreased when the level of either the fat or the protein or both was increased in the diet. Enrichment of the diets with inorganic phosphate seems to afford a moderate degree of protection against the injurious action of P^{32} . (NSA)

875

This abstract has been intentionally omitted.

876

Dent, J. N. LIMB REGENERATION IN TRITURUS VIRIDESCENS AS AFFECTED BY LETHAL DOSES OF RADIOACTIVE PHOSPHORUS. Anat. Record 105, 325-35(1949).

Phosphorus 32 injected intraperitoneally into adult male specimens of *T. viridescens* was lethal in single doses of 33, 66, and 166 microcuries per g of body wt. The average lengths of time which the animals of the 3 dosage groups lived after injn. were respectively, 36, 30, and 25 days. Right forelimbs excised in the carpal region and re-amputated 23 days later for histological study gave evidence of inhibited or greatly retarded regeneration. Distal tips of these limb stumps showed a scarcity of mitotic figures and distortion of epithelial cells. Blastemata were not present on the limb stumps from animals which had received 166 microcuries per g and were either lacking or rudimentary on the ones from animals injd. with the lower dosages. (BA)

877

Deysine, A. and B. Bonet-Maury. BIOLOGICAL EFFECTS OF THE BETA RADIATION OF P^{32} ON *B. COLI*. Compt. rend. soc. biol. 145, 1091-3(1951).

B. coli in nutrient media containing 0.1 mc of P^{32} /ml was carried through seven generations. The decrease in number of living cells was observed in each generation for 150 days. Development of radioresistance in the later generations was noted. Increasing the P^{32} concentration to 1 mc/ml caused a much more rapid decrease in viability. No distinction in respiration rates could be found by the Warburg method between proliferating and inactivated cultures. (NSA)

878

Doan, C. A., B. K. Wiseman, C. S. Wright, J. H. Geger, W. Myers, and J. W. Myers. SIX-YEAR CLINICAL EVALUATION OF RADIOPHOSPHORUS P^{32} (IN DISEASE). J. Lab. Clin. Med. 32, 943-69(1947).

A critical review of 100 cases treated with P^{32} is given. The main success of P^{32} has been in polycythaemia sera, in which the clinical and haematologic features were well controlled. In leukaemias, P^{32} was sometimes a valuable adjunct to other therapy, but in Hodgkin's disease it was without value. Deep bone pain and pruritus may be controlled in some cases. (NSA)

879

Erf, L. A. A NOTE ON THE EFFECT OF DERMAL AND ENTERAL IRRADIATION BY RADIO-PHOSPHORUS ON THE BLOOD LEVELS OF DOGS. *Am. J. Med. Sci.* **202**, 650-4(1941).

Beta-radiation (emitted by radio-phosphorus) applied dermally to dogs was followed by a slight in the absolute number of circulating lymphocytes; applied enterally, by significant decreases. (BA)

880

Finkel, Miriam P. THE RETENTION OF P^{32} BY YOUNG ADULT CF-1 FEMALE MICE. Argonne National Lab. Aug. 1, 1947. 172p. (AECD-2024-I)

The retention of radiophosphorus by the animals comprising the single dose chronic experiment was studied one month after injection. The external counts of those animals which received 0.1 - 0.5 $\mu\text{C/g}$ were too low to permit conversion to microcuries. The 10.0 - 0.5 $\mu\text{C/g}$ groups gave adequate external counts. At these levels it was found that the absolute retention ranged from 1.2 to 1.7 per cent. (NSA)

881

Friedell, Hymer L. and James H. Christie. THE SYNERGISTIC EFFECT OF PHOSPHORUS³² AND COLLOIDAL GOLD¹⁹⁸ ON SURVIVAL IN MALE ALBINO RATS. *Proc. Soc. Exptl. Biol. Med.* **76**, 207-10(1950) (NYO-1609)

Data are presented which indicate that colloidal Au^{198} and P^{32} administered as $\text{Na}_2\text{HP}^{32}\text{O}_4$ are synergistic in their killing effect on the male albino rat. A discussion of the distribution of P^{32} and colloidal Au^{198} and possible mechanism for the synergism are presented. (NSA)

882

Geffen, Abraham, Robert Loevinger, and Bernard S. Wolf. SURFACE ACTIVITY FOLLOWING ADMINISTRATION OF RADIOACTIVE PHOSPHORUS. *Radiology* **56**, 857-68(1951).

Thirty patients with various malignant diseases were studied, by means of an end-window Geiger-Müller counter, for β -particle surface activity following oral or intravenous administration of radioactive P. Surface activity appears at once, reaches a maximum between 3 and 50 min. after intravenous administration, and decrease approximately exponentially after 24 hours. Schematic surface activity curves for various areas are presented. The extreme variation in surface activity between sym. normal areas is about 15%, while the activity over the calvarium and the nipples is characteristically about 100% higher than over other areas. Over ulcerated and nonulcerated cutaneous malignant tissue, the surface activity may be 2 to 5 times that in normal areas. This differential appears within a few minutes after administration. Surface activity over lymph node metastases was in some patients higher than, and in other patients not appreciably different from, the control areas. Surface activity of the cervix was 3 to 4 times that of the thigh in normal patients, but was at least 6 times that of the thigh in 3 cases of carcinoma of the cervix. This ratio was reduced after radiotherapy. The measurement of surface β activity following administration of inorganic P^{32} does not appear to be necessary for the diagnosis of cutaneous malignant lesions, nor reliable for the diagnosis of subcutaneous lesions or metastatic lymph nodes. (CA)

883

Grad, B. and C. E. Stevens. HISTOLOGICAL CHANGES PRODUCED BY A SINGLE LARGE INJECTION OF RADIOACTIVE PHOSPHORUS (P^{32}) IN ALBINO RATS AND IN C3H MICE. *Cancer Research* **10**, 289-96(1950).

Twenty-two normal young male and female albino rats and eight adult female C3H mice received a single large

dose of radiophosphorus, P^{32} (0.5 to 4.0 mc), and were sacrificed from two hours to nine days later. The cellular destructions consisted mostly of pyknosis and karyorrhexis of mitotic nuclei. The cytoplasm of damaged cells showed vacuolation and reduced staining ability. The destructive effects of P^{32} were most marked in the lymphatic organs and bone marrow, the small intestine, granulosa of ovarian follicles, and mammary tumors. In the crypts of the small intestine, massive degeneration and pyknosis of dividing cells resulted in thinning of the epithelium of crypts and villi, probably because no new cells were supplied from the crypts to balance the continual loss of cells by extrusion normally occurring at villi tips. The mammary tumors showed many scattered pyknotic cells at 24 hours after injection; at 48 hours, large blood lakes had formed without much tissue damage; at nine days, most of the tumor was necrotic and liquefied. Lesser changes were noted in the stomach and colon, in the seminiferous tubules of the testis, and in the hair follicles; little or no damage was observed in the salivary glands, pancreas, liver, genitourinary system, endocrine glands (except the ovary), brain, and muscular and connective tissue. (NSA)

884

Graff, W. S., K. G. Scott, and J. H. Lawrence. HISTOLOGICAL EFFECTS OF RADIOPHOSPHORUS ON NORMAL AND LYMPHOMATOUS MICE. *Am. J. Roentgenol. Radium Therapy* **55**, 44-54(1946).

Mice were injected intravenously with 1.2×10^7 lymphoma cells and were given varying amounts of P^{32} in isotonic sodium phosphate solutions 7 or 13 days after injection. The results showed an initial depressing action of P^{32} on the lymphocyte series in the peripheral blood stream. After four days, when the granulocytes begin to drop off markedly, there already was an increasing deposition of P^{32} in bone. The retention of P^{32} in bone is of much longer duration than in lymphatic or any other tissue. There is no direct evidence that the neoplastic cells are more radiosensitive than other cells. It was found that, at corresponding stages in the lymphomatous process, the treated animals had less infiltration of organs by leukemic cells than the non-treated groups. In both the normal and leukemic animals, the greatest drop in white blood cells occurred during the first four days after administration of P^{32} . The chief cell type to be affected is the lymphocyte and the lymphoma or leukemic cell. During the following five days the rate of drop diminishes, but during this period the greatest decrease in granulocytes occurs. Studies of the exchange of P^{32} in leukemic tissues of mice revealed a higher uptake than in other soft tissue. This greater uptake in neoplastic tissue is of interest, since these cells receive relatively more radiation. The predominant effects of P^{32} on leukemic as well as normal elements of the marrow constitute its limiting factor in its use in the therapy of leukemia and make it of doubtful value in lymphosarcoma and allied diseases.

885

Hershey, A. D., M. D. Kamen, J. W. Kennedy, and H. Gest. THE MORTALITY OF BACTERIOPHAGE CONTAINING ASSIMILATED RADIOACTIVE PHOSPHORUS. *J. Gen. Physiol.* **34**, 305-19(1951).

Bacteriophage T4 containing assimilated P^{32} is inactivated at a rate proportional to the specific radioactivity of the constituent P. The β radiation from the P makes a negligible contribution to this effect. The inactivation is therefore a direct consequence of the nuclear reaction, which kills the phage with an efficiency of about $1/12$. Several phages related to T4 behave similarly. When radioactive phage is grown from a seed of nonradioactive phage, all the phage progeny are subject to killing by

radioactive decay. The phage is killed by β radiation from P^{32} with an efficiency of about $1/100$ per ionization within the particle volume. Bacteriophage T4 and its relatives contain about 500,000 atoms of P per infective particle. Virtually all this P is adsorbed to bacteria with the specificity characteristic of the infective particles, and none of it can be removed from the particles by the enzyme desoxyribonuclease. The P content per particle, together with the published data on analytical composition indicates a particle diameter close to 110m μ for the varieties of phage studied. (NSA)

886

Hollcroft, Joanne Weikel and Egon Lorenz. THE 30-DAY LD₅₀ OF TWO RADIATIONS OF DIFFERENT ION DENSITY. *J. Nat. Cancer Inst.* **12**, 533-44(1951).

The 30-day LD₅₀ x radiation was compared with that of the α particles emanating from short-lived decay products of radon injected intravenously in strain A male mice. The integral dose of x radiation necessary to produce 50% death was found to be 1.42 times that of α particles. Regression curves are given. The distribution of short-lived decay products of radon was followed for the 2-hr period following infection. The distribution of the dose was calculated. (NSA)

887

Hu, F. N., S. G. Holmes, C. M. Pomerat, C. S. Livingood, and K. P. McConnell. A METHOD FOR STUDYING THE EFFECT OF P^{32} ON LIVING ADULT HUMAN EPIDERMAL CELLS IN A PERFUSION CHAMBER. *Texas Repts. Biol. and Med.* **9**, 738-48(1951).

Experiments are reported on the effect of P^{32} on living adult human epidermal cells when introduced in a nutrient fluid within a perfusion chamber designed to permit still- and motion-picture photographic recordings of cellular structure. This preliminary study is designed to illustrate the feasibility of the method with respect to observations upon adult human tissues. (NSA)

888

Jones, H. B., C. J. Wrobel, W. R. Lyons. A METHOD OF DISTRIBUTING BETA-RADIATION TO THE RETICULO-ENDOTHELIAL SYSTEM AND ADJACENT TISSUES. *J. Clin. Invest.* **23**, 783-8(1944).

Chromic phosphate is precipitated from Na_2HPO_4 and $Cr(NO_3)_3$ solns. buffered by NaAc. The washed, dried precipitate is heated to 600°C. The heat drives off water of crystallization and converts the soluble precipitated $CrPO_4$ into an inert amorphous powder. This powder is ground to a colloidal state in isotonic saline by a glass-bead mill. The suspension (avg. particle size, 1 μ) is inert and non-toxic. As much as one mg/g body wt. is well tolerated by mice when given intravenously. Chromic phosphate can be prepared with radio-active P. Intraven. administered this material is taken up and retained by the reticulo-endothelial system; the β radiation of P^{32} is distributed to the endothelial system and adjacent tissues. The material accumulates in the liver, spleen, and lungs. In the dog 90% goes to the liver, 6% to the spleen, and 2% to the lungs. In the mouse the bulk goes to the liver, but the spleen and lungs acquire more than the same organs in the dog. The $CrPO_4$ is retained in the endothelial cells of mice for at least a year without detected decrement. Radioactive doses which delete the spleen do not affect the liver. Radioactive doses of the order of 80,000 r in the liver may induce hepatoma. The absorption of β radiation in tissues is discussed with special reference to tissues less than 0.6 cm thick. (BA)

889

Kisielewski, Walter E. and William P. Norris. THE EFFECT OF BAL ON THE DISTRIBUTION AND METABO-

LISM OF P^{32} AND Sr^{90} . *Proc. Soc. Exptl. Biol. Med.* **77**, 694-6(1951) 7p. (AECU-1368)

The effectiveness of 2,3-dimercapto-1-propanol (British antilewisite, BAL) in increasing the elimination of injected P^{32} and Sr^{90} in mice was investigated. It is concluded that BAL is essentially without effect although, in the case of P^{32} , the rate of uptake in bone appears to be reduced during the first hour. No such difference could be demonstrated after 24 hr. (NSA)

890

Kligerman, Morton M. THE EFFECT OF RADIOACTIVE PHOSPHORUS ON THE GROWTH OF THE ALBINO RAT. *Am. J. Roentgenol. Radium Therapy* **63**, 380-95 (1950).

Five groups of 21-day old Wistar Institute white male rats received P^{32} on the following basis: Group A (24 rats) 44 μ /kg body weight; Group B (24 rats) 132 μ /kg body weight; Group C (24 rats) 400 μ /kg body weight; Group D (24 rats) 1,200 μ /kg body weight; and Group E (20 rats) 3,600 μ /kg body weight. Five more groups of rats, 42 days old, received corresponding doses. Other details of the experimental procedures are included. It was found that doses as small as 44 μ /kg of P^{32} retarded normal weight gain in the 21-day old rats; doses of 132 μ retarded the growth of bone (femur) and larger doses produced a greater effect; 44 μ /kg seemed to accelerate the growth. The effect of P^{32} on growth (weight and long bones) ceased when its concentration fell below a threshold dose; this level was reached within 42 days after the last injection. The effect of the P^{32} was found to be temporary, treated rats equaling normal rats in weight, size, and appearance when 300 days old. However, when 1,200-3,600 μ /kg was given, the physical appearance and activity of the rats were affected, and half of the 42-day old rats receiving 3,600 μ /kg died before reaching 112 days of age; the 21-day old rats showed depression of all the cellular elements with profound changes in the white blood count. An increase in the densely calcified area on the metaphyseal side of the epiphyseal line also appeared. (NSA)

891

Koletsky, Simon, and James H. Christie. BIOLOGIC EFFECTS OF RADIOACTIVE PHOSPHORUS POISONING IN RATS. *Am. J. Pathol.* **27**, 175-94(1951).

Lethal doses of P^{32} produced extensive morphologic lesions in rats. These were similar to previously described effects of radiation, from either external or internal source, in both animals and man. Similar changes result also from the nitrogen mustards. By virtue of its distribution, P^{32} acted as a powerful hemopoietic poison producing aplasia of the bone marrow and hypoplasia of the lymphoid tissues of the body, including spleen and thymus. This was reflected in the peripheral blood by rapidly developing leukopenia, thrombocytopenia, and anemia. In addition, the intestinal tract, especially the small bowel, and the gonads were sensitive to radiation. Organs such as liver, pancreas, adrenals, kidney, heart, and brain were radioresistant. Destruction of tissue occurred rapidly, being well developed from 6 to 12 hr after injection of the P^{32} . The principal method of cell destruction was by karyorrhexis. Most of the resulting debris was removed by the 2nd or 3rd day. Involution of the hemopoietic organs was marked at the end of 24 hr and was then progressive over the next several days. During the period of necrosis and involution the animals usually were in good condition and asymptomatic. However, this latent interval was followed by progressive inanition, debility, and weight loss, terminating in death within 3 weeks after the administration of the P^{32} . At the time of

death there were aplasia of bone marrow, atrophy of lymphoid tissues, and persistent leukopenia, but the hemopoietic often revealed beginning or even fairly substantial regeneration; the intestinal damage was largely repaired, whereas the injury to testes was progressive. In animals that recovered there was usually good repair of bone marrow and lymph nodes after a few months. Regeneration was less effective in spleen and thymus, and in the testis generally ranged from slight to negligible. One of the late effects of P^{32} poisoning was the development of malignant neoplasms. The mechanism of radiation death is not established. With massive doses of P^{32} , after which death takes place within a few days, the outcome is usually attributed to a general toxemia resulting from extensive destruction of tissue. With LD_{50} doses of P^{32} , after which death occurs within a few weeks, the almost constant presence of infectious lesions suggests that bacterial toxemia may be significant. 30 references. (NSA)

892

Lawrence, John H., B. V. A. Low-Beer, and James W. J. Carpender. CHRONIC LYMPHATIC LEUKEMIA; A STUDY OF 100 PATIENTS TREATED WITH RADIOACTIVE PHOSPHORUS. *J. Am. Med. Assoc.* **140**, 585-8 (1949).

A study of 100 cases of chronic lymphatic leukemia treated with phosphorus-32 alone or in conjunction with roentgen rays is presented; the doses were usually 1-2 mc/week for 4-8 weeks, the treatment series being repeated if necessary (but not to exceed about 50 mc for the combined series). Comfortable life appears to have been prolonged as compared with the average life span after other methods of treatment. At the time of writing, 33% of the group have lived 5 or more years after onset and 10% 8 or more years; 24 of the patients are still living. When compared with 5-year end results in other types of neoplastic disease, such as carcinoma of the breasts, prostate, lung, stomach, and esophagus, these results are concluded to be relatively good and do not encourage the prevalent hopeless attitude taken by many doctors confronted with the problem of treating chronic leukemia. (NSA)

893

Lisco, H., Miriam P. Finkel and G. Hirsch. PROGRESS REPORT ON THE CHRONIC P^{32} MOUSE EXPERIMENT. Argonne National Lab. Nov. 1, 1947. 180p. (AECD-2009-E)

The data that are being collected on the CF-1 female mice that either received a single intraperitoneal injection or are receiving monthly injections of radiophosphorus are beginning to reach proportions which permit tentative analysis. At 290 days after the initial injection in each series (single and repeat doses), 20% of the total of 937 animals had died or had been sacrificed in a moribund condition. Although the final complete diagnosis of many animals must await histological study of one or more tissues, it is possible at this time to note some radiation effects. The tentative conclusions at this interval in the experiment (290 days) are that: (1) The incidence of lymphoma is increased in the groups which received 10.0-5.0 $\mu\text{C/g}$ and 1.0-0.5 (and probably 0.1) $\mu\text{C/g/mo}$ of P^{32} . There is no evidence at 290 days that animals receiving low doses of radiophosphorus have a decreased probability of developing lymphoma. (2) The incidence of mammary tumors among CF-1 female mice which received 10.0-0.01 $\mu\text{C/g}$ of P^{32} or which are receiving 1.0-0.01 $\mu\text{C/g/mo}$ is not different from the spontaneous occurrence of mammary tumors in this strain. (3) The incidence of lung tumors is increased by 10.0-5.0 $\mu\text{C/g}$ and 1.0-0.1 $\mu\text{C/g/mo}$ of P^{32} . (4) Growth is retarded by 1.0-0.5 $\mu\text{C/g/mo}$ of P^{32} . (ADD)

894

Low-Beer, Bertram V. A. EXTERNAL THERAPEUTIC USE OF RADIOACTIVE PHOSPHORUS. I. ERYTHEMA STUDIES. *Radiology* **47**, 213-22(1946).

For the study of skin effects of radioactive P, 69 exposures were made on the forearm and arm of 12 healthy subjects. The radioactive P was applied by using disks of blotting paper 2.5 cm in diam. and 0.4 mm thick, soaked with Na_2HPO_4 soln. Radioactive P applied to skin in this manner produces erythemata showing a monophasic course. The intensity of the erythema depends on the amount of exposure. "Threshold erythema" was produced by an exposure to 34 microcurie hours/sq. cm. Dry, scale epidermite was produced by an exposure to 2,000 microcurie hours/cm²; and bullous epidermite resulted from an exposure to 4,400 microcurie hours/cm². The depth of discernible biologic effect from externally applied radioactive P is approx. 5 mm for erythema producing doses. (BA)

895

Low-Beer, Bertram V. A. RADIOACTIVE PHOSPHORUS AS AN EXTERNAL THERAPEUTIC AGENT IN BASAL CELL CARCINOMA, WARTS, AND HEMANGIOMA. *Am. J. Roentgenol. Radium Therapy* **58**, 4-9(1947).

Superficial skin diseases were successfully treated with direct application of radioactive phosphorus (P^{32}) to the area of the lesion. Office type blotting paper, 0.4 mm thick and weighing 21 mgm per square centimeter, is cut to the size of the lesion with a 0.3-1.0 cm margin and backed with adhesive tape and dried. It is then soaked in active Na_2HPO_4 solution, dried and secured to the area of the lesion with adhesive tape. The threshold erythema dose was found to be 34 μC per sq cm; mild erythema was produced by 620 μC per sq cm and severe epidermitis by 4,400 μC per sq. cm. Treatment doses for basal cell carcinoma, hyperkeratosis, verruca, planter wart, subungual wart and haemangioma varied from 300 to 5000 $\mu\text{C-hr}$ per sq cm depending upon the size and type of lesion. Of the lesions treated, 88.6 to 100 per cent disappeared without recurrence. (EM)

896

Low-Beer, Bertram V. A. ISOTOPES: RADIOACTIVE; RADIOPHOSPHORUS AND RADIOSODIUM p.454-60 of MEDICAL PHYSICS, Vol. 2. Otto Glasser, ed. Chicago, Year Book Publ., Inc. 1950. 1227p.

P^{32} uptake and excretion are discussed for different routes; exchange problems, detection and measurement and therapeutic applications are considered. Clinical studies on uptake and excretion of Na^{24} show that equilibrium is reached in three hours following administration but that excretion is very slow. (R.D.B.)

897

Martin, A. THE EFFECTS OF RADIOACTIVE PHOSPHORUS ON *CRICETUS AURATUS*. *Genetics* **35**, 679 (1950).

This paper is reproduced here in its entirety.

Males of the golden hamster, *Cricetus auratus*, have been given intraperitoneal injections of various dosages of radioactive phosphorus and subsequently mated to untreated females. Histological and cytological examination of the tissues of the treated animals is in progress, and progeny are under observation. The maximum sublethal dose lies between 6 and 9 $\mu\text{C/g}$ of body weight. A few animals survive a dosage of 8 μC , and recover from radiation sickness in about 11 days. Three microcuries induce permanent sterility in 30 days or less. Dosages of 3 or more μC result in the degeneration of Sertoli cells and the filling of the seminiferous tubules with fibrous connective tissue. One microcurie has no effect on sperms in the tubules in 24 hr, but in 15 days the tubules are devoid of sperms. In 30 days, however, the testes again appear normal, and

the tubules contain apparently normal sperms. Following dosages of 1 and 3 μ c, the white blood cell count is much reduced. No statement is as yet available on effects on other tissues. The available progeny to date bear out the histological and cytological findings, in that none has been produced by males treated with 3 or more μ c. When not completely destroyed, the germ plasma seems to be remarkably stable, in that progeny show no phenotypic abnormalities, litter size is unaffected, and offspring are of normal viability. (NSA)

898

Muix, R. M. EFFECT OF RADIATION FROM RADIOACTIVE ISOTOPES ON THE PROTOPLASM OF SPIROGYRA. *J. Cellular Comp. Physiol.* **19**, 244-7(1942).

Beta radiation from radioactive P (P^*) increased the viscosity of protoplasm in *Spirogyra* when the radioactive strength of the solution was 4.0 millicuries/liter of 17.0 millicuries/liter but had no effect when the radioactive strength was 2.1 millicuries/liter. The total concentration of P fluctuated in filaments immersed in solutions of P^* , but remained relatively constant for 0.001 M and 0.005 M solutions of the nonradioactive P and showed an accumulation for the 0.01 M solution. Maxima occurred after periods of treatment which were shorter for the solutions which had greater radioactivity. Changes in total P content may result from permeability effects of beta radiation from P^* . (CA)

899

O'Neil, J. B., J. R. Jowsey, C. C. Lee, and J. W. T. Spinks. DISTRIBUTION OF P^{32} IN CHICK EMBRYOS. *Can. J. Research, D*, **27**, 223-32(1949).

By feeding a hen repeated daily doses of NaH_2PO_4 of equal P^{32} activity, eggs with high and nearly uniform P^{32} content were obtained for use in hatching expts. Eleven eggs were incubated. The embryos and chicks that died during or after incubation were dissected and analyzed for total and specific activities in the various fractions. Two of the chicks, both females, are still living. They are being raised so that observations may be made on their ability to reproduce and the effect of the radioactivity, if any, on their offspring. (BA)

900

Pal, R. K. and B. N. Mitra. EFFECTS OF RADIO-PHOSPHORUS IN MINUTE DOSES ON BLOOD AND SOME IMPORTANT ORGANS. *Indian J. Physiol. and Allied Sci.* **4**, 42-9(1950).

Rabbits were injected with a preparation of radiophosphorus (P^{32}) in an alkaline K_3PO_4 solution. The animals did not change weight within 18 days. The entire hematopoietic function of the red bone marrow, however, was deleteriously affected by β emanations. A great rise in the Ca content of the blood, through action of the tracer dose as an economizer and mobilizer of reserve supplies was found. There was no harmful action on the bone structure but adverse effects upon the thyroid gland, kidneys, and liver, were indicated. (CA)

901

Platt, W. R. EFFECTS OF RADIOACTIVE P^{32} ON NORMAL TISSUES. *Arch. Pathol.* **43**, 1-14(1947).

Radioactive P^{32} , administered as a dibasic salt to a series of human patients, produced characteristic changes in many tissues, varying in intensity but similar to those produced by other types of radiation. Prominent features of the changes were abnormal mitoses, producing giant irregular nuclei, fibrosis, hyalinization of collagen, thickening and hyalinization of small blood vessel and cellular death. Selective locationization of large quantities of radioactive P and greater injury was observed in tissues

most often involved by neoplastic cells of malignant lymphomatoses and myelomatoses, i.e. bone marrow, liver, spleen, and lymph nodes. Changes were demonstrated also in the lungs, kidneys, gastrointestinal tract, ovaries, and testes. (EM)

902

Powers, E. L., Jr., Deborah Shefner, M. J. Richard, and R. Sato. LETHAL EFFECTS OF P^{32} ON *PARAMECIUM AURELIA*. Argonne National Lab. Aug. 1, 1947. 17p. (AECD-2024-P; ANL-4078)

Further results on the response of *P. aurelia* to exposure to P^{32} , Sr^{90} , and Y^{90} have been obtained, and a partial summary statement of observations to date is presented. There is observed increasing death with increasing P^{32} radioactivity. Death following exposure to the Sr solution increases with increasing activity. Comparison of survival following phosphorus exposure to that following strontium treatment at the same activity level, reveals that in all instances survival of the P-treated animals is the same or significantly lower than survival of Sr-treated animals. From these data it appears that the P-treated animals are injured to a greater extent than the Sr-treated animals. (NSA)

903

Rubin, B. A. THE PATTERN AND SIGNIFICANCE OF DELAYED PHENOTYPIC EXPRESSION OF MUTATIONS INDUCED IN *E. COLI* BY ABSORBED P^{32} . *Genetics* **35**, 133(1950).

Biologically absorbed radioactive phosphorus (P^{32}) has been shown to induce significant increases in the proportion of streptomycin resistant cells among growing populations of *Escherichia coli* (strains B and B/r). Great differences in the absorption of P^{32} by the bacteria have been produced by varying carrier phosphorus. Calculations show that large increases in concentration of P^{32} , in a cell of bacterial dimensions, produce insignificant changes in specific ionization. The increase in mutation rate, however, is disproportionately high. When bacteria were grown in solutions of P^{32} (up to 8 mc per ml) the mutation rate increased with dose. But in all cases the relative size of the mutant population changed upon further cultivation. The pattern of change (diverse rates of increase, sometimes followed by decrease) varied with the concentration of P^{32} and with the amount of absorption, as controlled by carrier phosphorus levels. The complete phenotypic expression of the mutations produced seemed also to depend upon the number of bacterial divisions, since similar changes did not occur in resting cultures exposed in the same way, for similar periods. These patterns indicated a quantitative, as well as qualitative difference in distribution of mutant types produced by an effect which can not be accounted for by ionization alone. Calculations indicate that this effect may be attributed to the transmutation of P^{32} to S^{32} . (G)

904

Russ, Clem. EFFECTS OF PHOSPHORUS 32 ON THE HAMSTER. *Proc. Soc. Exptl. Biol. Med.* **74**, 729-31(1950).

Effects of intraperitoneal injection of the hamster with radiophosphorus, P^{32} , are described. Animals treated with 10 μ c/g of body weight died in 11 days. There were no apparent changes in the testes in this time. Toxic effects were observed in animals injected with as little as 6 μ c/g. Damage to the testes of animals treated with 6 and 8 μ c respectively, was extensive, consisting of marked decrease in size, absence of spermatogenic cells in tubules, and actual damage to the tubules themselves, suggesting permanent sterility. No changes in the testes of animals treated with 1 μ c/g were apparent in 24 hours. However, some damage was observed 30 days after treatment with

1 μ c. Spermatogenic cells were more sensitive than Sertoli cells. Some interstitial cells appeared to be affected. (NSA)

905

Russell, R. S., S. N. Adams, and R. P. Martin. **RADIATION EFFECTS DUE TO P^{32} IN FERTILIZER EXPERIMENTS.** *Nature* 164, 993-5(1949).

Barley was fertilized with the equiv. of 8 lb P/acre; this included from 0 to 4 μ c P^{32} /pot, or 0-460 μ c P^{32} /g P. There were no significant effects on dry wt. of shoot or root after 39 days; but at 4 μ c/pot there was a decrease in absorption of fertilizer P, and even at 0.8 μ c/pot, a significant decrease in ratio of fertilizer P to soil P absorbed. Increase of this ratio for shoots at 70 days (when activity had decayed to 3.4% of initial) may have been correlated with root regeneration in the surface layers of soil, as more short adventitious roots were found. (BA)

906

Schmidt, Clarence F. **THE EFFECT OF RADIOACTIVE PHOSPHORUS UPON A SUSPENSION OF *ESCHERICHIA COLI*.** *J. Bacteriol.* 55, 705-9(1948).

Radioactive phosphorus (P^{32}) added to a suspension of *Escherichia coli* in phosphate buffer has a definitely lethal effect upon the cells that in a general way is related to the initial concentration. Complete sterilization of the suspension was not obtained in the highest concentration tested. The survivor curve indicated a more rapid rate of killing during the first time interval, and the existence of a small percentage of the cells that were more resistant and survived to the end of the experiment. The present experiment does not suggest in any way the possibility of the application of radioactive materials to the sterilization of food products. (NSA)

907

Scott, K. G. and S. F. Cook. **THE EFFECT OF RADIOACTIVE PHOSPHORUS ON THE BLOOD OF THE GROWING CHICK.** *Proc. Natl. Acad. Sci. U. S.* 23, 265-72 (1937).

The administration of radioactive H_3PO_4 (birds were used as experimental animals) gives rise to effects upon the constituents of the blood that are not obtained by x-rays. The lymphocytes which are sensitive to x-ray radiation were not particularly affected. The administration of radioactive P ($_{15}P^{32}$) (I) brought about a great decrease in the number of polymorphonuclear leucocytes. This decrease is attributed to the selective deposition of I in the bones, which allows bombardment of the bone marrow with β -rays. The basophiles and monocytes were not appreciably affected, although an increase in eosinophiles was noted. Birds treated in this manner grew normally and any permanent ill effects from the administration of I were not observed. (CA)

908

Scott, K. G. and J. H. Lawrence. **EFFECT OF RADIO-PHOSPHORUS ON BLOOD OF MONKEYS.** *Proc. Soc. Exptl. Biol. Med.* 48, 155-8(1941).

The administration of radio-P to monkeys lowers the absolute numbers of red cells, lymphocytes, and granulocytes in the blood. Lymphocytes and granulocytes are affected to about the same degree. Red cells are not as radio-sensitive as the former. Monkeys tolerate doses of 0.76 and 0.71 millicuries of P^{32} per pound of body weight. 1.04 millicuries of P^{32} per pound of body weight was fatal. (BA)

909

Simon, Norman. **SUPPRESSION OF GASTRIC ACIDITY WITH BETA PARTICLES OF P^{32} .** *Science* 109, 563-4 (1949).

Irradiation of the gastric mucosa by x-radiations suppresses gastric acidity, but may also damage more sensitive adjacent organs, such as the liver and small intestine. In order to restrict the radiations to the gastric lining, applications of P^{32} were made, for the β -particle emission range for this isotope is only about 8 mm. The P^{32} was applied topically to the mucosal lining of the Heidenhain stomach pouches in dogs. A description of the applicator is included, and it was prepared to hold as much as 25 mc of P^{32} absorbed to its surface. The balloon was inserted into the stomach and held there for 2-6 hours. The radiation was followed after a few days by a decrease in total secretion as well as a decrease in the quantity and concentration of HCl in the pouches of all five dogs studied. Two of these dogs had anacid pouches and three had hypoacid pouches. Calculated doses of 1,800, 12,000, and 25,000 equivalent roentgens in the first mm of mucosa were given to one animal, while the rest received doses of 20,000-25,000 equivalent roentgens in the 1st of mucosa. The longest period of observation after irradiation of any animals was 125 days. There were no changes in blood count, weight, or general condition of the animals which could be attributed to the radiations. One dog returned to normal acidity after a period of three months, and an autopsy showed an ulcer of the stomach pouch. (NSA)

910

Stevens, C. E. **RADIO-AUTOGRAPHIC REACTIONS IN TISSUES OTHER THAN BONES AND TEETH AFTER INJECTION OF RADIO-PHOSPHORUS.** *Anat. Record* 103, 509(1949).

The following is an abstract and is reproduced here in its entirety.

After administration of radio-phosphorus to rats (as carrier-free phosphate), fairly large amounts of it may be detected by the Geiger counter in most organs and tissues. An attempt was made to locate this radio-phosphorus histologically by the autographic method after paraffin embedding. While some phosphorus containing compounds are removed by the fat solvents (dioxane, paraffin) used in the technique, it was found that several others are still retained in the tissues. However, quite different results are obtained according to the type of fixation. After fixation with formalin most of the radioactive material is removable with ribonuclease and is presumed to be ribonucleic acid. Some labeled desoxyribonucleic acid is present in cells which have recently divided by mitosis. Small amounts of other radioactive compounds (phosphoprotein, adenosine di-phosphate?) are also found. After fixation with bichromate containing fluids (Orth), much more intense autographic reactions are obtained in most organs and tissues. It is probable that bichromate retains, besides the above-mentioned phosphorus compounds, such substances as simple organic phosphates or even phospholipids which would normally be extractable with water or fat solvents.

911

Warren, S. and R. F. Cowing. **DISTRIBUTION OF LARGE DOSES OF RADIOACTIVE PHOSPHORUS IN RATS.** *Arch. Pathol.* 29, 730(1940).

Radioactive phosphorus, prepared by the department of physics of Harvard University by neutron bombardment of red phosphorus, was injected, in the form of dibasic sodium phosphate, intraperitoneally in rats. The dose given ranged from 16 to 30 microcuries per animal. The content in the blood dropped in the first 48 hours and the content in the urine fell sharply also. Approximately 6% of the amount injected was excreted in the first 3 hours. Measurements were made with a Lauritsen type electro-scope. The experimental error is probably 15%. The

tissues containing most phosphorus were: liver, voluntary muscle, bone, spleen, and kidneys. The histological observations will be reported. (AP)

912

Warren, S. and R. F. Cowing. **THE DISTRIBUTION OF DOSES OF RADIOACTIVE PHOSPHORUS IN RODENTS.** J. Lab. Clin. Med. **26**, 1014-16(1941).

Radioactive P was injected intravenously or intraperitoneally in mice, rats, and rabbits as an aqueous solution of Na_2HPO_4 . The dosages of active material injected ranged from 5 to 17.5 microcuries in the mouse, from 30 to 239 in the rat and from 50 to 84 in the rabbit. Measurements were made by a Lauritsen-type electroscope. The per centage partition between the various organs varied in the different species, but the spleen, liver, kidney and bone of all showed a material degree of absorption and retention. The urinary excretion of the active material was rapid; about $\frac{1}{4}$ the dose was excreted within 48 hours. There were minor variations in the percentage partition in various tissues among individual animals of the same species. (CA)

913

Warren, Shields, Margaret W. Holt, and Sheldon C. Sommers. **SOME EARLY NUCLEAR EFFECTS OF IONIZING RADIATION.** Proc. Soc. Exptl. Biol. Med. **77**, 288-91(1951).

Frozen-dried, dry-mounted, Feulgen-stained preparations of tissues of rats and mice intraperitoneally injected with large doses of P^{32} were employed to study early cytologic changes after ionizing radiation. Fine nuclear details are preserved by the freezing-drying method. Lethal radiation effects observed in radiosensitive cells include formation of large intranuclear vacuoles with stretching of nuclear membranes. Nonlethal changes in radioresistant tissues include small intranuclear vacuoles, decreased Feulgen stain of nuclear chromatin and sap, and loss of regular sharp staining of nuclear membranes. Such changes in liver cells may contribute to the acute radiation syndrome. (NSA)

914

Warren, Shields, Jane C. MacMillan, and Frank J. Dixon. **EFFECTS OF INTERNAL IRRADIATION OF MICE WITH P^{32} . PART I. SPLEEN, LYMPH NODES, THYMUS, BONE, AND BONE MARROW.** Radiology **55**, 375-89(1950).

A histologic survey of the effects of continuous internal irradiation of mice with varying dosages of P^{32} is presented. The tissue showing radiation injury earliest is the thymus, but the thymus also appears to possess a "radioresiliency" in that it returns to normal most rapidly and completely. Splenic tissue and bone marrow appear about the same in respect to sensitivity to P^{32} , but bone marrow is more nearly completely destroyed than splenic tissue by an equal dose. Repair and return of myelopoiesis can be seen in both tissues at 10 to 15 days following injection. The spleen becomes hyperplastic by 20 days, but the bone marrow does not become hyperplastic until some time later. Lymph nodes are the last tissue to show morphologic recovery from effects of radiation. In the group of animals given the minimal dose an overgrowth effect was observed in some of the tissues after a preliminary depressive effect. Marked lymphopoiesis, myelopoiesis, and hyperplasia occur, with resultant increase in the size of the spleen, thymus, and amount of bone marrow but not in the size of the lymph nodes, which appear permanently damaged and shrunken by this small dose. Also of interest is the histologic observation of repair and recovery in the lymphoid tissues and bone marrow. Restoration to almost normal was accomplished in some animals dying because of radiation injury. (NSA)

915

Warren, Shields, Jane C. MacMillan, and Frank J. Dixon. **EFFECTS OF INTERNAL IRRADIATION OF MICE WITH P^{32} . PART II. GONADS, KIDNEYS, ADRENAL GLANDS, DIGESTIVE TRACT, SPINAL CORD, LUNGS, AND LIVER.** Radiology **55**, 557-70(1950).

A study has been made of the histologic damage suffered by a series of mice injected with 25 μc , and 2 mc of P^{32} . The most characteristic and consistent change in the mouse ovary following injection of P^{32} is a reduction in total amount of ovarian tissue. An absolute sterilizing dose of P^{32} short of a lethal dose has not been found for mice. The 250 μc series of mice affords the best opportunity for study of progressive irradiation changes in the testes. Radiation injuries first the least mature of the spermatogenic cells, as evidenced by nearly complete loss of spermatogonia after 9 days of irradiation. The kidneys of the animals injected with 25 μc of P^{32} showed no morphologic changes. At 10 days, in the kidneys of the animals injected with 250 μc , there was occasional shrinking of the epithelial cells lining the renal tubules. The adrenals showed no specific radiation effects but slight variable congestion was observed, which was not correlated with the amount of radiation received. With doses of 25 and 250 μc the esophagus and stomach of almost all the experimental animals were apparently unaffected morphologically. In a few instances, small petechial extravasations of blood were noted in the ventral horns of the spinal cord of the mice receiving 250 μc . In addition, at least two large central hematomas extended vertically in the cord. Except for variable degrees of congestion, there were no specific radiation changes in the lungs of any of the animals. The maximum radiation effect on the liver, found about 20 to 50 days after injection, was a tendency toward regeneration of liver tissue shown by numerous mitotic figures in the liver cells. 39 illustrations. (NSA)

Plutonium

916

Abrams, R., et al. **METABOLISM AND DISTRIBUTION OF INHALED PU IN RATS.** Univ. of Chicago Metallurgical Lab. Oct. 29, 1946. 46p. (MDDC-677; CH-3655)

Several different techniques were used to introduce tracer quantities of Pu into the lungs of rats. When aerosols were produced by atomizing aqueous solutions of the nitrates it was found that approximately 20% of the dose was absorbed and deposited in the skeleton with tetra, hexa, and trivalent plutonium. Thus with these compounds, the lungs represent a more dangerous portal of entry than either oral (0.05%) or intramuscular (13%) administration. Tetravalent Pu was eliminated most slowly from the lung, the average half-time during the first month being 15 days. But when citrate was added to complex the Pu, over 70% was eliminated within one day. This was accompanied by a deposition of over 30% in the skeleton and over 20% in the liver. Presumably citrate breaks up the insoluble colloid in which Pu exists in the lungs. Complexing with cupferron which, unlike citrate, produces a "fat soluble" compound, greatly diminished the extent of absorption from the lungs. Plutonium oxide smokes which were produced at high temperatures were eliminated more slowly from the lungs (average half time of 30 days during the first month) and were deposited in the skeleton to a much lesser extent (6.2%) than was the case with the nitrates. (ADD)

917

Arnold, J. S. **RADIOAUTOGRAPHY.** Argonne National Lab. Jan. 1951. Decl. June 5, 1951. 4p. (AECD-3191)

In an effort to demonstrate the migration of Pu from its initial site of deposition 14 rats were given subtoxic amounts of Pu citrate intravenously and were sacrificed at weekly intervals. By radioautographic means it has been definitely shown that the Pu migrated from its initial endosteal site of deposition into the cortical bone by the process of having new nonisotope-containing bone laid down over it. Further, it seemed that the Pu that had migrated into the cortex was concentrated on the surface of the laminae of bone or in the cement substance between laminae. In a dog that had been given Pu 2 years before sacrifice, the retained Pu was distributed in a rather spotty manner in both trabecular and cortical bone. U^{233} , which had been administered intravenously as the nitrate, was found to appear in aggregates in the macrophages of the spleen of mice. A photograph of this phenomenon is reproduced in the report. The kidney accumulation of injected U^{233} appeared to be in the proximal convoluted tubes in the form of a cast deposition. The results of tests with NTA and NTB liquid nuclear track emulsions show that there is definite advantage in their use for localization studies. (NSA)

918

Barron, E. S. G., R. Abrams, R. D. Finkle, and R. P. Rhoades. **THE EFFECT OF PLUTONIUM ON TISSUE METABOLISM OF RATS.** Argonne National Lab. June 1946. 54p. (MDDC-1653; CH-3849)

Detailed information is given on metabolic changes in the various body tissues after introduction of Pu into the body by injection, after intratracheal instillation of Pu or after injection. Effects on the QO_2 , QO_2 succinate, anaerobic glycolysis, QO_2 pyruvate, Q pyruvate, Q and QO_2 butyrate, acetoacetate formation, phospholipid synthesis and removal are discussed. The various effected organs and tissues as kidney, liver, thymus glands, adrenals, submaxillaries, blood and lungs and the small intestine are treated specifically. P^{32} was used as tracer in some experiments. (TIS)

919

Bloom, William and Margaret Bloom. **SOME LATE HISTOLOGICAL CHANGES IN MICE AFTER LOW DOSES OF PLUTONIUM AND RADIUM, p.174-84 of BIOLOGICAL AND MEDICAL DIVISIONS; QUARTERLY REPORT, NOVEMBER, DECEMBER, JANUARY, 1949-50.** Argonne National Lab. [nd] 11p. (ANL-4401(p.174-84))

Mice were injected intravenously with plutonium nitrate (0.03 or 0.003 $\mu\text{C/g}$) or intraperitoneally with Ra (0.3 or 0.03 $\mu\text{C/g}$) and sacrificed at intervals of 2 months to a year thereafter. Results of histological examination of the spleen, lymph node, thymus, liver, testis, lung, skin, gastro-intestinal tract, and pancreas are given. The red pulp of the spleen was greatly increased after the higher doses of Pu and Ra and moderately increased after the low dose of Ra. The increase in hematopoiesis in the spleen was undoubtedly compensatory for the continued and progressive depression of the blood-forming mechanism of the bone marrow of these mice. Even where hematopoiesis in the marrow persisted, it was predominantly myelocytopoietic rather than erythropoietic. (NSA)

920

Brues, Austin M. **EFFECTS OF PLUTONIUM IN THE LIVER.** Trans Conf. Liver Injury, 7th Conf. 59-61(1948).

It has been determined that the early distribution of plutonium is in the liver and spleen and that it is gradually translocated to the bone. The effect of injecting a large dose (1 γ per g in the rat) was, as in total body radiation, to produce death. However, rats and mice given a smaller dose may survive for several months, although they show clinical evidence of liver disease, and severe cell damage and atrophy of the liver. Although liver carcinomas did

not develop, bone carcinomas frequently occurred nearly a year later. Hypertrophy of liver tissue around the margin of atrophic nodules has been attributed to the tendency of cerium-144 to concentrate in the liver. (NSA)

921

Finkel, Miriam P. **SOME FURTHER NOTES ON THE MICE TREATED WITH PLUTONIUM BEFORE WEANING.** Argonne National Lab. Aug. 1, 1947. (AECD-2024-H)

In August 1945 an experiment was begun to investigate the late effects of plutonium upon mice which were treated *in utero*. It was discovered that young mice obtained additional plutonium from the breast milk of their treated mothers. Therefore it was necessary to run another series of experiments which measured the Pu absorbed by suckling mice as well as the retention of the material by young animals. This information has made it possible to assign definite dose levels to the mice of the original experiment and to analyze the data which have been accumulating since the birth of these animals. Topics discussed are the dose levels, the relative contributions of plutonium from the placenta and the milk, the retention of plutonium by mice treated before weaning, and the effects of low levels of plutonium on growth. (NSA)

922

Finkle, R. D., et al. **THE TOXICITY AND METABOLISM OF PLUTONIUM IN LABORATORY ANIMALS.** Argonne National Lab. Aug. 1946. Decl. July 25, 1947. 144p. (MDDC-1140; CH-3783)

Methods used in tissue analysis after intracardial, intravenous, or intramuscular injection of Pu are discussed and new methods used are described. No species, strain, or sex differences were found in hematological effects of Pu. Doses of 0.0003 or 0.0006 $\mu\text{C/g}$ of Pu caused no detectable hematological alteration in the peripheral blood of mice, rats, and rabbits during 300 days of observation. A dose in the range of 0.003 $\mu\text{C/g}$ produced a minimum to moderate depression of the leucocytes and platelets in all 3 species within the first 100 days. A dose of 0.0063 $\mu\text{C/g}$ produced a moderate to severe and sustained leucopenia in all species studied and caused an anemia and early death in mice and rats (135 days). Doses of 0.0156 to 0.125 $\mu\text{C/g}$ produced correspondingly more severe and sustained anemia, leucopenia, reticulocyte reduction, and platelet deficiency; and early death in mice and rats. Pu intoxication produced morphological changes in the nucleated cells of the peripheral blood comparable to those which occur after exposure to external radiations. A macrocytic anemia developed in rats following the parenteral administration of Pu in doses between 0.0063 and 0.063 $\mu\text{C/g}$. This effect was less significant in mice and rabbits after comparable doses. (TIS)

923

Hamilton, Joseph G., D. H. Copp, D. M. Greenberg, M. J. Chace, L. Van Middlesworth, and E. M. Cuthbertson. **THE DEPOSITION OF PLUTONIUM AND CERTAIN FISSION PRODUCTS IN BONE AS A DECONTAMINATION PROBLEM.** [Radiation Lab., Univ. of Calif.] May 15, 1946. 98p. (AECD-2483; CH-3591)

Bone deposition of Pu and the fission products of radioactive Sr, Y, and Ce was studied in view of possible decontamination. Although most treatments had little influence on the absorption of Sr from the gut, both age and dietary Ca did have a profound effect, and growing rats, on a diet low in Ca, absorbed over 25 times as much of a given dose as did adult rats receiving ample Ca in the diet. There was also a 4-fold difference in the retention of injected radioactive Br but no appreciable effect on the retention of radioactive Y, Ce, or Pu. The chronic elimination by the rat of

radioactive Sr, Y, Ce, and Pu was followed for a period of several months. No appreciable decontamination was obtained by various prolonged treatments. Experiments on healing bone fractures showed that the peak uptake of radioactive Pu and Y by the callus occurred several days before the commencement of active calcification and deposition of radioactive Sr. There was a 4x reduction in the retention of radioactive Sr by animals suffering from a severe dietary P deficiency but no significance in the retention of Pu, Y, and Ce. It was found that the effects of severe P deficiency, including resorption of bone salts, could be produced by adding $\text{Al}(\text{SO}_4)_3$ or freshly precipitated $\text{AlO}(\text{OH})$ to a normal diet. Some demineralization of bone could be produced even in adult animals. Radioautographs of undecalcified bone sections from such animals showed that the radioactive Sr was deposited only in the presence of bone salts while radioactive Pu, Y, Ce, and Zr were laid down in the uncalcified organic matrix. These, and the preceding metabolic studies, indicate that while Sr follows the path of Ca and is deposited in the mineral of bone, the metabolism of the other elements is unrelated to that of Ca and they may be laid down in the organic bone matrix. Radioautographs or undecalcified bone sections of adult rat demonstrated the superficial deposition of Pu, and the relative immobility of these deposits. By this technique, it was shown that these Pu deposits in the skeleton may be overlaid with newly formed non-radioactive bone, thus shielding the sensitive cells of bone marrow and bone from the short range α particles. This has been suggested as a possible means of reducing the chronic toxicity of Pu in the skeleton. (TIS)

924

Katz, J., C. W. DeLong, M. E. Getzendaner, A. C. Case, and Esther S. Miller. **ABSORPTION OF PLUTONIUM FED CHRONICALLY TO RATS; I. EFFECT OF SEX ON FRACTION ABSORBED AFTER HIGH DOSAGE LEVELS.** Hanford Works. Mar. 13, 1951. 11p. (HW-20941(pt. 1))

Preliminary investigations undertaken to determine the percentage absorption from the rat's gastrointestinal tract of Pu administered chronically and to find whether the sex of the animal plays a role in the rate of absorption are described. Five male and five female rats each received perorally an average of $5.9 \mu\text{g}$ of Pu^{239} (+4) as the nitrate over a period of 90 days. Radiochemical analyses indicated that an average of 0.0095% of the administered dose was deposited in the total carcass. The pelt continued negligible amounts, but the gastrointestinal tract and contents retained considerable quantities of Pu even after a fast of 3 to 5 days. There was no evidence of any sex difference in Pu retention. (NSA)

925

Kawin, Bergene and D. Harold Copp. **A STUDY OF THE EFFECT OF 2,3-DIMERCAPTOPROPANOL (BAL) UPON THE METABOLISM OF PLUTONIUM.** Radiation Lab. Univ. of Calif. Jan. 23, 1950. Decl. Apr. 5, 1950. 8p. (AECD-2814)

The effects of 2,3-dimercaptopropanol (BAL) upon the metabolism of intramuscularly injected $\text{Pu}(\text{VI})$ in rats have been investigated. The use of BAL produced no significant alterations in the distribution and excretion of plutonium as compared to the pattern shown by control animals. The metabolism of plutonium does not appear to be related to sulphhydryl groups. On the basis of its ineffectiveness in changing the metabolism of plutonium, BAL does not appear to be an effective therapeutic treatment for plutonium poisoning. 10 references. (NSA)

926

Kisielewski, Walter E. and L. Woodruff. **STUDIES ON THE DISTRIBUTION OF PLUTONIUM IN THE RAT.** Argonne National Lab. [nd] 18p. (AECD-2009-F)

The citrate and nitrate salts of plutonium in the +6 valence states were injected intramuscularly into male rats at a dose of $0.1 \mu\text{g/g}$. Animals were sacrificed at intervals from 7 to 420 days, and the plutonium content of the various tissues was determined by the standard LaF_3 method for plutonium determination. When plutonium is injected intramuscularly as the citrate salt, the presence of the citrate as compared to nitrate seems to increase absorption of the plutonium from the site of injection. After 10 days 51% of the injected dose was found in the injected leg of the nitrate animals where only 30% was found in the citrate group. At the termination of the experiment (420 days) 20% was found after injecting the nitrate as compared to 12% with the citrate. The skeleton was the principal site of deposition regardless of the form in which the plutonium was injected. Liver was next in order, containing 2% of the injected dose at 10 days in the nitrate animals and 5% in the citrate group. The spleen contained only about 0.1% of the injected dose in both the citrate and nitrate animals, though in specific activity ($\mu\text{g/g}$ of wet weight) it was as high as liver or bone. Most of the other soft tissues contained insignificant amounts of plutonium activity and it was noted that this concentration decreased with time, the gonads being the exception, where a reverse trend was observed. There was no evidence to show translocation of plutonium from the soft tissues into bone. All of the tissues in the citrate groups showed a higher initial uptake than can be seen in the nitrate groups. The specific concentration of the various tissues gives a better picture of the increased initial uptake by the citrate group as compared to the nitrate. At seven days the specific activity in $\mu\text{g/g}$ of wet weight of liver in the nitrate group was $0.039 \mu\text{g/g}$, while the citrate was $0.214 \mu\text{g/g}$. The specific activity of the spleen was as high as liver having $0.043 \mu\text{g/g}$ at seven days in the nitrate group and $0.123 \mu\text{g/g}$ in the citrate group. Bone in the citrate group at seven days was $0.533 \mu\text{g/g}$, while it was $0.398 \mu\text{g/g}$ in the nitrate group. A significant difference was noted in the specific concentration in thymus in the two groups. The concentration was only $0.008 \mu\text{g/g}$ in the nitrate group at seven days, while it was $0.046 \mu\text{g/g}$ in the citrate group. (ADD)

927

Langham, W., et al. **METABOLISM OF PLUTONIUM.** J. Biol Chem. 171, 273-83(1947) (MDDC-719)

The purpose of the experiments conducted at this laboratory was to study the effect of citrate ion concentration, valence state, and various other factors on the body distribution and excretion of plutonium following its intravenous administration to the rat. The first day following intravenous injection of $\text{PuO}_2(\text{NO}_3)_2$ the urinary excretion of plutonium was 7.5% of the dose as compared to 0.33, 0.57, and 0.71% when administered as PuCl_3 , $\text{Pu}(\text{NO}_3)_4$, and Pu^{+4} citrate complex respectively. Fecal excretion during the first day was correspondingly lower following injection of $\text{PuO}_2(\text{NO}_3)_2$. On the 13th day following intravenous injection there were no significant differences in either urinary or fecal excretion of plutonium administered as PuCl_3 , $\text{Pu}(\text{NO}_3)_4$, Pu^{+4} citrate complex, and $\text{PuO}_2(\text{NO}_3)_2$. At this time the average urinary excretion was 0.014% of the injected dose and the average fecal excretion was 0.22%.

The average ratio of fecal to urinary excretion was 16/1. The skeleton was a major site of deposition regardless of the form in which the plutonium was injected. Four days following injection of plutonium as PuCl_3 , $\text{Pu}(\text{NO}_3)_4$, Pu^{+4} citrate complex, and $\text{PuO}_2(\text{NO}_3)_2$ skeletal deposition was 44.9, 29.3, 56.9, and 56.5% of the injected dose respectively. Deposition in the liver under the above conditions was 22.9, 39.7, 9.6, and 9.1% of the injected dose respectively. Deposition of plutonium in kidney, spleen, and in "balance" was not greatly affected by the form in which the plutonium was administered. The size of the injected dose of Pu^{+4} citrate complex did not affect the per cent of the dose excreted in the feces and urine. Likewise, the size of dose did not alter the per cent of injected material present in the various tissues six days following injection. Absorption of plutonium from the gastro-intestinal tract was quite low—0.01% of the administered dose. When Pu^{+4} was administered orally in 5% sodium citrate solution, the presence of the citrate seemed to increase absorption of the plutonium from the gastrointestinal tract. Absorption was still quite low—only 0.3% of the administered dose. Seventy-nine per cent of the plutonium absorbed from the gastrointestinal tract was deposited in the skeleton and 7.3% in the liver. Plutonium absorbed slowly via this route seems to give a higher deposition in the skeleton than it does when administered intravenously as PuCl_3 , $\text{Pu}(\text{NO}_3)_4$, Pu^{+4} citrate complex or $\text{PuO}_2(\text{NO}_3)_2$. Results are tabulated and graphed. (ADD)

928

MEDICAL AND HEALTH PHYSICS QUARTERLY REPORT, JANUARY, FEBRUARY, AND MARCH, 1950. Radiation Lab. Univ. of Calif. May 2, 1950. 105p. (AECD-2901)

The localization of Ca^{45} , Sr^{90} , Pm^{147} , Am, and Pu in the skeletal tissue of rats has been investigated by radioautography of the costochondral junction. The distribution of tracer Ca and Sr coincides exactly with that of bone salt and of Ca deposited in cartilage. Pm and Am is deposited at calcified surfaces and in potentially osteogenic tissues found free from osseous components, Pm is found in the same areas and also in spotty deposits in the vascular or perivascular regions within bone. Pu may have a transitory localization adjacent to Ca salts (1 hr after injection) and localizes mainly in actively osteogenic tissues, periosteal extension and inner and outer side of bone. Young rachitic rats show the same rapid initial uptake of $\text{Sr}^{90,90}$ as do young normal animals and the maximum uptake is as great, but $\text{Sr}^{90,90}$ does not remain fixed in the skeleton and is lost rather rapidly. The failure of the $\text{Sr}^{90,90}$ to remain fixed in the skeleton may be a result of the low P level and failure of actual new bone-salt deposition in the rachitic rats. The rapid removal of Sr in these rachitic animals suggests the possibility of important decontamination of $\text{Sr}^{90,90}$ deposited in the skeleton if similar conditions can be reproduced in normal animals. Results are tabulated of tissue distribution studies of Ta^{182} after intravenous or intramuscular administration and after inhalation. The intraperitoneal injection of inorganic phosphate, even in low concentrations, into young rats lowers the blood phosphatase level. The value of massive doses of Zr citrate as a decontaminant for Nb^{95} is demonstrated. The initial rapid drop in blood Nb^{95} level and the high urinary excretion rate are maintained by the Zr citrate action. Data on the effectiveness of Ca versenate (ethylenediaminetetracetate) in removing Y already deposited in the body are presented, and the toxicity of versene acid and Ca versenate to rats is determined. At has a highly selective destructive affinity for thyroid gland tissues. Photomicrographs of the thyroid

tissues are given and hematological studies are reported. Improved methods are given for the production of mc amounts of At^{211} and for the recovery and analysis of At in tissues. The preparation of carrier-free $\text{Re}^{183,184}$ from Ta and from W, and carrier-free Os^{185} from W is reported. (TIS)

929

Schubert, Jack. A STUDY OF THE TREATMENT OF PLUTONIUM AND RADIOYTTTRIUM POISONING BY ZIRCONIUM CITRATE. Argonne National Lab. Sept. 1, 1948. 23p. (AECD-2358; ANL-HDY-592)

A study was made of the effect of a single dose of zirconium citrate on the excretion and distribution of plutonium and radioyttrium in rats and a growing dog. It was found that the administration of zirconium citrate to rats increased the excretion of Pu from 1% to 50% and that of Y from 25% to 60% of the injected dose during a 24-hour period. The amount of Pu and Y deposited in the skeleton was reduced by factors of 6 and 2.6 respectively. No significant changes in the Pu or Y contents of the feces, liver, spleen, or kidneys were found. The administration of zirconium citrate to a dog five months after exposure to Pu was followed by a sustained increase in the urinary excretion of Pu. The extent of the increase was proportional to the dose of zirconium citrate. Two and one-half years after exposure to Pu the infection of a small amount of zirconium citrate was followed by a twofold increase in the urinary excretion of Pu. A discussion is given of the chemical concepts involved in applying metal displacement principles to the removal of radioactive metals from the body. (NSA)

930

Schubert, Jack. EFFECT OF ZIRCONIUM AND SODIUM CITRATE ON THE DISTRIBUTION AND EXCRETION OF YTTRIUM AND PLUTONIUM. J. Lab. Clin. Med. 34, 313-25(1949) (ANL-4206)

In a previous report it has been shown that zirconium, when administered as the citrate salt, increases the excretion of plutonium and yttrium and reduces its concentration in the bone (Schubert, Science, 105: 389, 1947). These studies have been extended and preliminary data are briefly described in this report. (NSA)

931

Schubert, Jack, Mariam P. Finkel, Marica R. White and Gertrude M. Hirsch. PLUTONIUM AND YTTRIUM CONTENT OF THE BLOOD, LIVER, AND SKELETON OF THE RAT AT DIFFERENT TIMES AFTER INTRA-VENOUS ADMINISTRATION. J. Biol. Chem. 182, 635-42 (1950).

Eighteen female Sprague-Dawley rats weighing between 236 and 254 g received an injection of 0.4 cc 1% Na citrate solution containing both Pu^{239} and Y^{91} into one of the lateral tail veins. The animals were sacrificed in pairs at 5, 15, 30, 60 min and at 2, 6, 12, 24, and 48 hr and blood, bone, and liver samples were analyzed by ashing and determining the alpha-radiations of Pu and beta-emissions of Y. Five min after intravenous injection about 50% of the Pu and 80% of the Y had disappeared from the blood. After this sharp initial drop Pu disappeared more slowly from the bloodstream; 12 hr after administration about 20% of the injected dose was still being circulated. Within 6 hr, almost all the Y had disappeared from the blood, 48 hr were required for removal of most of the Pu. The Pu content of the skeleton increased regularly until a maximum value of about 45% of the injected dose was reached in 24 hr; in 6 hr the Y concentration was near its peak of 45%. After an initial rapid increase of Pu and Y concentration in the liver, the level of Pu continued to rise at a diminished rate until it reached 24% of the injected dose at 24 hr. The Y

level decreased very slowly after the 2nd hr at which time the maximum value of close to 10% was attained. During the first 24 hr following injection the rat excretes about 3% of the Pu and 25% of the Y; after this period the body content of Pu and Y remains nearly constant. Interpretation of the data on the basis of a diffusion-controlled mechanism is discussed. (CA)

932

Schubert, Jack and Marica R. White. THE EFFECT OF DIFFERENT DOSE LEVELS OF ZIRCONIUM ON THE EXCRETION AND DISTRIBUTION OF PLUTONIUM AND YTTRIUM. *J. Biol. Chem.* **184**, 191-6(1950).

Early administration of zirconium citrate to rats previously injected with tracer levels of plutonium, Pu^{239} , and yttrium, Y^{91} , results in a marked increase in the urinary excretion and a considerable decrease in the bone content of the injected radioelements. Relatively large amounts of zirconium, about 200 mg/k, were used in these experiments. In order to clarify the mechanisms involved, graded dose levels ranging from 12.3 to 1336 mg/k as Zr have been given. (NSA)

933

Scott, K., et al. METABOLISM OF PLUTONIUM IN RATS. *J. Biol. Chem.* **176**, 283-93(1948) (MDDC-1018)

The results of detailed metabolic studies of plutonium following oral, intramuscular, intravenous, subcutaneous, and intrapulmonary administration are presented. Plutonium is not absorbed from the digestive tract. The skeleton is the chief organ of deposition for plutonium absorbed by the body following parenteral administration. The digestive tract is the principle channel of elimination and the degree of retention is very great. The rate of excretion is very slow and the half-period of retention of plutonium by the skeleton is estimated to exceed six months. No significant differences in the metabolic properties of plutonium absorbed by the body were observed for its three valence states. Considerable retention of plutonium by the lungs following intrapulmonary administration was observed and was found to be highest for the +4 state, less for +3 plutonium and least for +6 plutonium. A significant degree of absorption of plutonium from the lungs with subsequent deposition in the skeleton took place following the intrapulmonary administration of solutions of this element in its three valence states. (ADD)

934

Scott, Kenneth G., Dorothy Axelrod, Josephine Crowley, and Joseph G. Hamilton. DEPOSITION AND FATE OF PLUTONIUM, URANIUM, AND THEIR FISSION PRODUCTS INHALED AS AEROSOLS. *Arch. Pathol.* **48**, 31-54(1949).

The purpose of the experiments described was to ascertain the possible hazards resulting from the inhalation of fissionable materials and fission products. With the exception of one study on a human subject, young rats were used for all of the experiments, and after anesthetization, were given Pu, U, and mixtures of fission products containing Sr, Y, Zr, Cb, Ru, Ba, La, Ce, Cs, Pr, Nd, and element 61 in the form of smokes and sprays. The rats were given: plutonium oxide as smoke, plutonium nitrate as a spray; fission products, containing Pu and U, as aerosols; carrier-free fission products aerosols; aerosols of carrier-free Zr or zirconium oxide; and aerosols of Pa as protactinium oxide. The preparation of the aerosols is given in detail. The zirconium aerosol was administered to both a human subject and the rats. It was shown that the aerosols were almost totally retained by the head and lungs immediately after exposure; after four days the lungs contained the largest percentage of these elements. The ele-

ments deposited in the head and the bronchial tree were quickly eliminated through the gastrointestinal tract, while the nonciliated portions of the lungs removed the substances at a slower rate. The main pulmonary site of deposition of the substances was in the bronchial passages and alveoli; a small amount was absorbed and appeared in the skeletal structure, but none was found in the blood vessels or in the lymph nodes. (NSA)

935

Van Middlesworth, L. STUDY OF PLUTONIUM METABOLISM IN BONE. *Univ. of Calif. [nd]* 99p. Decl. June 6, 1947. (MDDC-1022; BP-69)

A method is described whereby Pu^{239} , Sr^{88} , and Y^{88} may all be distinguished in the same animal by differences in their radiations. The chronic excretion of Pu^{239} , Sr^{88} , and Y^{88} was followed for 11 weeks in rats injected simultaneously with these three elements. The very low rate of elimination of all three after the first month emphasizes the danger of chronic toxicity. Radioautographs of the tibia show radioactive strontium deposited throughout the bone with a heavy concentration in the region of new bone growth and active calcification beneath the epiphysis. Plutonium was shown to localize superficially in the endosteal and periosteal surfaces of the bone with no apparent concentration in the zone of bone growth and calcification. Severe phosphate deficiency was found to diminish greatly the retention of radioactive strontium in the skeleton. The retention of plutonium at the site of intramuscular injection was reduced in the phosphate deficient rats, but the distribution of plutonium in the body was otherwise unchanged. The maximum uptake of Pu^{239} and Y^{88} in the fracture callus occurred on the second or third day following fracture, before calcification had commenced. On the other hand, active Sr^{88} deposition did not begin until the 4-5 day, and reached a peak at 8-12 days when calcification was most active. Although plutonium and yttrium appear to deposit in uncalcified bone matrix, scurvy, which produces changes in connective tissue and osteoid matrix has no significant effect on the distribution of these elements, aside from a moderate decrease in the amount retained at the site of injection. A period of three weeks on a protein free diet did not alter the distribution of plutonium in the rat, although it did decrease somewhat the retention at the injection site. Following intramuscular injection, more Pu(IV) was retained at the injection site than Pu(VI), but the distribution in the body was otherwise similar. Following intravenous injection, Pu(VI) disappears from the blood stream much more rapidly than does Pu(IV). There was also a much larger proportion of Pu(IV) deposited in the liver. These results indicate that the Pu(IV) may be in a colloidal state. Methionine supplements resulted in a moderate decrease in the plutonium in the skeleton. When large doses of cysteine were injected one hour prior to the intramuscular injection of Pu(VI), the absorption from the injection site and deposition in the skeleton was reduced. There was no effect when the Pu(VI) was administered intravenously. (ADD)

Polonium

936

Finkel, Miriam P. and Gertrude M. Hirsch. POLONIUM AND CF-1 FEMALE MICE: THE 30-DAY LD-50. RETENTION, DISTRIBUTION, AND CONCENTRATION, p. 84-96 of BIOLOGICAL AND MEDICAL DIVISIONS; QUARTERLY PROGRESS REPORT, MAY, JUNE, JULY, 1949. Argonne National Lab. [nd] 12p. (ANL-4333(p.84-96))

Young adult CF-1 female mice were injected intravenously with polonium²¹⁰ chloride. It was found that the

30-day LD-50 lies between 0.04 and 0.03 $\mu\text{g/g}$. The per cent retention was independent of the dose within the range used (0.1 to 0.005 $\mu\text{g/g}$). The biological half-period was 26 days. Seventy-two per cent of the injected material was present in the mouse 10 days after injection, 90% was present at 100 days. Three days after injection 20% of the Po in the body was present in the liver, 12% in the kidneys, and 2% in the spleen. The following order of decreasing magnitude of specific activity ($\mu\text{g/g}$) was found: ovary, kidney, spleen, liver, mesenteric lymph node, lung, femur, gastrocnemius muscle. At 38 days concentration was greatest in the spleen. Doses higher than the 30-day LD-50 resulted in rapid loss of weight: 0.025 and 0.01 $\mu\text{g/g}$ prevented weight increase during the 120-day period of observation, while 0.005 $\mu\text{g/g}$ had little effect on weight increase. (S.V.S.)

937

Finkel, Miriam P., Gertrude Hirsch, Donald Gardiner, and Ruth McNunis. PROGRESS OF THE LONG-TERM POLONIUM-MOUSE EXPERIMENT; p.78-95 of BIOLOGICAL AND MEDICAL DIVISIONS; QUARTERLY REPORT, NOVEMBER, DECEMBER, JANUARY, 1949-50. Argonne National Lab. [nd] 8p. (ANL-4401(p.78-95))

An analysis has been made of a portion of the data that are being collected on the long-term toxicity of intravenously administered polonium chloride. The experiment involves 720 CF-1 female mice (including controls). At 280 days the unquestionable deleterious effects of 0.027 to 0.008 $\mu\text{g/g}$ and possible adverse effects of 0.004 $\mu\text{g/g}$ on survival, body weight, intestinal infection, spleen weight, and white blood-cell count were evident. Changes in the x-ray appearance of the long bones appeared in animals that received as little as 0.0009 $\mu\text{g/g}$, and osteogenic sarcomas occurred in two animals that were given only 0.00046 $\mu\text{g/g}$. (NSA)

938

Hursh, John B. THE THERAPEUTIC USE OF BAL IN POLONIUM TOXICITY. University of Rochester. July 12, 1949. 64p. (AECD-2852; UR-83)

British anti-lewisite (BAL) and related dithiol compounds have been tested for their effects on the toxicity of polonium in rats. When polonium is injected intravenously, BAL, the most effective of the dithiols tested, approximately doubles the 10-day excretion of polonium. Where polonium is injected subcutaneously, BAL is less effective than BAL acid (NDR 317) or the urea derivative of BAL (NDR 399). The tissue-distribution results show that the BAL rats at 10 days have consistently higher polonium concentration in muscle than do the control rats. If BAL is given as a single intramuscular injection one hour after intravenous polonium administration, the polonium concentration in the whole blood is very sharply decreased. Tissue distribution of polonium three hour post-administration is given for BAL and control rats. These data show that BAL mobilizes polonium from the blood into the muscle, intestine, and kidney. Twenty rats were injected with a dose of polonium (36 $\mu\text{g/kg}$) which was known to be associated with a median survival time of about 25 days. Ten rats were treated with intramuscular BAL. Records were kept of survival time, daily weight, and periodic blood-sample findings. The treated rats had a median survival time of 82 days, as contrasted with a median survival time of 21 days for the untreated rats. The data appear to indicate that the therapeutic effect of BAL is related to both the increased excretion of polonium and to the shift of polonium to less radiosensitive tissues. (NSA)

939

Kreyberg, Leiv and Finn Devik. OBSERVATIONS ON THE SKIN REACTION TO THE SUBCUTANEOUS AP-

PLICATION OF METALLIC POLONIUM IN MICE. Acta Radiol. 35, 356-62(1951).

A nickel plate covered by polonium was introduced under the skin in a series of mice. Some of the polonium was dissolved in the tissue fluid and caused general and local radiation damage. The local changes are described in some detail, and the mechanism of the very marked hyperplasia is discussed. The evidence in favor of the existence of an indirect effect through the connective vascular system is stressed. (NSA)

940

Watts, N. P. and K. P. McConnell. EFFECT OF POLONIUM²¹⁰ AND SELENIUM⁷⁵ IN EXPERIMENTAL SCHISTOSOMA MANSONI INFECTION IN MICE. Am. J. Hyg. 53, 11-6(1951).

Neither α nor γ radiation, as supplied internally by Po²¹⁰ and Se⁷⁵, have been observed to be damaging to the form of *Schistosoma mansoni* in the experimental infection in mice. (NSA)

Radium

941

Bloom, Margaret A. and William Bloom. LATE EFFECTS OF RADIUM AND PLUTONIUM ON BONE. Arch. Pathol. 47, 494-511(1949) (AECD-2053; ANL-HDY-496)

Radium injected into mice intraperitoneally at dose levels of 0.3 and 0.03 $\mu\text{g/g}$, and plutonium, 0.03 and 0.003 $\mu\text{g/g}$ given intravenously, produce an overgrowth of bone in the femurs and vertebrae. In the femur this overgrowth begins in the distal metaphysis and is more extensive there than in epiphysis or shaft. This atypical bone, surrounded by gelatinous marrow, fills the metaphysis and encroaches on the marrow of the shaft, which is also invaded by new bone from the endosteum, and in the extreme cases, the two processes combine in some areas to obliterate the marrow. The bone formed after radium treatment is atypical and fibrous, and much of it becomes devitalized. The cortical bone of the shaft also contains many empty lacunae. After plutonium treatment the newest bone is also fibrous, but the greatly thickened trabeculae of spongy bone becomes progressively more compact, although the extremely irregular arrangement of lamellae and osteocytes distinguishes them from normal bone. Empty lacunae are fewer than after radium. Early changes of an atypical proliferative nature were seen in a 3-month specimen after radium and in a 7-month specimen after plutonium, and may represent early sarcoma or a predisposing state. Resorption of the necrotic bone does not seem to have occurred. Infraction of the marrow was seen in two of the radium- and one of the plutonium-injected animals. The changes in the vertebrae are essentially like those in the femurs. (NSA)

942

Browning, Ethel. BLOOD CHANGES IN LUMINIZERS USING RADIOACTIVE MATERIAL. Brit. Med. J. 1, 428-31(1949).

In a 7-year study of 2,737 workers who used radioactive material (and 100 control workers), complete blood analyses were done while they were working, and, of these, 366 were followed up. Exposure was limited to small amounts by various precautionary methods and occurred from external irradiation by α particles, β and γ rays, radon inhalation, ingestion from hand contamination, and inhalation of radioactive dust. Transient lymphocytosis, the presence of Türk cells, premyelocytes, and premature large mononuclear cells were found, as well as a rare occurrence of anemia. The author discusses the findings and concludes that the blood changes are due to a slight temporary hyperstimulation of the reticuloendothelial system. (NSA)

943

Evans, R. D. RADIUM POISONING: A REVIEW OF PRESENT KNOWLEDGE. *Am. J. Pub. Health* **23**, 1017-23 (1933).

Radium poisoning results when a few micrograms of radium or other α -ray emitting solid radioactive substance become fixed in the system.

Its action is principally to destroy the blood producing centers, and to weaken the bones. Calcium therapy, following Aub's and Flinn's work seems the only hope of removing radium from a victim's system. Modes of entrance of radium include the ingestion or breathing of radioactive substances by watch dial painters, chemists, and miners, drinking radium water nostrums, and IV and other injections of radium by physicians. From 60 to 98% of the radium taken into the system is eliminated principally in the feces (90%) and urine (10%). Some radon is lost in the expired air; no radium is lost in perspiration. Necrosis of the jaw, osteogenic sarcoma, and regenerative anemia are among the most common symptoms of radium poisoning. At least six unambiguous physical laboratory tests are available for identifying radium poisoning. (Author's Summary)

944

Evans, R. D., E. S. Harris, and J. W. M. Bunker. RADIUM METABOLISM IN RATS, AND THE PRODUCTION OF OSTEOGENIC SARCOMA BY EXPERIMENTAL RADIUM POISONING. *Am. J. Roentgenol. Radium Therapy* **52**, 353-71(1944).

The oral or intradermal administration of 25-100 γ of Ra in young adult σ Wistar rats always resulted in chronic Ra poisoning and in a high percentage of cases in the development of primary osteogenic sarcoma. Many of the classic symptoms of Ra poisoning in humans were exhibited by the animals. There was hypercalcification at the ends of the long bones, which become fragile but healed satisfactorily, with marked concentration of the Ra at the site of repair. The tumors were usually primary in the vertebrae, with metastases in lungs and other organs, and were transplantable. At death 1-7% of the Ra administered orally remained in the body; whereas about 50% of that injected intradermally was retained. A terminal retention of 1 γ was sufficient to produce osteogenic sarcoma. The incidence of anemia was low and there was no correlation with the Ra content. It was shown that the rat cannot be used for obtaining an estimate of the toxic dose of Ra in humans; its tolerance/kg of body weight is much higher. (BA)

945

Fajerman, Henri, Pascaline Daudel, and Roland Muxart. METABOLISM OF RADIUM FIXED ON BONY TISSUE. *Compt. rend.* **222**, 1255-7(1946).

A procedure is given for the study of the retention of radioactivity in bones of white rats given subcutaneous injections of RaCl_2 . When radioactivated bones are decalcified in vitro with the aid of various acids, a notable portion of the radioactivity is removed with the Ca salts without destroying the bone structure; this suggests the possibility of treating radium poisoning in vivo. (GPR)

946

Fishman, Harold C. THORIUM-X INVESTIGATIONS: HISTOLOGICAL STUDY OF THORIUM-X APPLICATION ON RABBIT SKIN. *J. Investigative Dermatol.* **15**, 71-4 (1950).

The acceptance of thorium X (Ra^{224}) application in the treatment of skin disorders has been slow because of the possible radiation danger and the lack of histological studies on effects of the application in animals. The histological changes in the skin of rabbits was therefore investigated. Thorium X in alcoholic solution (1000 electro-

static units/cc) was applied to the barium sulfide-epilated backs of five adult white rabbits, and biopsy specimens were taken weekly for six weeks for histologic comparison with normals. The development of hyperkeratosis, vacuolization of the cytoplasm of the prickle cells, and acanthosis is detailed. The unique skin structure makes rabbits not the best choice as experimental animals for this type of investigation. (NSA)

947

Hoecker, Frank E. and Paul G. Roefe. STUDIES OF RADIUM IN HUMAN BONE. *Radiology* **56**, 89-96(1951).

Portions of several different bones from two cases of osteogenic sarcoma attributed to radioactive substances in the bones have been examined microscopically and autoradiographically. The radioactive substances (chiefly Ra and its disintegration products) are found to be concentrated in numerous microscopic localizations. The maximum density of Ra in these localizations appears to vary by a factor of only about 1.5 from one type of bone to another, but the frequency of occurrence of these localizations may vary by a factor of nearly 25. Certain regions of some bones may be entirely devoid of Ra. The mineral residue of the sarcoma of one case contained only a negligible amount of Ra. This is believed to indicate that Ra was not mobilized from other portions of the body, although this apparently did occur in the case of Ca. This is interpreted as one line of evidence to indicate that Ra is not biochemically similar to Ca in all respects. (NSA)

948

Hursh, John B. and Allan A. Gates. BODY RADIUM CONTENT OF INDIVIDUALS WITH NO KNOWN OCCUPATIONAL EXPOSURE. *Nucleonics* **7**, No. 1, 46-59(1950).

The radium content of the body of 25 adult individuals with no known occupational exposure to radium has been measured. The average value is believed to be 1.18×10^{-10} g radium per whole body. This agrees qualitatively with predictions based on the radium content of the water supply and known constants for radium metabolism by the body. The radium content of the body, as derived from measurements reported in this paper, is about $\frac{1}{100}$ as great as analogous figures previously existing in the literature and about $\frac{1}{50,000}$ of the radium content known to produce neoplastic bone changes. It is, therefore, concluded that to the extent to which the present measurements are representative, it is unlikely that irradiation of the bone by body-radium will be an important factor in the production of osteogenic sarcoma in individuals not occupationally exposed to radium. (NSA)

949

Jacobson, Leon O. and Eric L. Simmons. STUDIES OF THE METABOLISM AND TOXIC ACTION OF INJECTED RADIUM. PART II. THE HEMATOLOGICAL EFFECTS OF PARENTERALLY ADMINISTERED RADIUM. A COMPARISON OF PLUTONIUM AND RADIUM EFFECTS. *Univ. of Chicago Metallurgical Lab.* June 1946. 104p. (AECD-2372; CH-3884)

The effects of the parenteral administration of radium chloride on the hematological constituents of the peripheral blood of rats, mice, and rabbits have been studied. Intraperitoneal and intravenous doses of from 0.005 to 0.94 $\mu\text{c/g}$ have been given to rats; intraperitoneal doses of from 0.000066 to 0.85 $\mu\text{c/g}$, to mice; and intraperitoneal or intracardial doses of from 0.0016 to 0.1 $\mu\text{c/g}$, to rabbits. There appeared to be no significant species difference in the sensitivity of the hemopoietic systems of the rat and mouse to radium, but rabbits appeared to be slightly more resistant than the other two species. Also, CF-1 female mice appeared to be somewhat more resistant than ABC male mice, but whether this was a strain or sex difference

has not been ascertained. In the rat, mouse, or rabbit no significant hematological alteration occurred after an injection (by any route) of 0.01 $\mu\text{g/g}$ or less of radium chloride. A dose of 0.02 $\mu\text{g/g}$ produced an anemia and sustained leucocyte reduction in rats. A dose of 0.03 $\mu\text{g/g}$ resulted in a severe recurrent anemia in ABC male mice (but not in CF-1 females), comparable changes in heterophil levels in both strains, and in an initial moderate reduction in lymphocytes in the ABC male mice. Doses as high as 0.1 $\mu\text{g/g}$, however, failed to produce an anemia in the rabbit, but did cause a mild, early, persistent reduction in leucocytes. A dose of 0.94 $\mu\text{g/g}$ in the rat resulted in an initial reduction in reticulocytes with subsequent overproduction and in a marked reduction in platelets with only moderate recovery. Morphological changes were seen in the nucleated cells of the peripheral blood after radium administration. These were largely comparable to those previously described in animals following the external application of radiations such as x-rays, γ -rays, and fast neutrons, or internal radiation in animals following the parenteral administration of plutonium. As evidenced by an increased erythrocyte diameter and increased mean corpuscular hemoglobin, macrocytosis became apparent in rats, mice, and rabbits after the parenteral administration of doses of radium between 0.1 and 0.2 $\mu\text{g/g}$. (NSA)

950

Looney, William B. RADIUM TOXICITY PROGRAM; A PROGRESS REPORT OF CLINICAL STUDIES ON TWENTY-FOUR PATIENTS. Argonne National Lab. July 1951. 48p. (ANL-4666)

Clinical studies were made of a group of 24 patients who received radium chloride 20 yr previously. Clinical data presented include estimation of total-body radium by radon breath and γ -ray body measurements; clinical history; physical examination; hematological studies; serum calcium, phosphorus, and alkaline phosphatase determinations; Kahn test, dental examination, including dental x rays; and roentgenographic examination of the skeleton. The amount of radium present in the body was determined as the sum of the emanating and nonemanating fractions obtained by analysis of the radon content of the expired air and by measurement of γ -ray activity from the patients' bodies. Results of complete roentgenographic examination of the skeleton of 19 of the 24 patients are given. Seventeen of the 19 patients had changes in bone density, and, in 8 of the 19, changes in normal configuration of bone were present. No direct relationship was observed between the roentgenographic changes or symptomatology and the amount of radium remaining in the body. It was concluded that radium plus an unknown factor or factors combine to produce bone degeneration. (NSA)

951

Martland, Harrison S. and Harrison S. Martland, Jr. PLACENTAL BARRIER IN CARBON MONOXIDE, BARBITURATE, AND RADIUM POISONING. SOME ORIGINAL OBSERVATIONS IN HUMANS. *Am. J. Surg.* 80, 270-9(1950).

Seventeen children of 10 of the original New Jersey radium-dial painters, born during or subsequent to the time their mothers had ingested radioactive substances, have been examined for the presence of radium deposits in their bodies. Although 7 of the mothers later died of radium poisoning, none of the children show appreciable amounts of radioactivity in excess of 0.01 μg of radium, which is considered to be comparable with the upper limit of normal radioactivity in the human body. Although this does not prove that the gaseous emanations constantly present in the mother's blood do not cross the placental barrier and

render the fetus radioactive, should they do so, radioactive deposits in the children would be too small ever to produce harmful results in the children or their descendants. The effect on the fetus of CO and barbiturate poisoning of the mother has also been studied. (NSA)

952

Norris, William P. and Stanton H. Cohn. EFFECTS OF INJECTED RADIUM ON ALKALINE PHOSPHATASE ACTIVITY OF BONE AND TISSUES. Argonne National Lab. Oct. 1951. 22p. (AECU-1703; UAC-451)

The influence of radium as an internal α emitter on the phosphatase activity of bone and tissue was studied in a number of rats injected with varying amounts of radium chloride. The results indicate that: radium deposited in bone causes significant reduction in the alkaline phosphatase content of bone; at least a part of the serum phosphatase is derived from bone; the phosphatase content of the soft tissues analyzed is largely independent of that of bone and is not affected by injection of radium; radiation dosages, from deposited radium, of the order of 1 to 10 rep/hr will produce significant reduction in the alkaline phosphatase content of bone within 24 hr; in vitro studies with x-rays and with radium added to serum and bone homogenates produced no change in phosphatase activity up to 10,000 r (therefore, the effect of deposited radium as reflected by the reduction in alkaline phosphatase activity is almost entirely on the phosphatase-forming elements of bone). (NSA)

953

Norris, William P. and H. B. Evans. STUDIES OF THE METABOLISM AND TOXIC ACTION OF INJECTED RADIUM. Univ. of Chicago Metallurgical Lab. June 1946. 115p. (AECD-1965; CH-3852)

The most important period in defining the fate of radium in the animal body is that closely following administration, providing the material is readily available to the body fluids. This period is demonstrated in rats by the rapid disappearance of radium from the blood after intravenous injection and by the rapid uptake of radium from the peritoneal cavity as indicated by blood concentration curves following intraperitoneal administration. The excretion of intraperitoneally administered radium in rats and mice was very rapid and reached such a low value within 10 days that further excretion had a negligible function in determining the final retention. There exists a linear logarithmic dependence of per cent injected dose excreted per day ($\log E$) on time ($\log T$). More of the excreted radium was present in the feces than in the urine. The retention of radium administered intraperitoneally to rats, mice, and rabbits, increased concomitantly with dose level. There exists a linear logarithmic dependence of per cent retention ($\log R$) on dose level ($\log I$). Three possible explanations for this effect are offered. In rats and mice, intraperitoneally injected radium was found to cause calcification of some of the soft tissues. The effect was noted in high incidence in the aortas of both species. In rats, calcareous sites were also found in the pylorus, liver, peritoneal wall, the region of the upper mediastinum, and, occasionally, in the testicles. In mice, the only other observed site of calcification was on the trachea. Calcification of the soft tissues in rats was often accompanied by pathologic lesions throughout the abdomen and a high radium content in the viscera. The evaluation of the weight data in rats and mice, in terms of the ratio, $Q(I,t)$, of the injected to control animals shows simple quantitative relations between weight effects and amounts administered or retained. On an equivalent roentgen basis x-rays appear to be somewhat more effective in producing weight loss than radium. Evidence is presented to show

that there exists a linear dependence of mortality (log m) on retained microcuries of radium (log R). (ADD)

954

Read, J. RADIUM POISONING. *Brit. J. Radiol.* **12**, 632-7(1939).

The danger of radium poisoning has recently become a matter of importance because of the possibility of the scattering of Ra element by bombing. The literature on the subject has been surveyed and the results summarized. From a consideration of cases of Ra poisoning both experimental and accidental it is possible to obtain some idea of the distribution of the element in the various tissues when absorbed in different ways. Typical cases of poisoning are described, and particular attention is paid to the question of the retention of inhaled dust. The general conclusion is that about 100 μgm by mouth or 50 μgm inhaled would probably produce a permanent deposit of the order of 1 or 2 μgm , a quantity which may be lethal. These quantities may be much less in the case of RaSO_4 which has a low water solubility and this salt is therefore probably much more dangerous. A very comprehensive bibliography is attached. (PA)

955

Roofe, Paul G., Hal Bingham, Ralph Comer, and Martha Madison. EFFECT OF RADIATION FROM INTRAPERITONEALLY INJECTED RADIUM CHLORIDE UPON MEGAKARYOCYTE AND BLOOD PLATELET PRODUCTION IN ALBINO RATS. *Anat. Record* **108**, 537(1950).

This paper is an abstract and is reproduced here in its entirety.

Twenty-five rats were divided into groups of five, each group receiving respectively 10, 20, 30, 40, and 50 μg of RaCl_2 intraperitoneally. One rat from each group was sacrificed every 3rd day starting 3 days postinjection. Using a camera lucida, quantitative megakaryocyte counts were made from slides prepared from intact bone marrow of the femur. The platelet counts were made using a hemocytometer and a 2% sodium citrate diluting fluid. Megakaryocytes decrease progressively with time through the 9th day after injection of RaCl_2 . From this period to the 14th day, a trend toward regeneration was noted. The lowest number of megakaryocytes was observed in animals receiving 20 μg independent of time of sacrifice. Regeneration appeared earlier in the higher dosages. Following an initial increase of platelets on the 3rd day, there was a progressive decrease up to and including the 14th day. Regardless of time, higher dosages also produced a decrease from the normal. The initial destruction of the megakaryocytes is reflected on the 3rd day by an increase in platelets. As the megakaryocytes regenerate it appears that platelet production does not correspond quantitatively, presumably because young megakaryocytes do not fragment.

956

Roofe, Paul G. and Frank E. Hoecker. STUDIES OF APPARENT SUBMICROSCOPIC CHANGES IN BONE MATRIX AND PERIPHERAL BLOOD CHANGES ASSOCIATED WITH METABOLIZED RADIUM. *Anat. Record* **103**, 500(1949).

The following is an abstract and is reproduced here in its entirety.

Apparent submicroscopic structural changes in the bone matrix associated with metabolized radium are presented by photomicrographic technics. A new type of microtome enables us to cut serially thin sections of bone which are immediately exposed to NTA plates without further treatment. The radium distribution has been determined by means of tracts in the NTA emulsions produced by alpha particles. Exact registry between the microscopic bone

structure and the alpha-particle tracts is made possible by new autoradiographic technics. Ionizing radiation from radium intraperitoneally injected depressed the red cell count only slightly. White cells were depressed considerably. Two injections, 10 μg RaCl each, produced a much slower rate of whole body growth.

957

Roofe, Paul G. and F. E. Hoecker. THE EFFECT OF INTRAPERITONEALLY INJECTED RADIUM CHLORIDE UPON THE PERIPHERAL BLOOD OF ALBINO MALE RATS. *Anat. Record* **103**, 555-6(1949).

The following is an abstract and is presented here in its entirety.

Twenty-five albino rats were injected intraperitoneally with radium chloride in groups of 5, each separate group receiving the following dosages: 10, 20, 30, 40, 50 μg . Twelve animals served as controls. Complete blood counts and fragility tests were done prior to RaCl treatment. One animal from each group was sacrificed at 3-day intervals up to 15 days. Two controls were also sacrificed on those days. All tests were done on day of sacrifice. Results are grouped in two ways: those which received same dosage but at different time intervals; those which were sacrificed on same day but dosage varied. Normal red counts on 165 samples averaged 7,920,000 per cubic millimeter. Only a very slight drop in red cells was noticed after RaCl_2 treatment. Normal whites were 20,250 per cubic millimeter. Both increased time interval and increased dosage showed progressive drop in white cells. No great change occurred in the differential count. Platelet counts dropped from a normal of 852,000 to 142,000 per cubic millimeter, in those rats with 50 μg . Fragility tests remained unchanged.

958

Sabin, F. R., C. A. Doan, and C. E. Forkner. THE PRODUCTION OF OSTEOGENIC SARCOMATA AND THE EFFECTS ON LYMPH NODES AND BONE MARROW OF INTRAVENOUS INJECTIONS OF RADIUM CHLORIDE AND MESOTHORIUM IN RABBITS. *J. Exptl. Med.* **58**, 267-89(1932).

Authors began study of the effects of radioactive substances on the cells of the blood and connective tissues in rabbits in 1926. Radium chloride and mesothorium were used: these compounds were put up in sealed ampoules of such a strength that 2 cc of normal salt solution contained about 5 micrograms of the active material. In January 1928, the strength of this material was tested and was found to be for an ampoule of radium chloride the equivalent of 5.1 micrograms of radium and for one ampoule of mesothorium, 7.7 micrograms of radium. The dose of the mesothorium was also greater because it is known that it gives off 5 alpha particles to 4 from radium chloride. Nine rabbits were used for the experiment, five of which received radium chloride and four mesothorium. The injections were given intravenously once a month. The blood cells were counted once a week. The differential counts were made with the supravital technique. Each animal was killed when signs of some damage became evident, such as a fracture or marked weakness. Protocol for each rabbit is given. The observations in this work suggest that with certain doses of radioactive material, the fundamental damage in the lymphoid tissues is to the stem cell and that the damage is to the chromatin of the nuclei of these cells. The erythroid tissues are apparently less susceptible to radioactive material than the lymphoid tissues but an original anemia of secondary type from peripheral destruction may eventually be changed to one of primary type through decreased maturation of primitive cells in the marrow. The damage of lymph nodes and bone marrow leads to atrophy of these organs. The cells of the liver and

thymus suffer nuclear damage of the same general character as is seen in the lymph nodes, and there is an atrophy of these organs. The storage of the radioactive material in the bones gave rise to osteogenic sarcomata in 2 out of 7 rabbits surviving from 11 to 19 months. A repetition of the experiment has been undertaken with more intensive studies to test the validity of the findings. (S.V.S.)

959

Silberstein, Hannah E. **RADIUM POISONING; A SURVEY OF THE LITERATURE DEALING WITH THE TOXICITY AND METABOLISM OF ABSORBED RADIUM.** University of Rochester. May 26, 1945. 41p. (AECD-2122; M-1695)

This report is based upon a detailed survey of literature concerning radium poisoning from 1908 through 1944. Of 17 human fatalities following ingestion of radium mixed usually with meso-thorium described in the literature post-mortem activities were determined in nine; activities ranged from 1.2 to 126 micrograms radium equivalents. Only two were due definitely to radium alone. The actual intake was known in only one case, namely 2,800 micrograms of radium taken over a period of five years, leading to death about a year later: 73.66 micrograms were retained at death. All showed advanced regeneration type anemia, acute leucopenia, and varying degrees of bone destruction. Six deaths ascribed in the literature to inhalation of radioactive dusts occurred 5 to 15 years after beginning exposure. Dyspnea and lung fibrosis were the predominant signs, but bronchial carcinoma was also present in one case. There were only two early reports dealing with acute levels of dosage. One dog received 75 micrograms of radium per kilo body weight, in a single intravenous injection, and died at 14 days. Four groups of experiments with prolonged or intermittent dosage resulted in chronic poisoning. In four longstanding chronic human cases the coefficients of elimination were 0.002 to 0.005% per day, at which rate it would take 45 years to get rid of half the fixed radium in the body. The amount of radon lost through the lungs depends on the degree of fixation of radium in skeletal tissues and relative ease with which the radon produced can escape into the circulation. Deposition and distribution of radium in the body is analogous to that of lead and calcium. One early experiment has been said to indicate that at 3½ months after intravenous injection it is still widely distributed throughout the soft tissues, the highest concentrations being in bone marrow and liver, moderately high in lung. Deposition in bone probably continues to take place as long as any radium remains in soft tissues and in the circulation, going especially to regions associated with the most rapid uptake or turnover of calcium. Seven human cases are known to have carried more than 0.02 and less than 0.5 micrograms of radium in their system for 7 to 25 years without showing any clinical signs of poisoning, yet as little as 1.2 micrograms has been found in a fatal case. Therefore, the Bureau of Standards in 1941 set 0.1 microgram fixed in the body as the maximum level of radium content. (NSA)

960

Spieß, Heinz. **ANIMAL-EXPERIMENTAL INVESTIGATION OF PARENTERAL THORIUM X APPLICATION.** Z. ges. exptl. Med. 117, 567-86(1951).

The clinical effects on rabbits of intravenous injection of ThX (Ra²²⁶) in single or divided doses up to 1000 esu has been studied. The changes in the blood picture are reported, including effects on blood sugars, serum proteins, and serum Ca and P contents. Effects on the kidneys, reproductive system, and metabolism are noted. X-ray photographs and autoradiographs illustrate the localization and damage caused by ThX in bone and cartilage growth and fracture healing. (NSA)

961

Spieß, H., H. Poppe, and O. Wünsche. **EFFECT OF THORIUM X ON DYE UPTAKE BY CELLS.** Z. ges. exptl. Med. 116, 344-53(1950).

Injection of high doses (5 doses of 150 electrostatic units in 2.5 weeks) of ThX into rabbits, followed by 8 ml of 1% trypan blue, gave a higher serum and urine dye level in a period of 72 hours, than in animals not receiving ThX. Interposing 10 days between the last ThX injection and the dye injection maintained this difference. Smaller doses (15 doses of 25 units in 8 weeks) caused a reversal, in that serum and urine dye levels were lower than those of control animals not receiving ThX. (CA)

962

Weikel, J. and Egon Lorenz. **EXCRETION OF RADIUM FROM THE MOUSE.** Radiology 51, 865-70(1948).

The possibility exists that radium will form an organic protein compound and that its excretion might be influenced by BAL (2,3-dimercaptopropanol). Three groups of C₃H male mice, 50 in each group were injected intraperitoneally with 10 micrograms of radium element as bromide. One group of animals was injected with 5 mg of BAL daily for the first 20 days; the second group was given the same amount of BAL beginning at the 20th day for 20 days after injection of the radium. The excretion was measured by determining the amount of radium remaining in the animals. For this purpose a multiple Geiger Mueller counter was developed, in the inside of which the animals were placed. The number is described and the excretion data given. It was found that BAL does not influence the excretion of radium either in the acute or in the chronic stage of radium poisoning. (ADD)

963

Wilson, C. W. and J. R. Greening. **GAMMA-RAY PROTECTION IN RADIUM THERAPY.** Brit. J. Radiol. 21, 211-20(1948).

It is suggested that if the γ -ray dosage received by radium therapists during their radium work could be assessed (even if only roughly), more specific opinion might be formed as to what levels of exposure have proved to be safe. Calculations and measurements of local dosage and integral dose received by radium mould technicians and radium therapists are made in order to make each assessment. On the basis of these results the implications of the various proposed standards of protection are examined and set out in terms of actual working conditions. For this purpose protection is considered in the categories in which it seems the subject should be divided, viz., local exposure of the hands, local exposure of the gene material and integral dose throughout the whole body. In relation to medical work it is concluded (1) that many busy radium personnel may receive local exposure to the hands in excess of that now recommended in the U. S. A. as a safe amount (1 r per day), (2) that if circumstances dictate it should be practicable, by the use of suitable screenage, to reduce the local dose received by the genitals of mould technicians and therapists to the low figure recently suggested by Sievert (0.01 r per day), and (3) that this low figure may be impossible of realization for the integral dose received by personnel handling radium. It is suggested that in respect of integral dose, past experience indicates that a figure of 0.1 r per day may be safe. It is, however, desirable to achieve 0.01 r per day, particularly for personnel continually receiving radiation at a low but approximately uniform dose-rate over the whole body—this is because injury to the gene material is the foremost consideration. Suggestions are made for the future collection of data which will assist in placing protection standards on a surer foundation. (NSA)

964

Witten, Victor H., Milton S. Ross, Eleanor Oshry, Arthur B. Hyman, and Vera Holmström. **STUDIES OF THORIUM X APPLIED TO HUMAN SKIN; I. ROUTES AND DEGREE OF PENETRATION AND SITES OF DEPOSITION OF THORIUM X APPLIED IN SELECTED VEHICLES.** New York Univ. Hospital and New York Univ. [nd] 22p. (AECU-1470)

A basic problem which has remained unsolved in using thorium X (Ra^{224}) for therapy in dermatological conditions is whether Th X is confined to the surface or penetrates the skin in any way. A report is presented of an investigation of the routes and degree of penetration and sites of deposition, using nine pieces of tissue from eight different patients. Properties of Th X, including decay schemes, are discussed. Th X (adsorbed on CaCl in alcoholic solution) was applied to a small (about 5 mm²) area of skin, previously cleansed with alcohol and walled off with rubber on Duco cement. The amount applied varied from 0.001 to 0.015 cm³ and the strength from 0.06 to 3.0 μ c. The area was covered with collodion and allowed to dry. One to five days later the collodion was stripped off, and the treated area excised. Radioautograms prepared from frozen sections of the tissue show the isotope penetrates the epidermis and is distributed through the prickle cell and basal layers, flows down the hair follicle and penetrates the follicular wall, and passes down the sweat duct and into the sweat gland. Radioautograms showing the deposition of Th X in human skin are included. (NSA)

Radon

965

Arkin, Alvin M. and Norman Simon. **RADIATION SCOLIOSIS: AN EXPERIMENTAL STUDY.** J. Bone and Joint Surg. **32A**, 396-401(1950).

Examples are presented concerning the production of scolioses in rabbits by the direct action of radiation upon the spinal epiphyseal plates. A radon seed, containing 0.6 mc of radon, was placed adjacent to an intervertebral space in the lumbar spine of a rabbit in one case, and the radiation caused a suppression of the growth of the epiphysis on the side nearer the seed; a few months later, growth of the spine manifested asymmetry by a wedging of the vertebrae adjacent to the source of radiation. When radon seeds of 0.6 mc were placed opposite the middle of a vertebral body, or when 0.2-mc seeds were placed near one epiphyseal plate, no discernible wedging was noted. Growth suppression of the vertebral epiphyseal plate near the 0.6-mc seed was induced by a dose of about 2,700 r; the epiphysis next above the seed grew normally although it received a dose of 300 r. Similar asymmetrical growth arrest was effected by the use of an x-ray beam directed to one side of the spine; the radiations were delivered by a 140-kv machine through a filtration of 0.25 mm of Cu and 1 mm of Al at a target distance of 30 cm for an epiphyseal dose of 1,000 r; wedging appeared 7 weeks later. It is concluded that a single dose of 1,000 r is required to produce definite wedging in the spines of young rabbits. (NSA)

966

Cornfield, Jerome. **RETENTION OF RADON BY THE MOUSE. II. METHOD OF ESTIMATING BIODECAY FROM EXPERIMENTAL DATA.** Nucleonics **5**, No. 4, 68-75(1949).

This paper describes the method of estimating radon disintegration from the experimental data; the experimental data referred to is that which was presented by Hollcroft and Lorenz (Nucleonics, **5**: 63, 1949). A formula is derived for σD , the root mean square error, where D is

the number of radon disintegrations. The author suggests how the error formula can be applied to the planning of experiments. (NSA)

967

Hollcroft, Joanne Weikel and Egon Lorenz. **RETENTION OF RADON BY THE MOUSE. I. EXPERIMENTAL DETERMINATION OF BIODECAY AND ENERGY ABSORBED.** Nucleonics **5**, No. 3, 63-71(1949).

This report describes the elimination of radon from mice following the administration of an aqueous radon solution; biodecay and the determination of the energy absorbed by the animal from the disintegration of the radon and its subsequent short-lived decay products are discussed. The radon used in the experiments was obtained by the α bombardment of RaBr; 75-80% of the total radon prepared was obtained in solution. Two methods were used to study the elimination of the radon: in the first, groups of mice were sacrificed by cervical dislocation 5, 10, 30, 60, 90, 120, 180, and 240 minutes after the radon administration, and were sealed quickly in glass tubes for subsequent measurement; in the second, after the administration of the radon, the live animal was placed in a small vessel, and by means of an air transfer system and activated charcoal collection bulbs, the radon was collected from the exhalations and measured at intervals. Preliminary studies were also made on the modes of administration of the radon; an intraperitoneal injection of 0.25-0.5 mc of radon was given and the amount in the mouse was determined 5, 10, 15, and 30 minutes later; the rate of elimination after oral administration was also studied. The results showed that the elimination rate, at least for the first hour, differed according to the route of administration used and was generally higher for the intravenous than for the other methods. The amount of fat present in the animal influenced the radon retention only after intraperitoneal injections. (NSA)

968

Lange, K. and R. D. Evans. **ABSORPTION OF RADON THROUGH THE SKIN AND ITS EXHALATION THROUGH THE LUNGS.** Radiology **48**, 514-16(1947).

The authors followed the fate of radon originally contained in an ointment (44.4 microcuries of radon per cc of lanolin) to determine to what extent it enters the tissues. The experiments were carried out on normal intact skin, as well as on the surface of large postphlebotic leg ulcers. In the first group of experiments, samples of exhaled air were taken after 20 minutes, 2 $\frac{1}{2}$ hours, and 4 $\frac{1}{2}$ hours. Approximately 2.4% of the radon applied was exhaled within the first 4 $\frac{1}{2}$ hours when the ointment was applied to the leg ulcer while the amounts exhaled from cases of normal skin were only 0.13% and 0.08% for the same period. In the second experiment, the patient with the ointment on the intact skin exhaled during the first four hours approximately 1.2 microcuries or 0.4% of the amount applied, and during 23 hours 4.5%. The patient with the leg ulcer exhaled during the first four hours approximately 6.7 microcuries or 1.8% of the amount applied, and during 23 hours 10%. All calculations are based on the assumption that the subject exhaled 5 liters of air per minute. Precautions were taken in both experiments to prevent inhalation of radon during the application of dressings. It can thus be stated that appreciable amounts of radon applied in ointments are absorbed through the intact skin, and still more through open wounds. The radon exhaled must therefore have been carried to the patient's lungs internally as in circulating blood or lymph. (S.V.S.)

969

McClellan, Walter S. and Carl R. Comstock. **CUTANEOUS ABSORPTION OF RADON FROM NATURALLY**

CARBONATED MINERAL WATER AND PLAIN WATER BATHS. Arch. Phys. Med. 30, 29-36(1949).

Two subjects were studied under various conditions in baths of 30 min duration. The extent of Rn absorption during and after the bath was determined. The concentration of Rn in the expired air was greatest ($2.74-3.53 \times 10^{-10}$ curies/l air) when the subject bathed in CO₂ water containing Rn (0.107 uc/l) and breathed air over the surface of the tub. About the same amount of Rn was excreted by the subjects in a CO₂ bath containing Rn but breathing outside air through a mask ($1.77-2.89 \times 10^{-11}$ curies/l air) as when he bathed in plain water containing Rn and breathing air over the tub ($2.08-9.34 \times 10^{-11}$ curies/l air). When the patient was in a bath of plain water and Rn but breathed outside air, he excreted $0.17-0.62 \times 10^{-12}$ curies/l air. The Rn was eliminated almost completely in 3 hours. Rn is absorbed through the skin in greater amounts when the water contains CO₂. (CA)

Sodium

970

Evans, T. C., M. Lenz, C. P. Donlan, and M. J. LeMay. EFFECTS OF RADIOACTIVE SODIUM ON LEUKEMIA AND ALLIED DISEASES, PRELIMINARY REPORT. Am. J. Roentgenol. Radium Therapy 59, 469-81(1948).

Radiosodium, taken by mouth, in a suitable quantity and at appropriate intervals, is effective in reducing symptoms of chronic myelogenous leukemia, chronic lymphatic leukemia and polycythemia vera. The rate of response to each treatment appears to be intermediate between that of roentgen therapy and treatment with radiophosphorus. The contraindications are similar to those for other forms of radiation therapy. 18 references. (NSA)

971

Finkle, R. D., et al. THE ACUTE RADIOTOXICITY OF INJECTED Na²⁴ FOR MICE AND RATS. PART I. METABOLISM AND GENERAL TOXICITY. Univ. of Chicago Metallurgical Lab. June 1946. Decl. May 24, 1948. 29p. (AECD-2011; CH-3856)

Introductory work on the toxicity and metabolism of radioactive substances derived from uranium fission was started indirectly by using cyclotron bombarded sodium²⁴, an artificial radioactive isotope with a half-life of 14.8 hours. The isotope decays by emission of β -particles (1.4 Mev) and γ rays (1.4 to 3.6 Mev) to stable magnesium. Mice and rats were administered doses of radioactive sodium (Na²⁴) ranging from 12 to 150 microcuries per gram of body weight. It is apparent that the LD₅₀ lies between 20 and 40 μ c/g with the possibility that females may be more sensitive than males. Immediately after injection of 33 μ c/g or more, there was a drop in weight with the rate and magnitude of the loss varying with the dose. At the lowest dose level, 12 μ c/g, there was no significant effect on growth. Clinically, aside from loss of hair, encrusting of the eyelids, and hunched position of the animals at death, no characteristic lesions were noted. Rats that received 90 mg by intraperitoneal injection excreted 19% of the radioactive sodium in the first day and another 9% on the second day. Rats given smaller doses excreted an average of 15% on the first day and 12% on the second. The ratio of the fecal sodium content to the urinary content was 0.05 or less. In mice, the sodium turnover was somewhat faster than in rats. Mixed excreta measurements showed 33% of the sodium excreted by 24 hours and 50% by 72 hours. Analytical recovery of the injected sodium was between 80% and 100% in most groups. Discounting the systematic errors and the uncertainty for X-ray comparison, it might be said that the ratio of beta ray effectiveness to roentgen ray effectiveness is approximately one. (ADD)

972

Jacobson, Leon O. and E. L. Simmons. THE ACUTE RADIOTOXICITY OF INJECTED Na²⁴ FOR MICE AND RATS. PART II. THE EFFECT OF Na²⁴ ON THE LEUCOCYTES OF THE PERIPHERAL BLOOD OF MICE. Univ. of Chicago Metallurgical Lab. June 1946. Decl. June 9, 1948. 11p. (AECD-2036; CH-3857)

Groups of male mice of the ABC and CF-1 strains were injected intraperitoneally with Na²⁴ as the chloride in doses of 12, 23, 47, 65 and 90 μ c/g. Leucocyte counts and differential blood smears were made on all animals before injection of the radioactive isotope and at intervals thereafter; through 10 days in one experiment and through 15 days in another. A moderate to severe leucopenia followed the injection of all the above doses except the 12 μ c/g. Death of the animals in the groups which received 47, 65, or 90 μ c/g occurred before the eighth day. The number of neutrophils per cubic millimeter rose slightly for three days in the group which received 90 μ c/g. No further sampling was possible in this group because of the death of all the animals. No reduction of neutrophils followed the injection of 23 μ c/g in one experiment; 23, 47, and 65 μ c/g produced a marked neutropenia in another experiment. Lymphopenia occurred in all groups of animals which received 23, 47, 65, or 90 μ c/g and continued until sampling was discontinued or until death of the animals. (NSA)

973

Jacox, Harold W. THROMBOCYTOPENIC PURPURA FOLLOWING THERAPEUTIC ADMINISTRATION OF RADIOACTIVE SODIUM. Radiology 51, 860-1(1948).

Thrombocytopenia purpura developed following therapeutic administration of radioactive sodium in a case of metastatic sympatheticoblastoma. During a 5-month period a total of 202 millicuries of radiosodium (285 r) was administered to a 21-year old male. Pain was alleviated and repeated blood counts showed no abnormalities until after the last treatment when hemorrhagic manifestations appeared. The number of platelets fell rapidly but all the other blood elements continued to be normal. Death was attributed to aplastic anemia. An autopsy revealed punctate hemorrhages everywhere, clotted blood in the pelvis of the left kidney, and hemosiderosis in the spleen and bone marrow. In this case the purpura was caused by the radiosodium and not the disease itself. Although other patients have received much more radiosodium without a similar reaction, this patient seemed to become more susceptible to succeeding treatments. (NSA)

974

Snyder, R. H. and W. E. Kisieleski. THE RELATIVE BIOLOGICAL EFFECTIVENESS OF BETA AND RONTGEN RADIATION AS SHOWN BY THE RADIOTOXICITY OF SODIUM²⁴ FOR MICE. Radiology 54, 743(1950).

Mice were injected intraperitoneally with doses of radioactive Na²⁴ ranging from 12 to 150 μ c/g of body weight. The 20-day LD₅₀ (lethal dose for 50%) was found to lie between 20 and 40 μ c/g, the final value arrived at by interpolation being 30 μ c/g. The calculated radiation dosage corresponding to this 20-day LD₅₀, considering excretion and decay, was 680 rep. The ratio of x-ray to beta-ray effectiveness is approximately 1.4:1. (CA)

Strontium

975

Anthony, D., K. Lathrop, and R. Finkle. RADIOTOXICITY OF INJECTED SR⁹⁰ FOR RATS, MICE, AND RABBITS, PART II. METABOLISM AND ORGAN DISTRIBUTION. Univ. of Chicago Metallurgical Lab. June 1, 1946. Decl. Oct. 9, 1947. 36p. (MDDC-1363; CH-3846)

Mice, rats, and rabbits excreted Sr^{90} - Sr^{90} very rapidly following intraperitoneal or intravenous administration. The greatest part of the excretion took place during the first three days, and by 10-15 days virtually no more of the retained strontium was excreted. Average total excretion values were 54% of the injected dose for the mouse, 40% for the rat, and about 70% for the rabbit. Average total retention values were 45% of the injected dose for the mouse, 59% for the rat, and 21% for the rabbit. After three days almost all of the retained Sr^{90} - Sr^{90} was found in the skeleton. The concentration in bone was more than 100 times that in soft tissue. There does not appear to be any significant variation in retention of Sr^{90} on a per gram basis between different types of bone. The logarithm of the retention, the rate of excretion, and the blood concentration of radioactive strontium in each case was found to be a straight-line function of time. (ADD)

976

Anthony, D., K. Lathrop, and R. Snyder. **RADIOTOXICITY OF INJECTED Sr^{90} FOR RATS, MICE, AND RABBITS. PART III. LETHAL ACTION AND CLINICAL CHANGES.** Univ. of Chicago Metallurgical Lab. June 1946. Decl. Oct. 17, 1947. 20p. (MDDC-1364; CH-3845)

The LD-50 in 30 days was found to be between 7 and 8 $\mu\text{g/g}$ of Sr^{90} - Sr^{90} when administered intraperitoneally to mice; for rats it was slightly less than 5 $\mu\text{g/g}$; and for rabbits it was also slightly less than 5 $\mu\text{g/g}$. The food intake and gain in weight of rats and mice given doses of 2 $\mu\text{g/g}$ or more, but showing no apparent symptoms of radiation sickness, were less than those of the control animals. (ADD)

977

Asling, C. W., D. A. Heller, D. H. Copp, and J. G. Hamilton. **DEPOSITION OF RADIOACTIVE STRONTIUM AND THE RARE EARTH PROMETHIUM IN THE SKELETAL TISSUES OF THE RAT.** Anat. Record **103**, 420(1949).

The following is an abstract and is reproduced here in its entirety.

Radioautographs of sections through the costochondral junction of young normal and phosphorus-deficient rats were compared with undecalcified silver-stained sections to determine any differences which might exist in deposition of carrier-free radio-strontium (Sr^{90}) in bone, osteoid and hyaline cartilage (calcified and noncalcified). The rats were sacrificed one and 72 hours after intraperitoneal administration of the radio-element. Radio-strontium was found in the cortical bone of both normal and deficient rats as well as in the spongy bone of normal controls, but not in the osteoid of the deficient animals. The distribution and degree of deposition was comparable at one and 72 hours. In both control and deficient rats radio-strontium was demonstrated in the calcified cartilage but not in the non-calcified cartilage in the chondral segment of the rib. The degree of deposition approached that of the cortical bone of the same sections. The distribution of promethium (element 61) in normal adult rats 96 hours after injection differed remarkably from that of strontium. The promethium was observed in the region of periosteum, endosteum, and perichondrium and not within the cortical bone, calcified cartilage, or non-calcified cartilage.

978

Buchanan, D. L., B. Gasvoda, and E. S. Guzman Barron. **EFFECTS OF A SINGLE LETHAL INTRAVENOUS DOSE OF STRONTIUM CHLORIDE ON THE PLASMA OF A GOAT.** Argonne National Lab. June 1, 1947. 178p. (MDDC-1418-F)

Electrophoretic patterns of the plasma of a goat before and after the intravenous injection of a lethal dose of radioactive strontium are presented. Changes seen are a moderate decrease in albumin, α_2 globulin, and γ globulin. (ADD)

979

Chaikoff, I. L., M. C. Fishler, and C. Entenmann. **RADIO STRONTIUM (Sr^{90}).** Argonne National Lab. June 1, 1947. 1p. (MDDC-1142-D).

Tracer Studies—A continuation of this work with more complete data indicates that the retention of Sr^{90} by the skeleton was essentially as has been described in a previous report. The uptake of this material in the bones of the animals which received it by mouth was found to rise by almost a factor of two between the 4th and 16th days. Otherwise, there were no significant differences to be observed between the present more complete information and that which was given previously. The rate of excretion of Sr^{90} has now been followed for a period of 30 days, and after the 15th day its excretion is apparently less than the rate of decay of that which is retained in the body. (ADD)

980

Chaikoff, I. L., M. C. Fishler, and C. Entenmann. **RADIO STRONTIUM (Sr^{90}).** Argonne National Lab. [nd] 8p. (MDDC-1143-B)

Incomplete experiments with Sr^{90} indicate that the intraperitoneal injection of this element is followed by the prompt deposition of approximately 75% of the dose in the bones. The soft tissues contain negligible quantities of Sr^{90} as compared to the skeleton. The oral administration of Sr^{90} was followed by an uptake of approximately 10% of the administered dose at the end of 24 hours. The relative distribution of that which was absorbed was almost identical to the values observed after intraperitoneal injection. (ADD)

981

Cowan, Frederick P., Lawrence B. Farabee, and Robert A. Love. **HEALTH PHYSICS AND MEDICAL ASPECTS OF A STRONTIUM-90 INHALATION INCIDENT.** Brookhaven National Lab. [nd] 12p. (AECU-1169)

A number of health physics, medical, and chemical aspects of the management of an incident in which an individual became contaminated from activity released in the laboratory during the preparation of a Sr^{90} source are discussed. The results of the analysis of the urinary elimination of Sr^{90} - Y^{90} for the period following the inhalation are presented. (NSA)

982

Curtis, H. J. **THE EFFECT OF CLAY ON THE INTESTINAL ABSORPTION OF STRONTIUM.** Monsanto Chemical Co. Jan. 21, 1946. 8p. (MDDC-419; MONH-40)

Rats have been fed active strontium which was adsorbed on clay, while their controls were fed the same amount of active strontium in aqueous solution. There was no significant difference in the amount deposited in the skeleton between the two groups, and it is concluded that if ions are adsorbed on inert material, they will be eluted during their passage through the gastrointestinal tract. (ADD)

983

Finkel, Miriam P. **THE TRANSMISSION OF RADIOSTRONTIUM AND PLUTONIUM FROM MOTHER TO OFFSPRING IN LABORATORY ANIMALS.** Physiol. Zool. **20**, 405-21(1947).

Mice injected with radioactive Sr^{90} before conception had fewer litters than the controls. Injection of radioactive strontium or of plutonium increased the number of stillborn litters and the number of stillborn young in the litters that lived. Pregnant mice treated with either Sr^{90} or Pu lived longer than similarly treated nonpregnant female mice. Treated pregnant mice also suffered less radiation damage. After delivery, total Sr retained by mothers was the same as that of virgin females at similar time intervals after injection. The proportion of Sr or Pu transmitted to the young at birth varied with the injection—delivery period was within four days, the Sr activity per gram body weight of

the newborn mouse exceeded that of the mother. The initial excretion of radioactive Sr by very young mice was considerably lower than that of adult mice. Long bone malformation, anemia, retardation of growth, and osteogenic sarcoma occurred before weaning in animals that were treated in utero with Sr⁹⁰. No pathologic conditions developed in the animals treated with Pu. No difference in sensitivity to Pu or Sr⁹⁰ was found in young and adult tissues. (N)

984

Finkel, Miriam P. FIVE PUPPIES BORN WITH RADIO-STRONTIUM. A PRELIMINARY NOTE, p.71-82 of BIOLOGICAL AND MEDICAL DIVISIONS QUARTERLY REPORT, AUGUST TO NOVEMBER 1948. Argonne National Lab. Nov. 1, 1948. 12p. (ANL-4227(p.71-82))

On May 4, 1946, a pregnant dog of unknown ancestry was injected subcutaneously with 8 mc of radiostrontium (1.0 µc/g). Six days later she delivered five apparently healthy pups. The last of these died October 30, 1948. The mother died 18 days after receiving the isotope (12 days after delivery) with typical irradiation purpura. There was no gross evidence of infection. The results show clearly what damage a bone-seeking β emitter can do to the skeletal system when administered very early in the life of the animal. (S.V.S.)

985

Greenberg, D. M. and N. Kaplan. A PRELIMINARY STUDY OF THE REMOVAL OF RADIO STRONTIUM (Sr⁹⁰) FROM THE BODY. Argonne National Lab. June 1, 1947. 5p. (MDDC-1142-E)

Preliminary experiments on removal of Sr⁹⁰ from rats has indicated that sodium citrate, parathyroid hormone, ammonium chloride, and strontium chloride all apparently slightly enhance the removal of Sr⁹⁰. Massive doses of irradiated ergosterol has no such effect. This study must be repeated upon a much larger group of animals at varying periods after Sr⁹⁰ administration before any quantitative appraisals as to the relative effect of these different agents may be made. (ADD)

986

Jacobson, Leon O., Eric L. Simmons, and Matthew H. Block. THE EFFECT OF SPLENECTOMY ON THE TOXICITY OF SR⁹⁰ TO THE HEMATOPOIETIC SYSTEM OF MICE. J. Lab. Clin. Med. 34, 1640-55(1949)

In order to test the hypothesis that anemia fails to develop in CF-1 mice following the administration of large doses of Sr⁹⁰ due to the rapid development of an intense ectopic erythrocytopoiesis in the spleens of the animals, the experiments described were performed. Three groups of CF-1 female mice were provided: the mice in the first group were splenectomized; those in the second group received a single intraperitoneal injection of 2.0 µc of Sr⁹⁰/g of body weight; and the mice in the third group were first splenectomized and 24 days later treated with the same dose of Sr⁹⁰ as used in the second group. A second injection of 2.0 µc of Sr⁹⁰ was given to a representative number of animals from the second and third groups. Distribution, excretion, hematologic and histologic studies were made on the animals at intervals following the injections. A persistent leucopenia but no anemia of significance was produced in the peripheral blood of the mice; the same dose of Sr⁹⁰ produced both a leucopenia and an anemia in the splenectomized mice. Hematopoiesis was markedly reduced in the bone marrow of all irradiated mice within three days; recovery from the hematopoiesis and the anemia occurred usually by the 119th day. Ectopic erythrocytopoiesis and megakaryocytopoiesis were greatly increased in the spleen three days after the isotopic injection and lasted throughout the 119-day period of observation; splenic lymphocytopoiesis was reduced in three days and recovery was not complete

116 days later, while the process was essentially not affected in other tissues. Ectopic granulocytopoiesis increased more slowly in the spleen of the irradiated animals than normally. It is concluded that the rapid development and the persistence of ectopic erythrocytopoiesis in the spleen prevent anemia in the mice irradiated with 2.0 µc of Sr⁹⁰. (NSA)

987

Jones, D. C. and D. Harold Copp. STUDIES ON BONE METABOLISM WITH THE AID OF RADIOACTIVE STRONTIUM. Radiation Lab., Univ. of Calif. Jan. 16, 1948. 14p. (AECD-1962; UCRL-60)

The kinetics of skeletal uptake and urinary excretion of radio-strontium were studied during the critical first hour following intraperitoneal injection of a carrier-free dose. These experiments not only provided valuable data concerning the metabolism and fixation of this important fission product, but, because of the close similarity of strontium and calcium, also gave basic information on the process of calcification. Three groups of rats were compared: normal mature adults, young growing normal animals, and young rachitic rats. In all groups, the blood radioactive strontium rose to a maximum in 10-15 minutes, and then declined as the strontium continued to deposit in the skeleton or to be excreted in the urine. Muscle and skin strontium curves followed those of blood quite closely, suggesting a rapid equilibrium between their extracellular fluid and blood plasma. In all groups there was a continuous uptake of strontium by the skeleton. In the adults, this was almost constant, suggesting uptake by absorption and exchange with the calcium of the bone mineral. In the young rats, both normal and rachitic, the very rapid initial rate of uptake of radio-strontium tapered off sharply with time, indicating that some of this radioelement was coming back from the bone into the blood stream. This suggested a rapid labile combination of strontium in these animals, which, since it also occurred in the rachitic group in which normal calcification is inhibited, probably associated with the protein osteoid matrix present in both. A hypothetical calcification mechanism was suggested by these findings. Urinary excretion and renal clearance of strontium was constant in all three groups, but the clearance was almost ten times as great in the rachitic as in the normal young and adult rats. This would seem to indicate a direct effect of rickets on the renal mechanism of radio-strontium (and calcium) excretion. (ADD)

988

Jones, D. C. and D. Harold Copp. THE METABOLISM OF RADIOACTIVE STRONTIUM IN ADULT, YOUNG, AND RACHITIC RATS. J. Biol. Chem. 189, 509-14(1951)

The metabolism of carrier-free radio-Sr was studied in adult, young, and rachitic rats during the critical first 24 hrs. after intraperitoneal injection. Radio-Sr is removed from the plasma much more slowly in the adult animals than in the other 2 groups. The uptake by adult bone is continuous for the first 2 hrs., and reaches a maximum within 4 hrs. Skeletal uptake of radio-Sr is much more rapid in the young animals, reaching a maximum within 30 minutes; very little was lost in the urine. The deposited isotope remains fixed in the bone. In rachitic rats, the rapid initial uptake was similar to that in the normal young animals, but was followed by active loss from the skeleton; only 1/3 was left after 24 hours. A labile combination with bone is indicated. A large part of the dose of radio-Sr was excreted by the rachitic rats within the first 24 hrs., and the plasma clearance was 10-15 times as great as in the normal animals. Rickets may have a direct effect on excretion by the kidney. (CA)

989

Nelson, J. Eugene, John G. Gibson, 2nd, Bert L. Vallee, and Marvin A. Van Dilla. THE EFFECT OF RADIOACTIVE STRONTIUM ON THE PERIPHERAL BLOOD PICTURE OF THE NORMAL DOG. *Acta Unio Intern. contra Cancrum*. 6, 819-24 (1949).

A mixture of Sr^{90} and Sr^{90} was given intravenously as the nitrate to two normal male dogs and one castrated dog (2 mc, 7 mc, and 20 mc, respectively). The mixture consisted of 88% of Sr^{90} (half-life 55 days; 1.5 Mev maximum β radiation) and 12% Sr^{90} (25-year half-life; 0.6 Mev maximum β radiation). Sr^{90} is followed by a daughter Y^{90} (64-hours half-life; 2.5 Mev maximum radiation); Y^{90} and Sr^{90} come into equilibrium in four to five days, accounting for 22% of total radiation thereafter. Due to the interval between experiments the ratio of radiation due to Sr^{90} and Sr^{90} was greater in the dog receiving 20 mc than in the other two. All three animals showed a decline in the white count of venous (jugular) blood which reached a maximum 21 days after injection. It was found that the fall in count in dogs 1-S (7 mc injected) and 2-S (2 mc injected) was due entirely to a reduction in the number of granulocytes, there being no significant change in the absolute number of lymphocytes or monocytes. The venous hematocrit fell in all three animals by more than could be accounted for by red cells removed in sampling; the fall in per cent of pre-injection levels was proportional to dosage; the low points were reached at approximately the same time as the lowest white count: 21-25 days. In the dogs which survived the period of most intense leukopenia (1-S and 2-S) the hematocrit rose but not to pre-injection levels; these two animals gradually declined, lost weight, refused food and became apathetic. There was a terminal rise in rectal temperature to 41 to 42°C. and death was preceded by generalized convulsions; at postmortem there were no signs of acute infection other than early bronchopneumonia of the left lobes. Sections of bone marrow from the upper portion of the femur of dog S-3 showed evidence of marked diminution of erythropoiesis and myelopoiesis. The localization and distribution of Sr^{90-90} , based on radioactivity measurements in the organs and skeleton and the approximate radiation to which the bone marrow was exposed will be discussed. (NSA)

990

Norris, W. P. and W. E. Kisielski. THE EARLY DISTRIBUTION OF Sr^{90-90} IN RATS. Argonne National Lab. [nd] 12p. (AECD-2009-A)

Twenty white Sprague-Dawley rats (ca 200 g each) were infected intravenously (tail vein) with 0.5 ml of isotonic sodium chloride, pH 6, containing 115 μC of a mixture of carrier free Sr^{90-90} (ca 75% Sr^{90} , 25% Sr^{90}) in equilibrium with the Y^{90} daughter of Sr^{90} . Animals were sacrificed by decapitation at intervals of 1 minute, 2 minutes, 5 minutes, 20 minutes, 1 hour, 6 hours, 24 hours, 3 days, 10 days, and 30 days after injection. The intravenous administration of Sr into the tail vein was attended by a retention of Sr in the tail which is not identical, in the first 1½ hours, to the metabolic picture observed in the other bones of the rat. The consistency of the results from several rats indicates that the initial high concentration of Sr in the tail is not the result of variable injection technique, but rather a result of a consistent loss into tissue or some other physico-chemical process occurring around the injection site at the time of administration. During the period immediately after injection, there occurs a rapid uptake of Sr by the bones which continues for 1½ to 2 hours. This is shown graphically for the femur and scapula. The rate of uptake by the femur was almost exactly that for the scapula. A second quantitative difference is demonstrated by the fact that, whereas the femur has acquired only 11% of its maximum activity dur-

ing the first minute after injection, the scapula, in the same period, has reached 25.5% of its maximum value. The time-content curves for all the bones, femur, scapula, tail, and carcass (the Sr content of which is almost entirely in the bones after three days), indicate that the maximum bone Sr content, reached at about 90-120 minutes after injection, is maintained for about six days. In a preliminary experiment to determine whether x-irradiation can influence the gross picture of Sr metabolism, results obtained were identical, qualitatively and quantitatively, with that observed in the non-irradiated rats described. (ADD)

991

Sacher, George A. THE EXCRETION, RETENTION, DISTRIBUTION, AND CLINICAL EFFECTS OF STRONTIUM⁹⁰ IN THE DOG. PART II. STATISTICAL ANALYSIS OF EXCRETION AND RETENTION OF STRONTIUM⁹⁰ FOR INDIVIDUAL DOGS. Univ. of Chicago Metallurgical Lab. June 1946. 21p. (AECD-2108; CH-3866)

Excretion data of 17 dogs injected with Sr^{90} were analyzed. Excretion was assumed to conform to the function $\log E_t = \log E_1 + b \log t$, where E_t is the excretion per day at time t , E_1 is the instantaneous excretion at the end of the first day, and b is the slope of the $\log E$ versus $\log t$ diagram. Values of E_1 and b were estimated for urinary and fecal excretion of individual dogs. Errors of estimate were also computed. A negative correlation ($r = -0.575$) was found between the urinary and fecal excretion slopes of adult dogs. Slopes and intercepts of urinary and fecal excretion lines of beagle pups were lower than those for adult dogs. In the urine-feces correlation and in dependence of excretion parameters on age, the Sr^{90} results paralleled the results with plutonium. The total elimination, Q^∞ , was defined and estimated for individual adult dogs. It was found that on the average more than 90% of the injected Sr^{90} could be accounted for by extrapolation of the excretion line based on observed excretion in the first few weeks after injection. The calculated total elimination of pups, based on the observed excretion behavior, showed at least 40% of the injected Sr^{90} unaccounted for, presumably because of the increase of total-body strontium concomitant with bodily growth. (NSA)

992

Simmons, Eric L. and Leon O. Jacobson. RADIOTOXICITY OF INJECTED Sr^{90} FOR RATS, MICE, AND RABBITS. PART IV. THE HEMATOLOGICAL EFFECTS OF ENTERALLY AND PARENTERALLY ADMINISTERED STRONTIUM⁹⁰ IN MAMMALS. Univ. of Chicago Metallurgical Lab. Aug. 1946. 101p. (MDDC-1387; CH-3797)

Hematological studies of the peripheral blood of rabbits, rats, and mice, after the intraperitoneal or stomach tube administration of Sr^{90} in doses from 0.015 to 14.5 $\mu\text{C/g}$ for varying periods up to 108 weeks, are reported. With the techniques employed in this experiment, a reduction in the heterophil values was the most sensitive indicator of acute and subacute effects. Moderate but significant reduction in heterophil values followed the intraperitoneal injection of 0.068 $\mu\text{C/g}$ in ABC male mice; no effect was apparent after the administration of 0.015 $\mu\text{C/g}$ by the same route in two strains (ABC males and CF-1 females). Progressively more significant and sustained reduction in heterophil and lymphocyte values followed higher doses. No anemia occurred in mice with doses of 0.034 $\mu\text{C/g}$ or lower, but moderate and sustained anemias were apparent with doses of approximately 2.0 $\mu\text{C/g}$. The minimal exerting a mean detectable reduction in heterophil values in rats was between 0.22 and 0.25 $\mu\text{C/g}$. Doses above this level produced a progressively more severe heterophil depression and lymphopenia. Stomach tube administration of the isotope was studied in rats for comparison with the intraperitoneal route.

Approximately twice the intraperitoneal dose is required by stomach tube to produce a comparable effect on the hematological constituents of the peripheral blood. An intraperitoneal dose of 1.0 μg produced a reduction of heterophil values of significance in the rabbit. Following an intraperitoneal dose of 3.0 μg , a significant reduction in hemoglobin and erythrocyte values occurred with a rapid recovery. A sustained heterophil and lymphocyte reduction of significance was also apparent after this dose. Sr^{90} produced morphological changes in the cells of the peripheral blood in these three species comparable to those observed following the administration of plutonium, radium, or total body x-irradiation. Anemias that developed in these three species, after Sr^{90} intoxication, were characteristically normocytic, normochromic, but occasionally hypochromic, and macrocytic anemias were seen. Although drastic depletion of hemopoiesis in the bone marrow follows Sr^{90} intoxication, anemias failed to develop in mice with doses of 0.34 μg , due apparently to the rapid development of extramedullary erythropoiesis in the spleen and liver particularly. A dose of 2.0 μg , however, produced a moderately severe anemia in this species. (ADD)

993

Swift, Marguerite N. and C. Ladd Prosser. THE EXCRETION, RETENTION, DISTRIBUTION, AND CLINICAL EFFECTS OF STRONTIUM⁹⁰ IN THE DOG. PART I. REPORT OF EXPERIMENTAL WORK. Univ. of Chicago Metallurgical Lab. July 24, 1947. 83p. (MDDC-1388; CH-3843)

Three groups of dogs (adults, young adults, and puppies) were given intramuscular injections of Sr^{90} in doses of 0.1-3.13 μg . Excretion of Sr^{90} was rapid during the first three days, with fecal content 50% higher than that in the urine. Both excretion patterns were exponential with an average slope of 1.8 on log-log plot. Blood concentrations declined similarly. Survival time shows some, but not close, correlation with dosage. Symptoms in non-survivors were fever, lethargy, anorexia, loss in weight, cutaneous hemorrhages, ulcerated areas on the body or in the mouth, rapid decline in leucocyte count, and frequently edema of face, neck, or extremities. Survivors showed some or all of these symptoms in addition to lower red counts (up to 46% decrease) after three to six weeks. Analyses were made of the carcasses of some of the animals for Sr^{90} content. Autopsies on some of the animals showed extensive hemorrhages. (E.G.)

994

Swift, Marguerite N., C. Ladd Prosser, and Edward S. Mika. EFFECTS OF Sr^{90} AND X-RADIATION ON GOATS. Univ. of Chicago, Metallurgical Lab. June 1946. 16p. (AECU-108; CH-3888)

It seemed advisable to determine the toxicity and other effects of Sr^{90} for goats in the hope that such information would provide a rational basis for extrapolation to man; such studies have already been made for mice, rats, rabbits, and dogs. The study of x-radiation effects was included for comparison, and to provide a radiosensitivity correction factor applicable to Sr^{90} -toxicity data. The 30-day LD-50 for intramuscularly-injected Sr^{90} in goats appears to lie between 1.0 and 1.5 μg . The rate of excretion of Sr^{90} in urine and feces and the per cent retained varies considerably, but over a range similar to that reported for the dog. Toxicity on the basis of body weight is thus the same or less in the goat than in the dog (30-day LD-50, 1.0 μg), and if the goat be assumed representative of the larger mammals, this indicates that the slope of the curve,

relating animal size to Sr^{90} toxicity, does change in the range 30-60 kg, and toxicity is clearly not a simple function of body weight. The clinical course and gross pathology following sublethal and lethal doses are in general similar to those observed in the dog. The pattern of hematological change is similar in goats and dogs, but the decrease in leucocyte count is noticeably less in nonsurvivors as well as in survivors in the former species. The 30-day LD-50 for total-body x-irradiation in goats is about 350 r, a figure which approximates that obtained for the dog. The post x-irradiation syndrome is grossly indistinguishable from that following injection of Sr^{90} . There is some indication of a greater depression of the leucocyte count following x-irradiation. Blood coagulation times after x-irradiation were erratic and failed to show the definite rise characteristic of the x-irradiation, Sr^{90} , and Pu^{239} syndrome in dogs. (NSA)

Tellurium

995

Jacobson, Louis, Roy Overstreet, I. Chaikoff, and Associates. METABOLISM OF FISSION PRODUCTS—RADIO TELLURIUM. Radiation Lab., Univ. of Calif. Oct. 1944. Decl. June 5, 1947. 13p. (MDDC-1005; CH-2258)

Methods of preparing Te^{127} and Te^{129} without carrier are described. The results of oral and intramuscular experiments using tellururous tellurium (+4) and telluric tellurium (+6) are given. Tellurium, whether administered either in the tellururous or telluric state, is absorbed by way of the digestive tract. It seems quite possible that in these experiments the +6 tellurium was not as readily taken up by way of the digestive tract and that its assimilation takes place by it first being converted to tellururous tellurium which is then absorbed. The rates of elimination of absorbed tellurium in both valence states and by both oral and intramuscular administration are rapid and essentially comparable. The rates of excretion during the time intervals studied indicate an approximate half time of retention in the body of 16 days. This is substantially less than the half-lives of Te^{127} and Te^{129} which are 32 and 90 days, respectively. This observation places tellurium in the small list of the long life fission products whose rates of elimination are greater than their rates of radioactive decay. The other members of this group being ruthenium, xenon, and cesium. The principle organs of deposition for absorbed tellurium are blood, liver, and kidney. On the per gram basis the kidney tissue is from 2 to 5 times more active than any other of the tissues. In all of the intramuscular studies with tellururous and telluric tellurium the blood was more active per gram than the liver. The blood showed the highest per organ content of tellurium and it is of interest to note that these relative levels were maintained even up to the 32nd day interval. The small but constant retention of activity in the skeleton, which showed no significant change throughout the entire 32 day interval, together with the fact that the relative proportion of activity in the skeleton as compared to other tissues was somewhat lower in the oral experiments as compared to the corresponding intramuscular experiments suggests that there may have been from 2 to 5% of radioactive impurities in the tellurium preparations employed such as alkaline earths, rare earths, zirconium, and columbium. It does not appear that the tellurium shows any significant tendency to either deposition or retention by the skeleton. (ADD)

Thallium

996

Thyresson, Nils. EXPERIMENTAL INVESTIGATION ON THALLIUM POISONING IN THE RAT. DISTRIBUTION OF THALLIUM, ESPECIALLY IN THE SKIN, AND EXCRETION OF THALLIUM UNDER DIFFERENT EXPERIMENTAL CONDITIONS. A STUDY WITH THE USE OF THE RADIOACTIVE ISOTOPE THALLIUM 204. *Acta Dermato-Venereol.* **31**, 3-27(1951).

After 24 hours the subcutaneous injections to rats of 40 γ /g body weight $TlNO_3$, labeled with Tl^{204} , gave decreasing amounts Tl in the order: kidneys, intestinal tract, thyroid, testes, pancreas, skin, bone, adrenals, muscle, spleen, brain, spinal marrow, liver, fatty tissue. The whole blood, plasma, and red cells contained 2.4, 2.1 γ /ml and 2.7 γ /g wet weight, respectively. After injection of 20 γ $TlNO_3$ 4.4, 36.7, and 61.2% (feces 42.2, urine 19.0) of the dose was excreted in 24 hours, 1 and 4 weeks, respectively. Oral γ -time increased the excretion in the urine, but not in the feces after repeated doses; however, after a single dose, cystine as well as BAL, $Na_2S_2O_3$, and methionine did not affect the excretion. The amount of Tl in the skin 24 hours after an injection of 40 γ varied with the age of the rat; it increased to a maximum with the 20-30-day-old and reached another maximum with the 44-5-day-old, corresponding to the growth of the 1st and 2nd coats of hair. Radioautographs indicate Tl uptake by the hair follicles. (CA)

Thorium

997

Ackerman, H., R. P. Allen, G. Bonner, W. L. Downs, H. C. Hodge, E. A. Maynard, W. F. Neuman, J. K. Scott, A. Sparks, and H. E. Stokinger. PRELIMINARY STUDIES OF THE TOXICITY OF THORIUM. University of Rochester. Feb. 26, 1948. Decl. Sept. 15, 1948. 45p. (AEC-D-2283; UR-13)

LD_{50} values of $Th(NO_3)_4 \cdot 3H_2O$ injected intraperitoneally in adult albino rats are $\sim 1,770$ mg/kg, while with intratracheal administration the LD_{50} is ~ 85 mg/kg. With the latter test <1000 mg/kg of ThO_2 was tolerated. No consistent lesions which could be attributed to the Th compounds were found in any organs other than the lung. $Th(NO_3)_4 \cdot 3H_2O$ provoked a peculiar focal coalition of monocytes in the alveolar sacs. ThO_2 provoked minimal or no response. Weanlings fed 20% $Th(NO_3)_4 \cdot 3H_2O$ died promptly. The weanlings fed 10% grew very little but survived for 11 months. A small-scale paired feeding study demonstrated clearly that the weight depression was only partly due to the decreased food consumption. Labeled Th with UX_1 given intravenously to rats, rabbits, and guinea pigs shows that Th is lost very slowly from the blood and the major portion appears in the liver. After 14 days one-fourth has been excreted in the feces. When administered by other routes, the Th tends to stay where placed. (TIS)

998

Cassel, Chester, Julian M. Ruffin, and Robert J. Reeves. LATE EFFECTS OF THORIUM DIOXIDE IN MAN. *Arch. Internal Med.* **88**, 42-50(1951).

Three patients were studied, 17, 16, and 13 years, respectively, after ThO_2 administration. While the presence of ThO_2 could still be demonstrated no effect on hemopoiesis, hepatic function, or general health was disclosed. (CA)

999

Christensen, William R. and Sheldon C. Sommers. CYTOLOGIC CHANGES FOLLOWING INTRAVENOUS INJECTION OF THORIUM DIOXIDE. *Cancer Research Inst., New England Deaconess Hospital, Boston.* [nd] 7p. (AECU-1535)

In view of reports in the literature of the toxic and possible carcinogenic effects of thorium dioxide when used as a contrast medium for radiological diagnosis, an attempt was made to induce malignant changes in the reticuloendothelial systems of four rats following intravenous injection of colloidal thorium dioxide (Thorotrast—20% thorium dioxide by weight). After 15 months no gross changes of reticuloendothelial systems were observed by x-ray examination. Microscopic studies showed the livers of two rats to exhibit marked hyperplasia of reticuloendothelial cells, and anaplastic variation in size, shape, and chromatin arrangement of the affected cells. No invasion was found, but the areas were considered of precancerous significance. (NSA)

1000

Easton, Thomas W. RETENTION OF INJECTED COLLOIDAL THORIUM DIOXIDE IN THE BODY OF THE LABORATORY MOUSE. *Anat. Record* **108**, 515(1950).

This paper is reproduced here in its entirety.

Mice were injected intravenously through the tail vein with colloidal ThO_2 (Thorotrast), 0.2 cc/day on alternate days for three doses, a total of 0.6 cc. Success of injections was checked by roentgenogram, a heavy shadow at base of tail indicating poor injection. Such mice were not used. Thorotrast in the body was determined by ashing the entire mouse after dividing into various samples, and measuring the radioactivity with a Geiger counter. Thorotrast was determined in the whole body, in liver and spleen alone, and in the remainder of the body by comparing measured activity with that of measured amounts of the material injected. Values obtained were as follows: one day after last injection, mice retained from 0.4 to 0.59 cc of the original 0.6 cc. Of this the liver represented 25 to 55%; the spleen, 14 to 28%; and the remainder of the body, 17 to 51%. Ten days after last injection the total was 0.4 cc, with variations up to 0.1 cc. Of this, the liver held 55 to 70%; the spleen, 25 to 30%; and the remainder of the body, 5 to 20%. This level was maintained for 130 days, at least. Most of the variations observed in amount of thorotrast retained appear to be due to variations in liver content. Neither splenectomy nor fasting begun prior to injection appear to have any marked effect on retention or loss of ThO_2 .

1001

Engels, Alfred, Werner Maurer, and Annemarie Niklas. THORIUM RESORPTION IN THE RETICULOENDOTHELIAL SYSTEM. *Z. ges. exptl. Med.* **115**, 221-8(1949).

Tables give the distribution of radioactivity 24 hr after intravenous injection of $Th(NO_3)_4$ (5, 2, and 0.001 mg, or 10^{-11} g Th) containing Th^{232} into rabbits, rats, and pigeons. The liver and spleen contain the largest amount; moderate amounts are found in bone marrow, lymph nodes, and adrenals. Sensitizing rabbits with horse serum causes an increase in the radioactivity of the liver and spleen 8 hr after injection. Treating rats with a near lethal dose of trypan blue in an attempt to block the reticuloendothelial system did not affect the distribution of radioactivity. (CA)

1002

Engels, A., W. Maurer, and A. Niklas. BEHAVIOR OF THORIUM IN GRAVID AND NON-GRAVID RATS. *Z. ges. exptl. Med.* **115**, No. 5, 525-33(1950).

In a previous paper (*Deut. med. Rundschau* **3**, 261(1949)) the authors have shown that thorium injected into animals was accumulated mainly in the liver, the spleen, and the bones. In the present work the same technique (intravenous introduction of thorium nitrate into a rat's tail, Th being labeled with UX_1) was applied to a study of differences in the distribution of Th in gravid and nongravid rats. It was found that the above mentioned organs were chiefly involved in both cases; however, in gravid animals the Th concentrations were lower, and the decrease of Th content in blood

proceeded more slowly than in nongravid individuals. It was also established that the volume of blood contained in the adrenals of a gravid rat is twice that found in those of a nongravid animal, the body weight being only slightly increased in the former case. (NSA)

1003

Hall, R. H. INHALATION TOXICITY OF THORIUM OXALATE, p.72-5 of QUARTERLY TECHNICAL REPORT; JULY 1, 1950, THRU SEPTEMBER 30, 1950. University of Rochester. Nov. 1, 1950. 4p. (UR-142) (p.72-5)

As a means toward evaluating the nature and extent of this hazard, two experiments have been completed in which dogs, rabbits, and rats were exposed to thorium oxalate dust by inhalation. The sole evidences of toxicity following inhalation of thorium oxalate dust were decreases in the serum Ca concentrations of the dogs and decreases in the number of circulating red blood cells with a concomitant increase of mean corpuscular volume, resembling the development of a macrocytic anemia in the dogs and in one rabbit. (NSA)

1004

Krebs, A. CONCERNING THE TOXICOLOGY OF THORIUM EMANATION (G). *Naturwissenschaften* **28**, 766-7(1940).

The effect of Th on mice was studied. The tolerance dose of Th in air is less than 70 mst per cc (55-day test), the presence of 1,750 mst per cc causes death in five days. Relatively Th is less active than Rn. (CA)

1005

Maurer, W., A. Niklas, and A. Engels. PERMEABILITY OF RAT PLACENTA FOR THORIUM IONS WITH VARYING PREGNANCY PERIODS. *Z. ges. exptl. Med.* **115**, 510-24(1950).

After intravenous injection of $\text{Th}(\text{NO}_3)_4$ labeled with Th^{234} into pregnant rats, the specific activity of the fetus drops from 0.1%/g fetus at the 14th day of pregnancy to 0.001%/g on the 21st day. The permeability of the placenta decreases rapidly. (CA)

1006

Nordenström-Blomqvist, Björn E. W. AN ATTEMPT OF EXCRETING INJECTED THOROTRAST IN RABBITS BY 2,3-DIMERCAPTOPROPANOL (BAL). *Acta Radiol.* **34**, 533-45(1950).

An experimental attempt was performed to excrete intravenously injected thorotrast in rabbits by 2,3-dimercaptopropanol (BAL). No excretion of Th was found in urine. The radioactivity in urine depends upon disintegration products of Th, of which ThX (Ra^{224}) and MsTh_1 (Ra^{228}) were found. After BAL treatment there was no sign of increased radioactivity in urine or significant decrease of the radioactivity in liver, spleen, kidney, or yellow bone marrow. The radioactivity of the spleen was four times as high as that of the liver, measured on the γ intensity per gram. The radioactivity of the kidney was low in comparison with that of the liver and spleen. (NSA)

1007

Ruf, Fritz and Kurt Philipp. THE RADIOACTIVITY OF THOROTRAST. EVENTUAL DELAYED DAMAGE DUE TO ITS USE AS A CONTRAST MEDIUM. *Langenbecks Arch. klin. Chir.* **263**, 573-87(1949-50).

Injection of as little as 15 cc. of thorotrast deposits sufficient Th in organs such as the liver and spleen to expose each g. of organ to 0.5 r./day or twice the tolerance dose. Since the Th is not excreted, the dose of irradiation can exceed 1800 roentgens in 10 years. In most cases larger quantities of thorotrast are injected, leading to greater damage over a period of years. (CA)

1008

Salerno, Paul R. and Paul A. Mattis. ABSORPTION AND DISTRIBUTION OF THORIUM NITRATE IN THE RAT. *J. Pharmacol. Exptl. Therap.* **101**, 31-2(1951).

This paper is reproduced here in its entirety.

$\text{Th}(\text{NO}_3)_4$ was administered to adult male rats by several routes, and the tissue distribution was studied by means of $\text{UX}_1(\text{Th}^{234})$ as a radioactive indicator. Studies on rats given 30 mg/kg by stomach tube revealed that maximal absorption had occurred within 4 days and that more than 90% of the absorbed dose was deposited in the skeleton. After 32 days, 100% of the retained Th, which represented 0.06% of the administered dose, was found in the skeleton. When larger doses of Th (700 to 800 mg/kg) were administered by oral intubation, no absorption could be measured, which indicates that less than 0.001% is absorbed at this dosage level. Absorption following subcutaneous administration was found to be progressive in that 0.03 and 0.07% of the injected dose was found in the skeleton at 16 and 30 days, respectively. Following the intraperitoneal injection of 60 mg/kg of Th, 1% of the dose was deposited in the skeleton after 30 days. $\text{Th}(\text{NO}_3)_4$ administered intravascularly by intracardiac injection was retained to the extent of 95, 89, and 83% at 3, 8, and 14 days, respectively. Tissue distribution in terms of per cent of injected dose was 16% to the skeleton, 55% to the liver, and 5% to the spleen after 14 days. Two hours after intracardiac injection, 50% of the Th is removed from the blood, and 7.6% is found in the skeleton. Less than 1% is found in the blood after 18 hr. Most of the Th which is excreted is found in the feces and apparently is transported from the liver via the bile. (NSA)

1009

Schubert, Jack and Herschel Wallace, Jr. THE EFFECT OF ZIRCONIUM AND SODIUM CITRATE ON THE DISTRIBUTION AND EXCRETION OF SIMULTANEOUSLY INJECTED THORIUM AND RADIOSTRONTIUM. *J. Biol. Chem.* **183**, 157-66(1950). (AEC-2621)

The distribution and daily excretion of tracer levels of injected thorium and strontium were studied in rats receiving zirconium or sodium citrate intraperitoneally $\frac{1}{2}$ hour after the administration of the radio-elements ("early" treated) or three days later ("late" treated). One group of rats received no other treatment. In contrast to previous studies on plutonium and yttrium, zirconium citrate had no specific effect on Th or Sr metabolism other than that associated with the citrate part of the molecule. The early administration of zirconium or sodium citrate resulted in about a 3-fold increase in the urinary excretion of Th and a 2-fold increase in the urinary excretion of Sr during the following 24 hours. No effect on the fecal excretion was found. The Th concentration in the liver, mesenteric lymph node, pancreas, and spleen were markedly reduced as a result of early sodium citrate administration. No significant changes in the metabolism of Th or Sr were found in the late treated group. The deposition of Th/g was highest in the soft tissues, particularly in the liver, while Sr accumulated mainly in the skeleton. The results indicate that cationic radioelements are fixed in bone by at least three different mechanisms. An interpretation of the results in terms of ion exchange, surface absorption, and complex ion formation is presented. (NSA)

Tritium

1010

Brues, Austin M., Agnes N. Stroud, and Leola Rietz. TOXICITY OF TRITIUM OXIDE TO MICE. *Proc. Soc. Exptl. Biol. Med.* **79**, 174-6(1952).

The 30-day median lethal dose of H_2O for CF No. 1 female mice is about 1 mc per g body weight when given in a single injection. The estimated radiation dosage is about 800 rep in the first 3 days and about 1000 rep in the first 12 days after injection. It is concluded that no unexpected factor of biological effectiveness exists for tritium β rays in relation to X or γ rays. (Authors' Summary)

1011

Pinson, Ernest A. and Ernest C. Anderson. THE ABSORPTION, DISTRIBUTION, AND EXCRETION OF TRITIUM IN MEN AND ANIMALS. Los Alamos Scientific Lab. [nd] 4p. (AECU-937; LADC-867)

The tritium absorbed by rats from inspired air containing HT or HTO is proportional to the tritium activity in the inspired air. When present as HTO a very high percentage of the tritium activity inspired is taken into the body fluids indicating rapid exchange and absorption of activity across respiratory membranes. If present as HT in inspired air only about 0.05% of the inspired activity appears in the body as HTO. Apparently, biological catalyzation of HT to HTO takes place in the body. The activities studied were not high enough for the absorption of HT per se in body fluids to be detected. Three millicuries of HTO ingested by man in 200 cc of water was completely absorbed in about 45 minutes. Absorption is linear with time. Absorbed tritium dilutes with 57 to 68% of the body weight suggesting that body water is primarily involved. Tritium elimination from the body in both rats and man is an exponential function of total water turnover. The reservoir calculated from the rate constant is again 57 to 68% of the body weight. The biological half life of HTO in nine human subjects varied from 9 to 14 days on ad libitum water intake and was reduced to $2\frac{1}{2}$ days in one subject on high water intake. The biological half-life in rats ranged from 4 to 5 days on ad libitum water intake. The tritium activity in excreted sweat, insensible perspiration, expired water vapor, sputum, and urine is essentially the same as that in the blood. (NSA)

1012

Powers, E. L., Jr. and Deborah Shefner. TRITIUM-INDUCED EFFECTS IN *PARAMECIUM AURELIA*. Proc. Soc. Exptl. Biol. Med. **78**, 493-7(1951). (AECU-1485; UAC-403)

Isolated specimens of *Paramecium aurelia*, kept during 2 days in culture fluid containing 1 to 100 mc of T per ml, calculated to emit a radiation dosage of 630 to 64,450 rep/day, divided 6 to 8 times during that period. No effects were observed in the animals, washed after exposure, until autogamy occurred. Increasing death rates (1.9 to 98.1% after autogamy were observed with increasing radioactivity of the medium. The observed difference in the efficiency between T and $\text{Sr}^{90,90} \gamma^{90}$ in inducing the effects observed is consistent with the observations of others concerning the dependence of the mutation constant upon rate of energy loss by densely ionizing particles. (NSA)

1013

Stroud, Agnes N. and Austin M. Brues. THE EFFECT OF TRITIUM (H^3) ON CELLS CULTIVATED IN VITRO, p.111-17 of BIOLOGICAL AND MEDICAL DIVISIONS QUARTERLY REPORT FEBRUARY, MARCH, APRIL, 1950. Argonne National Lab. [nd] 7p. (ANL-4451(p.111-17))

A series of cultures of chick embryo muscle was treated with H_2O at dosage rates of 41.5 to 3000 rep/hr, up to total dosages of 72,000 rep. Under continuous irradiation, completion of the mitotic cycle becomes very much delayed even after the accumulation of a few hundred rep. Not all mitoses are equally delayed at a given stage, and the delay appears to result from a variety of processes, perhaps related to abnormal nucleic acid metabolism. Some cells eventually divide unequally, without evidence of spindle or

plate formation. Delay may occur in any stage of mitosis, perhaps excepting prophase. Cell degeneration occurs only in dividing cells at the lower dosages; after 20,000 rep and more, degeneration occurs suddenly in resting cells, beginning with an "explosion" followed by shrinkage of the nucleus. Others degenerate without exploding. Preliminary data suggest that at a given dose rate, the onset of mitosis is suppressed partially, an equilibrium rate of cell division being attained. Due to concomitant delays in completion of the cycle it is impossible to measure directly partial inhibition of onset. The cytoplasmic behavior of continuously irradiated cells is described. (NSA)

1014

Thompson, R. C. THE GROSS RETENTION AND METABOLISM OF TRITIUM OXIDE IN THE MOUSE. Hanford Works. Jan. 23, 1951. 13p. (HW-20092)

For evaluation of radiation hazard in handling of tritium, 0.5 ml of a 0.86% saline solution, containing 190 μC tritium per ml, was injected into mice intraperitoneally daily for 13 days. Tritium was determined in body water and in the ground combusted remains of the dried carcass. The initial biological half life for tritium oxide in body water was about 1.1 days; for tissue-bound tritium about 3 days. Thirty-two days after the final injection 90% of the tritium in the animal was in the bound state, being lost with a biological half life of approximately 30 days. (NSA)

1015

Thompson, R. C. RETENTION BY MICE OF TRITIUM ADMINISTERED AS THE OXIDE. Hanford Works. June 19, 1951. 14p. (HW-21494)

Tritium oxide was administered to mice by intraperitoneal injection. The retention of tritium activity in the body water and in the dry carcass was determined. The biological half life of body water in the mouse is approximately 1.1 days. The curve of tritium loss from the tissue-bound state can be fairly well resolved into components of 9-day and 90-day half lives. These components are thought to represent, respectively, groups of relatively dynamic body constituents, and of relatively stable body constituents. They are of comparable tritium binding capacity and under chronic exposure to tritium would accumulate about 17% as much activity as would be present in the body water. (NSA)

Uranium

1016

Arnold, James S. EXHIBIT-RADIOAUTOGRAPHS OF U^{233} IN BONE AND SOFT TISSUE. Argonne National Lab. Mar. 1951. Decl. June 6, 1951. 17p. (AECD-3176)

A series of radioautographs is presented showing deposition of U^{233} and Pu in the bone and soft tissues of animals, sacrificed at periods varying from 24 hr to 4 yr following injection. (NSA)

1017

Bauer, Frederick C., Jr., Grant C. Johnson, Lynn Carbonaro, and Edwin F. Hirsch. CHANGES IN THE SERUM LIPIDS OF RABBITS WITH ACUTE URANYL NITRATE POISONING. Arch. Pathol. **51**, 441-5(1951).

Uranyl nitrate poisoning in rabbits was associated with transient azotemia and lipemia of 2 to 3 weeks duration. All lipids participated in this increase, but the greatest increase was in the neutral fat fraction. The nonprotein N returned to near the control level several days before the lipids. The significance of these results with other forms of nephritis is discussed. (NSA)

1018

Brusa, Adolfo. HISTO-AUTORADIOGRAPHIC DETERMINATIONS OF RADIOACTIVE SUBSTANCES IN THE BODY. A STUDY ON EXPERIMENTALLY-INTRODUCED URANIUM. Boll. soc. ital. biol. sper. **26**, 673-5(1950).

Nonlethal doses of uranyl acetate were injected subcutaneously in guinea pigs, and sections from various organs were examined autoradiographically 1 to 6 days following the injection. The principal concentrations of U occur in the kidneys, being localized there in the cortical substance. In other organs the following main localizations are observed: the extreme portions of the bronchial ramifications of the lungs, the mucosa of the intestine, and the parenchyma of the lobuli of the liver. (NSA)

1019

Hodge, Harold C. PHARMACOLOGIC TOOLS IN THE STUDY OF THE MECHANISMS OF URANIUM POISONING. Arch. Ind. Hyg. Occupational Med. 2, 300-11(1950).

Application of fluorophotometric analysis for U, ultrafiltration of H_2CO_3 complex, protein precipitation, exchange adsorption studies of bone with radioisotopes, radioautographs of kidney, renal clearance studies, histopathology, enzymic activity in the urine, and cell physiology, U was found to enter the body as the uranyl ion, to be carried as a nondiffusible protein complex and diffusible H_2CO_3 complex, to be partly deposited in bone, and to be mostly excreted in the urine after damaging the tubules of the kidneys. (CA)

1020

Hodge, H. C., E. A. Maynard, and W. L. Downs. ANTI-DOTAL ACTION OF POLYPHOSPHATES IN URANIUM POISONING. J. Pharmacol. Exptl. Therap. 101, 17-18 (1951).

This paper is reproduced here in its entirety.

In previous studies it has been established that uranium nitrate hexahydrate fed at 2% of the diet or given intraperitoneally in a single dose of 2.5 mg/kg to adult albino rats produces approximately 50% mortality during the ensuing 21 days. Previous attempts to provide an antidote for acute U poisoning led to the suggestion of bicarbonate because this ion furnishes a diffusible complex with the uranyl ion. Following the recent demonstrations of the complex established between uranyl ion and bone surface (Neuman), between the uranyl ion and the surfaces of yeast cells (in both cases probably with phosphate groups), and between the uranyl ion and various polyphosphates (Rothstein), tests were carried out to see whether polyphosphates could be used in the treatment of acute experimental U poisoning. The excretion of Ca salts of polyphosphates in urine (Gosselin) prompted the trial of these compounds both in feeding studies and after intraperitoneal injections of U. The polyphosphate was administered sometimes as a single dose and sometimes in multiple injections intraperitoneally. There was considerable evidence that a marked reduction in mortality can be achieved. (NSA)

1021

Hurwitz, Leon. A KINETIC STUDY OF NORMAL AND URANIUM INHIBITED HEXOSE METABOLISM IN YEAST. University of Rochester. May 3, 1950. Decl. June 15, 1950. 108p. (AECD-2857; UR-117)

The industrial use of uranium in recent times has led to several toxicological problems. One of the most important of these is the deleterious effect of uranium on normal renal function. In order to gain some understanding of its poisonous action in the kidney, several investigators have found it valuable to determine the effect of uranium on cellular metabolism. Yeast cells being much easier to work with than kidney cells, they have been considered preferable for these studies.

Kinetically, glucose appears to form a loose complex with the active cell groups involved in aerobic and anaerobic metabolism, leaving the glucose mostly in the free state. The K_s (dissociation constant) for aerobic metabo-

lism is 3.6×10^{-3} and for anaerobic metabolism 4.4×10^{-3} . Fructose was also found to form a loose complex with the active cell groups under anaerobic conditions. Its K_s is 1.9×10^{-2} . The maximum velocities of anaerobic glucose and fructose metabolism are equal. The value is approximately 28 μ l CO_2 per milligram yeast per hour at 25°C and pH 3.5. This may indicate that a single enzyme system or that equal concentrations of two different enzymes dominate the rate-limiting step in the metabolic scheme. The rate-limiting step in the aerobic metabolism of glucose is slower than in the anaerobic metabolism of glucose. Its velocity is 13.30 μ l per milligram yeast per hour at 25°C and pH 3.5. It has been shown that the anaerobic production of CO_2 by yeast is proportional to the anaerobic utilization of glucose. Evidence was presented to show that the rate-limiting process on the yeast cell surface is an enzymatic reaction thus lending support to the theory of active transfer of material across the cell membrane. Anaerobically, there exists for the most part a noncompetitive inhibition of glucose metabolism by uranium. However, some degree of competition can be found in both aerobic and anaerobic glucose metabolism. In the fermentation of fructose, competition is apparently due to a uranium-substrate combination. The temperature characteristics of aerobic glucose metabolism is about 12,700 cal/mole between 18°C and 30°C and 20,850 cal/mole between 18°C and 10°C. When uranium is added the temperature characteristic becomes 23,400 cal/mole throughout the whole temperature range measured with no break at 18°C. In the anaerobic metabolism of both glucose and fructose, the temperature characteristics are about the same. They increase as temperature decreases whether uranium is present or not. In the control data, average (μ) values are about 21,800 cal/mole between 20 and 25°C, and 10,700 cal/mole between 25 and 30°C. In the presence of uranium, the anaerobic metabolism of fructose and glucose has an average temperature characteristic of 17,000 cal/mole between 20 and 25°C and 23,000 cal/mole between 25 and 30°C. The increase in aerobic (μ) values when uranium is added amounts in effect to a reversal of inhibition as the temperature is raised between 18 and 30°C. This also holds true for anaerobic glucose and fructose metabolism between 25 and 30°C. Uranium forms a complex in a 1/1 ratio with active groups in the anaerobic glycolytic system. The initial steps in the respiration and fermentation of glucose are accomplished by different systems, each possessing widely different characteristics. It has been postulated that either the aerobic, anaerobic, or both systems associated with glucose metabolism may be the composite of a number of dissimilar processes. 33 references. (NSA)

1022

Kisielewski, W. E., W. G. Faraghan, and W. P. Norris. THE RETENTION AND DISTRIBUTION OF U^{233} IN MICE. Argonne National Lab. Nov. 1950. Decl. Feb. 2, 1951. 2p. (AECD-3057)

A study of the metabolism and organ distribution of U^{233} injected intravenously in mice is reported. The major portion of the injected material was rapidly excreted; about 50% was retained at 3 to 4 days and only about 20% at 6 days. The bone was the principal site of deposition. (NSA)

1023

LaFrance, Leo J. A PARTIAL BIBLIOGRAPHY ON URANIUM AND ITS COMPOUNDS WITH ESPECIAL REFERENCE TO PHARMACOLOGY AND TOXICOLOGY. University of Rochester. May 11, 1951. 32p. (UR-166)

This annotated bibliography contains 414 references to papers dealing with pharmacological, toxicological, and physiological effects of U and its compounds on animals.

No references to the effects of U on plants are included. (NSA)

1024

MacNider, W. deB. **INABILITY OF 2-3 DITHIOPROPANOL (BAL) TO PROTECT THE LIVER AGAINST TOXIC ACTION OF URANIUM NITRATE.** *Proc. Soc. Exptl. Biol. Med.* **68**, 160(1948).

The author has shown that doses of BAL (10%, benzyl benzoate 20%, in peanut oil) equivalent to 15 mg/kg, when administered subcutaneously to dogs for 8 days, were ineffective against the hepatotoxic action of 4 mg/kg of uranium nitrate; instead, it tended to increase the toxic effects. The livers showed diffuse necrosis with advanced fatty degeneration. (NSA)

1025

Masturzo, Aldo. **PERIPHERAL-BLOOD AND BONE-MARROW TESTS DURING EXPERIMENTAL INTOXICATION WITH URANIUM.** *Folia med. (Naples)* **33**, 643-71(1950).

In continuation of observations on gradual intoxication of guinea pigs and rabbits with uranium chloride (*Folia Med. (Naples)* **33**, 535(1950)), an examination was made of the changes in the peripheral blood and the bone marrow; samples of marrow were obtained from the femur of living animals by means of a surgical operation. The alterations of the blood pointed to an anemia of a normochromic type, with a hyperchromic tendency in rare cases; the bone marrow exhibited hyperplasias, the hyperactivity extending mainly to the less mature elements. (NSA)

1026

Masturzo, Aldo. **BLOOD STUDIES IN INTOXICATION EXPERIMENTS WITH URANIUM CHLORIDE.** *Folia med. (Naples)* **33**, 748-59(1950).

Weekly blood tests of rabbits intoxicated by repeated doses of uranium chloride revealed notable modifications in the coagulation characteristics of the blood (lengthening of the prothrombin and coagulation times). (NSA)

1027

Neuman, W. F., M. W. Neuman, and B. J. Mulryan. **FAILURE OF NONISOTOPIC URANIUM TO INHIBIT RESORPTIVE PROCESSES IN THE RAT FEMUR.** *J. Biol. Chem.* **182**, 151-2(1950).

The previously described inhibition of the resorptive processes after injection of radioactive $\text{UO}_2(\text{NO}_3)_2$ was shown to be caused by radiation rather than by any specific chemical effect of U itself. (CA)

1028

Tannenbaum, Albert, ed. **TOXICOLOGY OF URANIUM.** McGraw-Hill Book Company, Inc., New York. 1951. 333p. (National Nuclear Energy Series, Division IV, Volume 23)

This volume contains report of investigations on the toxicology of uranium compounds together with associated studies. The report represents experiments performed for the Manhattan Project by the Metallurgical Laboratory of the University of Chicago and the Medical Research Institute of Michael Reese Hospital. Included are chapters on the nature of uranium poisoning, factors affecting uranium poisoning, distribution and excretion of uranium, biochemical effects of uranium poisoning, mechanism of action of uranium and the transport of uranium to the tissues, and the relation of experimental studies to uranium poisoning in man. Also included are sixteen papers in the collected papers section on the various aspects of the toxicology of uranium compounds. (S.V.S.)

1029

Voegtlin, Carl, and Harold C. Hodges, eds. **THE PHARMACOLOGY AND TOXICOLOGY OF URANIUM COMPOUNDS.**

McGraw-Hill Book Company, Inc., New York. PARTS I, II, 1949. 1084p. PARTS III, IV, 1953. 2466p. (National Nuclear Energy Series, Division VI, Volume 1)

This is one of the first available volumes of the National Nuclear Energy Series, Manhattan Project Technical Section. It summarizes years of research and many experiments on the toxicity of uranium compounds and the mechanism of uranium poisoning. Experiments on the toxic qualities of uranium compounds were made preceding various conditions, such as exposure by inhalation of dust or fumes, by skin and eye application, and by oral and parenteral administration. Large scale acute tests were made of the degree of air contamination by uranium compounds. The problems of aerosol production, control, and measurement are described; details are given on such aspects as the relationship of particle size to toxicity and the adaptation of the cascade impactor for routine dust measurements. Emphasis is placed on the mechanism of action of uranium. The physico-chemical rules which govern the formation of uranium-protein complexes and bicarbonate complexes are applied to the transport of uranium in the body and to its excretion through the kidney. The characteristic uranium in the kidney is described from histopathological and from function studies. The role of citrate in tolerance is also covered. Many of the methods and techniques are given in detail, such as the measurement of catalase in urine and the standardization of toxicological procedures for large scale investigation. New uranium methods presented are: skin and eye toxicity, the analytical method, inhalation toxicity, distribution and excretion, theory tolerance, enzyme and protein effects and the catalase method. (NSA)

Yttrium

1030

Anthony, D. S. **ACUTE RADIOTOXICITY OF INJECTED YTTRIUM⁹¹.** *Univ. of Chicago Metallurgical Lab.* July 3, 1947. Decl. Sept. 10, 1947. 16p. (MDDC-1240; CH-3838)

Male rats in groups consisting of five animals each were given intracardial injections of Y^{91} at dose levels of 1, 3, 5, 7, and 10 $\mu\text{C/g}$ of body weight. A control group of five animals was given isotonic saline. The excretion, retention, and distribution of the yttrium was measured, and its effect on survival and growth was observed. The average total excretion of Y^{91} to the time of death (from 76 hours to 24 days) was a little less than 30% of the injected dose. About 25% was excreted in the first four days. During the first four days, nearly 75% of the excretion was via the urine; while between the fourth and the ninth days, nearly 90% of the excretion was via the feces. The average total retention at death (average time, 8.5 days) in 15 rats was 66% of the injected dose. This retention was distributed grossly as follows: about 55% in the carcass, 11% in the entire viscera, and 2.5% in the femur. The highest total retention in the viscera was found in the liver (6%) while the highest retention/gram of soft tissue was found in the kidney (1.7%). The concentration in the femur was three times higher than the highest concentration in the soft tissues. The 30 day LD-50 was between 1 and 3 $\mu\text{C/g}$, indicating a toxicity nearly twice as great as that observed with other fission products. The explanation of the high toxicity of Y^{91} is not apparent from the data in this experiment. Although there were no deaths in the period between 4 weeks and 6 months, all four of the remaining rats that had been given 1 $\mu\text{C/g}$ died between 6 and 8 months. Three of these deaths were due to tumors. The growth rate, as measured by increase in body weight, was depressed approximately 10% even by the lowest (1 $\mu\text{C/g}$) dose of Y^{91} . (ADD)

1031

Brues, Austin M. and Leola Rietz. RESPONSES OF MITOTIC CELLS IN LIVER AND CARCINOMA TO CONTINUOUS INTERNAL IRRADIATION. *Cancer Research* **11**, 240(1951).

This paper is reproduced here in its entirety.

Regenerating rat liver was exposed to internal β irradiation by insertion of glass beads containing Y^{91} or $Ce^{144}-Pr^{144}$. The distribution of the absorbed energy around these point sources was such that concentric spheres of the tissue received graded dosages varying between zero and amounts sufficient to cause early necrosis. The frequency of mitotic figures was reduced more or less uniformly at a given dosage rate between 8 and 48 hr after insertion, and followed an exponential depression with increasing dosage. Mitotic figures decreased in number in the heavily irradiated areas within 1 hr after insertion of the radioactive source, and virtually disappeared between the 4th and 8th hour. A few residual figures probably represent prolongation of a few mitoses under continuous irradiation. Exposure of the Hall mouse carcinoma under the same conditions resulted in a similar picture. In addition to this, large cells appeared in the region of depressed mitotic activity. It appears probable that this results from continued nuclear and cytoplasmic growth where mitosis is inhibited. (NSA)

1032

Dobson, E. L., et al. STUDIES WITH COLLOIDS CONTAINING RADIOISOTOPES OF YTTRIUM, ZIRCONIUM, COLUMBIUM, AND LANTHANUM, PART II. THE CONTROLLED SELECTIVE LOCALIZATION OF RADIOISOTOPES OF YTTRIUM, ZIRCONIUM, AND COLUMBIUM IN THE BONE MARROW, LIVER, AND SPLEEN. *J. Lab. Clin. Med.* **34**, 305-12(1949) (AECD-2055; UCRL-92)

Studies with several colloids containing radioisotopes of zirconium, columbium, and yttrium have shown that the biological distribution of such materials depends upon the nature of the colloidal particles. Colloids of zirconium of relatively large particle size show rapid disappearance from the blood stream (half-life = 30 seconds to 1 minute), and are deposited primarily in the liver and spleen. Colloids of intermediate particle size, both of zirconium and yttrium, disappear much more slowly from the blood stream (half-life = 30 minutes to 80 minutes) and are deposited primarily in the bone marrow and spleen, the liver acquiring only $\frac{1}{2}$ the specific activity of marrow. Both types of colloids once deposited show no significant change in distribution pattern, at least over 2 to 4 week period, and only slow excretion from the body. (NSA)

1033

Foreman, Harry and Joseph G. Hamilton. THE USE OF CHELATING AGENTS FOR ACCELERATING EXCRETION OF RADIOELEMENTS. *Radiation Lab., Univ. of Calif.* June 14, 1951. Dec. Sept. 21, 1951. 18p. (AECD-3247)

The chelating action of (ethylenediamine)tetraacetic acid (EDTA) was investigated as a means of accelerating the excretion of radioelements which have become fixed in the animal skeleton. Rats injected with Y^{91} followed by the administration of Ca EDTA showed excretion of Y^{91} greatly increased when compared with controls which received Y^{91} alone. Rats receiving both Ce^{144} and Pu^{239} , followed by Ca EDTA showed an increase in urinary excretion of Ce when given during the first 24 hr following injection of the isotope. Ca EDTA enhanced urinary excretion of Pu to levels which were approximately 10 times greater than that of control animals. The effect lasted for several days after the cessation of treatment. Fecal excretion of Pu was not affected by the chelating agent except when Ca EDTA was administered during the first 24 hr, at which time there was a marked rise in Pu excretion. (NSA)

1034

Jacobson, Leon O. and Eric L. Simmons. THE EFFECTS OF INJECTED YTTRIUM⁹¹, PART VIII. HEMATOLOGICAL EFFECTS. *Univ. of Chicago Metallurgical Lab.* June 1946. 21p. (AECD-2037; CH-3859)

Radioactive yttrium (Y^{91}) was administered by gavage to rats in single acute doses of 5, 10, and 20 μ c/g. Daily doses of from 0.3 to 2.0 μ c/g were administered to other rats, and at some dose levels treatment was continued up to 178 days. A single dose of 20 μ c/g produced a marked initial elevation in erythrocytes and hemoglobin, followed by an erratic anemia due to bleeding. A 75% reduction in lymphocytes occurred within three days, but these elements reached a normal value by 42 days. The heterophil values after this dose were extremely variable. A dose of 10 μ c/g produced a temporary lymphopenia and an erratic heterophilia only. No hematological effect was observed after single doses of less than 10 μ c/g. The daily gavage of Y^{91} in amounts from 0.3 to 2.0 μ c/g produced no anemia. A sustained heterophilia was present in all groups receiving daily treatment. In one experiment a moderate lymphopenia, which reached its maximum at 60 days, was produced by the daily treatment of 0.3 and 1.0 μ c/g but the lymphocytes gradually recovered to normal values by 90 days even though yttrium administration continued through 178 days. In another experiment, daily ingestion of 0.3, 1.0 μ c/g produced a lymphopenia which reached its maximum at 98 days. By 14 days after the discontinuation of Y^{91} gavage (at 95 days) the lymphocyte values had returned to normal levels. It is suggested that the lymphopenia described above results from the local effect of β -radiation on the lymphatic tissue of the gastrointestinal tract. No significant morphological change in the nucleated cells or erythrocytes occurred after singly or chronically administered doses of ingested Y^{91} . (NSA)

1035

Kidman, Barbara, Margaret Tutt, and Janet Vaughan. EXCRETION OF YTTRIUM-91 IN RABBITS. *Nature* **167**, 658(1951).

The effect of age on excretion and retention of Y in rabbits has been demonstrated following injections of Y^{91} . The mean retention in three weanling rabbits 5 to 6 weeks old, on a medium calcium diet, killed 9 days after an injection was 0.63%/g of bone, while in three 7-month old rabbits it was 0.33% of the injected dose/g of bone. The mean excretion in the urine in weanlings was 12.0% of the injected dose, whereas in adults it was 24.0% of the injected dose. These findings confirm that the decay-curve method for estimating the excretion of Y^{90} has validity. (NSA)

1036

Kisielewski, W. E., B. E. Kline, and H. P. Rusch. A PRELIMINARY STUDY ON THE EFFECTS OF INJECTED YTTRIUM⁹¹ ON THE RIBOFLAVIN CONTENT OF RAT LIVERS, p.172-6 of BIOLOGICAL AND MEDICAL DIVISIONS, QUARTERLY REPORT, FEBRUARY, MARCH, APRIL, 1949. Argonne National Lab. [nd] 4p. (ANL-4291(p.172-6))

Data on the effects of injected yttrium⁹¹ on the riboflavin content of rat livers have been presented. Preliminary indications note a fall in riboflavin; however, no histological or morphological changes were noted, and this fall may be a sign of minimal radiation damage or, more likely, a part of a more general toxic picture that is manifested by loss in body weight. Calculations of the radiation dose to the livers and a method for riboflavin determination have been presented. (Authors' Summary)

1037

Lisco, H., Austin M. Brues, Miriam P. Finkel, and W. Grundhauser. CARCINOMA OF THE COLON IN RATS

FOLLOWING THE FEEDING OF RADIOACTIVE YTTRIUM. Cancer Research 7, 721(1947) (MDDC-1418-C)

Yttrium⁹¹, one of the common radioactive fission products obtained in a chain-reacting pile, is a pure β -emitter with an energy of 1.5 Mev and a half life of 57 days. It is essentially not absorbed and, since the material remains longer in the colon than in any other portion of the intestinal tract, most of the damage occurred in this region. One group of rats received a single feeding by stomach tube of from 1.0 to 6.0 millicuries of Y⁹¹. Of the 33 animals in this group, four died with adenocarcinoma of the colon. The earliest tumor was seen at 135 days and the latest, at 506 days. Additional animals died with acute and chronic ulceration of the colon accompanied by benign and atypical hyperplasia of the mucosa. A second group of rats was given 78 feedings of 0.46, 0.20, or 0.06 millicuries of Y⁹¹ per feeding over a period of three months. The total accumulated doses were 31.20, 15.60, and 4.68 millicuries, respectively. Clinically all animals appeared well during the feeding period and growth was not impaired. Six of the eight animals at the two higher levels died with carcinoma of the colon from 304 to 548 days after the first feeding. No malignancies were observed at the lowest level. However, many of these animals died with superficial ulcerative lesions of the colon. (ADD)

1038

Scott, K. **RADIO YTTRIUM (Y⁹⁰)** Univ. of Chicago Metallurgical Lab. [nd] (MDDC-1143-A)

Extended experiments covering a period of 64 days revealed that approximately 50% of Y⁹⁰ introduced into the peritoneal cavity is deposited in the bones. No significant decrease of this deposition was observed between the first and sixty-fourth day. The rate of elimination of Y⁹⁰ was extremely slow after the first few days of administration. The daily rate of elimination after the first week is negligible as compared to the rate of radioactive decay of this radio element. The oral administration of Y⁹⁰ indicates that the total absorption of this element from the digestive tract is less than 0.1%. When Y⁹⁰ is introduced as a solution of YCl₃ directly into the lungs apparently a large proportion of the administered material remains unabsorbed in this organ at four days. The proportion that underwent absorption was distributed in the tissues in a manner similar to the localization after intraperitoneal injection. (ADD)

1039

Walker, Leonard A. **LOCALIZATION OF RADIOACTIVE COLLOIDS IN LYMPH NODES.** J. Lab. Clin. Med. 36, 440-9(1950).

The purpose was to study the uptake by the lymph nodes of radioactive colloids injected into lymphatic channels. Unsuccessful attempts were made to cause colloids injected subcutaneously to enter lymphatic vessels and localize in regional nodes. A method for intralymphatic injections was developed and studies were made on the localization of yttrium 90 colloids. One type gave a concentration in the most active node of 284 times that of the most active tissue; a second colloid gave 7900. (CA)

Zirconium

1040

Overstreet, Roy, et al. **RADIO ZIRCONIUM (Zr⁹⁰)** Univ. of Chicago Metallurgical Lab. [nd] 5p. (MDDC-1143-D)

A satisfactory method has been developed for the preparation in the pure state of Zr⁹⁰ as ZrOCl₂ without the presence of carrier. When administered by intraperitoneal and subcutaneous injection approximately 80% at two and six day

intervals appear to remain at the site of injection. No marked degree of specific localization was noted in any of the tissues examined. (ADD)

IV RADIATION SICKNESS

Syndrome in Humans—General

1041

RADIATION SICKNESS. Brit. Med. J. 4585, 909-10(1948).

The cause of radiation sickness can probably be found in changes in the metabolism of cells which are sensitive to radiation. There is no general agreement on what the changes are, however. Breakdown of blood cells and release of substances, release of histamine, achlorhydric stomach, and change in endocrine function are all mentioned as possible causes. The following remedies are listed as having given good results in the hands of various workers: histaminase, "benadryl," hydrochloric acid, sodium chloride, magnesium chloride, high carbohydrate diet, large amounts of fluid, vitamin C, vitamin B, amphetamine, pancreatin, and pyridoxin. (NSA)

1042

Bean, William B., Tom D. Spies, and R. W. Vilter. **A NOTE ON IRRADIATION SICKNESS.** Am. J. Med. Sci. 208, 46-54(1944).

Nausea, vomiting, headache, cramps, and diarrhea comprise the syndrome of irradiation sickness often complicating the course of therapeutic irradiation. From previous successful attempts at treatment of this illness with nicotinic acid, and with the discovery that the behavior of urinary pigments and the cohydrogenases I and II following irradiation over the spleen resembled that in severely ill pellagrins, it was planned to make a comprehensive examination of the effects of a standard dose of radiation. Normal well-fed subjects, those given a vitamin-deficient diet with and without some of the vitamins, pellagrins and those with poor diet had resulted in illness without specific deficiency stigmata were investigated. The irradiation factors were: 200 kv, a Thoraeus filter, 20 ma, 20 cm distance, 33 r/min. The dose was 400 r over the upper abdomen and spleen. Five normal subjects consuming a good diet or various vitamin B supplements showed no ill effects. Irradiation sickness occurred in varying degrees of severity in the rest of those studied, including the normal subjects who had subsisted on a vitamin B deficient diet for six weeks. In all cases there was a rough correlation between the severity of the reaction and the degree of vitamin depletion as gauged clinically. Once the illness was established, large doses of thiamine or nicotinic acid were of relatively little value. Irradiation sickness could be prevented or reduced in severity if the vitamin supplements were given for a few days before therapy was started. A patient with myomata and carcinoma of the uterus suffered from severe radiation sickness because of repeated doses of radiation. She was not given supplements of vitamins and subsequently pellagra and beriberi developed. It would appear from these studies that the optimum time for vitamin therapy is before and not after irradiation sickness develops. The fact that patients needing radiotherapy often have a deranged nutrition makes careful dietary and vitamin therapy logical, if only on empiric grounds. (R)

1043

Brown, W. M. Court. **THE VALUE OF PLATELET COUNTS IN RADIOTHERAPY.** Brit. J. Radiol. 21, 221-5(1948).

The effect of wide-field irradiation on the blood platelet level is described, and it is suggested that the blood platelet level is a more reliable indicator of the effect of radiation on the bone marrow than the total white cell count. By using the blood platelet level in this manner it is possible to avoid altogether the production of partial or permanent marrow failure. The use of the platelet level in the planning of treatment is described. The relationship between the development of petechial haemorrhages and radiation-induced thrombocytopenia is discussed. (NSA)

1044

Brues, Austin M. **RADIATION SICKNESS**, p. 778-81 of **MEDICAL PHYSICS, VOLUME 2**, Otto Glasser, ed. Chicago, Yearbook Publ., Inc. 1950. 1227p.

Synopsis of the clinical picture, basis of acute radiation sickness, effects of sublethal doses, atom bomb injury, diagnosis and therapy of radiation exposure. (M.F.)

1045

Bryan, Fred A. **PROBLEMS RELATIVE TO POSSIBLE PHYSIOLOGICAL EFFECTS CAUSED BY RADIATION**. *Indust. Med.* **17**, 367-71(1948).

Some of the problems occurring in the use and manufacture of radioactive materials are discussed from the viewpoints of possibility of exposure, the physiological effects on personnel resulting from exposure, and the maintenance of safe practices and good health in personnel. The greatest hazard of all can be the lack of knowledge concerning the physiological and toxicological effects of radioactive materials by the people using them. It is pointed out, however, that if all safety procedures are well worked out and diligently applied, use of atomic energy or its by-products is as safe as any other type of manufacturing. (NSA)

1046

Butler, Nell and James F. Crenshaw. **POSITIVE CEPHALIN-CHOLESTEROL FLOCCULATION TEST IN X-RAY WORKERS**. *Am. J. Med. Technol.* **14**, 255-8(1948).

Carefully controlled experiments are described, testing cephalin-cholesterol serum flocculation in 28 x-ray workers who had been exposed for periods ranging between 4 months and 20 years. The data are presented in a table which correlates exposure time, age, sex, gastrointestinal symptoms, jaundice, liver tenderness, liver enlargement, and splenic enlargement with the results of 24-hr cephalin and 48-hr cholesterol flocculation tests. The authors conclude that at least 82% show some positive tests and suggest that this may be a measure of slight changes in liver function due to roentgen irradiation. (NSA)

1047

Cronkite, Eugene P. **THE DIAGNOSIS OF IONIZING RADIATION INJURY BY PHYSICAL EXAMINATION AND CLINICAL LABORATORY PROCEDURES**. Naval Medical Research Inst., Bethesda. Apr. 8, 1948. 15p. (Report No. 8)

The symptomatology and diagnosis of acute and chronic radiation illness is discussed. Characteristic symptoms of the acute illness are nausea, vomiting, diarrhea, hemorrhagic manifestations, agranulocytosis followed by non-purulent necrotizing infections, and epilation. The blood picture is the most sensitive biologic index of exposure to ionizing radiation. Lymphocytopenia appears promptly after the single intense exposure. The symptomatology and blood picture of chronic exposure is protean. In order to evaluate the blood changes of chronic exposure, rigid control data must be established. The most significant blood change following chronic exposure is a depression of the mean leukocyte count of the exposed groups below the control groups. Dosimetry, the measurement of radiation

intensities, must remain the basis of all protective measures. (NSA)

1048

Hempelmann, L. H. **THE ACUTE RADIATION SYNDROME**. Los Alamos Scientific Lab. [nd] 6p. (AECU-379)

The acute radiation syndrome is an acute generalized illness lasting only a matter of weeks and terminating either in death or in complete recovery of the patient. The syndrome differs in this respect from the chronic form of radiation injury caused by repeated or prolonged exposure of the body to radiation. Factors determining the severity of the injury are the dose rate, the type of radiation, and variation in the response of the individual. The clinical response of patients suffering with acute radiation syndrome are discussed in four phases occurring in the following chronological order: the initial reaction (prostration, nausea, and vomiting); a period of relative well-being; the gradual development of fever (toxemia) associated with diarrhea, bleeding, infection, and loss of hair; death or prolonged convalescence. Besides the easily discernible bodily reactions there are a number of equally and perhaps more fundamental responses of persons with the acute radiation syndrome which can be detected only by use of laboratory techniques. These are: changes in the 100 cells and in the male reproductive organs, distortion of the normal function of some of the internal organs of the body and certain kinds of cellular damage that are responsible for tissue injury and for the clinical response of the individual. It is concluded that there is no practical way of preventing the death of cells or tissues fatally injured by radiation. However, if the body can be helped to survive the acute state of the illness, even the most radiosensitive tissues, such as the bone marrow, may regenerate to the point where they can carry on their normal functions. Means by which the body can be helped through the acute state of the illness are: blood transfusions to replace temporarily the red and white blood cells; penicillin to prevent infection; certain materials (toluidine blue) to diminish the clotting time of the blood, and maintenance of the water and salt content of the body. (TIS)

1049

Henshaw, Paul S. **FURTHER PROBLEMS IN X-RAY PROTECTION. II. IRRADIATION INJURY AND THE TOLERANCE DOSE**. *Radiology* **44**, 569-80(1945).

The problem of tolerance dose and X-ray protection has been reviewed. It has been recognized that various effects such as skin ulceration, sterility, anemia, and even death may result from exposure to ionizing radiation in amounts not greatly exceeding those which accumulate in comparatively short periods of time in various laboratories, shops and clinics; that for such effects there are threshold levels of exposure; that other changes, such as premature aging and neoplasm may appear long after exposure; that for still other effects, irradiation induced mutations, there appears to be no threshold level of exposure, and that there is roughly a factor of 100 difference between the accepted permissible dose of 0.1 r/day and cosmic and earth radiation to which everyone is continuously exposed. (BA)

1050

Nuttall, John R. **THE EFFECTS OF OCCUPATIONAL EXPOSURES TO X-RAYS AND RADIOACTIVE SUBSTANCES**. *Clin. J. (London)* **72**, 181-5(1943).

A review of the effects of x-rays and radioactive substances, with particular reference to effects upon reproductive system and upon the skin, to radiation tiredness, and to blood changes. (CA)

1051

Nuttal, John R., J. C. Mottram, S. Russ, and J. M. Vaughan. **DISCUSSION ON THE EFFECTS OF OCCUPATIONAL EXPOSURE TO X-RAYS AND RADIOACTIVE SUBSTANCES.** *Proc. Roy. Soc. Med.* **35**, 717-22(1942).

A review of the dangers confronting workers in the field of X-ray and radioactive substances and the means of combating them; mutations produced by radiation in relation to mankind; harmful effects of radioactive substances; effect of occupational exposure to X-rays and radioactive substances upon haemopoiesis. (S.V.S.)

1052

Painter, E. E. and A. M. Brues. **THE RADIATION SYNDROME.** *New Engl. J. Med.* **240**, 871-6(1949).

A discussion is presented on the theoretical aspects and the clinical manifestations of the radiation syndrome. The initial shock, the acute, the subacute, and the chronic periods are described. The therapy for radiation damage is noted as not being adequate at the present time. It is observed that no single clinical reaction is peculiarly specific for the radiation damage, and many of the delayed effects of radiation can be duplicated by various toxic materials. In conclusion, it is stated, that damage to the radiosensitive cells will explain a great part of the picture, but much further understanding of the syndrome is required in the interest of prevention and therapy. (NSA)

1053

WHAT EVERY MEDICAL OFFICER SHOULD KNOW ABOUT THE ATOMIC BOMBS. PART IV. EVALUATION OF THE FIVE ATOMIC EXPLOSIONS. *Bull. U. S. Army Med. Dept.* **8**, 350(1948).

Lethal effects will be produced by air-burst atomic bombs over an area of 2 square miles and measurable effect over an area of 7 square miles as a result of the gamma radiation emitted at the time of detonation. There is little importance in the residual radioactivity except in the area close to the center of a low-altitude explosion. In an underwater detonation, radioactive fission products and unfissioned material will be spread by the cloud and base surge over a large area. The gamma radiation from these materials will be lethal to exposed personnel more than two miles downwind, and serious contamination will result at much greater distances. A serious hazard will be provided by this detonation for an indefinite period. At the time of the detonation prompt evasive action will permit the reduction of casualties. The pathologic effects of radiation are presented by outlining the early and late changes in tissue cells, organ systems, total body irradiation, and internal radiation by radioactive materials introduced into the body either accidentally or therapeutically. The sensitivity of various body tissues has been established and has been expressed largely as the relation of one tissue to another. (NSA)

1054

WHAT EVERY MEDICAL OFFICER SHOULD KNOW ABOUT THE ATOMIC BOMB. PART V. FUNDAMENTALS OF RADIATION PATHOLOGY. *Bull. U. S. Army Med. Dept.* **8**, 357-62(1948).

The pathologic effects of radiation are presented by outlining the early and late changes in tissue cells, organ systems, total body irradiation and internal radiation of radioactive materials introduced into the body either accidentally or therapeutically. A table is given which shows the relative radiosensitivities of various body tissues listed in decreasing order. (NSA)

1055

WHAT EVERY MEDICAL OFFICER SHOULD KNOW ABOUT THE ATOMIC BOMB. PART VI. PATHOLOGIC

ANATOMY OF RADIATION EFFECTS OF ATOMIC EXPLOSION. *Bull. U. S. Army Med. Dept.* **8**, 422-8(1948).

The radiation effects of an atomic explosion on the skin, pituitary, adrenals, heart, lungs, genitourinary system, gastrointestinal tract, spleen, lymph nodes, bone marrow and the reticulo-endothelial system are reviewed. The case history of a man at a distance of 0.7 kilometers from the explosion center is given. (NSA)

1056

WHAT EVERY MEDICAL OFFICER SHOULD KNOW ABOUT THE ATOMIC BOMB. PART VII. DETECTION OF OVEREXPOSURE TO IONIZING RADIATION. *Bull. U. S. Army Med. Dept.* **8**, 428-31(1948).

The effects of overexposure may be acute or chronic. The exposures may result from any type of radiation applied externally or internally. The clinical picture will depend on the amount, rate of delivery and depth of the dose. The signs and symptoms such as thermal burns, diarrhea, nausea, vomiting, headache, anuria, purpura, blood changes, fingernail brittleness, pigmentation, etc., are discussed. A procedure to be followed in studying a person suspected of being overexposed is given. (NSA)

1057

Warren, Shields. **THE PATHOGENESIS OF IRRADIATION SICKNESS.** *Chicago Med. Soc. Bull.* **51**, 957-9 (1949).

The syndrome of radiation sickness is discussed as it applies to mass radiation by atomic weapons. The cells of the body which have a short life-span are more effected by the radiation than those with long life-spans, and rapidly dividing cells, or those in mitosis, are more affected than cells in the resting phase. A dose of 400 r is usually fatal to about $\frac{1}{2}$ of the human population present. There is great variability in the sensitivity of different cells and organisms in general. It is believed that the heaviest types of doses cause disruption in the enzyme systems and vital functions of most of the body cells and death occurs promptly without much evidence of morphological change. Slides are presented which indicate specific and individual reactions to the radiation doses. These include multiple leukopenic abscesses and cellulitis of the neck. The different stages of development of the symptoms are pointed out. If the radiation dose is more than 500-600 r, the chances of survival are small. Future problems connected with mass effective medical care of radiation victims are discussed. Prevention rather than cure is suggested as the most promising method of handling the radiation sickness problem. Lecture with slides. (NSA)

1058

Warren, Shields and John Z. Bowers. **THE ACUTE RADIATION SYNDROME IN MAN.** *Ann. Internal Med.* **32**, 207-16(1950).

The pathogenesis, histopathology, symptomatology, clinical course, laboratory findings, complications, sequelae, therapy and prognosis of the acute radiation syndrome in man are discussed. Tables are included which demonstrate the variation in the sensitivity of the tissues of the human body to ionizing radiations and variations in sensitivity between species; such concepts of the mechanism of the effects of radiation on the body as the cell hydration theory and the target theory are outlined. Cellular, stromal and vascular effects of the radiation are noted, and the prominent manifestations of the syndrome (asthenia, diarrhea, nausea and vomiting, mucosal ulcerations, epilation, fever and tachycardia are correlated with three types of radiation illness seen: the fulminating form (most severe), the hemorrhagic form, and the pancytopenic form; hematological responses and bacterial infections are

discussed along with such sequelae as possible mutation effects and neoplasia. It is stated that the treatment of individuals exposed to damaging amounts of ionizing radiation is at this data supportive and nonspecific, there being no known specific agent which will ameliorate the injury. Such agents as folic acid, toluidine blue, rutin, protamine, adrenal cortical extract and parenteral therapy (for the correction of aberrations in blood electrolytes) are mentioned. Patients who develop the fulminating course of the radiation syndrome are concluded to have lethal amounts of radiation. However, those patients exhibiting the hemorrhagic and pancytopenic forms, with consequent delayed radiation effects, are said to have received either lethal amounts or sublethal amounts and a certain proportion can be expected to survive. (NSA)

1059

Wolf, B. S. MEDICAL ASPECTS OF RADIATION SAFETY. *Nucleonics* 3, No. 4, 25-9(1949).

This brief discussion emphasizes what the author calls psychomatic aspects. He takes up the following five items in connection with radiation which seem most worrisome to people and attempts to place these special hazards in their proper perspective. They are (1) the inability to detect exposure through the five senses, (2) the penetrating power of radiation, (3) the delayed effects of overexposure, (4) the sterilizing effect, and (5) the genetic effect. (NSA)

Syndrome in Humans—Hiroshima and
Nagasaki

1060

CLINICAL AND PATHOLOGICAL OBSERVATIONS ON THE EFFECTS OF THE ATOMIC BOMB. Atomic Bomb Investigating Groups, Manhattan District. [nd] 32p. (NP-1202)

Part I. Skin Burns. Nine cases are discussed demonstrating the pathology of skin burns caused by the atomic bomb explosion at Nagasaki. The nine victims were Japanese prisoners of war who were interned in "Camp No. 14" which was just outside the area of extreme atomic bomb destruction; the burns were thus caused by the explosion of a bomb well over a mile away.

Part II. Atomic Bomb Disease. Among the survivors of the atomic bombing of Nagasaki there developed a disease, often fatal, which was apparently independent of mechanical or thermal injuries. A clinical and pathological study of the disease showed it to be entirely comparable in all respects to the syndrome caused by a large generalized dose of gamma radiation. The mortality of the disease would have been much lower provided that adequate medical care had been given. (NSA)

1061

Beck, J. S. P. and W. A. Meissner. RADIATION EFFECTS OF THE ATOMIC BOMB AMONG THE NATIVES OF NAGASAKI, KYUSHU. *Am. J. Clin. Pathol.* 16, 586-92(1946).

Some observations are reported on the radiation effects of atomic bombing among the inhabitants of Nagasaki, Kyushu, during the sixth and seventh weeks after the bombing. Among 20 patients whose blood or bone marrow was studied, there was anemia, neutropenia, and thrombocytopenia, which were due to depression of the marrow. In 7 postmortem examinations there was confirmatory evidence of damage to the bone marrow. Evidence of recovery of bone marrow was found both clinically and post mortem. Histologic evidence of lipid depletion of cells of the adrenal cortex was found. Aspermatogenesis was noted in some instances. The mortality rate of "atom bomb disease" could have been lowered by adequate medical care. (BA)

1062

Benkwith, K. B. RETINAL HAEMORRHAGE AS SEEN IN AN ATOMIC-BOMB CASUALTY. *Am. J. Ophthalmol.* 29, 799-800(1946).

A fourteen-year-old Japanese girl who at the time of the atomic-bomb explosion at Nagasaki, Japan, was about one mile from the accepted hypocentre of the explosion has suffered from malaise, headache, fever and nausea ever since. Early in September she was admitted to the Ophthalmic Institute of the Kyushu Imperial University at Fukuoka suffering from a disturbance of vision. On examination massive pre-retinal haemorrhages were found and, in addition, superficial retinal haemorrhages and small "fluffy" spots of exudation close to the disc and to the retinal vessels. Petechiae in the skin, bleeding from the gums, and mild epilation were also noted by the patient. Although little treatment was attempted and she remained an ambulatory patient, the ill effects of the radioactivity subsided slowly, the vitreous remained clear, and by December 1945 the only pathological changes visible in the eye were a number of white discolored areas about the posterior pole. Initial laboratory tests showed the presence of a leucopenia with a W.B.C. of 2,200; and anemia with an R.B.C. of 2,200,000; a decrease in the number of blood platelets; and a prolongation of the bleeding time. There never was any evidence of blast wounds. (EM)

1063

Bernier, J. L. THE EFFECTS OF ATOMIC RADIATION ON THE ORAL AND PHARYNGEAL MUCOSA. *J. Am. Dental Assoc.* 39, 647-57(1949).

This report is concerned chiefly with the changes observed in patients who received both lethal and sublethal doses of γ ionizing radiation during the atomic explosions at Hiroshima and Nagasaki. The changes in the blood and the histopathologic changes are described in detail for the three significant stages (lethal irradiation, severe but sublethal irradiation, and mild irradiation). A very early depletion of the hematopoietic system occurred with resulting anemia, agranulocytosis (shown by pharyngeal angina, gingivitis and severe secondary infections) and thrombocytopenia (manifested clinically in a few weeks by the purpuric state); epilation became evident in about 10 days. Profound and early changes of both squamous and glandular types were noted in the epithelium; lesions appeared in the oral cavity and the gastrointestinal tract. It is concluded that further studies are necessary. (NSA)

1064

Bowers, John Z. ACUTE RADIATION SYNDROME. *J. Am. Med. Assoc.* 145, 63-5(1951).

The pertinent information that has been presented may be summarized as follows: The acute radiation syndrome is caused by sudden exposure to the penetrating radiations liberated by the atomic bomb. The resulting changes depend primarily on the inherent sensitivity of the exposed tissues and the type of radiation and are attributable to damage to the blood and blood-forming organs, the blood vessel endothelium and the bowel. These particular tissues all show a tendency toward ultimate regeneration, and it is on this fact that present therapeutic programs are based. The primary manifestations are hemorrhagic diathesis, nausea, vomiting and diarrhea and depression of the formed elements of the body. Treatment is at this date supportive in nature. (auth)

1065

Cogan, D. G., S. F. Martin, and S. J. Kimura. ATOMIC BOMB CATARACTS. *Science* 110, 654-5(1949).

Ten cases of cataract which seem to have been caused by exposure to the atom bomb blasts at Hiroshima and Naga-

saki are described. Of the 10 subjects, 7 were males and 3 females, ages at time of exposure varied from 13 to 55 years, all were within 550-950 m of the hypocenter of the explosion, all were in the open or were shielded by wooden structures at time of explosion, all had epilation of the head after a latent period 1-4 weeks with complete baldness lasting 3-7 months, and all had normal vision at time of explosion. The only ocular complaint of the subjects was failing vision, latent period varying from 6-30 months. The cataracts consisted of opacities in the axial zone of the posterior lenticular capsules over an area of 2-4 sq. mm, with occasional punctate dots farther toward the periphery; the findings were approx. symmetrical in the 2 eyes. Detailed nature of the cataracts is described. (BA)

1066

DeCoursey, E. HUMAN PATHOLOGIC ANATOMY OF IONIZING RADIATION EFFECTS OF THE ATOMIC BOMB EXPLOSIONS. *Military Surgeon* 102, 427-32(1948).

The effect of ionizing radiation on human anatomic structures was studied by means of necropsy findings conducted in Nagasaki and Hiroshima. Investigations were made on those dying during the early period (first two weeks), intermediate period (3-6 weeks) and late period (6 weeks - 4 months). The outstanding symptoms were nausea and vomiting on the day of the bombing, followed by fever, leukopenia, diarrhea, and after two weeks epilation, purpura and oropharyngeal lesions. The spleen showed gross change as early as the fourth day and there was almost total disappearance of blood forming cells in the bone marrow. All parts of the body in which hemorrhage is possible were affected. The gastro intestinal tract was among the first locations to present gross lesions. The tests showed prominent microscopic changes, all dying males having almost all their sex cells destroyed. The ovaries, except for hemorrhages, presented no distinct change and very little microscopically. About the surest macroscopic evidence of ionizing radiation and the most prominent external effect was the epilation of the scalp. (NSA)

1067

Enloe, C. F. SOME EFFECTS OF RADIANT ENERGIES ON THE EYE. *Sight Saving Rev.* 18, 77-83(1948).

The author reviews the various types of radiant energy, and reports in some detail present-day knowledge concerning the energy of the atomic nucleus and its relation to the eye. He notes that thus far the effects of radiation have not presented a great problem in the field of occupational ophthalmology and that the small amounts of radioactive material which might be found in factories in peacetime produce little direct effect upon the eye. It is stated that to date no primary damage to the ocular structures has been observed that could be interpreted as a direct result of atomic radiation. The lesions occurring from exposure to the flash during bomb detonation were found to be identical with those resulting from overexposure to infrared. The retinal changes and the four types of hemorrhage (flame, petechial, "Roth"-type and vitreous) observed in people subjected to atomic bombing are felt to be directly related to the deficiency in the blood elements and in no way directly related to the action of radiation on the eye. These lesions disappear after the blood returns to normal, and thus far there has been no report of permanent residual damage from the retinal lesions. (NSA)

1068

Howland, J. W. and S. L. Warren. THE EFFECTS OF IRRADIATION FROM THE ATOMIC BOMB ON THE JAPANESE. *Cancer Research* 6, 449(1946). (MDDC-1301)

A brief description is given of the medical effects following the atomic explosions at Hiroshima and Nagasaki. A discussion of the immediate clinical human pathology resulting from blast and burns is included. The effects of acute whole body irradiation on the human are considered in detail as well as pertinent observations on living individuals observed one year later. The comparative clinical and pathological effects of whole body irradiation on animals are given briefly. The pathological findings on tissues sensitive to irradiation namely lymphatic system, bone marrow, gastrointestinal canal and gonads are discussed. (ADD)

1069

Keller, Paul D. A CLINICAL SYNDROME FOLLOWING EXPOSURE TO ATOMIC BOMB EXPLOSIONS. *J. Am. Med. Assoc.* 131, No. 6, 504-6(1946).

Twenty-one patients who developed a delayed illness following their exposure to atomic bomb explosions in Japan, 20 of whom were indoors at the time, were affected similarly to excessive irradiation of the body with x-rays. There was destruction or suppression of the hemopoietic system, disturbed liver function, and increased erythrocyte sedimentation rate; evidence of extensive tissue destruction within the body. (BA)

1070

Kikuchi, T., et al. HEMATOLOGICAL OBSERVATIONS IN THE ATOMIC BOMB SUFFERERS IN HIROSHIMA CITY ONE YEAR AFTER THE BOMBING (SECOND REPORT). *Kyoto Imperial Univ., Japan.* [nd] 11p. (NP-305(J-6))

Hematological observations were made of atomic bomb sufferers (510 cases) one year after the bombing and of healthy Japanese (173 cases) as controls in Hiroshima city with results as follows: Red blood cell counts are less than 4 million in 71.7% of the sufferers and in 61.8% of the controls. Color index over 1.21 is found in 50.6% of the sufferers and in 8.8% of the controls. In white blood cell count, there is no case under 3,000 in 1 cmm of blood in the controls and the counts under 4,000 are found in 14.2% of the sufferers (counts under 3,000 in 2.1%) and in 3.5% of the controls. In differential count of leucocytes (eosinophils, neutrophils, lymphocytes, monocytes, and plasma cells) and Sugiyama's mean nuclear lobes of neutrophil leucocytes, there are no remarkable differences in both cases, but the curve of neutrophil leucocyte count in the sufferers shifts to lower percentage than that of controls and in the curve of lymphocyte count, this relation is contrary. Blood platelets count is under 90,000 in 28.9% of the sufferers and in 14.9% of the controls. Bleeding time is almost normal in both cases, but the cases with bleeding time over five minutes are found in 4.9% of the sufferers and in 5.2% of the controls. Tabular data show findings. (ACD)

1071

Kikuchi, T., G. Wakisaka, T. Yoda, S. Note, H. Yamada, and K. Miki. REPORT ON HEMATOLOGICAL OBSERVATIONS IN THE ATOMIC BOMB SUFFERERS IN NAGASAKI CITY ONE YEAR AND FOUR MONTHS AFTER THE BOMBING. *Kyoto Imperial Univ. Japan.* [nd] 12p. (NP-306(J-7))

Conclusions and tables of results of hematological examinations of 172 atomic bomb sufferers and 45 controls (healthy citizens who were not in Nagasaki city at the time of the bombing) are presented. It is concluded that the atomic bomb sufferers in Nagasaki city have returned to normal in the majority of cases, but there are still a few cases with anemia, leucopenia, thrombopenia and prolongation of bleeding time. (ACR)

1072

Larkin, John C. DISTRIBUTION OF RADIATION IN THE ATOMIC BOMBING OF NAGASAKI. *Am. J. Roentgenol. Radium Therapy* **55**, 525-32(1946).

This study is based on the clinical records of 95 patients in three hospitals in Nagasaki, who were still hospitalized six weeks after the bombing of the city. Some of the energy released was in the form of radiation, the remainder and greater part of the energy being released as heat. In order to facilitate this study the patients were grouped according to the zone of the city they happened to be in at the time of the explosion. There were few survivors in zone 1 (within 1,000 meters of the center of the explosion). Zone 2 (1,000 to 1,250 meters) was the zone where survivors showed maximum irradiation effects. Those in zone 3 (1,250 to 1,500 meters) showed slight irradiation effects. In areas beyond 1,250 meters, severe superficial burns but practically no irradiation effect were found. Protection by walls or roofs of buildings played a part in reducing the irradiation effects. There were nine people in concrete buildings in zone 2, four of whom had only mild evidence of roentgen sickness and no sign of burns. Twelve people in this zone, with less protection, suffered severe roentgen sickness—profuse vomiting, hematemesis, melena, and diarrhea. In zone 3 symptoms were much less severe and in the outer zone they were very slight. In no case was a typical erythema attributable to gamma radiation reported. Superficial radiation effects (i.e., ultraviolet, visible light, and infra-red) were by far the most widespread reactions, being found in all zones and as far as 2,500 meters from the radiation source. People in zones 3, 4, and 5 felt no heat but noticed burns several seconds after the explosion. Almost any particle of clothing seemed to give them adequate protection. A single layer of clothing might give partial protection, but several layers would not be penetrated. The burned areas were always facing the radiation source. These effects were not due to gamma radiation. In all cases healing was rapid and complete. Seventy-six per cent of persons in zone 2 and 22% of those in zone 3 lost part of their hair. Ten out of 11 women in zone 2 whose menses had been regular and 9 out of 12 in zone 3 had amenorrhea after the bombing. In some instances, this may have been due to psychological factors. Maximum depression of the white blood count was reached near the 28th day. The average count of 11 cases in zone 2 was 980. In zone 3 the average was 3,750. There was a normal count in a patient in zone 2 who was protected by a concrete roof. Patients who had combined irradiation effects and superficial burns died much earlier than those with pure irradiation effects. In the latter group the greatest number died at the end of the seventh week, demonstrating the delayed reaction to irradiation alone. (R)

1073

Leroy, G. THE MEDICAL SEQUELAE OF THE ATOMIC BOMB EXPLOSION. *J. Am. Med. Assoc.* **134**, 1143-8 (1947).

This paper concerns the investigations by the Army and Navy medical missions at Hiroshima and Nagasaki. The data was compiled before July 1946 as part of a report submitted to the Surgeon General of the U. S. Army. Two major subjects are considered: (1) the tremendous toll of casualties and (2) the syndrome of injury due to large amounts of gamma radiation. Effects of the blasts on bone marrow, blood cells, lymphatic organs, epilation, gastrointestinal disturbances, skin wounds and burns, the spleen, genital tissue, mucous membranes, and mortality are discussed in relation to ages, clothing, positions within buildings, time of maximum effects, distance from the explosion, attempted therapy, etc. A note by Dr. Verne R. Mason at the end of the paper emphasized that the study is not com-

plete, but that he expects to find correspondence between development of leukopenia in the patient, with the known life span of the white blood cell and between the time of death from aplastic anemia with the known life of the red blood cells. (E. G.)

1074

LeRoy, George V. HEMATOLOGY OF ATOMIC BOMB CASUALTIES. *Arch. Internal Med.* **86**, 691-710(1950).

Data from the detailed hematological studies made on Japanese injured by the atomic-bomb explosions over Hiroshima and Nagasaki indicate that it is possible to describe the syndrome of radiation injury in man in terms of typical clinical symptoms and a typical blood picture. The time trend of the syndrome is important, and the characteristic elements in the diagnosis become apparent at various times after exposure. In general, the severity of the symptoms paralleled the severity of the leukopenia. Likewise, the important symptoms became evident at about the time the lowest leukocyte count was observed. The changes in the thrombocytes paralleled those in the leukocytes. The onset and severity of a hemorrhagic tendency followed closely the variations in the thrombocyte count. The alteration in the red blood cells was less consistent and less useful in diagnosis or prognosis than was the time trend of the leukopenia. From the standpoint of prognosis, the Japanese physicians stated that patients with less than 500 leukocytes per mm³ were least likely to recover. The data presented here neither support nor deny this clinical observation. In the event of an emergency, it would be perfectly justifiable to perform only leukocyte counts and determinations of hemoglobin, hematocrit, and protein by the copper sulfate method. This would be an economical procedure and would provide the type of information required to evaluate cases and to aid in control of therapy. (NSA)

1075

Leucutia, T. RADIANT ENERGY INJURIES. *Am. J. Roentgenol. Radium Therapy* **59**, 890-3(1948).

In this editorial some of the medical aspects of the atomic bombing of Hiroshima and Nagasaki are considered. Most of the biological damage came from the heat and the radiations, above all from the gamma rays. The author reviews the various types of injuries sustained in the five zones arbitrarily determined by the distance of various sections from the bomb target. The effects of some of the injuries as they appeared two years after the bombing are mentioned briefly. (NSA)

1076

Liebow, Averill A., Shields Warren, and Elbert DeCoursey. PATHOLOGY OF ATOMIC BOMB CASUALTIES. *Am. J. Pathol.* **25**, 853-1028(1949).

A description is presented of the effects of the atomic explosions at Nagasaki and Hiroshima; the human injuries were mechanical, thermal, and ionizing in nature. Direct blast injuries analogous to those inflicted by high explosives were almost unknown among the survivors; however, damage produced by shattered glass and the like accounted for a high toll of injury. The burns among the survivors were mostly of the flash type, the result of an extremely large quantity of radiant heat acting for an extremely short period of time, and were characterized by sharply outlined areas; the effects of exposure extended up to 4,000 yards from the bomb. Depigmentation occurred in an area close to the bomb, but intense pigmentation occurred at larger distances from the explosion; the depigmentation occurred without destruction of the squamous epithelial skin surface, and was probably the result of the action of certain specific wavelengths. The radiation effects consisted of early symptoms of nausea and vomiting followed by diarrhea and fever, and developing into complications such as aplastic anemia,

leukopenia, and secondary infections such as pneumonitis or ulcerative enteritis. At necropsy, changes were found in the skin, gastrointestinal tract, gonads, and hematopoietic tissues. The specific radiation effects on these areas are described in detail. The remarkable resistance of the reticulum cell and the tendency of the bone marrow ultimately to regenerate are emphasized, and it is hoped that these phenomena indicate that successful defense measures against the radiations will be devised. Further studies are still in progress to investigate the relationship between life span and irradiation, the incidence of neoplasia among survivors, and the radiation effects on growth, sterility, and genetic mutation. (NSA)

1077

Nakaidzumi, Masanori. **THE RADIOACTIVITY OF THE ATOMIC BOMB FROM THE MEDICAL POINT OF VIEW.** Tokyo Imperial Univ. [nd] 10p. (NP-302)

The radiations which hit the human body were the following: neutrons and gamma rays in the air (including the primary neutrons and gamma rays from atomic bomb and gamma rays produced by the reaction between neutrons and nitrogen nuclei in the air), the radioactivities of the tissues of the human body and the soil resulting from the bombardment of neutrons (β and γ rays), and the fission fragments which fell on the ground (β and γ rays), etc. These all acted together, and the significance of each is complicated. Moreover, the scattering of γ rays by the buildings differed very much according to the type of building and its location. So the total dose received by each person may be different even when at the same distance from the explosion center or in the same building. The radiation intensity does not always decrease according to the inverse square law. Therefore, the factors affecting the total dose of radiation on the human body are very complicated and not easily calculated. In the estimation of total dose by clinical symptoms, epilation is a rather accurate indication. However, the effect of protection by shelter, etc., should be considered and its effect on the appearance of symptoms should be decided statistically. From the incidence of epilation the dose which was given to the human body can be estimated. Assuming the head epilation dose to have been 1,000 r, with 2 km, where 90% of all patients with epilation were, it is estimated that the dose directly beneath the explosion center was from 10,000 to 15,000 r. This also assumes explosion center to be 550 meters above the ground and the radiant rays to decay by the inverse square law. Protection from the radiant rays of the atomic bomb afforded by caves, concrete walls, and building structures is discussed. (ACD)

1078

Novy, Frederick George, Jr. **SURVIVORS OF BOMBING OF HIROSHIMA THREE YEARS LATER.** Arch. Dermatol. and Syphilol. 61, 379-83(1950).

The results of a survey on the skin condition of survivors of the atomic explosion at Hiroshima three years after exposure are presented. Careful examination was made for any ionizing radiation effect such as telangiectasia, atrophy, or hyperpigmentation of the skin, but in none of the patients could any of the burns be interpreted as due to radiation injury. It is concluded that there is a remote possibility that one or two instances of chronic cutaneous radiation injury may have occurred at Hiroshima, but it is not probable. (NSA)

1079

Oughterson, Ashley W., George V. LeRoy, Averill A. Liebow, E. Cuyler Hammond, Henry L. Barnett, Jack D. Rosenbaum, and B. Aubrey Schneider. **MEDICAL EFFECTS OF ATOMIC BOMBS; THE REPORT OF THE JOINT COMMISSION FOR THE INVESTIGATION OF**

THE EFFECTS OF THE ATOMIC BOMB IN JAPAN; Volume 1. Army Inst. of Pathology. Apr. 19, 1951. 246p. (NP-3036; AM-2837(Vol. I))

The first of five unclassified volumes (NP-3036 through NP-3040) first reproduces the original orders establishing the Joint Commission, lists the personnel, and gives original data on the mean and differential leukocyte counts of residents of Nagasaki not directly exposed to the atomic explosion but perhaps exposed to residual radioactivity. Copiously illustrated descriptions of the terrain, buildings, populace, and of the raids of Aug. 6 and 9, 1945, and their immediate effects on Hiroshima and Nagasaki are followed by eyewitness accounts of the atomic bomb explosions and of their consequences. 64 figures. 2 maps. (NSA)

1080

Oughterson, Ashley W., George V. LeRoy, Averill A. Liebow, E. Cuyler Hammond, Henry L. Barnett, Jack D. Rosenbaum, and B. Aubrey Schneider. **MEDICAL EFFECTS OF ATOMIC BOMBS; THE REPORT OF THE JOINT COMMISSION FOR THE INVESTIGATION OF THE EFFECTS OF THE ATOMIC BOMB IN JAPAN; VOLUME II.** Army Inst. of Pathology. [nd] 345p. (NP-3037; AM-2837(vol. II))

Clinical records and specimens taken by Japanese physicians following the raids on Hiroshima and Nagasaki and later collected by the Joint Commission are reviewed, and résumés of original Japanese reports are given. Clinical observations on the etiologic factors and consequences of injury by blast, heat, and ionizing radiation are reported in detail. Photographs of damage to structures, "shadow" effects, and selective destruction of clothing, etc., by heat are shown in addition to those of clinical interest. 129 figures. (NSA)

1081

Oughterson, Ashley W., George V. LeRoy, Averill A. Liebow, E. Cuyler Hammond, Henry L. Barnett, Jack D. Rosenbaum, B. Aubrey Schneider. **MEDICAL EFFECTS OF ATOMIC BOMBS; THE REPORT OF THE JOINT COMMISSION FOR THE INVESTIGATION OF THE EFFECTS OF THE ATOMIC BOMB IN JAPAN; VOLUME III.** Army Inst. of Pathology. [nd] 212p. (NP-3038; AM-2837(vol. III))

The studies made by Japanese sources and by the Joint Commission on the changes in peripheral blood, blood-clotting mechanism, and bone marrow of patients with radiation injury resulting from the atomic bomb explosions over Hiroshima and Nagasaki are reported in detail. (NSA)

1082

Oughterson, Ashley W., George V. LeRoy, Averill A. Liebow, E. Cuyler Hammond, Henry L. Barnett, Jack D. Rosenbaum, and B. Aubrey Schneider. **MEDICAL EFFECTS OF ATOMIC BOMBS; THE REPORT OF THE JOINT COMMISSION FOR THE INVESTIGATION OF THE EFFECTS OF THE ATOMIC BOMB IN JAPAN; VOLUME IV.** Army Inst. of Pathology. [nd] 324p. (NP-3039; AM-2837(vol. IV))

The present volume is devoted to the pathology observed in material obtained at autopsy of victims of the atomic bomb explosions over Hiroshima and Nagasaki. Particular attention is paid to the effects of ionizing radiation. Systematic organ-by-organ descriptions are given, with a statistical account of the material available and of the changes observed. 193 figures. (NSA)

1083

Oughterson, Ashley W., George V. LeRoy, Averill A. Liebow, E. Cuyler Hammond, Henry L. Barnett, Jack D. Rosenbaum, and B. Aubrey Schneider. **MEDICAL EFFECTS OF ATOMIC BOMBS; THE REPORT OF THE**

JOINT COMMISSION FOR THE INVESTIGATION OF THE EFFECTS OF THE ATOMIC BOMB IN JAPAN; VOLUME V. Army Inst. of Pathology. [nd] 343p. (NP-3040; AM-2837(vol. V))

A detailed statistical analysis is presented of the medical history of 6882 individuals in Hiroshima and 6621 in Nagasaki known to be alive 20 days after the atomic bombings. Burns, mechanical injuries, blast effects, radiation symptoms, hematology, and deaths are related to distance, shielding, age, sex, etc. (NSA)

1084

Pearse, Herman E. and J. Thomas Payne. **MECHANICAL AND THERMAL INJURY FROM THE ATOMIC BOMB.** New Engl. J. Med. **241**, 647-53(1949).

A description is given of the incidence and varieties of traumatic and thermal injury from the atomic bomb and the results of the clinical production of flash burns. The components of the atomic bomb flash were: a temperature of over 4,000°C; transmission largely by radiation; a spectrum high in ultraviolet, infrared and in visible light and brilliancy; and, a duration of less than a second. Shadow burning, the production of keloids, contracture and ulceration are described and correlated with the distance from the radiation source, the degree of protection afforded by clothing and other shelter, and the incidence of radiation sickness and traumatic injuries. The flash produced by magnesium was used to produce a flash burn similar in characteristics to the atomic radiation burns; extremely high intensity of radiation, short duration (0.1 sec) and other criteria were satisfied. It was noted that clinically there was an abrupt and diagrammatic demarcation between the burned and normal skin; the normal, basophilic cells changed on a straight line into acidophilic, burned cells. In the dermis the demarcation was at the burn border in the crypts and hair follicles. The method of healing of this type of burn was unusual; the burn consisted of a coagulative, fixed type of necrosis in the epidermis and dermis, with eschar formation and subsequent sequestration, rather than the organization seen in the noncoagulative, necrotic tissue of the moderate temperature burn. With a flash burn of moderate severity the epithelium grew out from normal borders and hair follicles and the healing was rapid; with widespread radiation injury and destruction of the epithelium in the crypts and hair follicles, delayed repair due to the lack of epithelial islands occurred. Prevention of infection and adequate shelter and diet are suggested as methods of treating these burns. (NSA)

1085

Price, F. L. **EFFECTS RESULTING FROM ATOMIC BOMB EXPLOSION.** J. Florida Med. Assoc. **34**, 651-3 (1946).

The atomic bomb explosions in Hiroshima and Nagasaki created a blast wave that lasted almost a second in contrast to the few milliseconds of pressure resulting from an ordinary explosion. No estimate of the number of deaths or symptoms caused by blast pressure could be made, but the pressure developed on the ground under the explosion was not sufficient to kill more than those people who were very near the center of damage. In Hiroshima 60% and in Nagasaki 95% of immediate deaths were caused by burns, and 90% of the burns suffered by patients who reached first aid stations were second degree. The radiations which caused injuries were primarily those created within the first second after the explosion; and it is estimated that gamma rays and neutrons caused about 7% of the deaths. The irradiation effects of nausea and vomiting, fever, diarrhea, purpura, ulcerations of the mucous membrane, and leukopenia varied in intensity according to the severity of irradiation. Death followed within 10 days of severe in-

jury, and mortality was 50% for those receiving moderate injury. There was almost complete disappearance of all cells of the myelopoietic and erythropoietic series. Men who had received enough radiation to produce symptoms did not have spermatozoa and most of the spermatogenic tissue was replaced by proliferating cells of Sertoli. The female reproductive system was affected to a much smaller extent. In Nagasaki the estimated radiation intensity at a distance of 1,250 meters from the point of explosion was 473 r. It is believed that the mortality rate for all types of injuries could have been reduced if electrolyte solutions, plasma, whole blood, and penicillin had been available. (NSA)

1086

Sassa, Kanshi. **CLINIC OF THE ATOMIC BOMB RADIATION SICKNESS.** Tokyo Imperial Univ. [nd] 27p. (NP-303)

This is a summarized report on the clinical observations of radiation sickness caused by the atomic bomb explosions in Hiroshima and Nagasaki. Over 10,000 patients were examined. Mechanically caused or heat injuries such as wounds and burns are not included. The etiological factors considered are age, sex, distance from center of explosion, and shelter. General symptoms such as fever and fatigue are described. Observations on the digestive, respiratory, and sex organs, the nervous system, the oral cavity, eyes, skin, blood and urine of victims of radiation sickness are discussed. (NSA)

1087

Schlaegel, T. G., Jr. **OCULAR HISTOPATHOLOGY OF SOME NAGASAKI ATOMIC BOMB CASUALTIES.** Am. J. Ophthalmol. **30**, 127-35(1947).

Sections of eyes of patients who had died from the effects of the Nagasaki A-bomb irradiation one month after the bombing were studied. Changes seen in the cornea and lens are apparently due to the direct effects of radiation, while the findings in the rest of the eye appear to be secondary to the systemic condition. The cornea and lens may have been damaged by direct irradiation. Some of the corneas are found to be denuded with evidence of epithelial regeneration. That lenses may be in the early stages of developing radiation cataracts is evinced by several vacuoles in the superficial cortex and a thickening of the posterior capsule. The following changes were due apparently to the patient's systemic condition: (1) serous exudation into and from the ciliary body; (2) invasion of the eye by bacilli; (3) septic choroiditis; (4) nodular cellular infiltration of the retina; (5) fibrin nets on the surface of the retina; (6) and, in one case, a striking distention of all the ocular vessels by white cells, most of which were mononuclears. In general, the damage to the eyes was less than that to other organs. Conjunctivitis and superficial keratitis were found in many patients, but the effects disappeared in about a month. Episcleritis in conjunction with corneal infiltration was found in some cases. (S.V.S.)

1088

Takahara, T., Akiko Mori, and Shigeko Natsumoto. **CONCERNING OTORHINOLARYNGOLOGICAL OBSERVATIONS DIAGNOSED AT THE TIME OF THE EXPLOSION OF THE ATOMIC BOMBS.** Osaka Medical College for Women, Japanese. [nd] 11p. (NP-313)

Research work with 83 patients had been reported about one month after the explosion of the atomic bombs. Principally from the view point of otorhinolaryngological investigations, data have been presented regarding the symptoms and the time of their appearance. Observations were made on peripheral blood cells as well as nucleated blood cells in the marrow of the bones, the distance from the explosion center in the bombed area, ages, sex, and injuries by burning, bleeding, falling-off of hair, diarrhoea, and other symptoms in general. (ACD)

1089

Timmes, Joseph J. **RADIATION SICKNESS IN NAGASAKI. PRELIMINARY REPORT.** U. S. Naval Med. Bull. **46**, 219-24(1946).

This report has been superseded by reports NP-3036-3040.

1090

Warren, S. **THE PATHOLOGIC EFFECTS OF AN INSTANTANEOUS DOSE OF RADIATION.** Cancer Research **6**, 449-53(1946).

The distinctive feature of the atomic bomb is the large amount of radiant energy that it produces. While this energy covers a wide range of the electromagnetic spectrum, its chief physiologic and pathologic effects may be divided into two groups: first, the effects of heat, producing primary thermal injury of the flash burn type, and secondary thermal injuries due to induced fires; 2nd, the effects of short-wave radiation and neutrons, paralleling closely the effects familiar to us from the experimental studies of the biologic effects of x-rays. The immediate effects from radiation injury were manifested as weakness, malaise, fever and often death, and appeared usually within 48 hours. These presumably present a syndrome of radiation sickness carried to an extreme degree. The delayed effects from radiation injury consist largely of damage to the hemopoietic tissue with resulting leukopenia, granulocytopenia, and anemia. (BA)

1091

Warren, Shields. **NAGASAKI SURVIVORS AS SEEN IN 1947.** Military Surgeon **102**, 96(1948).

The Atomic Casualty Commission is actively cooperating with the Japanese in a long range study of the surviving population of Hiroshima and Nagasaki. The explosions at Hiroshima and at Nagasaki were air burst so that little of the fission products remained at the site. Instead, they were widely disseminated through the stratosphere. Consequently, all of the bombed area is safe for habitation and for cultivation. The scars of flash burns are relatively frequent among the survivors. Special attention is being given to keloid formation in these scars. The incidence of the keloids appears to be somewhat greater among Japanese than whites, but there is no evidence that there is any specific relationship between the occurrence of keloid in scar tissue and exposure to the explosion of an atomic bomb. Disturbances of the hemopoietic tissue were evident in 1945, but by 1947 most of the survivors had returned approximately to normal. Up to the present time three cases of leukemia, one probable case of leukemia, and one of multiple myeloma have been reported among the survivors. An abnormal prevalence of monocytes and reticular cells suggests that the marrow in some may not be entirely normal. No tumors of gonads have been reported among the survivors. It will probably be 25 years before reliable data can be obtained on changes in genes. (NSA)

1092

Warren, Shields. **THE POSSIBLE CARCINOGENIC EFFECTS OF THE ATOMIC BOMB AT HIROSHIMA AND NAGASAKI.** Acta Unio Intern. contra Cancrum **6**, 874-7 (1949).

The explosion of the atomic bombs in Japan produced injury by air blast, thermal radiation, and ionizing radiation. Air blast, both its primary and secondary effects, produced much trauma, with extensive scarring and some keloid formation resulting as the injuries to the skin healed. Thermal radiation produced burns of varying severity which also healed with extensive scarring and keloid formation; no tumors have yet developed in these scars. It is stated that it is probable that some will ultimately appear, but not to a

greater extent than in burn scars from other sources. It is claimed that ionizing radiation in the amount received by survivors may be expected to produce some cases of leukemia and, possibly some ovarian tumors. As yet no significant increase in incidence of leukemia has occurred. (NSA)

1093

Warren, S. and R. H. Draeger. **THE PATTERN OF INJURIES PRODUCED BY THE ATOMIC BOMBS AT HIROSHIMA AND NAGASAKI.** U. S. Naval Med. Bull. **46**, 1349-53(1946).

Although injuries following the two explosions of atomic bombs in Japan ranged from instant death to delayed sickness, a clear pattern is discernible. To Draeger's classification of blast injury into that due to air blast, water blast and solid blast the authors now add the term "radiation blast injury." In the two Japanese cities water and solid blast injuries were absent, the casualties being the result of air and radiation blast. The unique feature here was the liberation of ionizing γ -rays and neutrons, with the result that, in addition to injuries from thermal burns, there was also observed the pathological changes which follow over-exposure to x-rays. In those exposed only to the ionizing rays there was at first no visible effect, but subjective malaise and nausea appeared early. Lymphocytopenia developed in a few hours in those heavily exposed, and death occurred in a few days. In those who lived longer there was evidence of injury to gonadal tissue and of bone marrow change, leukopenia, thrombocytopenia with hemorrhage, and anemia appearing in that order. Proof of induced radioactivity and residual radioactivity was not encountered. (BA)

Syndrome in Animals

1094

Bennett, L. R., P. E. Rekers, and J. W. Howland. **THE INFLUENCE OF INFECTION ON THE HEMATOLOGICAL EFFECTS AND MORTALITY FOLLOWING MIDL-LETHAL X-RADIATION.** Radiology **57**, 99-103(1951). (UR-140)

The careful analysis of blood cultures taken on 54 dogs following whole-body x irradiation had demonstrated the relative frequency of blood cultures of all types of organisms. Infection appears to be definitely related to mortality in those animals surviving the first 2 weeks of irradiation. This relation is less apparent in animals dying at an earlier time. No direct correlation between the definite leukopenia of dying animals and infection can be made. The presence of gram-negative organisms within the circulating blood appears to be definitely related to subsequent death of these animals. As a result of such observations preliminary experimentation has been carried out to determine the effect on morbidity and mortality of dogs and rats following various antibacterial agents. Aureomycin, streptomycin, sulfa drugs, penicillin, and terramycin have been studied extensively. Results will be reported. (NSA)

1095

Botkin, A. L., E. H. Praytor, Mary E. Austing, and J. Hensen. **THYROID RESPONSE TO TOTAL-BODY X-IRRADIATION.** Army Medical Research Lab., Fort Knox. Sept. 28, 1951. 9p. (AMRL-66)

Changes in thyroid and serum I^{131} content (inorganic and organic) of rats, after total-body x irradiation at 1000 r, indicate a stimulation of thyroid activity by 2 hr after irradiation. This increased activity is apparent until one day after irradiation, from which time until the sixth day there is a progressive decrease in activity. These changes in functional activity of the thyroid are probably due to sys-

temic damage caused by the radiation and are mediated through the hypophysis. The initial increased thyrotropin release from the hypophysis is followed by a shift of pituitary function toward increased adrenocorticotropin elaboration at the expense of thyrotropin production. (NSA)

1096

Bowers, John Z. and Kenneth G. Scott. **THE MOVEMENT OF SODIUM AND POTASSIUM IN THE TISSUES OF THE RAT FOLLOWING ACUTE RADIATION INJURY USING Na^{22} AND $\text{K}^{42,43}$ AS TRACERS.** Radiation Lab., Univ. of Calif. Jan. 1951. 20p. (UCRL-1101)

The purpose of the experiments was to determine alterations in Na and K content of various organs and tissues, and to check Na and K defecation and excretion at various time intervals after total-body irradiation. Two μc of Na^{22} with a half life of 2.6 hr, and 50 to 175 rep of K^{42} or K^{43} were injected subcutaneously. Radiations of LD_{50} and LD_{100} were used. Acute radiation injury is characterized by heavy and early losses of K from sensitive tissues (lymph nodes, small and large intestine, stomach, spleen) (irreversible injury), and less pronounced losses from other tissues (gonads, kidney, heart, lung, liver, brain, skin, skeleton, muscle, eyes) (reversible injuries). In sensitive tissues, there is an early loss of Na, but subsequently a penetration of Na into damaged cells, as indicated by an expansion of Na space. There are no characteristic or significant changes in the H_2O content of the various organs demonstrated in these experiments. (6 tables, 2 charts) (NSA)

1097

Brues, Austin M. **PATHOLOGIC EFFECTS OF IONIZING RADIATIONS AND RADIOACTIVE MATERIALS.** *Biochem. J.* 42, 22(1948).

Certain purely chemical effects of ionizing radiations are understood. These include the dissociation of water into H and OH radicals and the inhibition of certain enzymes such as those containing sulfhydryl groups. In addition to these proximate effects, various forms of genetic and cell damage have been extensively studied. The relation of these changes to most clinical radiation effects remains largely to be established. In acute lethal radiation exposure in mammals, an immediate response is seen corresponding to clinical x-ray sickness. Susceptible animals will show hypertension, vomiting, or erythema of the skin. By the second day, acute symptoms have largely abated, but there is a marked decrease in circulating white cells which continues until death. During the ensuing week, animals refuse food and water and lose weight. There is increasing anaemia, increased plasma and extracellular volume, accelerated sedimentation rate, increased renal excretion of phenol red, and decreased levels of blood non-protein nitrogen, urea and polypeptides. Histologic damage is most marked in the blood-forming organs, gonads, and intestinal tract. During the second week, the clotting time is greatly increased due to an overabundance of circulating heparin; fever and subcutaneous oedema appear and death occurs, attended by loss of blood, bleeding into vital areas, such as the heart and central nervous system, ulceration of mucous membranes and a terminal shock-like state. A shift in the plasma protein pattern (increased beta and gamma globulin) has been seen in dogs, but is not specific for radiation sickness. Later effects in surviving animals include anaemia, lymphoid atrophy, and in mice, an enhanced tendency to lymphoma. Chronic effects include decrease in life span, greying of hair and an increased tumor incidence. Acute effects of absorbed radioelements generally resemble those of total body radiation. Their late effects depend upon localization of the element and, as in the case of radium, a great increase in bone tumors is seen after absorption of radiostrontium, as well as plutonium and many of the radioactive rare earths. Since

C^{14} has been shown to deposit in bone (Bloom, Curtis, and McLean, 1947), the question is raised whether it may present a human hazard analogous to radium. An attempt has been made to consider the human tolerance on the basis of known facts and it is presently thought that a total human absorption in excess of 30 microcuries must be considered hazardous until further knowledge is gained regarding the retention of carbon administered in various forms. In the case of a hypothetical carbon compound, such as a steroid, which might remain localized in a very small organ, even this figure may need revision. (NSA)

1098

Brues, Austin M., ed. **DIVISION OF BIOLOGICAL AND MEDICAL RESEARCH; QUARTERLY REPORT, MAY, JUNE, JULY, 1951.** Argonne National Lab. [nd] 112p. (ANL-4676)

Data are given on blood cell counts of guinea pigs having received bone-marrow injections before or after lethal x-ray doses. The prophylactic effect of bone-marrow injections against radiation injuries varies with the strain of mice. In 30-day LD_{50} comparisons of radon and x-radiation effects, the x-ray LD_{50} was 564 r with a standard deviation of 23 r or 52,400 ergs/g, the radon solution was $0.1415 \pm 0.001 \text{ mc/g}$ or 36,800 ergs/g. The energy absorbed from the x radiation was 1.42 times that of the particle energy. The biologic effects observed in mice injected intravenously with radon are caused 86% by α and 14% by β radiation. The histological changes in the retina of new-born mice due to 1000 r x radiation are illustrated; data are given on percentage of cataract formation and length of latent periods elapsing before these are visible. Information is given on the effects of spleen shielding during x radiation on blood cell counts, and effect of injection of embryonic suspensions, mashed placental tissues, and frozen spleen implants on sensitivity to x radiation. Spleen shielding of rabbits during irradiation with lethal x-ray doses preserved the capacity of forming antibodies, even though the spleen was removed 24 hr after irradiation and the antigen given 24 hr after splenectomy. Data on the effect of marrow suspensions from normal and estrogen-treated mice and of p-chloromercuribenzoate on the sensitivity of mice to total x irradiation are given. Supernatant plasmas of blood-perfused spleen of dogs were protective when injected in 1-ml dosage into mice immediately before giving the mice 800 r total-body x irradiation. The effects of massive doses of cortisone on mortality in the initial period following x irradiation of young chicks were small. In newly hatched chicks, the shielding of different small areas of the body during 1000 r x irradiation resulted in similar decreases in mortality, indicating that some lesions were effects of direct radiation. Renal failure was one of numerous factors contributing to the deaths. Preparation of C^{14} -labeled dextran by biosynthesis is described. Effects of diethanolamine salt of maleic hydrazide on killer clones of *Paramecium* are reported. Studies with sea-urchin eggs and sperm showed inhibition of respiration of the cells when exposed to large doses of x radiation, the dose depending on the degree to which the cell is sensitive to ionizing radiation, and increase of respiration after small doses. Some results of experiments of ionization in air from β -ray point sources are given. An ionization-type halide detector for use in quantitative measuring has been developed. (NSA)

1099

Brues, Austin M., ed. **PHARMACOLOGY; THEORETICAL BIOLOGY, EXPERIMENTAL PATHOLOGY, AND TREATMENT OF POSTIRRADIATION INFECTION WITH ANTIBIOTICS, p.109-24 of DIVISION OF BIOLOGICAL AND MEDICAL RESEARCH; QUARTERLY REPORT, AUGUST, SEPTEMBER, OCTOBER, 1951.** Argonne National Lab. [nd] 16p. (ANL-4713(p.109-24))

Preliminary data from a study of the pharmacodynamics of compounds derived from ribonucleic acid and the effects of these compounds upon physiological changes following total-body irradiation showed that the blood pressure of rats is appreciably decreased by small amounts of adenosine and 3-adenylic acid, while other nucleic acid derivatives have much smaller effects. An approximate formula for the standard error of an absolute white cell count is used to show the dependence of the standard error on the blood count parameters and sample sizes and to develop formulas for minimum error at fixed cost as well as for minimum cost at fixed relative error. Data on the survival and incidence of malignant bone tumors in mice that had received less than 22 μ c per kg of U from 210 to 415 days previously, and experimental design and survival figures at 221 days of mice which had received injections of Ra²²⁶ and Pu²³⁹ are presented in tabular form. Biometric analysis of data on the effects of various patterns of antibiotic therapy on the survival of mice following a fixed dose of x rays showed streptomycin dosages ranging from about 3000 to 6000 units per day were protective to the same degree. Penicillin plus streptomycin appeared to be less protective than streptomycin alone. Aureomycin, chloramphenicol, and terramycin, all supplemented with streptomycin, conferred about equal degrees of protection. (NSA)

1100

Carter, Robert E., Payne S. Harris, and James T. Brennan. **THE EFFECT OF ACUTE DOSES OF X-IRRADIATION ON THE SPLENIC AND THYMIC WEIGHT OF CF-1 FEMALE MICE.** Los Alamos Scientific Lab. Mar. 7, 1950. 8p. (LA-1075)

A high correlation is obtained between x-radiation received during a single exposure and loss of weight of the spleen and thymus of female mice. A 250-kv peak x-ray machine was used with a 3.9-mm Cu filter in addition to the inherent filtration of the tube (equivalent to approximately 2.00 mm of Al). The exposure rate was 14 r/min. Curves of the log of the total dosage (in roentgens) and the per cent weight loss of the thymus and spleen are linear on a semi-log graph. The use of splenic and thymic weight change as a means of biologically comparing various ionizing radiations is suggested. 15 references. (NSA)

1101

Chrom, Sv. A. **STUDIES ON THE EFFECT OF ROENTGEN RAYS UPON THE INTESTINAL EPITHELIUM AND UPON THE RETICULO-ENDOTHELIAL CELLS OF THE LIVER AND SPLEEN.** Acta Radiol. 16, 641(1935).

Histological and bacteriological studies were made on white mice irradiated with x rays. Universal radiation with 250-550 r resulted in a general infection with intestinal bacteria. Abdominal irradiation with the spleen and liver protected did not produce the infection characteristic of irradiation of the entire abdomen. The effect of irradiation was evidently damage to the protective functions of the intestinal epithelium and of the liver and spleen. (BA)

1102

Conard, Robert A. **EFFECT OF X-IRRADIATION ON INTESTINAL MOTILITY OF THE RAT.** Am. J. Physiol. 165, 375-85(1951).

The effect of x irradiation on intestinal motility of the rat was studied in vivo. Kymographic studies showed that x-ray doses of 100 r and above produced a consistent pattern of intestinal response characterized by a latent period of about 1 min followed by increased tone and motility, the degree and length of tone rise, in general, increasing with dose. Using doses of 800 r x ray, propulsive motility was found to be accelerated during the first hr with a tendency to a decrease below normal from the third hr through the third day and a return to normal after the third day. The most

striking feature of both studies was the shortness of the latent period. A study of the influence of various drugs on the response indicated that the action of x irradiation resulted in a stimulation of the cholinergic nerves. The site of action was found to be largely localized in the intestine with little systemic component, and the chief site of action on the vagus appeared to be at the level of the enteric ganglia. (NSA)

1103

Coulter, M. P., F. W. Furth, and J. W. Howland. **THE INCIDENCE OF BACTEREMIA IN THE X-RADIATED RAT, p.44-6 OF QUARTERLY TECHNICAL REPORT; OCTOBER 1, 1950 THRU DECEMBER 31, 1950.** University of Rochester. Feb. 1, 1951. 3p. (UR-152(p.44-6))

A total of 294 rats received 700 r of whole-body radiation and were sacrificed at intervals postradiation for heart blood culture studies. Blood cultures were obtained on 55 normal rats for control studies. From 20 to 64% of the cultures from radiated rats were positive during the second week postradiation. The greatest mortality also occurred during this period. The organisms recovered were those normally found in the gastrointestinal tract. (NSA)

1104

Cronkite, Eugene P. **THE CLINICAL MANIFESTATIONS OF ACUTE RADIATION ILLNESS PRODUCED IN GOATS BY EXPOSURE TO AN ATOMIC BOMB, TEST ABLE, BIKINI, 1946, WITH COMMENTS ON THERAPY.** Naval Medical Research Inst., Bethesda. Mar. 8, 1948. 42p. (NP-574; Report No. 10)

The clinical manifestations of acute ionizing radiation illness in the goat at which it progresses are functions of the amount of radiation received. The fully-developed illness consists of apathy, anorexia, diarrhea (often bloody), purpura, epilation, marked leukopenia, and a high mortality. However, many signs may be absent with overwhelming or sublethal radiation. The therapeutic use of penicillin and transfusions suggests that these agents may be of value. (NSA)

1105

Cronkite, E. P. **PATHOGENESIS AND THERAPY OF RADIATION ILLNESS.** Med. Ann. Dist. Columbia 18, 239-42(1949).

The radiation sickness produced by whole body radiation is discussed from a descriptive and therapeutic standpoint. The syndrome is initiated by protoplasmic injury, through the following mechanisms: (1) enzyme inhibition, particularly sulphydryl enzymes; (2) some alterations in the osmotic properties and the cell permeability; (3) generalized protein denaturation and (4) an intoxication by histamine-like compounds supposedly liberated as a result of the radiations. There is a reciprocal relationship between the degree and reversibility of the enzyme inhibition, the protein denaturation, and the alterations in osmotic properties and cellular permeability. As the dosage increases, the degree of reversibility decreases and the mortality rises. A list of varying degrees of susceptibility of different tissues to necrosis is included. Toxic symptoms develop immediately after or during the diffuse radiation. These consist of nausea, vomiting, diarrhea, malaise, etc. and they subside within 24-48 hours. A latent period follows in which leukopenia, thrombopenia, and a slowly progressive leukemia develop. Physiopathologic manifestations involving the adrenal function, the adaption syndrome, the intoxication by histamine-like substances, and bacterial invasion also take place. Finally, the panleukopenia and hemorrhagic symptoms develop 4-6 weeks after the radiation. Capillary fragility and clotting defects also occur. It is suggested that an adequate method of separating hopeless cases from the casualties is essential to conserve time, personnel, and therapeutic

agents. Among the specific therapeutic methods which may be used are: sulfhydryl agents to reverse enzyme inhibition; anti-histamine compounds to neutralize toxins; adrenal hormones to replace losses; agents to maintain the water and electrolyte metabolism; prophylaxis treatments of infections in the presence of a granulocytopenia; the prevention and therapy of anemia; the treatment of hemorrhagic tendencies; and means to prevent and remedy the marked loss of tissue and negative nitrogen balance. The use of penicillin, aureomycin, chloromycetin, rutin, and protamine sulfate are also discussed. (NSA)

1108

Cronkite, Eugene P. **THE CLINICAL MANIFESTATIONS OF ACUTE RADIATION ILLNESS IN GOATS.** U. S. Naval Med. Bull. 49, 199-215(1949).

The goats considered in this report were exposed to ionizing radiations in amounts ranging from 100 r to more than 10,000 r at Bikini. They were divided into four groups based on the severity of their illness and the depression of their leukocyte counts. In group 1, severest radiation illness, the animals survived less than six days, mortality was 100%, and sudden death occurred. An extremely marked depression of the leukocyte developed. There was no visible evidence of hemorrhage during life and no epilation. The animals in group 2, severe radiation illness, survived manifestations with a variable clotting defect occurred, epilation was prominent, and mortality was 100%. In group 3, less severe radiation illness, survival was in excess of 44 days and two were alive 1½ years later. The signs were similar to group 2 but developed with less rapidity and severity. A moderate leukopenia was present, and epilation was minimal. Hemorrhagic phenomena were less prominent and a clotting defect was not found. In group 4, mild radiation illness, survival was in excess of 184 days. Six of 9 were alive 1½ years after irradiation. Signs were mild and of short duration. Hemorrhage, epilation, and rhinitis were absent. The clinical picture in goats is similar to that of man except for the absence of vomiting and the more rapid progression of signs. Penicillin and whole blood transfusions were used therapeutically. For lack of comparatively exposed control animals definite conclusions cannot be drawn about the usefulness of these agents. The data suggest that they may be of value. (NSA)

1107

Cronkite, E. P. **THE HEMORRHAGIC SYNDROME OF ACUTE IONIZING RADIATION ILLNESS PRODUCED IN GOATS AND SWINE BY EXPOSURE TO THE ATOMIC BOMB AT BIKINI, 1946.** Blood 5, 32-45(1950) (NP-1902)

This preliminary paper based on field tests at Bikini in July 1946 is concerned with a description of the hemorrhagic syndrome encountered in goats and swine following irradiation by an atomic bomb. Of 176 goats exposed to the aerial atomic explosion, 31 developed detectable effects of radiation; 14 of these showed purpura, while four exhibited a prolonged clotting time. A total of 20 swine were exposed to the underwater atomic explosion; all animals were below decks and it is concluded that most of the irradiation to which they were subjected was γ radiation at the time of the explosion or γ emission from fission products showered upon the ships after the explosion; the greater part of this irradiation was received within two days. Red blood cell counts, prothrombin and whole blood clotting times, hemoglobin determinations, hematocrit readings, white and differential blood cell counts and clot retraction times were taken on the swine and goats before and at intervals after exposure. The hemorrhagic syndrome is considered to be predominantly a result of a combination of "increased vascular fragility" and thrombopenia. Infrequently, a blood

coagulation defect characterized by a prolonged clotting time due to a circulating antibody with heparinlike properties may occur, but only in fatally irradiated animals. Evidence is presented suggesting that serum fibrinolysins may have been activated by the irradiation. It is concluded that a hemorrhagic syndrome can develop in irradiated dogs, goats, swine, rats, chickens, and guinea pigs without the appearance of a prolonged clotting time and without a detectible "heparinemia." The most common phenomena observed in the syndrome, it is stated, appear to be an increased vascular fragility, thrombopenia, and ulcerations. (NSA)

1108

Dillard, G. H. L., G. Brecher, and E. P. Cronkite. **SEPARATION, CONCENTRATION, AND TRANSFUSION OF PLATELETS.** Proc. Soc. Exptl. Biol. Med. 78, 796-9 (1951).

A simple method is presented for the efficient separation and concentration of platelets from burrow, dog, and guinea pig blood in quantities sufficient for transfusion. This method depends upon the use of Sequesterene Na₂ as an anticoagulant, which prevents the development of platelet stickiness and clumping in shed blood. Platelets prepared by this method and transfused into the thrombopenic, irradiated dog remain in the circulation, reverse the coagulation defect, and prevent hemorrhages. (auth)

1109

Draeger, R. H. and S. Warren. **MEDICINE AT THE CROSSROADS--A REPORT BY THE MEDICAL CORPS OF THE NAVY ON THE STUDY OF ANIMALS USED IN THE BIKINI TESTS.** U. S. Naval Med. Bull. 47, 219-25 (1947).

The biological experiments conducted during Operations Crossroads are outlined and their results summarized. Twenty-two scientists, 200 goats, 200 pigs, 5,000 rats, 120 mice, and 60 guinea pigs were transported to Bikini on U.S.S. Burleson, which served as the laboratory. In addition to the mammals, other biological material—insects, bacteria, seeds, sera, hormones, etc.—and inorganic substances such as soil and drugs were included. Most of the animals were used in Test Able, where the atomic bomb was exploded above the ground. All were retrieved within two days. It was found that the majority of early deaths were due to blast injury, radiation effects being a lesser cause of death at this time and flash burns being minimal because of the furry coats of the animals. The animals which were exposed to appreciable amounts of radiation developed the same signs and symptoms as were noted in the human survivors of Hiroshima and Nagasaki. The first sign was atrophy of lymphoid tissue; then appeared a hemorrhagic diathesis and severe enteritis, often with necrosis of mucosa and submucosa. Marked changes in the blood picture occurred and, some weeks later, partial depilation. The sequence of the pathologic changes is being studied by means of sections from the tissues of animals sacrificed at intervals after the exposure. Information obtained by placing swatches of different cloths on fir plywood confirmed the impression gained in Japan that white material protects against flash burns better than dark cloth. After Test Baker, in which the bomb was exploded under water, the test subjects could not be recovered for several days because of the intense residual radioactivity resulting from the flooding of the target ships with radioactive "rain." The animals thus received not only a more intense radiation but also a much longer exposure than those at Test Able. The surviving animals and the inert materials are now being studied at the Naval Medical Research Institute. (BA)

1110

Edelmann, Abraham and W. J. Eversole. **CHANGES IN ANTIDIURETIC ACTIVITY OF RAT SERUM AFTER**

X-IRRADIATION. Am. J. Physiol. 163, 709(1950) (AECU-1081)

The report is reproduced here in its entirety.

The experiments reported here concern an attempt to determine the physiology involved in the previously reported (Federation Proc. 8, 39(1949)) diuresis occurring within 24 hr after whole-body x irradiation of the rat. A test dose of water, 4 ml/100 cm² body surface, was given by stomach tube 30 min or 24 hr after whole-body x irradiation (160 kvp, 10 ma, 0.2 mm Cu). Control animals were similarly treated except they were not irradiated. Exposed animals excreted the administered water at a more rapid rate than the controls. Serum taken from irradiated rats at various times after exposure was tested for antidiuretic activity by the method of Birnie et al. (Proc. Soc. Exptl. Biol. Med. 70, 83(1949)). Significant decreases in antidiuretic activity were found at 12 and 24 hr after irradiation. These results indicate that a decrease in amount of circulating antidiuretic substance or substances is a factor involved in the increased urine flow after irradiation. (NSA)

1111

Evans, T. C., Grace Clarke and Estelle Sobel. **INCREASE IN ¹³¹I UPTAKE OF THYROID AFTER WHOLE BODY ROENTGEN IRRADIATION.** Anat. Record 99, 577(1947).

Adult male rats were exposed to x-rays (500 r and 1000 r) and 2 days later a tracer dose of radioactive iodine was given subcutaneously. Twenty-four hours after ¹³¹I administration, thyroids were removed and relative amount of radioactivity determined. The activity in the thyroids of the irradiated animals was much higher than that of the controls. Animals were tested at different times after irradiation and the maximum increase in activity (relative to that of the controls) occurred during the third day after the irradiation. At this time the leukocyte count was very low. Increased activity of the thyroid in the irradiated animals occurred even when the thyroid itself was not irradiated. In fact, the largest relative activity of the thyroid occurred in an animal receiving irradiation over the abdomen (head and thorax protected with lead). The ¹³¹I content of the blood of the irradiated animals was usually higher than that of the controls. In one experiment, the thyroid of adrenalectomized rats did not retain as much radio-iodine as did those with the gland. Irradiated animals without adrenals showed an increase in ¹³¹I over their controls (without adrenals) in about the same proportion as if adrenals were present. New born rats (3 days of age) did not respond in the same way as did the adults. Irradiation of the babes resulted in a partial depression of the ¹³¹I uptake of the thyroid. (NSA)

1112

France, Owen. **CHANGES IN THE WATER CONTENT AND DISTRIBUTION IN RATS AND MICE AFTER CHRONIC AND ACUTE TOTAL-BODY X-IRRADIATION.** Univ. of Chicago Metallurgical Lab. June 1946. 34p. (AECU-131; CH-3889)

In order to determine something of the nature of the changes in water metabolism that occur after total-body irradiation, studies were made of the relative water contents of muscle, plasma, and the entire carcass of rats and mice. Water distribution, as measured by the volume of distribution of injected thiocyanate ion and of intravenously-administered blue dye, T1824, was used as an estimate of changes in the extracellular and vascular compartments, respectively. A transient increase in thiocyanate space occurred in rats at an x-ray dosage that was about 15% of the LD-50. A similar increase was observed in the total-body water of mice that was about 30% of the LD-50. No changes occurred in relative muscle or plasma water, or in plasma

volume, until the lethal levels of x-irradiation were approached, at which time increases were observed in all five types of measurements. The increases occurred in at least some cases in the terminal period, and in the presence of a negative water balance. Chronic irradiation with x-rays and with α -rays from injected plutonium resulted in a state of relative hydration. The thiocyanate space, again, was the most sensitive indicator of change in water metabolism, although some increases in plasma and muscle water did result from the higher dosages. By means of studying the effects of pre- and post-irradiation water restriction on the survival time of rats and mice, it was determined that the dehydration resulting from this procedure was apparently helpful in that the irradiated animals so treated lived longer than the x-irradiated controls. (NSA)

1113

Haley, T. J., Margaret R. Andem, Richard F. Riley, and Idamae Williams. **THE PRESENCE AND IDENTITY OF VASOTROPIC SUBSTANCES IN THE BLOOD OF RATS SUBJECTED TO ACUTE WHOLE BODY ROENTGEN RAY IRRADIATION.** Univ. of Calif., Los Angeles. Oct. 18, 1951. 17p. (UCLA-161)

A systematic study has been made of the effect of 600 r of acute whole and regional x irradiation on the peripheral vascular system of the rat. The effects of such radiation upon the formed elements of the blood, the intestinal tract, and other body tissues have been correlated with the published data concerning radiation damage of these tissues. It has been demonstrated that peripheral vascular function is not impaired by a direct action of the radiation on the precapillary sphincters and terminal arterioles but is mediated through the release of a vasodepressor material (VDM) by the liver. This material, which is present in the circulation during the first post-irradiation week, has been shown to be the same as that which appears in the blood of animals in irreversible shock. It fits all the criteria for ferritin. However, the sequence of its appearance is different from that reported for physiological shock states. A vasoexcitor material (VEM) has been found in the blood of irradiated animals during the second post-irradiation week. This material fits the criteria established for the VEM found in the blood of animals in the reversible phase of shock. (NSA)

1114

Hollicroft, Joanne and Egon Lorenz. **SYSTEMIC EFFECTS IN THE IRRADIATION TREATMENT OF A TRANSPLANTED MOUSE LYMPHOSARCOMA,** p. 173 of INTERNATIONAL CONGRESS OF RADIOLOGY, 6th Congress, London. 1950.

The lymphosarcoma used in these experiments originated in an irradiated strain A mouse. When subcutaneously or intramuscularly transplanted this tumour grows at the site of inoculation and kills the animals in 30 to 40 days. Whole body irradiations were carried out with roentgen radiation or intravenously injected radon in equilibrium with its short-lived decay products. The radon dose in rep equalled the roentgen radiation dose in r. It was found that a whole body irradiation with 400 r or rep of either roentgen radiation or radon caused regression of only the tumor and a few permanent cures. Roentgen irradiation of the tumour or of the body alone with the same dose of 400 r had almost no effect on tumour regression. Doses to the tumour alone of 1,300 r had little effect while doses of 4,000 r were approximately as effective as a whole body exposure of 400 r. Similar effects, however, could be obtained by giving a tumour dose of 1,000 r or more followed by a whole body exposure to 100 r. This subsequent whole body exposure is

only effective if given within a few hours of the irradiation of the tumour. The experimental findings suggest that a systemic effect is involved in tumour regression induced by radiation.

1115

Johnson, C. G., C. F. Vilter, and T. D. Spies. IRRADIATION SICKNESS IN RATS. *Am. J. Roentgenol. Radium Therapy* **56**, 631-9(1946).

Groups of Sprague-Dawley albino rats fed either on a vitamin free diet or a nutritionally complete stock diet, adjusted in quantity so that no appreciable weight changes occurred from day to day, received single x-ray doses in the range 600-800 roentgens (200 kv excitation, filtration 0.5 mm Cu plus 1 mm Al). These doses were chosen so that approximately half of the rats died. Other groups, similarly treated, received daily oral vitamin supplements, or parenteral medication, commencing three and two days, respectively, before irradiation and continuing until the end of the experiment. A third treatment was with three subcutaneous doses of crude liver extract. The protective action of these treatments was judged by mortality, post-irradiation survival time, weight changes, activity, food consumption, and autopsy findings. Results are summarized below:

Diet	Medication	Protective Value
Vitamin-free	Crude liver extract, subcutaneously	0
Stock	Vitamin K, intraperitoneally	0
Stock	Pyridoxine, intraperitoneally	Plus (?)
Stock	Thiamine and nicotinamide, intraperitoneally	Plus (?)
Vitamin-free	Folic acid, subcutaneously	Plus (?)
Vitamin-free	Daily oral supplements	Plus
Thiamine	0.2 mgm. Nicotinamide	2.5 mgm
Pyridoxine	0.2 mgm. Calcium pantothenate	10.0 mgm
Inositol	0.2 mgm. Choline hydrochloride	20.0 mgm
Riboflavin	0.2 mgm. Cod-liver oil preparation containing vitamins A and D	

Young rats were more susceptible to severe irradiation sickness than were older rats, and young rats receiving a vitamin-free diet were markedly more susceptible than rats maintained on an adequate diet. The daily oral vitamin supplements greatly decreased the incidence of fatal irradiation sickness. In all, 824 rats were used in 20 experiments, usually in groups of 52. (EM)

1116

Kimeldorf, D. J. and D. C. Jones. PERFORMANCE STUDIES ON ANIMALS EXPOSED TO EXTERNAL RADIATION. II. EXHAUSTIVE EXERCISE TESTS ON RATS EXPOSED TO X-RAYS IN THE LETHAL DOSE RANGE. Naval Radiological Defense Lab. Aug. 25, 1950. 23p. (AD-241(B))

The performance of rats in a standardized exhaustive performance test was depressed following whole-body irradiation with relatively lethal doses of x-rays (700 and 860 r). The extent of performance depression appears to be related to the post-irradiation survival time. The extent and rate of mortality following irradiation, with the doses described, were markedly increased by repeated periods of exercise in the post-irradiation survival time. (NSA)

1117

Kimeldorf, D. J. and D. C. Jones. THE RELATIONSHIP OF RADIATION DOSE TO LETHALITY AMONG EXERCISED ANIMALS EXPOSED TO ROENTGEN RAYS. *Am. J. Physiol.* **167**, 626-32(1951) (AD-321(B))

The mortality of exercised irradiated rats was compared with that of nonexercised irradiated rats following x-ray doses ranging from 200 to 1000 r. Swimming to exhaustion under standard conditions of testing constituted the exercise. Where exposure to x rays if followed by daily exhaustive exercise the mortality is significantly greater than with irradiation alone. For exercised irradiated rats LD₅₀ was found to be 510 r and for nonexercised irradiated rats LD₅₀ was 710 r, 28% higher. The mortality is not affected by exercise undertaken prior to irradiation. Experiments exposing the rats daily to water of different temperatures without exercise had no influence upon the postirradiation mortality of exercised irradiated animals, showing that the specific environment associated with the method of exercise is not responsible for the mortality increase observed with exercise. (NSA)

1118

Kohn, Henry I. CHANGES IN THE COMPOSITION OF THE BLOOD PLASMA OF THE GUINEA PIG DURING THE ACUTE RADIATION SYNDROME. *Am. J. Physiol.* **162**, 703-8(1950). (ORNL-464)

The plasma of the guinea pig was studied during the 8 days following a single total-body exposure to 250 kvp x-rays. The changes came in two phases with respect to time, the first phase beginning within 1 day of exposure, the second phase beginning about 3 or 4 days later and corresponding to the time when the first serious symptoms were noted. The changes after 200 r, the approximate LD₅₀, were smaller than after 600 r, but the patterns of change were alike. After 200 r, the following was observed. Glucose concentration rose 60 mg% during the first day and gradually returned to normal during the next 5 days. The non-protein nitrogen was elevated by 10 mg% for 5 days. The albumin-globulin ratio rose from a normal of 3.1 to 4.5 during the first 2 days and returned to normal during the next 3 days. The rise was due to nonprotein material which could be rendered ineffective by extraction of the plasma with ether. The total protein level fell about 1 g% during the 5th to 7th days after exposure. The chloride concentration was elevated by as much as 50 mg% during the 3d to 5th days. Cholesterol was elevated by 20 mg% during the 4th and 5th days. A peculiar, transient syndrome was also noted during the first hour or two immediately following exposure, especially after 600 r, whose signs were abnormal posture, labored respiration, and lacrimation. 16 references. (NSA)

1119

Lawrason, F. Douglas and E. P. Cronkite. INCIDENTAL FINDING OF MEGALOBlastic-LIKE CELLS IN BONE MARROW OF ONE OF TWO SWINE WITH MACROCYTIC ANEMIA AND ACHLORHYDRIA. *Yale J. Biol. and Med.* **22**, 57-6(1949).

Extensive hematological observations were made on two swine (Z) for 17 months after they were exposed to atom bomb ionizing radiation at Bikini. Red blood counts were compared with test swine beyond the range of significant radiation, several surviving heavily irradiated swine, and controls; white blood counts were compared with test swine beyond the range of significant radiation and surviving swine subjected to heavy radiation. The results are discussed in terms of nutrition, radiation, age, and previous history of the animals. The authors found in blood microscopic analyses and marrow smears evidence for true macrocytic anemia in both animals (Z) and a hyperplastic megaloblastic-like bone marrow in one. Achlorhydia was found in both animals (Z). (NSA)

1120

Lourau, M. and O. Lartigue. MODIFICATION OF THE

GLYCEMIA PRODUCED BY IRRADIATION OF THE ENTIRE BODY WITH X-RAY. Arch. sci. physiol. **4**, 197-208(1950).

Irradiation caused guinea pigs to exhibit a hyperglycemia after 15-48 hours fasting. It also strongly diminished their tolerance to injected glucose. The tolerance curves, differing from diabetic curves, may be the result of modification of intestinal absorption. (CA)

1121

Miller, C. Phillip, Carolyn W. Hammond, and Marianne Tompkins. **THE INCIDENCE OF BACTEREMIA IN MICE SUBJECTED TO TOTAL BODY X-RADIATION.** Science **111**, 540-1(1950) (AECU-739)

Male, white mice of a strain having an LD-50 (30 days) of approximately 400 r were subjected to total body x-radiation in a single exposure of 600 or 450 r. Cultures of hearts, blood and spleen were made on mice killed at daily intervals post-irradiation. The results showed that bacteremia occurred most frequently during the period of greatest mortality, and its incidence roughly paralleled the daily death rate. Among the mice receiving 600 r the incidence of bacteremia reached a maximum of 85% on the 9th day post-irradiation, and among the mice receiving 450 r a maximum of 54% on the 10th day. With few exceptions the bacteria were all members of the species normally inhabiting the lower intestinal tract of this strain of mice. (NSA)

1122

Miller, C. Philip, Carolyn W. Hammond, and Marianne Tompkins. **THE ROLE OF INFECTION IN RADIATION INJURY.** J. Lab. Clin. Med. **38**, 331-43(1951) (AECU-1543)

Male white mice averaging 20 g in weight were subjected to 600 or 450 r total-body x irradiation in a single exposure. In the 600 r series, 288 mice were killed and cultured (at the rate of 20 a day). Of these, 113 showed positive cultures from heart's blood and/or spleen. Eighty per cent of the positive cultures occurred during the 2nd week postirradiation, the period of greatest mortality. In the 450-r series, 595 mice were killed and cultured (at the rate of 35 a day). 152 showed positive cultures from heart's blood and/or spleen. 66% of the positive cultures occurred during the 2nd week postirradiation. In a majority of the animals the bacteremia was severe enough to be regarded as an overwhelming sepsis. The bacteremia was caused by microorganisms normally present in the lower bowel of this strain of mice. Control cultures on unirradiated mice were all sterile. It is concluded that septicemia caused by microorganisms of enteric origin is in large measure responsible for the death in mice irradiated with these doses of x rays. (NSA)

1123

Montgomery, Philip O'B. and Shields Warren. **THE MECHANISM OF ACUTE HYPOTENSION FOLLOWING TOTAL BODY IRRADIATION.** Proc. Soc. Exptl. Biol. Med. **77**, 803-7(1951) (AECU-1488)

The effect of doses of 1500, 2000, and 2500 r of total-body x irradiation upon the blood pressure, blood volume, and hematocrit were similar regardless of the dose. Blood pressures, hematocrits, and blood volumes of rats irradiated with 1500 r 30 hr after cutting the spinal cord at the level of C6 were the same as found in nonirradiated controls that had undergone the same operation. Bilaterally adrenalectomized rats after 1500 r total-body irradiation exhibited behavior identical to that shown by normal rats given the same dosage. It is concluded that the cause of the immediate hypotension following large doses of total-body irradiation is depression of the nervous system. (NSA)

1124

Moon, V. H., K. Kornblum, and D. R. Morgan. **THE PATHOLOGIC NATURE OF IRRADIATION SICKNESS; A NEW METHOD FOR PRODUCING SHOCK.** Arch. Pathol. **29**, 723(1940).

Irradiation sickness was produced in dogs in order to make observations on the hemo-concentration and on the visceral changes. From 1,400 to 2,800 r was given in divided doses over different parts of the abdomen. After an interval of 60 to 72 hours, severe illness developed, and hemoconcentration, ranging from 15 to 50 per cent, appeared. Urination was decreased, and blood was seen in the urine, feces, and vomitus. The illness progressed rapidly, and death occurred by circulatory failure within 24 hours. The gross and microscopic features were those characteristic of shock. They included capillovenous congestion of the viscera, petechial hemorrhages in mucous and serous surfaces, edema of the lungs and of the mucosae, and parenchymatous degeneration of the liver and kidneys. The results were concordant in 12 animals so treated. An additional feature was degeneration, progressing to necrosis, of the gastrointestinal mucosa. The epithelium lining the crypts and covering the villi showed all stages of disintegration. Some crypts contained nuclear and cellular debris; others were denuded and empty. Some of the villi retained their epithelial covering while that in the crypts was necrotic and disintegrating. Our results corroborate those of Whipple and others: Roentgen radiation of high voltage causes delayed necrosis of the intestinal mucosae, accompanied by shocklike manifestations. Apparently the latter are due to absorption of material from the damaged mucosa. The condition is accompanied by progressive hemoconcentration, and the visceral changes observed post mortem are characteristically those of shock. These results provide experimenters with a new method for inducing shock by causing damage to the tissues. This method eliminates pain and emotional responses, sympathoadrenal hyperactivity, hemorrhage and anesthesia, conditions which are assigned as causes for shock by some writers. (AP)

1125

Moon, V. H., K. Kornblum, and D. R. Morgan. **PATHOLOGY OF IRRADIATION SICKNESS: A NEW METHOD OF INDUCING SHOCK.** Proc. Soc. Exptl. Biol. Med. **43**, 305-6(1940).

Dogs given abdominal roentgen irradiation developed delayed sickness. Vomiting, diarrhea, low blood pressure, hemoconcentration, prostration and death resulted. Post-mortem findings were those of shock: capillovenous congestion, petechial hemorrhages in mucosae and serosae, edema of soft tissues, and parenchymatous degeneration. Injury by X-rays caused delayed necrosis of the intestinal mucosa. The syndrome of shock resulted from this injury, independent of anesthesia, hemorrhage, emotional reactions and of sympatho-adrenal hyperactivity. The results substantiate the interpretation that shock may result from tissue damage, independent of other confusing factors. (BA)

1126

Painter, Elizabeth E. **PATHOPHYSIOLOGICAL EFFECTS OF TOTAL BODY IRRADIATION.** Chicago Med. School Quart. **11**, 96-9(1950).

The author describes various pathophysiological effects of total-body irradiation. Some of the physiological and biochemical alterations occurring after exposure to ionizing radiation appear to result from direct damage to the tissue concerned, while others result from indirect effects by agents carried in the blood from one region of the body to another; the signs and symptoms are similar with every

kind of ionizing radiation. A list is included which covers the single total-body dosage of x-rays needed to kill 50% of the animals involved. The characteristic phases in the radiation-effect pattern (initial shock, acute period, sub-acute period, and chronic period) are discussed under separate headings. The total-body dosage either of 25, 50, 100, or 200 r is correlated with such specific effects in the guinea pig, dog, rabbits, and rats as lymphopenia, granulocytopenia, reduction in the platelet count, reduction in blood pressure, elevation of basal metabolism, inhibition of intestinal absorption of glucose, elevation of sedimentation rate, anemia, absence of reticulocytes, and prolongation of clotting time. (NSA)

1127

Painter, Elizabeth E. and M. C. Moore. **SUSCEPTIBILITY OF X-RAYED ANIMALS TO HISTAMINE AND TO ADENOSINE.** *Federation Proc.* 7, 90(1948).

The report is reproduced here in its entirety.

A study was made to determine the susceptibility of x-rayed animals to the blood pressure lowering effects of tissue breakdown products, such as histamine and adenosine. The compounds were infused at a constant rate over 4-min. periods. The amounts required to produce a perceptible decrease (5-8 mm Hg) in carotid blood pressure were determined for the controls and for the x-rayed animals during the first 4 hours after exposure. All animals were anesthetized with pentobarbital before carotid cannulation. Rabbits given a single total body dose of 800 r require only 2-5 µg/kg/min. of histamine base at 1 to 2 hours after radiation to produce a perceptible decrease in blood pressure. At 3-4 hours, however, the amount required, 3-8 µg/kg/min., approaches that for the control animals, 10-15 µg/kg/min. With adenosine this change in susceptibility is not so apparent: 70-100 µg/kg/min. for the X-rayed rabbits during the first 4 hours as compared with 90-130 µg/kg/min. for the controls. Preliminary experiments on dogs given a single total body dose of 400 r show a significant change in susceptibility to both compounds. These findings may be correlated with the following changes occurring in the animal body during the early period after exposure to x-radiation sickness: (1) liberation of tissue breakdown products, (2) alteration in the detoxifying powers for such substances, and (3) alteration in the compensatory mechanisms for reducing the effects of such substances.

1128

Painter, E. E., C. Ladd Prosser, and M. C. Moore. **PHYSIOLOGICAL OBSERVATIONS ON RABBITS EXPOSED TO SINGLE DOSES OF X-RAYS.** University of Chicago Metallurgical Lab. [1946] Decl. Mar. 4, 1947. 79p. (MDDC-761; CH-3727)

Most of the acute deaths among rabbits after single total-body x-radiation occur in the first two days or at 10-15 days after irradiation. Signs of clinical depression are seen in survivors of sublethal doses during each of these periods, termed the initial shock period and the principal acute radiation death period. The femoral arterial blood pressure of unanesthetized rabbits declined rapidly from a control of approximately 98 mm Hg to a minimum of about 50 mm Hg at 1½ hours after doses of 600 r or greater. Proportionately smaller reductions in blood pressure occurred after 400 and 200 r. The threshold for 10-20 mm drop was approximately 50 r. During the first few hours the heart rate increased. Survivors of the initial shock period showed partial recovery of blood pressure, but at about 10 days, blood pressure again declined, particularly in rabbits which died acutely. Low blood pressures were not observed at this time after doses of 400 r or less. Plasma protein concentration declined slightly during the acute post-irradiation period. Plasma volume as measured by Evans blue space

was not significantly altered in the initial shock period after a dose of 800 r. Intradermally injected dye (Evans blue) spread more rapidly in the irradiated than in non-irradiated skin during the first few hours after irradiation. At the same time intravenously injected dye appeared in the interstitial space of a patch of irradiated skin much earlier than in non-irradiated skin. Recovery in survivors occurs gradually over about a month. Average weight loss is marked (10-15%) in the first three days; weight remains diminished for about one week, after which some rabbits die and others begin a gradual recovery in weight which is not complete by 30 days. Some individual rabbits show two minima in food and water intake and in weight; one, at 1-2 days, and the second at 10-15 days. Rabbits show a polyuria on the 2nd to 4th day after receiving 800 r. Thereafter urine output decreases slightly below control values but not as much as water intake decreases. Blood removed from rabbits 1½ hours after 800 r caused an average fall of 26.2 mm in arterial blood pressure of non-irradiated hosts, blood removed 5-12 days after irradiation caused variable but much smaller fall in the pressure of the host. The plasma of non-irradiated rabbits had an average of 0.3 µg/ml, while plasma removed about 1½ hour after 800 r contained a mean of 0.6 µg/ml. The values for whole blood declined due to removal of cells in subsequent sampling. (ADD)

1129

Prosser, C. Ladd, Elizabeth E. Painter, and Marguerite N. Swift. **THE CLINICAL PHYSIOLOGY OF DOGS EXPOSED TO SINGLE TOTAL-BODY DOSES OF X-RAYS.** Univ. of Chicago Metallurgical Lab. Dec. 12, 1946. Decl. Sept. 2, 1947. 187p. (MDDC-1272; CH-3738)

The median lethal dose of single exposures of 200 kvp x rays in the dog is approximately 315 r. During the first several hr after receiving a dose in the lethal range, dogs are lethargic, often have diarrhea, and vomit. Blood pressure, heart rate, and temperature remain relatively constant until 10-15 days after treatment, then heart rate and temperature are elevated and blood pressure depressed until death, 3 to 7 days later. Dogs that survive doses of 250 r, or above, usually show a similar rise in temperature for a few days during the same acute period. Detailed information is given on changes in the blood picture including counts of lymphocytes, leucocytes and erythrocytes at various periods after irradiation with from 50 to 350 r, blood sedimentation rates, clotting times, plasma volume and protein contents. Body weight declined very little during the first 7 to 10 days after a midlethal dose but thereafter fell rapidly to a minimum of about 80% of control weight in non-survivors. Some loss in weight by survivors of doses of 100 r and above also occurred in the 10 to 15 day period. Food and water consumption were usually slightly diminished for 1 to 3 days after irradiation and were reduced nearly to zero in the acute "depression" period. Metabolic balance data also indicate an increase in catabolism after irradiation. Fecal output corresponded roughly to food intake, but urine output was diminished much less than was water intake. N balance became negative as food consumption was reduced, and in the terminal period N excretion was relatively undiminished even when N intake was zero. Details in metabolic changes are given and the onset of hemorrhages are described. (TIS)

1130

Quastler, Henry, Elizabeth F. Lanzi, Mildred E. Keller, and James W. Osborne. **ACUTE INTESTINAL RADIATION DEATH. STUDIES ON ROENTGEN DEATH IN MICE. III.** *Am. J. Physiol.* 164, 546-56(1951).

Mice were subjected to x irradiation, delivered in one or two exposures to the whole body or to parts, and the time

elapsing between irradiation and death was recorded. A survival time of $3\frac{1}{2}$ days is stable over a wide range of doses. It occurs with radiation of different qualities, in mice of various strains and different weights. Because of its stability, a survival time of $3\frac{1}{2}$ days is considered a manifestation of some intrinsic property of mice, and called a characteristic value of the response spectrum. If a dose which will produce death in $3\frac{1}{2}$ days has been given, additional irradiation does not further reduce the life expectancy. A mouse can be made to die $3\frac{1}{2}$ days after a small dose has been given if a supplementing treatment with a large dose is given within a certain time, which depends on the amount of the small dose. In order to produce the reaction which supersedes the $3\frac{1}{2}$ -day process after large doses, it is necessary and sufficient to irradiate the head. In order to elicit the $3\frac{1}{2}$ -day process, it is necessary and sufficient to irradiate any portion of the intestine. (NSA)

1131

Rekers, Paul E. INDUCED PREGNANCY IN A MAMMALIAN HOST FOLLOWING SEVERE TOTAL BODY X-IRRADIATION. *J. Lab. Clin. Med.* **37**, 331-41(1951).

Pregnancy was readily and naturally induced in dogs after large doses of total-body irradiation of LD₅₀ or more. A full-term, viable pup was whelped from the dam receiving the largest dose of irradiation. A second dam aborted following a pulmonary infection. The third dam delivered three living pups, one of which was underdeveloped and succumbed. This dam and the two offspring have remained well. During the gestation period of 50 days or more there were normal gross alimentations, constant weights, and varying degrees of depression of the peripheral blood elements without bacterial invasion of the blood stream or intravascular hemolysis. After whelping or aborting there was a rapid decline in the physical condition of two of the three dams, subsequent death, and the findings of sepsis and degeneration including the hemopoietic tissues. From the data presented it does not appear that fetal tissue provided an active hemopoietic center for the irradiated dam. The question, however, of the protective action of embryonic tissue for maintaining resistance to infections and of benefit from fetal endocrine or enzyme systems is raised. 29 references. (NSA)

1132

Rosenthal, Robert L. OPALESCENCE OF SERUM AFTER TOTAL BODY RADIATION AS A PROGNOSTIC SIGN OF DEATH. *Science* **110**, 43-4(1949).

During an investigation of the clotting reaction of blood after irradiation with 200 kv x-rays, the appearance of a marked opalescence was noted in the serum and plasma of rabbits which subsequently died a few days after exposure to a single lethal dose of total body irradiation.

This opalescence appeared within 24 hours following exposure to radiation. In all cases, it disappeared completely 72 hours after exposure. A review of the literature failed to reveal any mention of this phenomenon. An attempt was made to find a correlation between varying intensities of the opalescence and the death rate of the rabbits. At present, there is no clear explanation of the mechanism by which radiation produces this opalescence. In view of its apparent relation to death, this phenomenon may not only provide a valuable early measurement of the effect of acute exposure to radiation, but may lead to further knowledge concerning the nature of radiation sickness and its lethal mechanisms. (NSA)

1133

Shacter, Bernard. EFFECT OF X-RADIATION AND OF RADIOMIMETIC SUBSTANCES ON THE SULFHYDRYL CONTENT OF PLASMA: RELATIONSHIP TO ADRENAL

ACTIVITY FOLLOWING STRESS. *Cancer Research* **11**, 277-8(1951).

An abstract of this paper appeared in *Cancer Research* **11**: 277-8(1951) and is reproduced here in part.

A study was undertaken on the effects of x radiation and of radiomimetic substances on the sulfhydryl content of rat plasma. In addition, because of the possible relationship between sulfhydryl groups and adrenal activity, the effect of adrenalectomy and of sham operation on plasma sulfhydryl levels was also determined. Exposure of rats to 750 r total body x radiation was followed after several days by a marked decrease in the sulfhydryl content of the plasma. Similar effects were observed following administration of the radiomimetic substances, nitrogen mustard and tris-ethylene triazine. A decrease in plasma sulfhydryl levels was observed within 24 hr after surgical treatment of rats. Since the plasma sulfhydryl changes occurred concomitantly with the initiation of active tissue regeneration, it is suggested that decreased plasma sulfhydryl levels may be indicative of an increased demand for sulfhydryl groups in tissues during periods of accelerated cellular proliferation, and that the plasma proteins may serve as sources of sulfhydryl groups for tissue requirements. (NSA)

1134

Smith, D. E., G. Svihla, and H. M. Patt. THE EFFECTS OF X-RADIATION ON CIRCULATION IN THE WING OF THE BAT. *Physiol. Zool.* **24**, 249-57(1951).

Direct observations and cinemamicrophotographs were made of the blood vessels in the wing of the living bat, *Myotis lucifugus*, each day following total body irradiation and following local irradiation of a portion of the wing. No circulatory changes were noted after total-body irradiation with dosages of less than 10,000 r. Doses over the range of 10,000 r to 60,000 r elicited sticking of leucocytes to blood vessel walls, aggregation of red cells into clumps and stagnation of blood. No other changes were seen. In the areas locally irradiated no alterations in circulation were noted following dosages of less than 50,000 r. After 50,000 r to 5,000,000 r leukocyte sticking, red cell clumping, white cell clumping, platelet thrombi and stagnation of blood occurred. With the exception of red cell clumping the various intravascular changes were quantitatively related to radiation dosage. The authors discussed the significance of the several intravascular reactions in relation to the stagnation of blood. (auth)

1135

Soberman, Robert J., Richard P. Keating, and Roy D. Maxwell. EFFECT OF ACUTE WHOLE-BODY X-IRRADIATION UPON WATER AND ELECTROLYTE BALANCE. *Am. J. Physiol.* **164**, 450-6(1951).

Simultaneous repeated measurements of total body water, extracellular space, sodium space, whole blood, red cell, and plasma volumes, and plasma electrolytes were carried out in adult female dogs following 450- to 500-r whole-body x irradiation. Except for an increase in plasma volume and a decrease in red-cell volume, no consistent changes were noted in any of the determinations. (NSA)

1136

Tullis, John L. THE RESPONSE OF TISSUE TO TOTAL BODY IRRADIATION. *Am. J. Pathol.* **25**, 829-52(1949).

Two series of experiments involving whole body irradiation of swine are described and the results are discussed. The results of the Bikini atomic bomb experiments were found to be similar to experiments performed separately at the Naval Medical Research Institute (experiments which consisted of irradiating swine from a 100 kv source with no filtration, at a distance of 1 m with whole body x-radiations and at a rate of 30 r); in the latter experiments the 50%

lethal dose/30 day period was found to be 275 r measured in air. The lesions produced in both series were characterized by hemorrhage, necrosis and secondary infections; lymphoid cells, myeloblasts, germ cells and intestinal epithelium were found to be particularly radiosensitive, injury to these cells causing anemia and lowering of resistance to infection. Irradiation caused a dilatation of capillaries, and impairment of circulation and tissue anoxia; the pathological state was self-perpetuating. It is concluded that since the most primitive hematopoietic stem cells, the reticular cells, are relatively radio-resistant, the effort to reduce mortality does not appear to be hopeless; management of the effects of total body irradiation should be directed at the prevention of secondary infections, such as pneumonia, which often occur when the organism is in a weakened condition, and the treatment of anemia, impaired circulation and anoxia. (NSA)

1137

Tullis, J. L. and S. Warren. GROSS AUTOPSY OBSERVATIONS IN THE ANIMALS EXPOSED AT BIKINI. A PRELIMINARY REPORT. *J. Am. Med. Assoc.* **134**, 1155-8(1947).

Goats and pigs are approximately as sensitive to total body irradiation as man, guinea-pigs are more sensitive, and rats more resistant. Ionizing radiations were responsible for most of the mortality in the first test, and the animals were sheltered from blast in the second. The deaths which were due to the effects of total body irradiation occurred in the acute phase, and no latent or chronic effects had been observed at the time of the report. Almost all the deaths occurred within one month of the test, the mortality reaching a peak within two weeks of the test. Details of the case histories are given for these animals. The conclusions drawn include the following: (1) the flimsiest of shielding seems to afford ample protection from thermal radiation, but heavy armor does not always protect from the ionizing radiations. (2) An underwater atomic bomb explosion is more lethal than an air explosion, since the spray which showers down on the ships in the vicinity carries with it fission products; these contaminate the ships' surfaces, cannot be removed easily, and remain dangerously radioactive for long periods of time. (TIS)

1138

Van Dyke, D. C. and R. L. Huff. EPILATION IN THE NON-IRRADIATED MEMBERS OF PARABIOTICALLY UNITED RATS. *Proc. Soc. Exptl. Biol. Med.* **72**, 266-9 (1949).

After X-irradiation of one member of parabiotically united rat pairs both members showed marked hair loss. The non-irradiated member lost its hair earlier and to a greater degree than the irradiated member. An effect such as epilation must result from the transfer of material from one member to the other through their common circulation. Whether the epilation represents the passage of physiologically active material from the irradiated to the non-irradiated or is a manifestation of loss of material from the non-irradiated to the irradiated is not demonstrated. (BA)

1139

Wilder, Helenor Campbell and Russell M. Maynard. OCULAR CHANGES PRODUCED BY TOTAL BODY IRRADIATION. *Am. J. Pathol.* **27**, 1-19(1951).

Pathological changes in the eyes of 21 goats and 31 pigs receiving varying amounts of total-body ionizing radiations at Operations Crossroads, Bikini, have been compared with those in the eyes of 24 pigs exposed to 200 to 600 r of total-body roentgen radiation and of 4 fetuses from x-irradiated sows. Nine control goats and 15 control pigs were examined. The pathological changes in the bomb-exposed and x-irradiated animals were similar. For the most part, they

were regarded as results of bone marrow depression and secondary systemic changes, rather than as direct effects of the rays. The hemorrhages were attributed to thrombocytopenia and to a heparin-like substance. Serous exudates were the result of increased vascular permeability, possibly secondary to anemia. Septic choroiditis and bacteria in the vessels were manifestations of the septicemia. Vacuoles were present in the lenses of many of the irradiated animals but were found also in the controls and therefore were not regarded as a specific manifestation of irradiation. Massive cataract in irradiated animals may have been due to direct radiation, although secondary nutritional effects associated with anemia and severe hemorrhages could not be ruled out. Immediate changes in the lens specific for irradiation were not apparent in the young or mature animal. Although the secondary effects of ionizing and roentgen radiation were similar in the eyes of both pigs and goats, there were no ocular changes which could be attributed to unequivocally to direct irradiation. 11 figures. (NSA)

Prophylaxis and Therapy—General Reviews

1140

Allen, J. G., P. V. Moulder, and D. M. Enerson. PATHOGENESIS AND TREATMENT OF THE POSTIRRADIATION SYNDROME. *J. Am. Med. Assoc.* **145**, 704-11(1951).

The postirradiation syndrome is characterized by infection, hemorrhage, anemia, and malnutrition. Progress has been made in the treatment of these important disorders, and there is reason to anticipate even better results when several rational therapeutic programs are combined. Anemia can be controlled by blood transfusion, but this does not increase the platelet or leukocyte counts. Transfusion alone did not increase the survival period in our dogs irradiated with 450 r, although it may appear more beneficial in less serious exposures. Transfusion every second day plus daily doses of aureomycin, however, did increase the survival time, and two of 11 animals so treated have survived the critical period of 6 weeks. The general nutritive status of the person can be cared for orally for 1 or 2 weeks after exposure, but there after parenteral feeding may be necessary for several weeks. Frequent transfusion of blood and probably plasma are perhaps the best means to achieve this end. This is a new and serious problem which is largely foreign to previous experiences in burn therapy of nonirradiated persons, for whom extensive oral feedings are generally possible. Irradiation injury is a systemic disease. Wounds, burns, and other injuries must be considered in the light of the entire body economy, for the careful management of local wounds is of little consequence if the subsequent general physiological disorders are not taken into account. (Authors' Summary)

1141

Brues, Austin M. THE NATURE AND THERAPY OF RADIATION SICKNESS. *Chicago Med. School Quart.* **11**, 105-8(1950).

A description is presented of some of the symptoms present in humans after atomic irradiation. Leucopenia, epilation, sterility, and keloids are mentioned in connection with the chronic and acute forms of radiation sickness. Such methods of therapy as blood transfusion, injection of toluidine blue, general supportive measures, and injections of antibiotics are named and outlined. Pretreatment with cysteine and phenylhydrazine is mentioned; the radiosensitivity of tissues and genetic mutation are briefly considered. (NSA)

1142

Lacassagne, A. CONCERNING RECENT RESEARCH ON

PROTECTION AGAINST HIGH-INTENSITY WHOLE-BODY EXPOSURE TO PENETRATING RADIATIONS. Fortschr. Gebiete Röntgenstrahlen 75, Suppl., 98-105 (1951).

The author reviews the investigations carried out since 1909 on chemical prophylaxis and treatment of radiation sickness and describes an experiment of his own in which adult rats were injected with Loiseau's solution (glucose, cysteine, thiourea, ascorbic acid, and succinic acid) 15 min before or after x irradiation with 666 to 836 r. Histological observations are reported briefly. The lower mortality of the treated animals is apparently caused by survival of a greater number of stem cells in the hematopoietic tissue. 53 references. (NSA)

1143

Langendorff, H. **CHEMICAL PROPHYLAXIS OF RADIATION INJURIES.** Strahlentherapie 85, 391-400(1951).

When acting on higher organisms, high energy radiations always produce a local radiation injury and also a general stress situation caused by the upset of interaction between the vegetative nervous system and endocrine gland function. The prophylactic action of certain chemicals is explained: cysteine, glutathione, p-chloromercuribenzoate, BAL, KCN, and HgCl effect cell reactions locally; general stress-damping effects result from usage of doca (desoxycorticosterone acetate), rutin, pyridoxin (Vitamin B₆), nicotinamide, d-catechol, and antibiotics. The importance of compounds protecting free SH-groups is stressed. (NSA)

1144

Selle, W. A. **ATTEMPTS TO PREVENT AND COUNTER-ACT EFFECTS OF IONIZING RADIATIONS BY CHEMICAL AND PHARMACOLOGICAL MEANS.** NEPA Div., Fairchild Engine and Airplane Corp. Sept. 15, 1949. 30p. (NEPA-1127)

The purpose of this report is to summarize available information concerning attempts to prevent or reduce radiation injury by pharmacological means. The pathogenesis of lethal and sublethal radiation exposures, and the theories and therapies of radiation sickness are discussed. The effects of the following agents on human radiation sickness are summarized in tabular form: desoxycorticosterone acetate and pyridoxine; antihistaminics, vitamins, and miscellaneous drugs; antihistaminics, transfusions, and antihemorrhagic substances; ascorbic acid, riboflavin, thiamin, nicotinamide, and nucleic acid compounds; rutin and related drugs; folic acid; adrenal cortex, desoxycorticosterone, and related drugs; estrogens and other sex hormones; cysteine, cystine, and glutathione; and penicillin and blood transfusions. (NSA)

Anoxia

1145

Bennett, Leslie R., Sarah M. Chastian, Jerry S. Flint, Robert A. Hansen, and Alvin E. Lewis. **LATE EFFECTS OF ROENTGEN IRRADIATION; I. STUDIES ON RATS IRRADIATED UNDER ANOXIC ANOXIA.** Univ. of Calif., Los Angeles. Sept. 7, 1951. 24p. (UCLA-154)

Late effects have been studied to 540 days in rats receiving 600 to 1400 r of whole-body roentgen irradiation under anoxia and surviving the acute post-irradiation period. The findings were marked shortening of life span, high death rate due to pneumonia with a rather specific cellular type in the granuloma, nephrosclerosis and generalized arteriosclerosis, hypertension, blood dyscrasia characterized by thrombocytopenia and anemia (possibly suggesting hypersplenism), cataracts in the animals sur-

viving 10 months or more, general cachexia, and late epilation over head and back. (NSA)

1146

Bennett, Leslie R., Robert A. Hansen, and Andrew H. Dowdy. **THE EFFECT OF ANOXIA ON THE HEMATOLOGICAL INJURY IN RATS CAUSED BY ROENTGEN IRRADIATION.** Univ. of Calif., Los Angeles. Sept. 12, 1951. 18p. (UCLA-156)

Hematograms were made on rats following 500 or 1000 r of whole-body x irradiation administered while the animals were subjected to extreme anoxic anoxia (4% O₂). The results showed that the peripheral blood elements receive a partial degree of protection under these conditions. (NSA)

1147

Dowdy, Andrew H., L. R. Bennett, and Sarah M. Chastian. **PROTECTIVE ACTION OF ANOXIC ANOXIA AGAINST TOTAL-BODY ROENTGEN IRRADIATION OF MAMMALS.** Radiology 55, 879-85(1950).

The effects of brief extreme anoxic anoxia on the LD₅₀ and on the radiation syndrome observed in mammals after total-body roentgen irradiation has been investigated. The 30-day LD₅₀ for rats irradiated in 5% oxygen appears to be between 1200 and 1400 r as contrasted with an LD₅₀ of slightly higher than 600 r in irradiated control rats. Anoxia produced by injection of NaCN failed to protect rats from roentgen irradiation. These experiments support the theory that radiochemical reactions involving free oxygen play a vital role in radiation injuries. (NSA)

1148

Lacassagne, A. **LACK OF SENSITIVITY TO X-RAYS ON THE PART OF NEWBORN MICE IN A STATE OF ASPHYXIA.** Compt. rend. acad. sci. U.R.S.S. 215, 231-2 (1942).

For newborn mice sensitivity to X-rays was reduced by exposure to a temperature just below 0°, by N asphyxia and by CO₂ asphyxia. (CA)

1149

Limperos, George. **EFFECTS OF VARYING OXYGEN TENSION ON MORTALITY OF X-RAYED MICE.** J. Franklin Inst. 249, 513-4(1950).

Oxygen tension is reported to play an important part in the biological effects of x radiation. The production of H₂O₂ and HO₂ and the "release" of the OH radicals from a back reaction may account for increased mortality of mice x rayed under a higher-oxygen atmosphere. The low-oxygen atmosphere exerts a protective effect possibly because it decreases the concentration of OH and HO₂ radicals and of H₂O₂. (NSA)

1150

Smith, D. E., H. M. Patt, and Ella B. Tyree. **PROGRESS REPORT; THE EFFECT OF ANOXIA UPON THE SURVIVAL OF ADULT FROGS AND DAY-OLD RATS,** p.53-6 of BIOLOGICAL AND MEDICAL DIVISIONS, QUARTERLY REPORT FEBRUARY, MARCH, APRIL, 1950. Argonne National Lab. [nd] 4p. (ANL-4451(p.53-6))

Pairs of male frogs (*Rana pipiens*) were exposed to total-body x radiation consisting of single doses of 3000, 6000, or 12,000 r. One of each pair was subjected to anoxia in 100% N₂ during irradiation while the other was irradiated in room air. Daily checks on mortality indicated that subjecting frogs to anoxia during x irradiation does not alter their radiosensitivity as measured by survival. One-day-old Sprague-Dawley rats were given single total-body doses of 500 r in 100% N₂ or in 20% O₂-80% N₂. Sixteen of the 17 rats exposed in 100% N₂ were surviving at 20 days post-irradiation, while none of 17 irradiated in the 20% O₂-80% N₂ mixture were alive. Death in the con-

trol group occurred from the 9th to the 13th day after x irradiation. It appears that the survival of one-day rats is greatly increased by anoxia during irradiation.

1151

Smith, Willie W., Robert Dooley, and Edwin C. Thompson. **SIMULATED HIGH ALTITUDE FOLLOWING WHOLE-BODY RADIATION OF MICE.** *J. Aviation Med.* **19**, 227-37(1948).

Mice exposed to single doses of 400 to 500 r were subjected to simulated high altitudes of 20,000 to 25,000 feet at periods of 1 to 6 days after irradiation while circulating leukocytes were undergoing reduction, and after 10 to 12 days when platelets and erythrocytes were greatly reduced. Radiation was given at the rate of 64 r/min. (189 kvp, 20 ma, and 0.25 mm of copper and 0.55 mm of aluminum added filtration). Five litter-mate pairs were kept in each cage and irradiated simultaneously. One from each pair was taken for the ground group (total 336) and one for the altitude group (total 341). Several non-irradiated mice were always subjected to altitude with the exposed groups. The extent of damage was determined by weight loss, deaths, and hematological changes. There was no evidence found that altitude adversely affected the probability of survival nor did it affect the total or differential counts of circulating leukocytes when they are maximally reduced. The course of diminution and recovery of platelets, erythrocytes, and hemoglobin was not altered by altitude. It is pointed out that the conclusions relative to the absence of altitude effect are based on results with high energy radiation alone, where no vascular effects were observed such as would result from flash burns occurring after atomic bomb detonations. (NSA)

Antibiotics

1152

Arons, Isidore and J. W. Freeman. **THE USE OF AUREOMYCIN AS AN ANTIDOTE IN RADIATION SICKNESS.** *Harlem Hosp. Bull.* **3**, 123-6(1950-51).

The authors studied the effect of aureomycin on five patients with radiation sickness who did not respond to pyridoxine or to the combined use of penicillin and sulfathalidine. All of the patients responded favorably to the treatment. The authors conclude that although there are several therapeutic agents which, when administered prior to therapy, are capable of preventing radiation sickness, aureomycin apparently is the only drug which can bring about regression of all the symptoms once they have become manifest. (S.V.S.)

1153

Felsenfeld, Oscar, Sachiko Janet Ishihara, Thora Waters, and Jeannette Norsen. **IRRADIATION DAMAGE TO MICE.** *Lab. Digest* **14**, 18-19(1951).

Experiments were conducted to examine the influence of some antibiotics on radiation sickness in mice. The results show that the number of surviving animals after the irradiation, which was an approximate of LD₅₀, was significantly increased when given Neomycin, Glucomycin, Neobacin, or Prodigiosin in doses which would be well-tolerated by humans. Thus oral treatment of bacteremia resulting from total-body irradiation is possible. (NSA)

1154

Furth, F. W. and M. P. Coulter. **THE EFFECT OF AUREOMYCIN ON THE RADIATION SYNDROME IN DOGS.** *University of Rochester.* Dec. 15, 1950. 18p. (UR-146)

Observations are presented on a group of 24 dogs that were exposed to 450 r of 250-kv x radiation. One-half of

these dogs received aureomycin, 100 mg/kg daily beginning immediately after irradiation and continuing for 28 days. The remaining dogs served as controls. Dogs treated post-radiation with clinical doses of aureomycin have shown decreased mortality as compared with the control animals. The onset of morbidity and mortality was delayed for 5 to 7 days in the treated dogs. Pathological studies revealed severe gastrointestinal hemorrhage and ulcerations of the small intestine in the control dogs and minimal gastrointestinal hemorrhage and absence of small-bowel ulcerations in the treated dogs. Bacteriological studies showed a greater number of positive blood cultures in the control animals post-radiation than in the treated animals. Bacteria recovered from autopsy material from the control dogs were sensitive to aureomycin, while those recovered from the treated dogs were resistant to aureomycin. (NSA)

1155

Furth, F. W., M. P. Coulter, and J. W. Howland. **FAILURE OF ALPHA TOCOPHEROL TO PROTECT AGAINST RADIATION INJURY IN THE RAT,** p.34-8 of **QUARTERLY TECHNICAL REPORT; OCTOBER 1, 1950, THRU DECEMBER 31, 1950.** *University of Rochester.* Feb. 1, 1951. 5p. (UR-152(p.34-8))

The administration of large amounts of alpha tocopherol or aureomycin just previous to exposure to large doses of x radiation fails to alter the lethality of the irradiation in rats. The experimental method is described, with results shown by a graph. (NSA)

1156

Furth, F. W., M. P. Coulter, and J. W. Howland. **EFFECT OF CRUDE AND CRYSTALLIZED AUREOMYCIN ON THE WEIGHT OF NORMAL AND X-RADIATED RATS,** p.39-43 of **QUARTERLY TECHNICAL REPORT; OCTOBER 1, 1950, THROUGH DECEMBER 31, 1950.** *University of Rochester.* Feb. 1, 1951. 5p. (UR-152-(p.39-43))

Aureomycin administered orally in either the crude or crystalline form failed to increase the weight gain of normal or x-irradiated rats, although the incidence of diarrhea in the x-irradiated rats was markedly diminished. (NSA)

1157

Gustafson, Gordon E. and Simon Koletsky. **EFFECT OF ORAL TERRAMYCIN PRIOR TO WHOLE BODY X-RADIATION.** *Proc. Soc. Exptl. Biol. Med.* **78**, 489-90 (1951).

Terramycin has been shown to be effective in reducing the mortality in rats when administered for a period of only 48 hours prior to 660 r of whole body x-radiation. (Authors' Summary)

1158

Hammond, Carolyn W. and C. Philip Miller. **THE EFFECT OF TERRAMYCIN ON POST-IRRADIATION INFECTION IN MICE.** *Ann. N. Y. Acad. Sci.* **53**, 303-8 (1950). (AECU-873)

Cultures of heart's blood and spleen of mice subjected to a single dose of x-radiation showed a high incidence of bacteremia during the second week, the period of greatest mortality. The septicemia was caused by microorganisms normally present in the lower bowel of the stock mice. In a majority of animals, the infection was severe enough to be regarded as an overwhelming sepsis. The administration of terramycin protected irradiated mice against the septicemia occurring the second week post-irradiation, unless it was caused by terramycin-insensitive bacteria. The most common of these was *Pseudomonas* against which no antibiotic or combination of antibiotics tested

thus far has been found to be effective. Preliminary experiments suggest that the administration of streptomycin together with terramycin may prove more effective than terramycin alone in controlling infections caused by drug-sensitive organisms. (NSA)

1159

Howland, Joe W., Frank Furth, L. R. Bennett, Molly Coulter, and G. M. McDonnel. STUDIES ON FACTORS EFFECTING THE RADIATION SYNDROME I THE EFFECT OF AUREOMYCIN AND ANTIBIOTICS ON WHOLE BODY IRRADIATION. University of Rochester. Oct. 14, 1949 35p (UR-94)

Results are presented in considerable detail on the exposure of more than 600 rats and 8 dogs to lethal doses (LD_{90-100}) of 250 kvp x-radiation. Observations of the treatment of a proven lymphoma (Hodgkin's type) of liver and spleen are also given. Clinical doses of aureomycin given therapeutically to rats in the diet or drinking water can cause almost complete alleviation of the diarrheal state following lethal doses (LD_{90}) of 250 kvp x-radiation. As such it is superior, to date, to other antibiotics tested, including chloromycetin, streptomycin, sulfadiazine, and penicillin. Survival of life is prolonged an additional 5 to 7 days. The animals die of a hemorrhagic death which is not considered to be typical of a radiation death for this species. Animals may regain pre-radiation weights as early as 3 or 4 days following the exposure. Bacteriological studies indicate a suppression of the normally occurring gram negative organisms in the intestinal tract. Possible causes of the sudden mass mortality are discussed. Dogs treated with clinical doses of aureomycin or combined aureomycin-streptomycin have definitely shown no evidence of radiation sickness and have had bleeding tendencies associated only with local trauma. Three of six animals treated in this manner have survived cumulative doses of as much as 750 r in the last 14 months, including 450 r at the time of the experiment. Pathological findings in the late deaths resemble somewhat atypically those noted in the hemorrhagic period for the species 14 to 28 days. Bacteriological studies show depression of sensitive organisms. The case history of one patient with proved lymphoma of Hodgkin's type is included. From a careful study of the presented data one can state that a favorable step has been made toward the understanding of the radiation sickness which follows localized abdominal irradiation in the human subject under treatment for malignancy of the abdominal viscera and adjacent areas. Caution is advised in the further treatment of human cases before a better understanding of the nature of the coagulation of abnormality is determined. An analysis of the physiological approach necessary in the study of the biological effects of penetrating ionizing radiation is given. (NSA)

1160

Howland, Joe W., Frank Furth, and Molly Coulter. THE EFFECT OF AUREOMYCIN AND ANTIBIOTICS ON WHOLE BODY IRRADIATION. Federation Proc. 9, 334 (1950) (AECU-748)

The document is in abstract form; it is reproduced below in its entirety.

Results are presented on the exposure of more than 1,200 rats and 18 dogs to lethal doses of filtered 250 kvp x-radiation. Clinical doses of aureomycin or other combined antibiotics given to rats after lethal x-radiation results in almost complete alleviation of the diarrheal state. Survival of life is prolonged an additional 5 to 7 days. Animals die of a sudden hemorrhagic death. Preradiation weight may be regained as early as 4 days after exposure. Bacteriological studies show suppression of normally occurring gram-negative organisms in the intestinal tract.

Dogs treated with only clinical doses of aureomycin (equivalent to 50 to 100 mg/kg) or combined aureomycin-streptomycin have shown no evidence of radiation sickness. Occasional bleeding tendencies are associated only with local trauma. Survival of life is prolonged from 10 to 14 days. Deaths in control animals occur between the 10th to 14th day; in treated animals, after the 22nd day. Mortality in the dog is considerably improved. To date all dying treated animals have shown sepsis with aureomycin- or streptomycin-resistant organisms 48 hr before death, with the same organism being cultured post-mortem from all tissues examined. Pathological findings in the treated animals have not been, in general, typical of radiation disease. Lesions of the gastrointestinal canal have not been observed in the treated animals. Bacteriological observations indicate a general alteration in the bacterial flora of the intestinal canal with a suppression of gram-negative organisms.

1161

Howland, J. W., F. W. Furth, and M. P. Coulter. EFFECT OF TERRAMYCIN ON ACUTE RADIATION SYNDROME IN DOGS. Federation Proc. 10, 67(1951).

This report is reproduced here in its entirety.

During the course of investigations on the role of infection in the acute radiation syndrome in dogs various antibiotics have been administered to dogs which have received large doses of x-radiation. Previous investigations showed that aureomycin reduced the morbidity and mortality of the acute radiation syndrome in dogs. Terramycin has a similar effect. Twenty-seven adult mongrel dogs were exposed to a single dose of 450 r of x-radiation from a 250 kv source. Immediately after irradiation 14 of the animals were started on a dose of approx. 100 mg/kg/24 hours of terramycin administered in divided doses every 6 hours for 28 days. The remaining 13 dogs served as controls. By the 60th day post-radiation 12 (92%) of the control dogs had died whereas 7 (50%) of the treated dogs had died. A delay of 4-5 days in the onset of mortality in the treated group was found. The dogs in the treated group did not appear as sick as those in the control group. Blood cultures on both groups of dogs showed no significant difference in the incidence of positive cultures between the groups. No significant difference in the decrease in peripheral blood elements or in weight loss was noted in the two groups.

1162

Koletsky, Simon and James H. Christie. EFFECT OF ANTIBIOTICS ON MORTALITY FROM INTERNAL RADIATION. Proc. Soc. Exptl. Biol. Med. 75, 363-6(1950). (NYO-1614)

Streptomycin and penicillin in combination proved effective in reducing the mortality of rats given lethal doses of radioactive phosphorus. Morbidity was also reduced and survival time prolonged. (NSA)

1163

Lambert, G., J. Maisin, M. Mandart, E. Pluygers, and G. Podio. EFFECT OF PERORAL ADMINISTRATION OF AUREOMYCIN ON THE SURVIVAL OF RATS EXPOSED TO LETHAL DOSES OF X RAYS. Compt. rend. soc. biol. 144, 1558-60(1950).

Severe leukocytopenia, observed in animals submitted to lethal x-ray doses, points to infection as a possible cause of death. Rats totally irradiated with 500 and 600 r received aureomycin hydrochloride (6 mg twice daily) by mouth until death, or until the 21th day in cases of long survival. Although in the 500-r group this treatment produced a notable increase in the survival rate, no favorable result was observed in the 600-r group. (NSA)

1164

Miller, C. Phillip, Carolyn W. Hammond, and Marianne Tompkins. **THE TREATMENT OF POST-IRRADIATION INFECTION.** Chicago Univ. [nd] 16p. (AECU-1816)

These experiments seem to demonstrate that generalized infection played a significant role in the death of mice exposed to moderate doses of total-body x radiation. Infection was caused by bacteria belonging to the intestinal flora. Treatment with antibiotics reduced the mortality to a significant degree; and, among the antibiotics tried, streptomycin was the most effective. Next in order of effectiveness were chloroamphenicol, aureomycin, and terramycin, among which there was no demonstrable difference in therapeutic value. (NSA)

1165

Miller, C. Phillip, Carolyn W. Hammond, and Marianne Tompkins. **REDUCTION OF MORTALITY FROM X-RADIATION BY TREATMENT WITH ANTIBIOTICS.** Science 111, 719-20(1950) (AECU-738)

Previous experiments (AECU-739) have suggested that infection might be a significant factor in death from radiation injury. An attempt has therefore been made to reduce the mortality from x-radiation by controlling the bacteremia by the administration of antibiotics. Treatment with streptomycin alone or combined with penicillin caused a significant reduction in the mortality (30 days) of mice following total body x-radiation with 450 r. Chloroamphenicol although somewhat less effective was the best of the other antibiotics tested. (NSA)

1166

Miller, C. Phillip, Carolyn W. Hammond, Marianne Tompkins, Gertrude Shorter, George A. Sacher, Sylvanus A. Tyler, and Joan Gurian. **THE TREATMENT OF POST-IRRADIATION INFECTION WITH ANTIBIOTICS; AN EXPERIMENTAL STUDY ON MICE. PART I AND PART II.** Institute of Radiobiology and Biophysics, Univ. of Chicago. [nd] 65p. (AECU-1730)

Young adult mice were subjected to total-body x radiation in a single exposure, varying from 450 to 600 r. After irradiation the mice were treated daily with antibiotics; one only or several in combination were used. Streptomycin, given by subcutaneous injection, decreased mortality from 73% in control animals to 14%. Penicillin given in addition to streptomycin did not increase its effectiveness. Chloramphenicol, aureomycin, and terramycin (mixed in food) caused significant reductions in mortality; their supplementation by daily injections of streptomycin during the second and third weeks post-irradiation increased the protection. Neomycin was ineffective, polymyxin too toxic. Infections or epidemics by drug-resistant strains could not be controlled by the antibiotics used and the importance of infection as a lethal factor in mice exposed to moderate doses of x radiation is stressed.

Data on the effects of various patterns of antibiotic therapy on the survival of mice following a fixed dose of x rays were subjected to biometric analysis. Streptomycin dosages ranging from about 3000 to 6000 units per day were protective to the same degree. Penicillin plus streptomycin alone. Aureomycin, chloramphenicol, and terramycin, all supplemented with streptomycin, conferred about equal degrees of protection. The measure of protection employed was the difference of probits of mortality for control-therapy cage pairs. This measure was validated by an analysis of the relation between per cent mortality in cages and mean survival time of decedents. The probit difference was shown to have a small positive regression on level of killing in cages. (NSA)

Antihistamines

1167

Beeler, John W., Jan H. Tillisch, and Walter C. Popp. **A NEW DRUG IN THE TREATMENT OF RADIATION SICKNESS.** Proc. Staff Meetings Mayo Clinic 24, 477-83(1949).

A description of a new drug, dramamine (β -dimethylaminoethylbenzohydryl ether 8-chlorotheophyllinate) for the treatment of radiation sickness is presented; the similarity between the symptoms of motion and radiation sickness suggested the use of dramamine for the latter. Excellent results were obtained in 25% of the 82 cases treated, while good results were shown in 53%; maximal effectiveness was achieved when 100 mg of the drug was given 30-60 minutes before the radiation treatment and repeated 1.5 hours and 4.5 hours after treatment, for a total dosage of 300 mg. One or more of the side reactions such as drowsiness, "bad taste," paresthesias, and nausea occurred in about 30% of the cases. It is concluded that a combination of dramamine and pyroxidine should be of valuable therapeutic aid in the control of radiation sickness, especially in severe cases. (NSA)

1168

Brown, W. M. Court and R. B. Hunter. **ANTI-HISTAMINE DRUGS AND RADIATION SICKNESS.** Brit. Med. J. 116, 984(1948).

It had been claimed by some that radiation sickness is due to histamine release and that antihistamine drugs alleviate this condition. The authors experimented with neoantergan in radiation sickness. One group of 17 patients was given 600 to 1,000 mg of the drug daily for five days before radiation, another group, of 15, placebo tablets, and a third group no medication at all. Irradiation symptoms occurred in 94.1% of the group treated with neoantergan, actually a higher incidence than in the other groups. Between the 3rd and 5th days following the radiation, five of the neoantergan group developed a rash between the shoulder blades which persisted until the neoantergan was discontinued. The eruption may be due to the toxic action of the rays on tissues which normally would protect themselves by a defense mechanism. In the presence of the antihistaminic drug the defense mechanism may not operate, so that the toxic effect is increased. (EM)

1169

DeFeo, Edward, Paul H. Reitman, and M. Herbert Nathan. **RADIATION SICKNESS AND ITS TREATMENT WITH DRAMAMINE.** Radiology 56, 420-2(1951).

One hundred patients were given dramamine as soon as symptoms of radiation sickness appeared following radiation treatments. In only 46 of these patients was any improvement noted following treatment with dramamine. One-half of this number had no recurrence of symptoms after administration of the drug for 1 day (400 mg). In the remainder, it had to be given daily throughout the period of irradiation. In the latter group symptoms recurred on an average of 2.1 days after the drug was discontinued. Because of this recurrence of symptoms, it was possible to observe the effect of placebos given at intervals during irradiation in 24 of the 46 patients claiming improvement with dramamine. The placebo was identical in appearance and taste to the drug. Seventeen of the 24 patients (70%) did as well with the placebo as with the drug itself, reducing the actual number of patients whose improvement could be credited to dramamine to 29. These results emphasize the important role of psychogenic factors in radiation sickness, and the care which must be exercised in drawing conclusions as to the effectiveness of any drug in a syndrome in which criteria of improvement are

mainly subjective. In 11 of the cases dramamine produced undesirable side effects, consisting of intense drowsiness in 6, giddiness in 3, and a metallic taste in 2. The drowsiness was of such a degree that the medication had to be discontinued, since this side effect was more debilitating than the radiation sickness. As a result of this experience the authors believe that the effectiveness of dramamine in radiation sickness is proportional to its antihistaminic effect. It is generally known to be one of the less effective of the antihistamines. The problem of radiation sickness will not be solved until there is more general agreement as to its cause. Only then can treatment be directed to the underlying factors and not to the symptoms alone. (NSA)

1170

Fetzer, H. and E. Werle. X-RAY SICKNESS TREATED WITH ANTISTINE. *Strahlentherapie* **78**, 619-24(1949).

12 patients with a marked irradiation syndrome (X-ray sickness) after heavy X-ray irradiation were treated with antistine; 11 of them responded very well. It is questionable if the influence of antistine is predominantly histamine—antagonistic. Like the other antihistamine substances, antistine also influences the cholinesterase—acetyl choline system by inhibiting cholinesterase and by decreasing the reaction on the organs affected by acetylcholine. (EM)

1171

Field, John B. and Paul E. Rekers. A PROPHYLACTIC APPROACH TO THE ANAPHYLACTIC FACTORS IN IRRADIATION DISEASE. *Lancet* **254**, 489(1948) (MDDC-1658; M-2009)

Both of two dogs each given 25 mg benadryl or pyribenzamine three times daily beginning two weeks prior to exposure with 350 r single dose total body x-irradiation succumbed with typical severe signs of radiation disease. This compares with a mortality of 64% (16 of 25) untreated dogs. Five of 10 rats given approximately 20 mg pyribenzamine daily succumbed 15 days after exposure to 750 r single dose total body irradiation compared with the death of 6 of 10 control rats at 10 days. When ethylene disulphonate in distilled water was injected in various schedules, only 2 of 11 (18%) dogs given 350 r single dose whole body x-irradiation succumbed. The treated animals in general had fewer signs of irradiation toxicity. However, when 450 r was the irradiation dose given, 4 of 5 (80%) dogs succumbed compared with 3 of 4 (75%) of untreated dogs. The injection of ethylene disulphonate into rats and rabbits which were irradiated did not affect the extent of toxic signs or the mortality. (ADD)

1172

Gelber, Louis J. THE USE OF ANTIHISTAMINE OINTMENT IN CONJUNCTION WITH DEEP X-RAY THERAPY. *N. Y. Physician* **34**, 22, 24, 46, 48(1950).

A series of experiments was carried out to determine to what degree antihistamine substance in ointment form reduces skin reactions to irradiation and whether or not there is an increase in skin tolerance to irradiation. A total of 31 cases was studied, some with a 1% solution of Euphorbia pilulifera, some with Rayderm Ointment, and some with both agents; irradiation was carried out at 1,300 to 2,200 r in air, the radiation being delivered by a 200-kv machine at a 50-cm target distance through a filtration of 0.5 mm Cu and 1 mm Al. The results of five of the cases are presented in tabular form. It was found that all methods achieved good results, the combined method yielding the most satisfactory results; with it, 2,200 r in air could be delivered with less reaction than 1,300 r without medication. (NSA)

1173

Glenn, J. C. Jr. and R. J. Reeves. TREATMENT OF RADIATION SICKNESS WITH TRASENTINE AND TRASENTINE-PHENOBARBITAL: PRELIMINARY REPORT. *Radiology* **47**, 392-6(1946).

To 65 patients suffering from radiation sickness, trasentine-phenobarbital tablets were given (three 75 mg tablets four times a day up to totals of 1,000 mg). Complete relief of symptoms was obtained in 39 cases, no relief in six. (BA)

1174

Haley, T. J. and D. H. Harris. THE EFFECT OF SEVERAL ANTIHISTAMINIC DRUGS ON MORTALITY DUE TO X-IRRADIATION. *Stanford Med. Bull.* **8**, 1-7 (1950).

A study has been made of the effect of several antihistaminic drugs on mortality due to x-irradiation in guinea-pigs. The drugs investigated were synergistic with the radiation, increasing its lethality. A significant decrease in the coagulation time was observed after antihistaminic therapy in both the medicated and the medicated irradiated groups. The antihistaminic drugs caused a pronounced leukocytosis in normal guinea-pigs that received the drug daily for periods of 14-23 days. Gall bladder rupture and enlargement of the common bile duct and gall bladder were observed in guinea pigs chronically medicated with antihistaminic agents. Pyranisamine was the only drug investigated that caused ulceration and perforation of the stomach. The leukocyte count in x-irradiated, medicated or nonmedicated guinea-pigs follows the pattern seen in other species after irradiation. (AWM)

1175

Hiemisch, Willi. CONTRIBUTION TO THE PATHOLOGY OF GENERAL X-RAY INJURIES, WITH SPECIAL EMPHASIS ON THE ROLE PLAYED BY HISTAMINE. *Strahlentherapie* **84**, 255-71(1951).

A test was made of the theory of Reding and Much which ascribes general injurious actions of x rays to protracted anaphylactic toxic shocks. Since this view is essentially related to another rather widely accepted one of the influence of accumulations of histamine in the body, 20 guinea pigs were submitted, after a determination of their histamine-sensitivity threshold, to a fractionated irradiation leading to the lethal dose. Although the intracutaneous histamine-sensitivity increased 3- to 7-fold, parallel experiments in which protective injections of antistine were made did not show any effect of the latter on the lethal dose. It was concluded that the histamine accumulation did not play a decisive part in the general injury of the body produced by x rays. Death was caused by grave lesions of the blood-forming system; no pathologico-anatomical changes pointed to anaphylactic processes. Views ascribing decisive significance to the latter and to general intoxications in x-ray effects should be rejected. (NSA)

1176

Kullander, S. SOME OBSERVATIONS ON RADIATION SICKNESS AND ITS TREATMENT. *Acta Radiol.* **28**, 221-4(1947).

A definite insufficiency in the production of HCl in the stomach occurs during severe radiation sickness. When HCl is given, the symptoms of radiation sickness disappear. Injections of histamine were also effective in alleviating the symptoms of radiation sickness. These observations definitely contradict the theory that histamine or similar substances are the etiologic factors in the causation of radiation sickness. (BH)

1177

Larkin, John C. EFFECT OF ATROPINE ON ACUTE

IRRADIATION SICKNESS IN MICE Am. J. Roentgenol Radium Therapy 62, 547-9(1949).

Experiments were performed on mice to determine whether the alleviation of the effects of ionizing radiations by antihistamine drugs was due to their anti-histaminic effect or their slight atropine effect. Albino Swiss female mice were irradiated in groups of 10 in a circular chamber by a 200-kv machine; a 1 mm Al filter was used, the distance from the target to the chamber was 30 cm, and the irradiation rate was about 192 r/min. The mice were injected daily, beginning 24 hours before irradiation, with 0.1 cc of a $0.45 \times 10^{-3}M$ solution of atropine sulfate; the injections were continued to the 15th day. The typical signs of irradiation sickness were observed in all of the control mice; in the treated groups, the symptoms were not noted as early, but frequently mice which exhibited no signs of severe irradiation sickness one day, were found dead the following day. When the radiations exceeded 910 r, the treated groups failed to survive, while all of the control groups receiving 740 r perished. The increase in survival rate which was observed in the treated groups is concluded to be greater than chance probability; the average survival time for the lethal dose of 1,152 r was seven days longer for the treated group. It is concluded that: the ionizing radiations must produce multiple injurious reactions; and, the particular effect which atropine produces does not involve the most important of these reactions since the protection afforded by this drug is incomplete. (NSA)

1178

Lofstrom, J. E. and C. E. Nurnberger. **EFFECTS OF RADIATION. IRRADIATION SICKNESS: HISTAMINE EFFECT TREATED WITH BENADRYL; A PRELIMINARY REPORT.** Am. J. Roentgenol. Radium Therapy 56, 211-19(1946).

Relief of severe symptoms of irradiation sickness in 19 cases by administration of benadryl (beta-dimethylaminoethyl) benzyhydrol ether hydrochloride is reported by the authors. The complaints of anorexia, nausea, vomiting, weakness and headache were used as index of the efficacy of the drug. For intravenous injection, 5 to 10 cc (50 to 100 mg) of benadryl was given. Patients thus treated experienced a side reaction consisting of dizziness, unsteady motion, weakness, and drowsiness lasting for one to four hours. Later a general feeling of well-being developed. In seven cases benadryl was given by mouth only, in the form of 50 mg capsules, one every four hours during the day. These patients showed no marked side reactions, and satisfactory relief was obtained in most cases. The causes of irradiation are unknown. There is evidence to suggest that histamine-like bodies are developed in the blood of the patient subjected to roentgen therapy, and the relief afforded by benadryl may be the result of its antihistamine reaction.

1179

Mains, M. P. **ANTI-HISTAMINE OINTMENTS FOR SKIN PROTECTION IN RADIATION THERAPY.** Radiology 52, 579-81(1949).

Some anti-histamine ointments, beneficial in combating radio-dermatitis caused by the release of histamine and histamine-like substances during tissue damage, are discussed. The author advocates the use of Aquaphor as a base for both Benadryl and Pyribenzamine in 5% strength. Using 200 kv at 50 cm target distance with 0.5 mm Cu and 1.0 mm Al filters, 1,800 r in air formerly produced marked skin reactions. Doses as high as 2,400 r in air produce less reaction when the anti-histamine ointments are applied to the treated skin. Examples are given of the beneficial and protective effects of oral and local anti-histamines in specific cases treated by the author. (NSA)

1180

Panzironi, P. E. and E. Zilli. **HISTAMINE AND ROENTGEN INTOXICATION. REPORT ON THE THERAPEUTIC ACTION OF A SYNTHETIC ANTIHISTAMINE PREPARATION: DIMETINA** Nuntius Radiol., Belluno, 13/3-4, 167-85(1947).

After a brief review of the various theories advanced since the beginning of the roentgen period to elucidate the roentgen intoxication an extensive exposition is given of the conception of the occurrence of roentgen intoxication and its various expressions, which are generally accepted today; viz that is to be put down to a toxic state of the organism provoked by histamine or histamine-resembling substances. According to the various theories the therapeutic substances suggested were different, too, until synthetic antihistamine drugs were prepared in connection with the histamine theory. The favorable results obtained by these preparations (the author treated 30 patients with a new synthetically prepared drug, dimentina, with success in 26 patients) are thought to substantiate ex juvantibus the histamine theory of the origin of the roentgen intoxication. (EM)

1181

Salva, J. A. and M. Badell. **TREATMENT OF RADIATION DISEASE BY A SYNTHETIC ANTIHISTAMINIC DRUG.** Presse méd 57, 888(1949).

A study is presented concerning the therapeutic qualities of various antihistamines in the treatment of radiation disease. The case studies are divided into three groups: the prophylactic treatment of the radiation symptoms; the curative treatment of patients exhibiting intolerance to irradiation; and, the treatment of the sequelae of irradiation. Several drugs are discussed; among them are benadryl, neoantergan, and phenergan. The results indicate that treatment by phenergan seems to be effective in relieving the radiation symptoms, the drug is well tolerated and conducive to sleep. Phenergan's influence on the capillary changes produced by various agents is also discussed. (NSA)

1182

Salva, J. A., and M. Badell. **THE CONTRIBUTION OF THERAPEUTICS IN IRRADIATION SICKNESS** Med clin. (Barcelona) 13, 30-3(1949)

Six cases of irradiation sickness caused after anterior irradiation are presented, and the effects of Phenergan on the relief of the radiation sickness syndrome are noted. The Phenergan was administered orally once a day in doses of up to 25 mg; complete radiation protection was afforded by the Phenergan for the radiation doses noted; it was also found that Phenergan was of greater value in the treatment of irradiation sickness than the classical medications and the other antihistamines. (NSA)

Cyanide Studies

1183

Bacq, Z. M. and A. Herve. **CYANIDE AND X-RAYS.** J. physiol. (Paris) 41, 124-5A(1949).

In a previous note it was shown that an injection of 0.1 mg NaCN made immediately before x-irradiation of 580 r reduced to 30% what would have been 100% mortality in mice. New experiments are reported here on mice which received larger doses of NaCN and x-irradiation of 650 r. An injection of 0.1 mg NaCN immediately before irradiation reduced the 100% mortality to 50% while the same amount of NaCN immediately after irradiation delayed the 100% mortality for three to four days; if the injection was made 15 minutes after the irradiation, no reduction in the mortality rate occurred. Sulfocyanide produced no reduc-

tion in mortality when injected before irradiation; when irradiation producing a mortality rate of 10-40% was administered, a prior injection of 0.1-1 mg of the sulfocyanide augmented the mortality rate. The injection of 1 mg of α tocopherol 40 hours and 24 hours before the irradiation reduced to 30% a mortality rate of 60% in the controls. The author's theory of the protective action of these compounds is that important chemical reactions take place in the organism which are influenced by the cyanides; the reactions are connected with the formation of peroxides by x-irradiation and the action of peroxides on the cells of the organism. (NSA)

1184

Bacq, Z. M. and A. Herve. PROTECTION OF MICE AGAINST A LETHAL DOSE OF X RAYS BY CYANIDE, AZIDE, AND MALONONITRILE. *Brit. J. Radiol.* **24**, 617-21(1951).

Cyanides (but not thiocyanate or cyanate), azide (NaN_3) and malononitrile protect a significant percentage of mice irradiated by a single lethal whole-body dose of x rays; these poisons are ineffective when given after irradiation. The protective effect of previously injected glutathione has been confirmed; the action of cyanide is increased by simultaneous administration of glutathione. (NSA)

1185

Bacq, Z. M., A. Herve, J. Lecomte, and P. Fischer. CYANIDE PROTECTION AGAINST X-IRRADIATION. *Science* **111**, 356-7(1950).

Mice of pure breed (C-57 black or A.K.A.), weighing about 30 g and 4 to 6 months old, were irradiated by groups of 10, using 230 kv, 12 ma, copper filter 0.25 mm, focal distance 50 cm, field 100 cm², mean output 30 r/min. The 42 control mice receiving 500 to 600 r all died between the 4th and 8th or 9th day. Animals receiving 0.1 mg NaCN just before similar irradiation showed 50 to 80% survival. The same dose of NaCN given immediately after irradiation only delayed mortality. When the cyanide was injected 15 minutes after irradiation, the mortality curve was exactly the same as that of the controls. This protective action is attributed to the CN anion, and the possible modes of action of this protective factor are discussed. (NSA)

1186

Betz, H. MECHANISM OF THE PROTECTIVE ACTION OF POTASSIUM CYANIDE AGAINST THE LETHAL ACTION OF X-RAYS IN MICE. *Compt. rend. soc. biol.* **144**, 593-5(1950).

In mice exposed to 720 r, an immediately previous injn. of 0.1 mg of KCN intraperitoneally protected against shock and death but did not prevent the cellular lesions in the thymus, lymphatic ganglions, spleen, and testicles which usually appear 1-7 days after the irradiation. (CA)

1187

Betz, H. and L. Fruhling. INFLUENCE OF POTASSIUM CYANIDE ON THE MORTALITY OF MICE X-IRRADIATED IN FRACTIONAL DOSES. *Compt. rend. soc. biol.* **144**, 595-7(1950).

Mice were exposed to 84 r daily for 12 consecutive days, with intraperitoneal injn. of 1/60 mg of KCN just before each treatment. Instead of protecting, the KCN increased the mortality. Possibly this was due to accumulation of SCN^- , which is known to augment the toxic effects of X-rays. (CA)

1188

Betz, H. and L. Fruhling. REGENERATION OF HEMATOPOIETIC ORGANS IN HEAVILY-IRRADIATED MICE PROTECTED BY KCN INJECTION. *Compt. rend. soc. biol.* **144**, 1013-15(1950).

Adult C57 mice were irradiated with 700 r of 250-kv x rays immediately following an intraperitoneal injection of 0.05 mg of KCN. The 75% of animals surviving the irradiation were sacrificed after periods of 24 hr to 10 months. The regeneration of blood, bone marrow, spleen, thymus, lymphatic nodes, and liver is described in some detail. The delay in regeneration is the same as that observed at much lower radiation doses. In addition, the rate of regeneration exceeds that of normal animals. The present results confirm the view that mortality in irradiated animals is not due to cell destruction but to a more general disturbance involved in the "alarm reaction." (NSA)

1189

Betz, H. and A. Herve. PROTECTIVE ACTION OF KCN AGAINST MORTALITY IN MICE IRRADIATED WITH VARIOUS DOSES OF X RAYS. *Compt. rend. soc. biol.* **144**, 1015-17(1950).

Experiments have been performed to determine whether the protective action of KCN injected prior to irradiation with the minimal x-ray dose (700 r) persists at higher exposures. Six control lots of 30 to 40 C57 adult mice were irradiated with 500, 700, 900, 1200, 1800, and 3000 r of 250-kv x rays. Five identical lots were irradiated with the same doses (except 3000 r) following intraperitoneal injection of 0.05 mg of KCN. The 500-r exposure caused no mortality in either control or injected mice; at 700 r the KCN reduced the death rate from 100% at 10 days to 75%; and at 900 r 22% of the injected mice survived. The mortality curves of control and injected mice were very similar at 1200 r, the KCN prolonging the lives of a few animals by only 2 days, and were identical at the 1800-r irradiation. The mechanism of radiation damage causing this reduced effectiveness is discussed. (NSA)

1190

Herve, A. and Z. M. Bacq. CYANIDE AND A LETHAL DOSE OF X-RAYS. *Compt. rend. soc. biol.* **143**, 881-3 (1949).

Mice of the black C-57 strain were irradiated by a single exposure to 500-600 r of x-radiations, delivered by a 230 kv machine with a 0.25 mm Cu filter, at a focal distance of 50 cm and at the rate of 30 r/min. The technique consisted in dividing the mice into three series: the first series received the x-radiation alone; the second series received an intraperitoneal injection of 0.1 mg of NaCN in an aqueous solution; the treatment for the third group consisted of giving the radiations immediately after the administration of the NaCN and while the animals were still in the state of prostration from the injection. The mortalities of the groups were recorded every 24 hours. The results indicate that the NaCN injection reduced the mortality of the mice, for the radiation dosage given, from 100% to 30%. (NSA)

1191

Herve, André, Z. M. Bacq, and H. Betz. CHEMICAL MODIFICATION OF THE LETHAL EFFECT OF X-RADIATION AND THE MECHANISM OF THE ACTION, p.169-70 of INTERNATIONAL CONGRESS OF RADIOLOGY, 6th Congress, London. 1950.

A series of experiments to study the protective action of different substances on the mortality of X-irradiated mice (single dose of 700 r) has shown that an injection of 0.1 mg of NaCN given immediately before irradiation reduces the mortality from 100 per cent (control animals) to 30 per cent.

The same amount injected immediately after irradiation retards death by 4 days. If injected 15 minutes after the end of irradiation, the NaCN has no effect.

Sodium nitrite gives a similar protective effect.

Histological study of the most sensitive organs from irradiated and "protected" animals shows no difference in the intensity of the radiolesions.

Regarded, on the other hand, from the aspect of "shock," the animals show important differences (suprarenal discharge very slight, and a small excess of fat in the liver among the protected animals). This indicates that death of irradiated mice, unprotected by NaCN, is due to shock rather than to cellular lesions produced by radiation, since among protected animals the mortality is greatly diminished while the cytological lesions are similar to those in unprotected animals.

1192

Herve, A., Z. M. Bacq, and H. Betz. PROTECTIVE PROPERTIES OF SODIUM CYANIDE AND SODIUM NITRIDE AGAINST X RAYS. *J. chim. phys.* **48**, 256-7 (1951).

Injection of 0.1 mg of NaCN immediately prior to irradiation reduces by 50 to 80% the mortality rate of mice totally irradiated by 700 r. Administered after the irradiation, the injection is ineffective. The above treatment does not protect against higher x-ray doses. Similar effects (40 to 50% mortality decrease) are obtained with 0.1-mg doses of Na_3N or 2-mg doses of glutathione; a simultaneous injection of 0.1 mg of NaCN and 2 mg glutathione produces additive effects (90 to 95% mortality decrease). While no differences are observed in anatomical radiolesions, the injections tend to prevent such characteristic effects of the irradiation as the disappearance of corticoadrenal lipids and the accumulation of liver fats. (NSA)

Flavonoids

1193

Arons, I., S. Weintraub, I. Wright, B. Sokoloff, and R. Dutcher. THE PROTECTIVE ACTION OF FLAVONOIDS AGAINST RADIATION, p.170 of INTERNATIONAL CONGRESS OF RADIOLOGY, 6th Congress, London. 1950.

Using a vitamin P compound containing four identical flavonoid factors, the authors demonstrated a decrease in capillary fragility in rats and rabbits. In another series of experiments 100 rats received 800 r total body X-radiation in a single exposure. 40 of the rats served as controls, while the remaining 60 rats were given vitamin P compound isolated from citrus fruit. Mortality rate of the control group was 80 per cent. All rats of this group showed gross haemorrhages of varying gravity and pronounced pathological lesions in the reticular zone of the adrenal cortex. The rats which had received 5 milligrams vitamin P daily for 7 days prior to exposure and for 23 days after radiation, had a mortality rate of 10 per cent, with much less pronounced hemorrhagic diathesis.

Histological investigation of the group of vitamin treated animals revealed only minor injury to the capillary wall with intercellular pores remaining intact. It appears that vitamin P factors have a specific affinity for the intercellular cement of the capillary wall by strengthening it and giving it considerable protection against a total body, near lethal dose of ionising radiation.

1194

Clark, W. G., R. P. Uncapher, and M. L. Jordan. EFFECT OF FLAVONOIDS (VITAMIN P) ON MORTALITY FROM TOTAL-BODY ROENTGEN IRRADIATION. *Science* **108**, 629-30(1948).

A flavonoid preparation derived from lemons was administered in the drinking water of a group of guinea pigs

subjected to 225 r (dose in air) total-body irradiation in a single dose. The experiment was designed to confirm the anti-hemorrhagic effects of vitamin P, and for this purpose the visible manifestation of purpura and anemia were checked at intervals. Of a control group which was similarly irradiated, but not given the flavonoid preparation, 67% died, whereas of the (protected) group only 35% died. In addition, the hemorrhagic symptoms of the protected group were considerably less than those of the control series. (EM)

1195

Cronkite, E. P., W. H. Chapman, and F. W. Chambers. FAILURE OF A FLAVONOID TO REDUCE RADIATION MORTALITY IN MICE. *Proc. Soc. Exptl. Biol. Med.* **76**, 282-4(1951).

A flavonoid (vitamin "P") compound isolated from citrus fruit was given subcutaneously twice daily to white Swiss inbred male mice, beginning 5 days before irradiation with 750, 850, 950, or 1050 r of 2000-kvp x rays, and continuing until the mice died or for 15 days after irradiation. Total daily dose was 0.13 mg/g of mouse. At the doses of radiation used the compound gave no protection. There was no evidence of any toxicity of the compound in mice at the dose used. It is concluded that a flavonoid compound is of no value in the treatment of radiation injury in the LD_{50} to LD_{100} range in mice. (NSA)

1196

Cronkite, E. P., D. C. Eltzholtz, C. R. Sipe, W. H. Chapman, and F. W. Chambers. FAILURE OF RUTIN TO DECREASE THE MORTALITY OF ACUTE IONIZING RADIATION ILLNESS IN MICE. *Proc. Soc. Exptl. Biol. Med.* **70**, 125-8(1949).

Rutin, a crystalline rhamnoglucoside of quercetin, has been found to be beneficial in the hemorrhagic syndrome of acute radiation sickness in dogs. It also accelerates healing of skin lesions due to radiation in rats. Increased capillary fragility is in some way influenced by this substance, especially where there is no deficiency of ascorbic acid. An extensive experiment has demonstrated that, in mice, mortality from lethal-range doses of x-rays is not reduced by rutin administration but is rather increased. Rutin was fed to mice in drinking water (10 to 13 mg/ml) or in food (20 mg/100 g). Treated mice and untreated controls (as many as 400 at a time) were subjected to x-radiation at 1,000 kv and 3 ma. The specially constructed cages were arranged in two tiers as segments of a circle of 1 metre diameter. (Full details of the cages and their arrangement are given in a previous paper.) The average output of the tube was 31.2 r per minute at the geometric centre of the cages 104.4 cm from the target. From cage to cage the variation was at most ± 0.5 r. The exposure time was 22.5 minutes for all mice, the dose being 705 ± 11 r. All mice were weighed daily before and after irradiation. The clinical signs of radiation illness were identical in all mice. A few were selected for necropsy and appearances were typical. By the 17th day the mortality rate in the rutin group was significantly greater than in the control group, although at the end of the 28-day observation period the mortality rates had reached the same level, a little over 40%. There was no significant difference in the weight-loss rates in the two groups, the maximum loss in weight occurring at 12 to 14 days after exposure. The authors point out that, of the many factors influencing survival from radiation exposure, capillary integrity may not be the critical one. Irradiated animals often die with only minor hemorrhage. It is suggested that similar investigations be carried out on guinea pigs, whose requirements for maintenance of capillary integrity more nearly resemble those of man. (AWM)

1197

Field, John B. and Paul E. Rekers. STUDIES OF THE EFFECTS OF FLAVONOIDS ON ROENTGEN IRRADIATION DISEASE. I. PROTECTIVE INFLUENCE OF RUTIN IN IRRADIATED DOGS. *Am. J. Med. Sci.* 218, 1-15(1949).

Sixty per cent of a group of dogs given a single dose of 350 r total body x-irradiation died when left untreated, 36% of a similar group succumbed when treated with a preparation derived from lemon peels, and 11% of a third group died when rutin was given before and after the radiations. When rutin was only given before the radiations, 33% of the dogs died, and when only given afterwards 60-80% of the animals succumbed. Hemorrhagic diathesis appeared more frequently in the untreated specimens and those receiving rutin than in the remainder of the animals. Rutin prevented petechiae and caused a reduction in hemorrhagic signs despite a depression in the blood platelet count and a moderate hypo-coagulability; the rate of anemia production and the magnitude of the increased sedimentation rate were reduced while the erythroblast forms and the nucleated red blood cells were increased. Septicemia was present in 62% of the dead dogs, but it is suggested that the primary cause of death in animals receiving the 350 r was a bleeding tendency associated with a vascular dysfunction, as well as a thrombocytopenia. The existence of "vitamin P" is claimed to be supported by this report and it is suggested that this investigational method may be used as part of an assay for this vitamin substance. (NSA)

1198

Field, John B. and Paul E. Rekers. STUDIES ON THE EFFECTS OF THE FLAVONOIDS IN RÖNTGEN IRRADIATION DISEASE. II. COMPARISON OF THE PROTECTIVE INFLUENCE OF SOME FLAVONOIDS AND VITAMIN C IN DOGS. *J. Clin. Invest.* 28, 747-51(1949).

When normal dogs were exposed to 350 r single dose, total-body x-radiation, 60% succumbed with a prominent hemorrhagic syndrome. Five flavanone substances appeared to be roughly equal in activity in reducing the hemorrhagic signs when administered continuously, pre- and post-irradiation. When rutin was fed, 11% of the dogs succumbed; with hesperidin 17%; with epimerized d-catechol 10%; and with homoeriodictyol and morin none. Other flavonoids had little effect, including quercetin, quercitrin, and naringen. Benzopyrone and coumarin had slight anti-irradiation activity. Ascorbic acid alone had no effect, but when given with quercetin (which alone had no effect) it was markedly protective. Potent hyaluronidase inhibitors such as dopa and Na gentisate had no influence. Hyaluronidase plays little or no role in this syndrome. (CA)

1199

Griffith, J. Q. Jr., E. Anthony, E. P. Pendergrass, and R. Perryman. EFFECT OF RUTIN ON RECOVERY TIME FROM RADIATION INJURY IN RATS. *Proc. Soc. Exptl. Biol. Med.* 64, 332-3(1947).

All animals were given 2,385 r of radiation to one leg (single dose, 200 kv, 15 ma, 1/2 mm Cu + 1 mm Al filter, 26 cm skin target distance). Half were used as controls and the other half were given rutin, 20 mg every third day, implanted subcutaneously as a pellet. The time of onset of reaction and the height of reaction were essentially the same for the two groups but the rats treated with rutin recovered more rapidly. (BA)

1200

Kohn, Henry I., P. W. Robinett, and M. N. Cupp. THE EFFECT OF RUTIN UPON THE RESPONSE OF THE RAT TO TOTAL BODY X-IRRADIATION. Oak Ridge National Lab. June 7, 1948. Decl. July 22, 1948. 13p. (AECD-2176)

Experiments were performed to determine whether rutin can influence the reaction of the rat to 250 kv x-rays. The drug is the rhamnoglucoside of 3, 5, 7, 3', 4', pentahydroxyflavone. In all cases 5 mg per day were given subcutaneously, beginning either on the day of irradiation or one week before, and continued for at least 18 days. Oral supplements were also given in some experiments. It was found that rutin did not affect the LD-50, the survival following two sublethal exposures, the coagulation time, the thrombocyte count, the total white cell count, and the hemorrhage into the lymph nodes and the gastrointestinal tract. Because rutin is said to affect the hemorrhagic tendency in certain conditions, in vitro studies were carried out on normal human and rat blood. The prothrombin time is not affected, nor the coagulation time. It does not prevent the action of heparin. However, it does antagonize the anti-heparin action of toluidine blue. (NSA)

1201

Paris, R., Edmond Vairel, and J. Vavasseur. PROTECTIVE EFFECT OF FLAVONE DERIVATIVES ON MORTALITY IN IRRADIATION OF THE RABBIT AND MOUSE. *Ann. pharm. franç.* 9, 68-78(1951).

Rutin prevented in the rabbit irradiated with 700 r the increase in capillary fragility and often, the prolongation of clotting time. It slightly decreased the mortality. At 800 r no beneficial effect was observed. Alimentation low in green vegetables caused a decrease in resistance, but in these cases the effect of flavone compounds was most marked. Rutin, hesperidin-methylchalcone aphiol, quercitol, and naringoside given orally before irradiation exerted a slightly favorable action on the mortality of mice irradiated with 600 to 800 r. (CA)

1202

Rekers, P. E. and J. B. Field. CONTROL OF HEMORRHAGIC SYNDROME AND REDUCTION IN X-IRRADIATION MORTALITY WITH A FLAVANONE. *Science* 107, 16-17(1948).

Fifty dogs were exposed to 350 r of total body x-irradiation. Twenty-five were given 50 mg of rutin, orally, 3 times daily, starting one week prior to exposure and continuing through the test period; of the rutin-treated animals 10% died, of the untreated animals 64% died. (CA)

1203

Sokoloff, Boris, Walter H. Eddy, and James B. Redd. THE BIOLOGICAL ACTIVITY OF A FLAVONOID (VITAMIN "P") COMPOUND. *J. Clin. Invest.* 30, 395-400 (1951).

A flavonoid preparation from citrus fruit and containing four identified factors was tested, experimentally and clinically, on its biological activity. In addition to demonstrations of protective action against leukotaxine and bacterial polysaccharide, it was shown that the flavonoid gave a considerable but not complete protection to rats against a total-body, near-lethal dose of x radiation. Ninety-two human patients, undergoing deep x-ray therapy and given the mixed flavonoids, 300 to 600 mg/day orally, for 5 days prior to the exposure and during the whole period of radiotherapy, manifested considerable diminution in radiation erythema of the skin and in some cases a complete absence of erythema. Nausea and vomiting, however, persisted in some of the treated patients. (NSA)

1204

Sokoloff, Boris, James B. Redd, and Raymond Dutcher. VITAMIN P PROTECTION AGAINST RADIATION. *Science* 112, 112-13(1950).

Rats were fed vitamin P (CVP compound), isolated from citrus waste, both before and after a total-body radiation of 800 r of x-rays. Considerable protection against the near-

lethal dose was observed, probably due to the prevention, by the flavonoids present, of an increase in capillary fragility. (NSA)

1205

Sokoloff, Boris, James B. Redd, and Raymond Dutcher. **CAPILLARY FRAGILITY AND VITAMIN 'P' PROTECTIVE ACTION AGAINST RADIATION.** *Proc. Soc. Exptl. Biol. Med.* **75**, 6-9(1950).

Administration of leukotaxine, a bacterial polysaccharide, or an exposure to ionizing radiation induces increased capillary fragility. Injury to the capillary wall, whether it is caused by ionizing radiation, by leukotaxine, or by a bacterial polysaccharide, can be prevented to a considerable degree by the administration of a vitamin "P" compound composed of flavonoids naturally present in citrus fruit. (NSA)

Hormones

1206

Betz, H. **EFFECT OF ACTH ON THE MORTALITY OF IRRADIATED MICE.** *Compt. rend. soc. biol.* **145**, 1240-2(1951).

Adult C57 mice injected daily with 0.5 mg of ACTH for 7 days before irradiation with 700 r of 250-kv x rays had a lower rate of mortality than untreated controls, and there was 20% survival. However, when the daily injection was started after the irradiation, the mice died more rapidly than the controls; all succumbed by the 8th day, in contrast to the 11th day for controls. Mice injected intraperitoneally with 0.05 mg of KCN immediately before a 700-r x irradiation had a 75% survival rate without further treatment, but only a 30% rate when a daily 0.5-mg ACTH injection was begun after the irradiation. The ACTH clearly increases activity of the adrenal cortex, which in the irradiated animals is already excessively affected by radiation stress. (NSA)

1207

Betz, H. **INFLUENCE OF THE ADRENALS ON HEMATOPOIETIC REGENERATION IN THE X-IRRADIATED RAT.** *Compt. rend. soc. biol.* **145**, 465-7(1951).

Adrenalectomy of rats before x-irradiation prevents formation of erythroblastic and myeloblastic changes in the spleen. This effect is overcome by injection of desoxycorticosterone acetate. It thus appears that the adrenals play a part not only in the regulation of the lymphoid system, but also in that of myeloid tissue. (CA)

1208

Blount, Henry C. Jr. and Willie W. Smith. **THE INFLUENCE OF THYROID AND THIOURACIL ON MICE EXPOSED TO ROENTGEN RADIATION.** *Science* **109**, 83-4 (1949).

Experiments to determine the effects of thyroid and thiouracil feeding, and heat on mice exposed to damaging roentgen radiations are summarized. Radiation doses delivered with an effective voltage of 170 kv, 20 ma, through aluminum and copper filters, were administered. Mice on thyroid and thiouracil diets for 13 and 8 days before radiation were examined up to four weeks later. Mortality rates and temperature experiments indicate that metabolic activity rather than body temperature is the predominant factor in increasing the mortality of mice exposed to the rays. Further experiments are in progress. (NSA)

1209

Craver, B. N. **EFFECT OF ADRENAL CORTICAL INJURY ON THE TOXICITY OF ROENTGEN RAYS.** *Am. J. Roentgenol. Radium Therapy* **59**, 404-7(1948).

Two series of 25 white male rats (Wistar strain) were exposed in the following manner to irradiation by roentgen rays: (1) the "protected" rats were covered over the adre-

nal area of the back with a lead strip 1 inch wide maintained in that position by confining the rats in cellophane cones; (2) the "unprotected" rats had two 1/2 inch lead strips shielding them, one over the upper chest and the other over the lower abdomen. Since the 1 inch strip protected the lower chest and upper abdomen, the two 1/2 inch strips were placed as described so that they might protect approximately equivalent amounts of like tissue. The technical factors of the exposure were as follows: 250 kv, 15 ma, 24 in. target skin distance, 660 r total dose, 19.6 r/min. output, an exposure of 33 minutes and 40 seconds. All 50 of the rats survived for 30 days following exposure, except three of the "unprotected" series which died 12, 12, and 16 days after exposure. Twenty-nine days after the first exposure, the animals were exposed again, to 880 r. The technical factors of the exposure were as follows: 250 kv, 15 ma, 24-in. target skin distance, 880 r total dose, 21.9 r/min. output, an exposure of 40 minutes. After this exposure two of the "protected" animals died, one on the fourth and one on the twelfth day after exposure. Seven of the "unprotected" animals died on the 3rd, 9th, 16th, 17th, 24th, 26th, and 30th days after this exposure, after which the remaining animals were destroyed. In the "protected" series, three rats were in poor health; in the "unprotected" series six rats were in poor condition. This evidence suggests that rats whose adrenals are "protected" are less susceptible to the lethal effects of radiation than rats receiving equivalent doses but not so protected. The possible relation of the adrenal-lymphoid system to irradiation sickness and the lethality of roentgen radiation is discussed.

1210

Cronkite, E. P. and W. H. Chapman. **EFFECT OF ADRENALECTOMY ON RADIATION INDUCED MORTALITY OF THE MOUSE.** *Proc. Soc. Exptl. Biol. Med.* **74**, 337-40(1950).

Adrenalectomized and control mice were exposed at the rate of 15 r/min to the beam of a 2-Mv x-ray tube. The results were: (1) The adrenalectomized or "adrenal insufficient" mouse is more sensitive to irradiation than the normal mouse. (2) The survival time of adrenalectomized mice is shortened. (3) Mice adrenalectomized 48 hr before irradiation were more sensitive than those adrenalectomized 15 days before irradiation. (4) The cause of death in the adrenalectomized irradiated mouse is apparently due to mechanisms other than infection and hemorrhage. (NSA)

1211

Edelmann, Abraham. **THE EFFECT OF ADRENALECTOMY UPON SURVIVAL OF RATS AFTER X-RADIATION.** *Brookhaven National Lab. [nd] 3p. (AECU-325)*

Bilaterally adrenalectomized male albino rats (Sprague-Dawley) were given 650 r of whole body x-radiation. The average survival of the adrenalectomized irradiated rats was 4.1 days as compared to 7.8 days for the adrenalectomized controls. Subjection of these data to an analysis of variance reveals that the irradiation significantly shortened the lives of the adrenalectomized rats. (NSA)

1212

Edelmann, Abraham. **ADRENAL CORTEX AND SURVIVAL OF RATS AFTER X-IRRADIATION.** *Federation Proc.* **9**, 36(1950).

This report is reproduced here in its entirety.

Protecting the adrenals of male rats by means of lead shields placed about the glands significantly increased the survival incidence following 850 r of x-irradiation (160 KVP, 10 ma, 0.15 mm Cu). The x-irradiation (650 r) shortens the lives of adrenalectomized rats from an average of 8 days to 4 days. Substitution therapy in the adrenalectomized rat is effective inasmuch as 3 cc/day of a whole gland ad-

renal extract (Upjohn) or 5 mg/day of desoxycorticosterone acetate resulted in 20 and 40% mortalities respectively at 15 days after 600 r, whereas 90% of the adrenalectomized controls were dead at this time. It is thought that the adrenal cortical response to x-irradiation is similar to that following any other stress.

1213

Edelmann, Abraham. ADRENAL SHIELDING AND SURVIVAL OF RATS AFTER X-IRRADIATION. *Am. J. Physiol.* **165**, 57-60(1951).

Lead shields placed around the adrenal glands of rats appreciably decreased the number of deaths following 700 or 800 r of whole-body x radiation. It is thought that the shielding prevents direct radiation damage to the glandular cells so that they retain their ability to respond to nonspecific stress. The gland was extruded from the shield by 3 months, probably because of the formation of connective tissue within the shield. Enucleation with degeneration of the medulla appeared to result. It is thought that available histological and histochemical techniques do not reveal the true radiosensitivity of the adrenal cortex. (NSA)

1214

Edelmann, Abraham. SURVIVAL OF ADRENALECTOMIZED RATS WITH AND WITHOUT REPLACEMENT THERAPY FOLLOWING X-IRRADIATION. *Am. J. Physiol.* **167**, 345-8(1951). (AECU-1599)

The average survival time of rats whole-body irradiated with 650 r of x rays 4 days following adrenalectomy was 4.1 days compared to 7.8 days for adrenalectomized, untreated controls. In contrast, 80% of adrenalectomized, irradiated rats given 3-cc daily doses of adrenal extract and 60% given 5-mg of desoxycorticosterone acetate (DOCA) daily were alive 20 days after irradiation. The length of survival after discontinuance of therapy of the irradiated adrenalectomized rats treated with DOCA or adrenal extract was similar to that of the unirradiated, untreated adrenalectomized rats. (NSA)

1215

Edelmann, Abraham and Seymour Katsh. THE SURVIVAL OF RATS ADRENALECTOMIZED AFTER X-IRRADIATION. *Federation Proc.* **10**, 38(1951) (AECU-1137)

This report is reproduced here in its entirety.

Rats were adrenalectomized at various times after a dose of whole-body x irradiation (600 r, 160 kvp, 0.2 mm Cu, a dose which does not kill normal control rats in this laboratory), and the time of death was noted. It was observed that the life span was reduced when the time interval between irradiation and adrenalectomy was decreased. This relation was not linear, a greater effect being noticed at the shorter intervals. If the irradiation was given 5 or more days before the adrenalectomy, the life span of the irradiated-adrenalectomized rats approached that of the unirradiated-adrenalectomized rats. This may be interpreted to mean that the need of the animal for adrenal hormones to survive is most acute immediately after irradiation and rapidly diminishes after 3 to 5 days.

1216

Ellinger, Friedrich. PROTECTIVE ACTION OF DESOXYCORTICOSTERONE ACETATE AGAINST X-RAY INDUCED LIVER CHANGES. *Science* **104**, 502(1946).

Total-body irradiation with x-rays was given to white male mice. The doses were 500 and 1,000 r/air in one exposure or in fractions of 100 r daily. The radiation factors were: 200 kv, 10 ma, 0.25 mm Cu + 1.0 mm Al filters, 50 cm distance, 20×20 cm field, 23.4 r/min., HVL - 0.75 mm Cu. Daily doses of 0.25 to 0.5 mg desoxycorticosterone acetate (in oil) were administered subcutaneously six times weekly to one group of irradiated animals. The other group of irradiated animals served as con-

trols. Total doses varying between 2.5 and 8.0 mg were given within 10 to 18 days. The effects of mortality rate, fat content of the liver, and radiation changes in other organs were studied over a period of 40 days. The outstanding observation made was a striking reduction in the amount of sudanophile fat in the irradiated and desoxycorticosterone-treated group of animals as compared with those receiving irradiation only. There was a slight decrease in the mortality rate produced by the various doses of x-rays in favor of the desoxycorticosterone-treated group. This protective action of desoxycorticosterone against x-ray-induced liver changes supports the value of desoxycorticosterone in the treatment of radiation illness. The results also seem to support the histamine hypothesis of radiation effect.

1217

Ellinger, Friedrich. EFFECTS OF DEOXYCORTICOSTERONE ON MICE IRRADIATED WITH X-RAYS. *Proc. Soc. Exptl. Biol. Med.* **64**, 31-5(1947).

Fatty changes in the liver brought on by irradiation of mice with LD-50 of x-rays caused death. The percentage of mortality and liver damage was reduced to an extent proportional, within limits, to the dose of desoxycorticosterone administered. The toxic action of x-rays is due to the liberation of histamine like substances by tissue breakdown, since some histamine effects are known to be antagonized by desoxycorticosterone, while this substance has no effect on x-ray damage to the spleen and bone marrow. (NSA)

1218

Ellinger, Friedrich. INFLUENCE OF PHARMACOLOGICAL AGENTS ON EFFECTS OF IRRADIATION. *Radiology* **50**, 234-43(1948).

A simple method for the evaluation of the action of pharmacologic agents on the effects of irradiation is described. The criteria selected (mortality rate produced in total body irradiation and changes in spleen, bone marrow, and liver) were easily observable and lent themselves to statistical analysis. By means of this method, the following results were obtained. Desoxycorticosterone acetate markedly decreased the lethal effect of various x-ray doses in mice and prevented the radiation-induced fatty changes in the liver. The chemically closely related steroid pregnenolone failed to show these effects. Vitamin B complex showed a definite reduction of the fatty changes in the liver. Both vitamin B complex and vitamin C failed to produce significant changes of the radiation effects on the spleen. The importance of pharmacologic analysis of radiation effects for the understanding of their mechanism is discussed. The significance of the demonstrated possibility to decrease the mortality rates of ionizing radiations produced in total body irradiation for the improvement of radiation therapy of widely spread cancers and the possible utilization of these experiences in the treatment of persons accidentally exposed to lethal doses of radiations generated during nuclear fission are indicated. (BA)

1219

Ellinger, Friedrich. THE USE OF ADRENAL CORTICAL HORMONE IN RADIATION SICKNESS. *Radiology* **51**, 394-9(1948).

In the light of recent studies radiation sickness appears to be caused by a general intoxication brought on by tissue decomposition products of histamine-like substances, or histamine itself, and adrenal cortical insufficiency. An important accompanying condition is the fact that there are fatty changes in the liver. Since a synthetic hormone of the adrenal cortex, desoxycorticosterone acetate (DCA), is known to counteract mineral losses caused by adrenal-cortical insufficiency and to play an important part in the

inactivation of histamine, it seemed logical to use DCA in the treatment of radiation sickness. In an earlier series of tests (Science, 104: 502, 1946; Radiology, 50: 234-242, 1948) the author gave mice varying doses of total body irradiation and found that DCA protects the liver against radiation-induced fatty changes and that this liver-protecting action is accompanied by a decrease in the mortality rates. Here the author has extended his studies on the influence of DCA on the effect of x-rays to include the effects on the spleen, bone marrow, and adrenal cortex. One hundred Swiss white mice (average weight 25 g) were exposed to 500 r/air of x-rays (h.v.l. 0.75 mm Cu) given as total body irradiation in one exposure. Part of the animals were given daily doses of 0.5 mg DCA. They were killed at different intervals and the tissues examined histologically. The irradiation changes in the spleen were not affected by the hormone. However, there were well defined changes in the marrow observable in the DCA group, and there was a decreased depletion of the sudanophile fat in the adrenal cortex during the first week only. This seems to be explainable by the fact that cortical fat content had returned to normal. The lack of observable change in the spleen may have been factual, or the result of faulty method. The conclusion is made, taking other studies into consideration also, that the administration of DCA prevents exhaustion of the adrenal cortex caused by irradiation. Mention is made of a clinical study by the author and others on a group of 50 patients under treatment for radiation sickness where 37 patients were relieved of nausea and/or vomiting upon administration of DCA. (NSA)

1220

Ellinger, Friedrich. SOME EFFECTS OF TESTOSTERONE PROPIONATE ON MICE IRRADIATED WITH X-RAYS. Proc. Soc. Exptl. Biol. Med. 74, 616-19(1950).

Administration of testosterone propionate in daily doses of 0.25 and 0.5 mg, respectively, following exposure of mice to the LD₅₀ of x-ray, up to 14 days, markedly increased the lethal effect of irradiation. No changes in the x-ray induced organ effects were accomplished in all investigated organs with the exception of the liver. Radiation induced accumulation of sudanophile fat in this organ was definitely suppressed with a larger dose of testosterone. Radiobiological and some clinical implications of these findings are discussed. 15 references. (NSA)

1221

Ellinger, Friedrich, J. Blagg, and W. Brooks. PHARMACOLOGICAL STUDIES ON IRRADIATED ANIMALS. II. EFFECTS OF CORTISONE ON X-RAY MORTALITY OF MICE. Proc. Soc. Exptl. Biol. Med. 80, 214-17(1952).

Injection of 0.25 mg/day of cortisone intramuscularly for 14 days after the higher LD doses of x-rays increased the mortality rate. With the lower LD doses it did not increase the mortality but it shortened the latent period between irradiation and death. Simultaneous treatment with ascorbic acid did not significantly modify these effects. (CA)

1222

Ellinger, Friedrich, B. Roswit, and S. M. Glasser. THE TREATMENT OF RADIATION SICKNESS WITH ADRENAL CORTICAL HORMONE (DESOXYCORTICOSTERONE ACETATE). Am. J. Roentgenol. Radium Therapy 61, 387-96(1949).

The authors analyze the response of 50 patients suffering from radiation sickness to desoxycorticosterone acetate (DOCA). This clinical investigation was based on the assumption that irradiation of animal tissues liberates some toxic histamine-like substance. One of the authors has previously adduced evidence from animal experiments that DOCA protects the liver against the fatty changes induced by irradiation, and also reduces the lethal effect of irradiation on mice.

The authors claim that the present investigation corroborates his findings. Symptoms of radiation sickness are classified in five groups: (1) general; (2) gastrointestinal; (3) hematological; (4) cardiovascular; (5) psychic. This report deals with the effects of DOCA on groups 1 and 2 only—mainly on nausea and vomiting. Five mg in peanut oil was injected I.M. every eight hours until relief of symptoms (but for not more than five days). All of the patients in this series suffered from nausea and/or vomiting, as well as other symptoms, after irradiation therapy for a variety of benign and malignant lesions. Only three patients failed to respond in any way to DOCA and two of these had advanced brain tumors. Of the remaining 47 cases, 37 were completely relieved of the most distressing symptoms, nausea and/or vomiting and 19 became symptom-free. Of 27 cases in which the liver was included in the irradiated area, 23 patients were relieved of nausea and/or vomiting. In the individual case records "body section irradiated" (that is thorax, abdomen, neck, groin) is cited but no details are shown of actual field sizes and volumes irradiated. Details of dosage are not given but the correlation of daily and total cumulative dose with onset, frequency and severity of symptoms will be presented at a later date with a larger series of cases. (AWM)

1223

Graham, J. B. and R. M. Graham. THE MODIFICATION OF RESISTANCE TO IONIZING RADIATION BY HUMORAL AGENTS. Cancer 3, 709-17(1950).

Methods of modifying resistance to radiation in animals are reviewed. Experiments on Swiss mice exposed to total-body x-ray radiation are recorded. A number of substances including horse serum, stilbestrol, estradiol, estrone, testosterone, and adrenal cortical extract given either 10 days before or immediately after exposure to x-rays were found to increase or decrease the mortality rate. The effect produced was determined not only by the substance but also by the time of its administration. The ability of the hormones to modify radioresistance could not be correlated with their established endocrine activity. The sensitivity of animals to ionizing radiation was reflected in the appearance of their epithelial cells. Characteristic cytological alteration was observed in vulnerable animals after exposure. Experiments here and elsewhere indicate that the adrenal cortex has little to do with resistance to radiation. A variety of substances, including stilbestrol and some steroids, have been found to induce a cellular response in animals closely resembling that produced by radiation. This suggests that these materials and radiation have a similar effect on the organism and may explain the ability of these agents to modify resistance to radiation. (NSA)

1224

Graham, J. B., R. M. Graham, and A. J. Graffeo. THE INFLUENCE OF ADRENAL CORTICAL HORMONES ON SENSITIVITY OF MICE TO IONIZING RADIATION. Endocrinology 46, 434-40(1950).

More than 2000 adult Swiss mice including controls were given cortical extract (ACE), desoxycorticosterone (DCS) and 11-dehydrocorticosterone (HCS) at varying times before and after total body irradiation of 400 to 600 r. The procedure is outlined, and the results are tabulated and discussed. The authors conclude that ACE given 10 days prior to irradiation increases the survival rate in both sexes, when given immediately before irradiation raises the mortality in females, and does not alter the survival rate under any other conditions tested; despite reasonable postulates that the adrenal cortex plays a significant role in the resistance to radiation, the authors did not find any evidence for the mediation of radioresistance by the adrenal cortical hor-

mones used, and probably not by the cortex itself; they further conclude that the demonstrable effects of adrenal compounds on radioresistance are in the nature of a non-specific stimulus since they may be duplicated by injection of other material such as foreign protein or estrogen. (NSA)

1225

Gray, John L., Elizabeth J. Moulden, John T. Tew, and H. Jensen. **THE PROTECTIVE EFFECT OF PITRESSIN AND OF EPINEPHRINE AGAINST TOTAL BODY X-RADIATION.** *Proc. Soc. Exptl. Biol. Med.* **79**, 384-7 (1952) (AMRL-64)

The survival of rats, exposed to lethal x-ray dosage, was found to be significantly increased after pretreatment with pitressin or epinephrine. The protective effect is attributed to their property of producing a temporary tissue anoxia. (NSA)

1226

Halberstaedter, L. and M. Ickowicz. **THE EFFECTS OF X-RAYS ON THE LYMPHATIC ORGANS OF NORMAL AND ADRENALECTOMIZED RATS.** *Radiologia Clin.* **16**, 240-57(1947).

A series of normal and adrenalectomized rats were irradiated with an X-ray dose of 2,000 r. Histologic reactions are reported concerning the pycnotic reaction in thymus, spleen, and mesenteric lymph node within a few hours following the irradiation. It was found that: (a) The greater the volume dose, the stronger the pycnotic reaction. (b) Following irradiation of one part of the body, an indirect influence is demonstrable in the non-irradiated part of the body. (c) Adrenalectomy diminishes the X-ray effect, especially the indirect effect. (d) Thymus, spleen, and mesenteric lymph node do not react to X-ray with equal pycnotic intensity, especially if the effect is an indirect one. The thymus shows the greatest sensitivity. This is in conformity with the finding of Dustin, that the thymus generally exhibits a greater degree of susceptibility to toxic substances than either spleen or lymph node. (NSA)

1227

Haley, Thomas J., Samuel Mann, and Andrew H. Dowdy. **A COMPARISON OF THE RESPONSE OF NORMAL AND HYPOTHYROID MICE TO ACUTE WHOLE BODY ROENTGEN RADIATION.** *Science* **112**, 233-4(1950). (UCLA-61)

The ability of antithyroid drugs to protect animals against the lethal effects of x-irradiation has been investigated with adult mice. It has been concluded from the results that the hypothyroid state does not protect the mouse from x-irradiation damage. The amount of available oxygen and not its rate of utilization determines the extent of such damage. (NSA)

1228

Haley, Thomas J., Samuel Mann, and Andrew H. Dowdy. **THE EFFECT OF ROENTGEN RAY IRRADIATION ON NORMAL, HYPOTHYROID, AND HYPERTHYROID RATS.** *Endocrinology* **48**, 365-9(1951). (UCLA-81)

Thyroparathyroidectomy does not significantly increase the survival time nor decrease the total mortality of roentgen-ray irradiated rats. Hyperthyroidism produced by the subcutaneous injection of thyroxine or thyroglobulin into rats causes a significant increase in mortality rate as compared with normal and hypothyroid animals even though there are no significant differences in total mortality. Thyroxine and thyroglobulin premedication of hypothyroid rats decreases their survival time, as compared to non-medicated hypothyroid and normal animals, but total mortality was practically unchanged. (NSA)

1229

Haley, Thomas J., Samuel Mann, and Andrew H. Dowdy. **THE INABILITY OF THIOUREA TO MODIFY ROENTGEN RAY IRRADIATION MORTALITY IN RATS.** *Science* **114**, 153-4(1951). (UCLA-112)

The hypothyroid state induced by feeding 0.1% thiourea confers no protection on rats subjected to 600 r of acute whole-body roentgen irradiation. Hyperthyroidism produced by thyroxine injections results in a slight increase in the rate of mortality under the same experimental conditions. However, the greatest increase in the rate of mortality was seen in those animals which had been treated with both thiourea and thyroxine. (NSA)

1230

Ickowicz, M. **EARLY EFFECTS OF X-RAYS ON OVARIES OF NORMAL AND ADRENALECTOMIZED RATS.** *Proc. Soc. Exptl. Biol. Med.* **66**, 646-9(1947).

The appearance of pycnotic lesions of the cells in the granular layer of the ovarian follicles of rats four hours after x-ray irradiation was inhibited by previous adrenalectomy. (BA)

1231

Joel, C. A. **EFFECT OF TESTOSTERONE PROPIONATE ON THE REGENERATION OF TESTES INJURED BY X-RAYS.** *Endokrinologie* **24**, 310-17(1942).

Adult white rats were irradiated with 360-450 r. Some of the animals were then treated with testosterone propionate (total dose 30 mg in four weeks) while others served as controls. After 25 days the testes of the treated and untreated animals were about alike but after 50 days, when the reparative processes had already been started, the testes of the treated rats had manifested regeneration to the normal condition, whereas those of the untreated rats showed only beginning regeneration. (CA)

1232

Katsh, Seymour and Abraham Edelmann. **THE ADRENAL CORTICAL REQUIREMENTS OF ADRENALECTOMIZED, X-IRRADIATED RATS.** *Federation Proc.* **10**, 73(1951) (AECU-1134)

Adrenalectomized male rats were maintained with whole-gland adrenal extract (Upjohn), the amount being adjusted so that the animals had a slight weight gain during the period of observation. The animals were irradiated with 600 r of x-rays (160 kvp, 10 ma, 0.2 mm Cu). It was found that the level of cortical extract had to be increased several fold for 3 to 4 days after irradiation to inhibit weight loss. A gradual reduction in extract requirement then occurred, basal levels being reached after 5 days. This clearly indicates the need for increased adrenal hormones following x irradiation.

1233

Kohn, Henry I. **EFFECT OF IMMATURITY, HYPOPHYSECTOMY, AND ADRENALECTOMY UPON CHANGES IN BLOOD PLASMA OF RAT DURING ACUTE RADIATION SYNDROME.** *Am. J. Physiol.* **165**, 43-56(1951).

Following whole-body irradiation of the immature rat, the pattern of change in the plasma was like that in the mature animal, but the LD₅₀ was about 200 r less and diarrhea appeared sooner. The effect of hypophysectomy upon the radiation reaction depended upon the age at which operation had occurred. In the adrenalectomized mature animal, the glucose and NPN reactions to irradiation were greatly diminished, the chloride reaction was modified, and the cholesterol, protein, and A/G reactions were unchanged or somewhat enhanced. Irradiation of the head and neck alone led to no changes in the plasma. Whatever role the pituitary or thyroid glands played was therefore an in-

direct one. Some conclusions are drawn about the role of the pituitary-adrenal system. (NSA)

1234

Kohn, Henry I., Nancy Swingley, W. J. Robertson, and Marian Kirsliis. EFFECT OF IMMATURITY, HYPOPHYSECTOMY AND ADRENALECTOMY UPON THE CHANGES IN THE BLOOD PLASMA DURING THE ACUTE RADIATION SYNDROME IN THE RAT. Oak Ridge National Lab. June 7, 1951. 32p. (ORNL-656)

Changes that occur, during the 10 to 14 days following total-body x irradiation of the rat, in the plasma levels of glucose, nonprotein nitrogen (NPN), phosphorus, total protein, albumin/globulin ratio (A/G), chloride, and cholesterol were reported previously (*Am. J. Physiol.* **165**, 43-56(1951)). The effect of immaturity, hypophysectomy, or adrenalectomy on the pattern of these plasma changes has now been investigated using the same experimental conditions. Following irradiation of the immature animal (aged 35 to 40 days) the pattern of change in the plasma was like that in the mature animal (aged 90 days plus), but the LD₅₀ was about 200 r less and diarrhea appeared sooner. Hypophysectomy in the immature animal prevented the chloride reaction. In the mature animal, it modified the cholesterol reaction. In both, it greatly reduced the glucose and NPN reactions. It had no effect on the protein and A/G reactions in either type. A striking difference due to age also was seen in the unirradiated hypophysectomized animals; in the mature group, fasting had no effect on the level of NPN. Following adrenalectomy in the mature animal, the glucose and NPN reactions to irradiation were greatly diminished, the chloride reaction was modified, and the cholesterol, protein, and A/G reactions were unchanged or somewhat enhanced. A system is proposed in which radiation effects are classified as primary or secondary, depending on whether they occur within the irradiated cell or elsewhere. It is suggested that the A/G reaction might be an indication of a primary injury, whereas the other reactions were more likely to be indications of secondary effects. (NSA)

1235

Lambert, G., J. Maisin, M. Mandart, F. Meersseman, G. Podio, and E. Plugers. INFLUENCE OF DESOXYCORTICOSTERONE, n-HEXYL BUTYRATE, ALPHANAPHTHYLTHIOUREA, AND ACACIA GUM ON THE SURVIVAL OF RATS RECEIVING A LETHAL DOSE OF X-RAYS. *Compt. rend soc. biol.* **144**, 449-52(1950).

The injection of small doses of desoxycorticosterone acetate or α -naphthylthiourea before and after the irradiation had no significant effect on the survival time. Injections of hexyl butyrate or acacia gum shortened the survival time. (CA)

1236

Loiseleur, Jean and Georges Velley. IMMUNITY CONFERRED BY HYPERGLYCEMIA AGAINST LETHAL DOSES OF X-RAYS. *Compt. rend* **231**, 182-4(1950).

Fifty-four adult rats were given total body lethal doses of x-rays (950 r at 180 kv) for 45 minutes. Forty-five minutes prior to irradiation, 27 of them were given an intraperitoneal injection of glucose (4 cm³ containing 2 g glucose per 150 g body weight). All controls died, between a period of 5 and 23 days following irradiation, with the usual symptoms of radiation exposure accompanying death. Among the glucose treated rats, five died. All the others showed no ill effects and, in fact, exhibited an average gain of weight of 15.5%. The authors discuss the reason for this high immunity. (NSA)

1237

Marder, Sumner N., Henry S. Kaplan, and Egon Lorenz. LACK OF EFFECT OF ADRENALECTOMY ON THE LYMPHOPENIC RESPONSE OF C-57 BLACK MICE TO

TOTAL-BODY IRRADIATION AT A LOW DOSAGE LEVEL, p.21-27 of BIOLOGICAL AND MEDICAL DIVISIONS, QUARTERLY REPORT, AUGUST, SEPTEMBER, OCTOBER, 1948. Argonne National Lab. Nov. 1, 1948. 6p. (ANL-4227(p.21-7))

Marked variation in the level of circulating lymphocytes of C-57 black mice has been noted, and the difficulties thus imposed on the demonstration of minimal acute changes are discussed. Lymphopenia within six hours following total-body irradiation with 30 r has been demonstrated in both splenectomized and nonoperated male mice of this strain. (Authors' Summary)

1238

Patt, H. M., R. L. Straube, E. B. Tyree, M. N. Swift, and D. E. Smith. INFLUENCE OF ESTROGENS ON THE ACUTE X-IRRADIATION SYNDROME. *Am. J. Physiol.* **159**, 269-80(1949) (AECU-524; UAC-92)

The phenomenon of estrogen protection against x-rays has been investigated. Several types of experiments were performed. The following results are reported. Pretreatment with estradiol benzoate improves the survival of male mice after lethal x-irradiation has been confirmed. It has been demonstrated further that the estrogen protective effect occurs in female mice as well and that benzenestrol, but not progesterone and testosterone, is also effective. The time of injection of estrogen relative to the time of irradiation is critical, for estradiol is most effective when it is given 10 days before the exposure. Estrogen injection 5 or 15 days before irradiation also protects but administration at other intervals fails to increase survival and, indeed, may even potentiate toxicity. Estradiol in dosage sufficient to protect against x-rays does not influence survival after poisoning with a nitrogen mustard. Estradiol (0.166 mg per mouse I.M.) increases adrenal weight and accelerates thymic involution but has no appreciable effect on weight of the spleen, inguinal nodes or kidneys. Although the increase in adrenal weight after x-irradiation is somewhat greater in mice pretreated with estrogen, the radiation-induced involution of spleen, thymus, and inguinal nodes is not altered by the treatment. A leukopenia with maximal depression around 10 to 14 days after estrogen injection has been observed. The reduction in heterophils is more marked and somewhat more consistent than the lymphocyte response. Little change is noted in erythrocyte count following the single injection of estradiol. Leukocytes are decreased to the same levels in both the estrogen-treated and control irradiated animals, although maximal depression and recovery occur earlier in the former. The more rapid recovery of leukocytes in irradiated mice which received a prior injection of estrogen residues in the heterophil component. The anemia of radiation is also less severe in the estrogen-treated animals. Significantly, the maximal estrogen protective effect is observed when mice are irradiated during their leukopenic period. That there is some correlation between heterophil response and lethal effect is indicated in the finding that a rapid recovery of heterophils but not of lymphocytes occurs in mice treated with estradiol 10 days before x-irradiation. (NSA)

1239

Patt, Harvey M., Marguerite N. Swift, Robert L. Staube, Ella B. Tyree, and Douglas E. Smith. INFLUENCE OF A CONDITIONING INJECTION OF ESTROGEN ON THE HEMATOLOGIC AND ORGAN WEIGHT RESPONSE TO X-IRRADIATION. *Federation Proc.* **8**, 124(1949) (AECU-487; UAC-38)

Estradiol benzoate (0.166 mg I.M. in a single injection 5-15 days before exposure) greatly enhances resistance of mice to total-body x-irradiation. Progesterone and testosterone are ineffectual. To elucidate this phenomena we

have studied the effect of estradiol on organ weights, blood count, and microscopic anatomy in control and irradiated mice. Estrogen increases adrenal weight by 35-40% four days after injection and accelerates thymic involution but has no appreciable effect on weight of spleen, inguinal nodes, or kidney. Leukopenia with maximal depression around 10-14 days after injection has also been observed. Decreases are noted in lymphocytes and heterophils. Little change is seen in erythrocytes. Significantly, the maximal estrogenic protective effect is observed when mice are irradiated during their leukopenic period. Estrogen injection at the time of irradiation or 25-35 days before exposure does not protect. Radiation-induced involution of spleen, thymus, and inguinal nodes is not altered by estradiol. However, the increase in adrenal weight is somewhat greater in these animals. Leukocytes are decreased equally in both estrogen and control (sesame oil injected) irradiated animals, although maximal depression and recovery occur somewhat earlier in the former. Erythrocyte count of irradiated controls is decreased by 45% at 11 and 14 days after exposure. Estrogen-treated animals manifest a smaller decrease in red count (25%) seven days after irradiation and normal levels at 11 and 14 days. The possibility that the protective action of estrogens is mediated by the adrenals is being investigated. (NSA)

1240

Patt, H. M., M. N. Swift, E. B. Tyree, and E. S. John. ADRENAL RESPONSE TO TOTAL BODY X-RADIATION. *Am. J. Physiol.* **150**, 480-6(1947).

The changes in adrenal cholesterol content and adrenal weight observed after total body x-radiation at 650 r and 900 r suggest a considerable adrenal response to these dose levels. After 200 r, there is little change in adrenal activity as judged by these indices of response. (GPR)

1241

Patt, H. M., M. N. Swift, E. B. Tyree, and R. L. Straube. X-IRRADIATION OF THE HYPOPHYSECTOMIZED RAT. *Science* **108**, 475-6(1948).

In order to determine whether hypophysectomy would prevent adrenal response to x-radiation and to note whether survival and some of the typical changes in organ weights would be altered, 30 white male rats were hypophysectomized one week prior to a single exposure of 750 r (200 kv; dose rate 18 r/min). The animals were sacrificed three hours and four days after irradiation and the adrenals, spleen, thymus and left kidney were removed. The per cent changes in organ weights and in adrenal cholesterol were determined. Hypophysectomy appeared to potentiate x-ray toxicity. It was concluded that the initial, intermediate, and terminal adrenal changes resulting from x-ray exposure were prevented by the operation, and that under these conditions the extent of the splenic and thymic involution is not altered, although toxicity appears to be enhanced. (NSA)

1242

Smith, Willie W. and Falconer Smith. EFFECT OF THYROID HORMONE ON RADIATION LETHALITY. *Am. J. Physiol.* **165**, 639-50(1951).

The effect of the thyroid hormone in increasing x-radiation lethality was evaluated, and the critical period of susceptibility to the thyroid effect delineated. Dinitrophenol was found to increase the proportion of deaths after irradiation. Thiouracil and propylthiouracil failed to protect against radiation lethality. A yeast supplement failed to prevent thyroid from increasing the mortality after irradiation. Weights of adrenal, lymphoid tissue, and kidney were determined and blood studies made in thyroid-treated and control irradiated mice. No evidence was found to indi-

cate that the thyroid effect is secondary to its action on the adrenal. After sublethal radiation, leucocytes and hemoglobin were more depressed in thyroid-treated than in control mice. (NSA)

1243

Smith, Willie W., Falconer Smith, and E. C. Thompson. FAILURE OF CORTISONE OR ACTH TO REDUCE MORTALITY IN IRRADIATED MICE. *Proc. Soc. Exptl. Biol. Med.* **73**, 529-31(1950).

Intraperitoneal injections of cortisone, or subcutaneous injections of ACTH, failed to increase survival time or number of irradiated mice surviving. (Authors' Summary)

1244

Straube, R. L., H. M. Patt, E. B. Tyree, and D. E. Smith. INFLUENCE OF THE LEVEL OF ADRENAL CORTICAL STEROIDS ON SENSITIVITY OF MICE TO X-IRRADIATION. *Proc. Soc. Exptl. Biol. Med.* **71**, 539-41(1949) (AECU-529; UAC-102)

The radiosensitivity of intact mice with and without whole adrenal cortical extract or desoxycorticosterone has been determined. Data on the sensitivity of adrenalectomized mice which were obtained as part of another study have been included for comparison. From these data it is concluded that the survival of x-irradiated mice appears to be independent, at least within certain limits, of the amount of adrenal cortical steroids present. The adrenals are apparently involved only secondarily as part of the organism's buffer response to the stress of irradiation. The rationale of employing adrenal corticoids to alter radiation mortality is therefore open to question. (NSA)

1245

Swift, M. N., H. M. Patt, and E. B. Tyree. THE EFFECT OF ADRENAL CORTICAL EXTRACT ON ADRENAL RESPONSE TO TOTAL BODY X-IRRADIATION. *Federation Proc.* **7**, 121-2(1948).

This paper is an abstract and is reproduced here in its entirety.

The transient 20-50% decrease in adrenal total cholesterol observed in albino male rats three hours after a mid-lethal total body exposure to x-radiation (Patt, et al., *Am. J. Physiol.*, **150**, 480, 1947) is largely prevented by subcutaneous injection of adrenal cortical extract (Wilson). Total doses of 0.3-1.8 cc/200 g rat were similar in effect, with no graded response over this range. This is additional evidence that the early cholesterol fall reflects increased adrenal activity. In order to investigate the nature of the marked rise (70-109%) in adrenal cholesterol observed 3-7 days after midlethal exposure to x-radiation, a second similar exposure was administered to rats four days after the first. No fall in adrenal cholesterol occurred by three hours after the second exposure, and the cholesterol level at this time was unaffected by cortical extract dosage sufficient to prevent the early decrease seen after a single x-ray exposure. Elevated adrenal cholesterol is reported to occur only after prolonged stimulation by adenotrophic hormone, and may in this case also represent overstimulation in excess of cortical hormone demand. Rats given 0.1 cc of extract three times daily, an amount sufficient to prevent the early cholesterol fall, show adrenal cholesterol changes of slightly lesser degree than do controls over a 15-day post-irradiation period. Survival is not enhanced by this treatment. Larger amounts of extract might possibly prove effective since increased survival has been reported after x-irradiation by shielding the adrenals (Craver, *Fed. Proc.*, **6**, 319, 1947).

1246

Torda, Clara and Harold G. Wolff. EFFECT OF LYMPHOID NECROSIS DUE TO NITROGEN MUSTARD AND

ROENTGEN IRRADIATION ON NEUROMUSCULAR FUNCTION OF HYPOPHYSECTOMIZED ANIMALS. *Am. J. Physiol.* **163**, 201-8(1950).

Hypophysectomized rats exhibited a marked decrease of the ability of nerve to maintain the amplitude of action potential during repetitive stimulation, and a decrease of the ability of nerve tissue to synthesize acetylcholine. Roentgen irradiation and administration of nitrogen mustard increased acetylcholine synthesis in hypophysectomized rats about 30%, and increased by about 30% their ability to maintain the amplitude of action potential during repetitive stimulation. Administration of ACTH restored in hypophysectomized rat the acetylcholine synthesis and the ability to maintain the amplitude of action potential to normal. The effect of ACTH in improving the function of nerve is probably dependent only in part on the reduction of the mass of thymus (perhaps also the lymphoid tissue). (Authors' Summary)

1247

Treadwell, A., W. U. Gardner, and J. H. Lawrence. EFFECT OF COMBINING ESTROGEN WITH LETHAL DOSES OF ROENTGEN RAY IN SWISS MICE. *Endocrinology* **32**, 161-4(1943).

Groups of mice were given 400 to 550 units of x-ray. Estrogen was given 1/3 of the mice at the time of irradiation. One-third of the mice had received estrogen nine days before irradiation. At the end of four days the survival of the irradiated mice was 20.6%, of mice given estrogen and x-rays at the same time, 11.7% and estrogen nine days before irradiation, 75%. (BA)

1248

Van Eck-Vermande, G. J. and J. Freud. ACTION OF GONADOTROPHINS AND OF OESTROGENS ON X-RAYED MOUSE OVARIES. *Arch. intern. pharmacodynamie* **78**, 67-78(1949).

Mouse ovaries irradiated with 330 r and 660 r are moderately responsive to human placental, mare seral, and horse hypophyseal gonadotropins. The response of irradiated ovaries is continually simplified in comparison with those of normal mice as the time after irradiation increases and prospective follicle forming structures disappear. The final result is eutrophy of interstitial ovariocytes, when hardly anything else remains in the irradiated ovary. The estrus and progestational activity of these ovariocytes is indicated in the genital accessories. The immediate destruction of follicles by x-rays is irreparable. But the "secondary" damage caused by irradiation on follicles that develop in subsequent batches is greatly reduced either by estrogens or by hypophyseal gonadotrophin. After such treatment primary follicles show abundant granulosa, secondary follicles do not fail to develop, luteinisation follows, and corpora lutea can assume the pregnancy type. Poorly enveloped oocytes and anovular follicles are found. The theoretical implications, especially doubt as to the existence of follicle stimulating hormone and luteinizing hormone, concerning the cycle and the alleged inhibition of the hypophysis by moderate doses of estrogens are discussed. (NSA)

1249

Velley, Georges and Jean Loiseleur. AUGMENTATION OF THE CUTANEOUS RADIOSENSITIVITY OF THE RABBIT RESULTING FROM THE ACTION OF INSULIN. *Compt. rend.* **230**, 2132-3(1950).

Rabbits were irradiated with various doses of x-radiation (2250 to 3000 r) after receiving an injection of insulin (0.5 clinical units per kilogram). The onset of epilation at the exposed area was greatly accelerated by the insulin injection. The explanation the author offers for this is as follows:

When cellular oxygen becomes activated by x-rays, its activity is shared by the metabolic molecules, principally glucose, and the cellular components (the cause of the appearance of radiolesions). The insulin hypoglycemia, causing the oxidation of the cellular constituents to be preponderant, results in an increase in the cutaneous radiosensitivity. (NSA)

Sulphydryl Compounds

1250

Chapman, W. H. and E. P. Cronkite. SULFHYDRYL-CONTAINING AGENTS AND THE EFFECTS OF IONIZING RADIATIONS; II. FURTHER STUDIES OF THE BENEFICIAL EFFECT OF GLUTATHIONE ON X-IRRADIATED MICE. *Proc. Soc. Exptl. Biol. Med.* **75**, 318-22(1950). (NP-1833)

The effects of the subcutaneous injection of glutathione, prior to irradiation, were studied in four consecutive experiments in which 2343 male, Swiss Albino mice were exposed to various doses of total-body x radiation. The lethal dose curves for glutathione-injected and nontreated mice were simultaneously determined in each experiment. The 28-day LD₅₀ for the nontreated mice was 740 r; for mice that received 1.6 mg of glutathione per gram of mouse, the 28-day LD₅₀ was 840 r, and for mice that received 4.0 mg of glutathione per gram of mouse, the 28-day LD₅₀ was 950 r. These results indicate a quantitative relationship between glutathione dosage and the degree of protection it affords against x-ray damage. Weight change and the effect of trauma were studied in the irradiated survivors in an attempt to demonstrate differences in the recovery rates of the glutathione-injected and the nontreated mice. For these studies, all mice were weighed daily throughout the 28-day observation period of each experiment and on the 29th day all surviving animals were subjected to controlled mechanical trauma produced by a Noble-Collip drum. The glutathione-injected mice lost less weight and were more resistant to trauma than their nontreated controls. (NSA)

1251

Chapman, W. H., C. R. Sipe, D. C. Eltzhoft, E. P. Cronkite, and F. W. Chambers, Jr. SULFHYDRYL-CONTAINING AGENTS AND THE EFFECTS OF IONIZING RADIATIONS. I. BENEFICIAL EFFECT OF GLUTATHIONE INJECTION ON X-RAY-INDUCED MORTALITY RATE AND WEIGHT LOSS IN MICE. *Radiology* **55**, 865-73(1950).

Male and female mice were exposed to total-body x-ray irradiation, in doses of 800 r. Four hundred were given glutathione before or both before and after irradiation. Two hundred were given control saline injections, and 200 received no treatment. The survival rates of the glutathione-treated groups were greater (63.8%) than the survival rates for the comparable control groups (40 to 46%). Statistical analysis showed that the differences in survival rates were definitely significant. The surviving glutathione-treated irradiated animals lost less weight and recovered weight more rapidly than the surviving irradiated control animals. Glutathione-treated survivors, when traumatized, had a lower mortality than the nontreated controls. (NSA)

1252

Cronkite, Eugene P., George Brecher, and W. H. Chapman. SULFHYDRYL-CONTAINING AGENTS AND THE EFFECTS OF IONIZING RADIATIONS; III. STUDIES ON THE MECHANISM OF THE PROTECTIVE ACTION OF GLUTATHIONE. *Military Surgeon* **109**, 294-307(1951). (NP-1876)

After injection of reduced glutathione, clearance and tissue distribution studies were performed in mice, dogs,

and rats. Animals were irradiated during a period when tissue concentration of reduced glutathione was significantly elevated. Following irradiation of mice with 820 r, granulocytes and lymphocytes were apparently absent from the blood of the untreated mice for a few days. During this same period granulocytes and lymphocytes were seen in small numbers in the blood of glutathione-treated mice. The spleen and thymus of irradiated glutathione-treated mice recover normal weight more rapidly than untreated mice. Histologically hematopoiesis returns earlier and with greater frequency in the treated mice than in the untreated mice. Dogs are also partially protected from radiation by intravenous glutathione, 50% recovering from a dose of radiation that has so far been uniformly fatal in untreated dogs in this laboratory. 15 references. (NSA)

1253

Cronkite, E. P., G. Brecher, and W. H. Chapman. MECHANISM OF PROTECTIVE ACTION OF GLUTATHIONE AGAINST WHOLE BODY IRRADIATION. *Proc. Soc. Exptl. Biol. Med.* **76**, 396-8(1951).

White Swiss inbred male mice weighing 20 to 24 g were irradiated with the radial beam of a 2.0-Mev x-ray tube. All mice were given 820 r with the exception of the mice in which the testicles were studied. The latter received 750 r. Before irradiation the mice received either 4 mg of glutathione per gram of mouse subcutaneously as a 10% solution at pH 6.5 or isotonic saline in the same volume. The similarity of the glutathione-treated and untreated irradiated mice in respect to their radiosensitive-organ weights, blood counts, and histologic picture during the first 3 to 5 days is highly suggestive that cellular destruction of radiosensitive tissues (bone marrow, thymus, spleen, and testis) is of equal degree in the two groups. It is impossible to prove this conclusively by histologic techniques because a few blasts might survive and be undetected. In contrast to the similarity in the destructive phase the bone marrow, spleen, and thymus regenerated much more rapidly in the glutathione-treated animals as judged by the criteria used. (NSA)

1254

Cronkite, E. P. and W. H. Chapman. EFFECT OF ADRENALECTOMY AND GLUTATHIONE ON X-RAY INDUCED MORTALITY IN MICE. *Federation Proc.* **9**, 329(1950).

The 28-day mortality of mice simultaneously exposed to various doses of 2.0 mev X-ray was studied on 3 groups of the same age and sex. Group 1: adrenalectomized 10-15 days before exposure and maintained on 1% saline; Group 2: normal control mice; Group 3: injected subcutaneously with glutathione 4 mg/gm immediately before exposure. It is of interest that adrenalectomy 10 days before reduces the total body and hepatic reduced glutathione concentration significantly. The present data indicate that adrenalectomy increases the sensitivity of mice to radiation, this may be related to sulfhydryl levels of tissue. In addition this data refute in part the statement of Straube, et al (*Proc. Soc. Exptl. Biol. Med.* **71**, 539, 1949) "the radiosensitivity of intact or adrenalectomized mice, with or without exogenous adrenal cortical steroids, is similar."

Estimated Percentage Lethal Doses in r
from Mortality Dose Curve

	Adrenalectomized	Control	Glutathione treated
LD ₀	<450	550	550
LD ₅₀	<620	730	840
LD ₁₀₀	<790	940	>1050

1255

Cronkite, E. P., W. H. Chapman, and George Brecher. RELATION OF CLEARANCE AND DISTRIBUTION OF INJECTED GLUTATHIONE TO PROTECTION AGAINST RADIATION INJURY. *Proc. Soc. Exptl. Biol. Med.* **76**, 456-9(1951).

It has been demonstrated by experiment that: (1) The clearance of intravenously injected reduced glutathione from the blood of dogs is rapid (30 min). (2) The disappearance of subcutaneously injected glutathione from the body of the mouse is much slower (>3 hr). (3) The distribution of injected reduced glutathione is not uniform throughout the body. Of the organs studied it concentrates to a considerable extent in the liver, spleen, and kidneys. (4) These experiments suggest that concentration of glutathione at sites vital for survival may be the prime factor in glutathione protection of the irradiated mammal. (NSA)

1256

Fischer, P., L. de Landtsheer, and J. Lecomte. REDUCED GLUTATHIONE CONTENT OF THE BLOOD AND TISSUES AFTER TOTAL-BODY IRRADIATION WITH LETHAL DOSES OF X-RAYS. *Bull. soc. chim. biol.* **32**, 1009-11(1950).

In mice and guinea pigs fatal x-ray doses did not alter the reduced glutathione content of blood, liver, kidney, heart, or muscle. Parenteral administration of dilute H₂O₂ to unirradiated animals caused a decrease in reduced glutathione in the kidney but not elsewhere. (CA)

1257

Forssberg, Arne. POSSIBILITY OF PROTECTING THE LIVING ORGANISM AGAINST RÖNTGEN RAYS BY CHEMICAL MEANS. *Acta Radiol.* **33**, 296(1950).

Attempts to protect living organisms against the effects of Roentgen rays are reported. Cysteine, given to bacterial cells immediately before the irradiation, partly protects the culture from the irradiation injury. Other SH-containing chemicals act similarly, but not related chemicals without a sulfhydryl group.

Cysteine, injected into the skin of guinea pigs, prevents epilation more or less after doses which without cysteine treatment result in epilation. (CA)

1258

Goldie, Horace, Gadson J. Tarleton, Jr., and Paul F. Hahn. EFFECT OF PRETREATMENT WITH CYSTEINE ON SURVIVAL OF MICE EXPOSED TO EXTERNAL AND INTERNAL IRRADIATION. *Proc. Soc. Exptl. Biol. Med.* **77**, 790-4(1951).

Mice pretreated with small doses of cysteine before irradiation with lethal doses of x rays showed a high percentage surviving 10 to 14 days after irradiation. In mice receiving high doses of cysteine the x-ray treatment was followed immediately by death or agony. The condition of mice treated with one factor alone was affected only after several days indicating a potentiation of treatment with cysteine (high doses) and x irradiation. The effect of high doses of cysteine was absent in x-ray treated mice possessing copious peritoneal exudate due to the growth of free S-37 cells in the peritoneal fluid. This action was attributed to the inactivation (oxidation) of cysteine by some factor of the peritoneal fluid. Pretreatment with small doses of cysteine had unfavorable effects on survival of mice injected with radioactive colloidal gold. A possible explanation offered is the increased cysteine penetration from the blood stream into tissues after increase of blood vessel permeability due to high doses of irradiation. (NSA)

1259

Hennessy, Thomas G. and Fleming B. Folsom. THE INABILITY OF CYSTEINE TO PROTECT ERYTHROPOIETIC BONE MARROW AGAINST IRRADIATION IN-

JURY AT A DOSE LEVEL OF 800 r. Naval Radiological Defense Lab. Nov. 6, 1950. (AD-266(B))

Studies of the radioiron, Fe^{59} , red-blood cell uptake in rats that had received cysteine previous to x irradiation were conducted. Control groups of irradiated and nonirradiated rats were also studied. It is concluded that cysteine shows no protective effect against depression of erythropoiesis at the 800-r level of x irradiation. (NSA)

1260

Hennessy, Thomas G., Fleming B. Folsom, and John K. Glover. THE INABILITY OF GLUTATHIONE TO PROTECT ERYTHROPOIETIC BONE MARROW AGAINST IRRADIATION INJURY AT A DOSE LEVEL OF 300 r. Naval Radiological Defense Lab. Nov. 6, 1950. 11p. (AD-267(B))

The uptake of radioiron, Fe^{59} , in the red blood cells of rats that had received subcutaneous injections of glutathione 0.5 hr previous to total-body x irradiation was studied along with that of control groups of irradiated and nonirradiated rats. It is concluded that glutathione shows no significant protective effect against depression of erythropoiesis at the 300-r level of total-body x irradiation. (NSA)

1261

Limperos, G. and W. A. Mosher. PROTECTION OF MICE AGAINST X-RADIATION BY THIOUREA. Science **112**, 86-7(1950).

Varying amounts of thiourea were given to mice by intraperitoneal injection in a single dose five minutes before irradiation with a 650 r dose of x-rays and by administration in the drinking water in a concentration of 1% for a period of six days before irradiation. Mice receiving thiourea had a lower mortality rate than control mice. The authors believe that thiourea and possibly other reducing agents lower the mortality due to x-radiation because of the protection afforded to certain vital cellular constituents such as nucleic acid. (NSA)

1262

Loiseleur, Jean and Georges Velley. CURATIVE TREATMENT OF RADIOLESIONS RESULTING FROM THE ADMINISTRATION OF LETHAL DOSES OF X-RAYS. Compt. rend. **231**, 529-31(1950).

From a brief analysis of phenomena taking place in cells following lethal doses of x-rays, the hypothesis was made that prompt administration of oxygen acceptors capable of penetrating the cells and reducing the dissolved oxygen would be a curative treatment for radiation injury. Eighteen rabbits were exposed to 950 r of whole-body x-irradiation, and ten of these were immediately injected intraperitoneally with 20 cc of a solution of cysteine and ascorbic acid. Additional 10 cc doses were injected after 30 minutes and 2 hours. Six of the ten survived, are in good health, and have gained weight 2 to 4 months after the irradiations. All the untreated controls died 5 to 28 days after receiving the irradiation. (NSA)

1263

Mole, R. H., J. St. L. Philpot, and G. R. V. Hodges. REDUCTION IN LETHAL EFFECT OF X-RADIATION BY PRETREATMENT WITH THIOUREA OR SODIUM ETHANE DITHIOPHOSPHONATE. Nature **166**, 515(1950).

A few substances, selected in the hope that they would enter cells without being too toxic or too rapidly metabolized, and would protect against radiation damage by competing for hydroxyl radicals, were administered intraperitoneally to mice a few minutes before or after x-irradiation. Saline solution was used as a control. The protective effects of thiourea and dithiophosphonate were highly significant, those of glycerol barely so. Thiourea given im-

mediately after the irradiation was ineffective, and saline was not deleterious. (NSA)

1264

Patt, Harvey M., Margaret E. Blackford, Robert L. Straube, and Douglas E. Smith. THE EFFECT OF X RAYS ON THYMOCYTES AND ITS MODIFICATION BY CHEMICAL MEANS. Am. J. Physiol. **167**, 815(1951). (AECU-1557; UAC-409)

The report is reproduced here in its entirety.

X radiation decreases the life span of rabbit thymocytes in vitro, the percentage of surviving cells (eosin resistant) decreasing exponentially with increasing radiation dosage. The LD_{50} at 24 hr is 150 r and definite effects appear with 50 r. Sensitivity is decreased by a factor of 2 over the range of 50 to 1500 r when cysteine (0.02M) is added to the cell suspension before irradiation. The small reduction in toxicity which occurs when cysteine is added after exposure may be due in part to persistence of a toxic substance in the medium, as well as to reversal of a chain of radiation action, since irradiation of only the medium (serum-phosphate buffer) is slightly toxic to cells added subsequently. Anoxic anoxia and cysteine afford comparable protection to thymocytes irradiated with 200 r but they are not additive under these conditions. Packed cells are less radiosensitive than cells suspended in serum and are not protected by cysteine or anoxia. This may be attributed perhaps to the fact that packed cells are already anoxic since cells exposed to oxygen before centrifugation are as sensitive as cells in suspension. These findings suggest that at least two mechanisms are concerned in the cytotoxic action of x rays, one of which is subject to the influence of cysteine and anoxia. It is assumed that these factors act on toxic chemical intermediates that are formed during irradiation, though not necessarily in the same manner. A specific metabolic action cannot yet be ruled out, however. (NSA)

1265

Patt, Harvey M., Douglas E. Smith, Margaret E. Blackford, and Robert L. Straube. PROGRESS REPORT; THE EFFECT OF X RAYS ON THE OXIDIZABLE SULFHYDRYL GROUPS OF RATS RECEIVING CYSTEINE, p.75-7 of BIOLOGICAL AND MEDICAL DIVISIONS QUARTERLY REPORT, NOVEMBER, DECEMBER, JANUARY, 1949-50. Argonne National Lab. [nd] 3p. (ANL-4401(p.75-7))

The oxidizable sulfhydryl content of tissues obtained from irradiated (800 r, total-body) and nonirradiated rats receiving cysteine has been compared. Cysteine (950 mg/kg intravenous) increased the sulfhydryl content of serum, kidney, thymus, small intestine, and liver. Similar increases were noted in cysteine-pretreated x-irradiated rats. X radiation had little effect on the oxidizable sulfhydryls of the control-irradiated animals. The studies suggest that cysteine apparently does not protect against x radiation because it acts as a substrate for oxidation by the free radicals that are presumably formed during exposure. (NSA)

1266

Patt, Harvey M., Douglas E. Smith, and Eugenia Jackson. THE EFFECT OF CYSTEINE ON THE PERIPHERAL BLOOD OF THE IRRADIATED RAT. Blood **5**, 758-63 (1950).

A single intravenous injection of cysteine (950 mg/kg) five minutes before total-body exposure of rats to x-rays (800 r) significantly modified the radiation-induced hematologic changes. Depression of the heterophils, lymphocytes, and erythrocytes was less severe and recovery more rapid. The hematologic observations are consistent with the thesis that cysteine reduces the biological effectiveness of the radiation. (NSA)

1267

Patt, Harvey M., Douglas E. Smith, Ella B. Tyree, and Robert L. Straube. **FURTHER STUDIES ON THE MODIFICATION OF SENSITIVITY TO X-RAYS BY CYSTEINE. I. TIME COURSE OF THE PROTECTION AND COMPARISON OF CERTAIN RELATED SUBSTANCES.** *Proc. Soc. Exptl. Biol. Med.* **73**, 18-21(1950). (AECU-599; UAC-148)

Cysteine (950 mg/kg, neutralized I. V.) greatly reduces sensitivity of rats to total-body x-irradiation (800 r, 250 kv), provided that the amino acid is given before the exposure. Comparable protection is obtained when cysteine is administered intravenously immediately or one hour before irradiation (87% survival of 79 cysteine irradiated; 16% survival of 82 irradiated controls). Injection immediately after exposure or 6 or 24 hours before is without influence. Oral cysteine (1,900 mg/kg) affords a significant protection when given 30-60 minutes prior to x-irradiation. However, oral administration is not as efficient as intravenous. Cysteine, unlike its reduced counterpart, cystine, is not effective by either route. Glutathione, on the other hand, can reduce x-ray toxicity but only when it is given intravenously before exposure. Oral glutathione does not protect rats or mice even though the oral dose is equivalent to the effective oral doses of cysteine in sulfhydryl content. Methionine, ascorbic acid, and sodium sulfide do not alter survival after lethal x-irradiation. Results with colloidal sulfur are equivocal and further work is necessary. These findings suggest first that the critical reactions leading to morbidity are complete when the irradiation is terminated and that these reactions are apparently not reversible. Secondly, a sulfhydryl group distinguishes the substances which can protect from those which cannot. It is important to bear in mind, however, that all sulfhydryl-containing materials may not necessarily protect and that other reducing substances which are properly distributed, temporally and spatially, may. (NSA)

1268

Patt, Harvey M., Douglas E. Smith, Margaret E. Blackford, and Robert L. Straube. **NATURE OF CYSTEINE INDUCED RADIORESISTANCE: SULFHYDRYL LEVELS AND DISTRIBUTION OF CYSTEINE SULFUR.** *Am. J. Physiol.* **163**, 740-1(1950).

The report is reproduced here in its entirety.

Cysteine may increase radioresistance by: 1) decreasing free radical production, 2) competing directly for oxidizing free radicals, 3) shifting the redox potential of critical cell elements, thus protecting them against oxidation, and 4) altering metabolic pathways. Assuming selective action on sulfhydryl groups by products of irradiated water, less than 1% of nonprotein-SH (as cysteine) could theoretically be oxidized when a 200-gm rat is exposed to 800 r. X-irradiation had no immediate observable effect on -SH levels in control and cysteine rats, although cysteine per se (950 mg/kg intravenously) increased the oxidizable -SH content of TCA filtrates of serum, kidney, thymus, intestine, and liver. Rather identical retention of S^{35} was noted in blood of rats receiving labeled cystine, cysteine, or cysteine followed by X-irradiation, (60 mg cystine or cysteine, 5×10^5 counts/min. intravenously). Uptake of S^{35} by liver and intestine was more rapid in cysteine injected rats. X-radiation appeared to decrease rate of uptake and retention. The initial concentration of S^{35} in bone marrow was similar in cystine and cysteine animals but fell sharply during the first hour in the latter. Marrow uptake was diminished by irradiation. No clear relationship between S^{35} concentration in these tissues and the time course of cysteine protection was evident. Our data do not support the concept of direct or indirect competition by

cysteine for oxidizing radicals. If such a mechanism is operating, oxidation must be localized in specific sites where -SH or other essential substances are few and their inactivation critical.

1269

Patt, Harvey M., Ella B. Tyree, Robert L. Straube, and Douglas E. Smith. **CYSTEINE PROTECTION AGAINST X-IRRADIATION.** *Science* **110**, 213-14(1949).

Some observations concerning the influence of cysteine and cystine on the radiosensitivity of rats are reported. Brief exposures to intense irradiation were employed and the radiation factors were a 250 kv machine delivering radiations through 0.5 mm Cu and 3.0 mm Bakelite filters at a target distance of 27.5 cm and at a dosage rate of 210 r/min. Male and female rats weighing 150-250 g received 800 r of total-body x-radiation in a single exposure. Cysteine was injected into the tail vein one hour before, 5 minutes before, or five minutes after the exposure. Four different doses of cysteine were compared (175, 350, 575, and 875 mg of cysteine/kg body weight), and a 20% solution was used, the cysteine being injected slowly over a period of minutes; irradiated controls were injected with an equivalent volume of saline solution. The results show that pretreatment with cysteine markedly reduced the toxicity from total-body x-irradiation since there was an 82% survival from the treated group as compared with a 19% survival from the controls. Cystine, however, did not influence the survival rate. There were variations in the degree of protection per gram of cysteine depending on the pH of the administered solution; the injection of cysteine immediately after exposure was ineffectual. It is concluded that cysteine, but not cystine, administered to rats prior to x-irradiation in the nearly completely lethal range, greatly diminishes toxicity. (NSA)

1270

Rosenthal, Robert L., Leontine Goldschmidt, and Bryant I. Pickering. **HEMATOLOGIC CHANGES IN RATS PROTECTED BY CYSTEINE AGAINST TOTAL BODY X-IRRADIATION.** *Am. J. Physiol.* **166**, 15-19(1951). (AD-215(B))

Following 800 r total body x-irradiation, cysteine-protected rats showed significantly higher neutrophil values in the blood, and more myeloid cells of all stages in the bone marrow, than did saline-injected rats. The possible significance of these findings in relation to mortality and infection is discussed. (NSA)

1271

Smith, D. E., Harvey M. Patt, and Ella B. Tyree. **PROGRESS REPORT; NOTES ON THE EVALUATION OF MATERIALS THAT MIGHT BE EXPECTED TO ALTER RADIOSENSITIVITY, p.72-4 of BIOLOGICAL AND MEDICAL DIVISIONS QUARTERLY REPORT, NOVEMBER, DECEMBER, JANUARY, 1949-50.** Argonne National Lab. [nd] 3p. (ANL-4401(p.72-4))

Thirty-day survival, time to 50% mortality, and average survival time of rats subjected to a single total-body exposure of 1000 r were taken as criteria of the capacity of materials to alter sensitivity to x radiation. Of materials so tested, BAL and cysteine + KCN administered prior to irradiation significantly decreased radiosensitivity; while thiamine-HCl, L-taurine, and tyrosine were without effect. Moreover, cysteine + KCN reduced radiosensitivity to the same degree as the same dose of cysteine alone, indicating that cysteine owes its protective ability to factors other than its reducing powers. (NSA)

1272

Smith, Douglas E., Harvey M. Patt, Ella B. Tyree, and Robert L. Straube. **FURTHER STUDIES ON MODIFI-**

CATION OF SENSITIVITY TO X-RAYS BY CYSTEINE.
Proc. Soc. Exptl. Biol. Med. **73**, 18-21(1950).

Cysteine greatly reduces the sensitivity of rats and mice to lethal amounts of x-rays delivered at either high or low dose rates provided that the amino acid is given before the exposure. Rather comparable protection is obtained when cysteine is injected intravenously in rats immediately or one hour before irradiation with 800 r (90% reduction in the 28-day mortality). Injection immediately after exposure or 6 or 24 hr before is without influence. Cysteine also improves survival significantly when it is given orally 30 to 60 minutes prior to the irradiation. Glutathione (IV but not oral) can also diminish radiation toxicity. Cystine, methionine, ascorbic acid, and sodium sulfide do not alter survival of the irradiated animal. Results with colloidal sulfur are equivocal. The possible significance of these observations is discussed. (Author's Summary)

1273

Smith, D. E., H. M. Patt, E. B. Tyree, and R. L. Straube. **QUANTITATIVE ASPECTS OF THE PROTECTIVE ACTION OF CYSTEINE AGAINST X-RADIATION.** *Proc. Soc. Exptl. Biol. Med.* **73**, 198-200(1950).

Three groups of male Sprague-Dawley rats received a 10% solution of cysteine intravenously and within five minutes after the dose were irradiated by whole body exposure at 250 kv through a filter of 0.5 mm Cu and 3.0 mm Beryllium at a target distance of 26.5 cm with a dose rate of 210-220 r/min. Each group had controls and they were divided into groups as follows: 50-950 mg/kg of cysteine was given in graduated doses to test protection from 800 r and 1,000 r; the protective value of 950 mg/kg of cysteine was determined for graduated doses from 600-1, 800 r; a dual injection composed of one dose of 475 mg/kg followed in 45-60 minutes by a second dose of 950 mg/kg was given and then the animals were irradiated as before with a total dose of 1,200 r. Results are briefly given and discussed and the authors conclude that the protection given by cysteine is roughly proportional to the amount of cysteine given. (NSA)

1274

Straube, Robert L., George Svihla, Margaret E. Blackford, and Harvey M. Patt. **EFFECT OF CYSTEINE ON THE RADIOSENSITIVITY OF THYMIC CELLS IN VITRO.** *Am. J. Physiol.* **167**, 829(1951) (AECU-1532; UAC-407)

The report is reproduced here in its entirety.

The effect of cysteine on the radiosensitivity of thymic cells incubated in vitro has been studied cinematographically. Normal thymic cultures and cultures to which cystine has been added, as well as irradiated cultures, are shown for comparison, both immediately and 20 to 24 hr following preparation. Cysteine (0.02M) does not alter the activity of normal cells. Motility, protoplasmic streaming, pseudopod extension, nuclear granulation, and vacuolization, occur to the same degree in both preparations. Loss of motility and rounding up of the cells to form indistinctly granular spheres, with occasional nuclear vacuolization, is usually preceded by a flurry of activity. Such spherical, quiescent cells stain with eosin or safranin. More quiescent cells are found after incubation for 20 to 24 hr in all preparations. Since the mature thymic cells almost never divide, population reduction due to cellular senescence and death is a constant factor. Irradiation of a thymic suspension with 1000 r greatly reduces the number of cells surviving at 20 to 24 hr. The majority of surviving cells, unlike those in the cystine 1000-r series, are non-motile. Thus, on a qualitative basis, control cells and cells to which cystine has been added are essentially similar at both 0 and 24 hr. Control irradiated cells and cystine ir-

radiated cells are similar at 0 hr, but at 24 hr preparations of the latter contain almost as many motile forms as the normal, whereas those of the former show predominantly quiescent forms. (NSA)

1275

Works, Lee, John H. Grotts, and Gordon W. Raleigh. **EFFECT OF BAL ON RADIATION MORTALITY RATE IN MICE.** *Quart. Bull. Northwestern Univ. Med. School* **24**, 295-6(1950).

A group of 66 mice irradiated with 550 r of 210-kvp x rays showed a 5% survival rate at the end of 5 weeks, in contrast to a 39% survival rate in a group of 61 animals of the same strain, each of which had received a subcutaneous dose of 2.6 mg of BAL (2,3-dimercaptopropanol) 1 hr prior to the irradiation. A 94% survival rate was found in mice subjected to the BAL treatment only. (NSA)

Surgical Treatment

1276

Brown, James Barrett, Frank McDowell, and Minot P. Fryer. **RADIATION BURNS, INCLUDING VOCATIONAL AND ATOMIC EXPOSURES. TREATMENT, AND SURGICAL PREVENTION OF CHRONIC LESIONS.** *Ann. Surg.* **130**, 593-607(1949).

Acute and chronic radiation burns and their treatment are discussed. For the treatment of the acute burns, such as those caused by single, large exposures, atomic radiation and the like, rest, sedation, prevention of infection, and alleviation of the severe pain are advised, as well as grafting of open wounds as soon as possible. Chronic burns, commonly seen on the hands of radiologists and due to repeated exposures over a long period of time to small amounts of radiation, are treated by excision and repair of the skin defects with grafts or flaps; the treatment should be done in the early or the quiescent stages, rather than in the ulcerated stage. The authors conclude that the pathology of atomic radiation burns is probably similar to that of the burns under discussion and the same types of therapy will be beneficial; chronic skin lesions in heavily irradiated areas may be prevented by excision and grafting before the chronic changes (coagulation, atrophy, endarteritis of the small arterioles, telangiectasis and similar phenomena) occur. (NSA)

1277

Brown, James Barrett, Frank McDowell, and Minot P. Fryer. **SURGICAL TREATMENT OF RADIATION BURNS.** *Surg. Gynecol. and Obstet.* **88**, 609-22(1949).

The treatment by excision and grafting of burns due to excessive radiation on normal skin and regions with acne, eczema, and other abnormalities is described. Pathological effects of the radiation, such as loss of appendages of skin and obliteration of blood vessels, are noted, and specific treatment in these cases is detailed. The symptoms of severe burns are excessive pain, swelling, weeping skin, and possible sloughing of the epidermis. Treatment for this type of burn and for chronic improvement-resisting burns is, and should be, entirely surgical. Anatomical regions most commonly affected are described separately. In special cases immediate flap closure, delayed pedicle closure, or pedicle grafts are called for instead of the regular procedure. Surgery becomes necessary frequently to prevent the development of carcinoma in the affected areas. (NSA)

1278

Greeley, Paul W. **RECONSTRUCTION FOLLOWING IRRADIATION INJURIES.** *Arch. Surg.* **56**, 741-9(1948).

Although present knowledge of x-ray and radium therapy is extensive, a surprisingly large number of irradiation injuries still occur. They result from incidental reactions following treatment of deep lesions and mismanagement by untrained or inexperienced operators. It is emphasized that all types of treatment by x-rays under disguised names and usually in the hands of lay operators are a serious menace to the public. X-rays produce irreversible reactions that are characterized by severe pain, itching, ulceration, and eventual malignant degeneration. These symptoms can be relieved promptly and permanently by wide surgical excision. The resulting defects are then closed by one of several different plastic surgical procedures. (NSA)

1279

Huff, R. L., W. F. Bethard, J. F. Garcia, B. M. Roberts, L. O. Jacobson, and J. H. Lawrence. **THE EFFECT OF SPLEEN PROTECTION ON IRON DISTRIBUTION IN IR-RADIATED RATS.** *J. Lab. Clin. Med.* **36**, 40-51(1950) (ANL-4401(p.33-4))

Eighty female Curtis-Dunning rats were divided into 4 groups treated as follows: (I) maintained as normal controls, (II) surgical mobilization of the spleen, but no radiation, (III) single total-body exposure to x radiation, as well as a sham operation in which the spleens were mobilized but not protected, and (IV) irradiated with the mobilized spleen in a lead chamber. Each of the x-irradiated animals received 500 r. Three days thereafter, and at comparable times for controls, each rat received intravenously approximately 10,000 cpm of Fe^{59} . Bone marrow of groups I and II contained 60% of injected Fe^{59} within 3 hr after injection. Similar curves for groups III and IV yielded maximum uptakes of 11 and 16%, respectively. Unexpectedly, the bone marrow in group IV animals showed significantly greater function than that in group III. Uptake of Fe^{59} in liver was greatest in group III (56%). Groups I, II, and IV gave values of 15, 15, and 43% in the order given. The uptake of Fe^{59} in spleen was nearly equal (1%) for groups I, II, and III. In the irradiated, spleen-protected animals, however, 7% of the injected tracer was found in the spleen. (NSA)

1280

Jacobson, Leon O., Edna K. Marks, Evelyn Gaston, Melba J. Robson, and Raymond E. Zirkle. **THE ROLE OF THE SPLEEN IN RADIATION INJURY.** *Proc. Soc. Exptl. Biol. Med.* **70**, 740-2(1949).

A technique different but related to that previously described by Jacobson et al (*Anat. Record* **100**, 1948; *National Nuclear Energy Series Div. IV Vol. 22B*) for the study of the significance of the spleen in recovery from or compensation for radiation injury is presented. The materials and methods are described in detail. Radiation consisted of 600 r whole-body x-radiation administered to mice with or without their spleens protected by lead boxes covering all but the pedicles. Hematologic and histopathologic studies were carried out at intervals. The mean hemoglobin, erythrocyte, and hematocrit values of the lead-protected mice were not significantly altered while marked reduction in the unprotected mice was noted. The mean platelet and reticulocyte values of the unprotected group also fell appreciably. These data indicate that severe anemia, leucopenia, and thrombocytopenia develop in mice after a single dose of 600 r whole-body x-radiation. Ectopic erythropoiesis, in the lead-protected spleens compensates with such rapidity and so extensively for the destruction and interruption of this activity in the marrow spaces that no anemia of significance becomes apparent. Ectopic granulocytopenia and megakaryocytopenia in the lead-protected spleens compensates significantly but at a slower

pace and less completely for the bone marrow destruction. A marked and sustained decrease in the amount of lymphatic tissue is produced in the lead-protected spleens. This decrease in lymphatic tissue may perhaps be a result of (a) unsuccessful competition of the lymphatic tissue with the ectopic hematopoiesis for nutritional requirements, (b) actual indirect effect of radiation, and (c) a differential humoral suppression from some unknown site. This technique provides a method of studying potential sites and mechanisms of the production of ectopic blood formation, possible secondary effects of radiation as well as offering possibilities for determining the potential role of such sites in immune reactions, in preventing or alleviating radiation-induced hemorrhagic phenomena and in the study of survival or recovery from radiation injury. (NSA)

1281

Jacobson, Leon O., Eric L. Simmons, W. F. Bethard, Edna K. Marks, and Melba J. Robson. **THE INFLUENCE OF THE SPLEEN ON HEMATOPOIETIC RECOVERY AFTER IRRADIATION INJURY.** *Proc. Soc. Exptl. Biol. Med.* **73**, 455-9(1950).

Young adult female mice were exposed to 1,025 r whole-body x-irradiation delivered by a 250-kv source through an 0.25 mm Cu filter. The spleens of these mice were mobilized surgically through an abdominal incision and lead-protected during irradiation in one group and mobilized but not lead-protected during irradiation in another group. The bone marrow and lymphatic tissues were destroyed, and no regeneration was apparent on the tenth day in the animals irradiated without lead protection of the spleen. In the animals with lead protection of the spleen during irradiation, these tissues were not depleted of free hematopoietic cells, and the bone marrow and the lymph nodes were normal in cellularity eight days after irradiation. Several possible interpretations of the role of the spleen under the conditions of these experiments are discussed. (NSA)

1282

Jacobson, Leon O., Eric L. Simmons, Edna K. Marks, and J. H. Eldredge. **RECOVERY FROM RADIATION INJURY.** *Science* **113**, 510-11(1951).

An attempt has been made to clarify some of the factors involved in the greatly increased LD_{50} of spleen- or liver-shielded mice (*J. Lab. Clin. Med.* **34**, 740(1949) and **35**, 746(1950)). The results indicate that the factor involved in the shielding or transplant experiments is definitely effective after irradiation, and that the factor responsible for recovery from radiation under these conditions is probably a substance of a noncellular nature. (NSA)

1283

Jacobson, Leon O., Eric L. Simmons, Edna K. Marks, Evelyn O. Gaston, Melba J. Robson, and J. H. Eldredge. **FURTHER STUDIES ON RECOVERY FROM RADIATION INJURY.** *J. Lab. Clin. Med.* **37**, 683-97(1951).

The 28-day LD_{50} for spleen-shielded mice is ~1100 r of whole-body x-radiation compared to ~550 r for mice without spleen shielding. Unlike glutathione, cysteine, O_2 deprivation, or cyanide intoxication, the "factor" in spleen shielding which effects a significant increase in survival of mice from whole-body x-radiation is unnecessary during the actual irradiation process and is definitely effective after irradiation. In these experiments the general assumption is made either that (1) the shielded tissues produce a substance of a noncellular nature which exerts a beneficial effect on the recovery of the irradiated animal or (2) that cells migrate from the shielded tissue which enhance recovery of the irradiated tissues. The evidence appears to be in favor of the first assumption. The potential significance of these observations to the therapy of radiation injury and other clinical syndromes is discussed briefly. (NSA)

1284

Jacobson, Leon O., Eric L. Simmons, Edna K. Marks, Melba J. Robson, W. F. Bethard, and Evelyn O. Gaston
THE ROLE OF THE SPLEEN IN RADIATION INJURY AND RECOVERY. *J. Lab. Clin. Med.* **35**, 746-70(1950).

In a study to compare the effect of 1,025 r on the blood and blood-forming tissue of mice which had had lead protection of the surgically mobilized spleen during radiation with the effect of this dose on mice without lead protection, 165 female CF-1 mice aged 10 to 12 weeks were divided into four groups, including one control group of 40 animals and three other groups which were prepared by surgical mobilization of the spleen under nembutal anaesthesia. Two of the three groups received X-ray doses with irradiation delivered by a 250-kv machine through a 0.25 mm Cu filter, with a dose rate of 53.9 r/min at 55 cm, hematological, gross and microscopic tissue examinations, and determinations of body weight at various intervals were done. The data and results are extensively presented in graphs, tables, and plates; they are thoroughly discussed. (NSA)

1285

Lorenz, Egon, Delta Uphoff, T. R. Reid, and Emma Shelton.
MODIFICATION OF IRRADIATION INJURY IN MICE AND GUINEA PIGS BY BONE MARROW INJECTIONS. *J. Natl. Cancer Inst.* **12**, 197-201(1951).

Data indicate that bone marrow injected either intravenously or intraperitoneally postirradiation gives excellent protection to mice and guinea pigs from the acute irradiation syndrome. (NSA)

1286

Mason, Michael L. **THE SURGICAL TREATMENT OF IRRADIATION INJURIES.** *Illinois Med. J.* **95**, 20-6(1949).

The five large groups into which irradiation injuries of the skin and subcutaneous tissues may be grouped are reviewed. Examples are given of injury treatment which consists in removal of all involved skin and plastic repair of the resultant defect. Additional irritants, particularly irradiation of any sort, must be avoided since they increase the severity of the process and delay surgical repair (NSA)

1287

Rekers, Paul. **TRANSPLANTATION OF BONE MARROW INTO DOGS THAT HAVE RECEIVED TOTAL BODY SINGLE DOSE RADIATION.** University of Rochester. [nd] 5p. (AECD-1968; UR-11)

The major results of this paper are condensed in Rekers, Coulter and Warren (*Arch. Surg.* **60**, 635-67 (1950)). See abstract 1348

1288

Robtson, David W. **THE SURGICAL REPAIR OF IRRADIATION DEFECTS.** *J. Kansas Med. Soc.* **49**, 456-61 (1948).

The types of injuries caused by irradiation in different tissues are briefly described and the surgical repair techniques for different structures and different locations are discussed. Cases are classified with respect to etiology as follows: (1) accidental x-ray burns of physicians, (2) injury from intentional massive dosage for neoplasm, (3) late change from repeated small dosage given for superficial therapy, and (4) burns to patients from prolonged exposure under the fluoroscope. The repair of injuries is described in reports of illustrative cases for each etiologic group (NSA)

1289

Simmons, Eric L. **PRELIMINARY REPORT; FURTHER STUDIES OF THE PROTECTIVE EFFECTS OF SHIELDING,** p.27 of **DIVISION OF BIOLOGICAL AND MEDICAL**

RESEARCH QUARTERLY REPORT, MAY, JUNE, JULY, 1950. Argonne National Lab. July 1950. 1p. (ANL-4488(p.27))

A brief report states that data from experiments show that a marked increase in survival occurs in both male and female rats when the intestine is surgically mobilized and lead-protected during total-body x irradiation. Initial studies of survival of the x-irradiated, spleen-shielded rat show less positive results than those obtained when mice were irradiated with spleen protection. Preliminary experiments have failed to show any increased capacity of the spleen to aid survival following x irradiation when priming doses of 100, 200, or 300 r were given before 800 r. However, there was an increase in mortality with increase in the total dose administered. (NSA)

1290

Stevenson, Thomas W. **SURGICAL TREATMENT OF X-RAY BURNS.** *Rocky Mt. Med. J.* **46**, 198-200(1949).

There are two types of deep ulceration following irradiation. In the acute type the initial erythema progresses rapidly, vesicles appear, and later the skin becomes necrotic. The sloughing off of necrotic tissue is greatly retarded and may not occur for several months. Granulation tissue fails to appear and no sign of marginal epithelialization is seen. The retarded slough and lack of granulation tissue and epithelialization distinguish this lesion from any other form of traumatic wound. Pain is usually a striking feature, the slightest drying of the surface or pressure of dressing causing extreme discomfort. In the chronic form, ulceration may take place in an area which had remained healed for several years. This usually results from progressive fibrosis and consequent reduction in local blood supply, which eventually leads to ischemic necrosis. Intense pain is also a feature of this type of ulceration. Complete excision of the involved area with skin grafting is the treatment of choice. In the author's experience the source of the largest group of superficial injuries was the treatment of hypertrichosis, fracture reduction, and various dermatologic conditions. (RA)

1291

Talbot, John M. **BONE MARROW IN THE TREATMENT OF RADIATION INJURY,** p.125 of **INTERNATIONAL CONGRESS OF RADIOLOGY**, 6th Congress, London. 1950.

An initial group of rats with bone marrows depressed by benzene received intrahepatic, intramuscular, and subcutaneous injections of fresh femoral marrow from animals of the same strain. Healthy marrow growths were found in the livers at six, fourteen, and twenty-six days. A second series received acute LD₅₀ doses of whole body X-radiation with tibiae, fibulae, and about one-half of each femur shielded by lead. Total WBC and RBC showed significantly less depression during the two weeks' observation periods than did the unshielded controls. Deaths occurred in both the shielded and unshielded animals. Following acute LD₅₀ doses of total body X-radiation two series of rats were given intrahepatic and intramuscular injections of approximately 0.05 cc of fresh femoral bone marrow from donors of the same strain. Healthy survival of the implants was found in animals sacrificed at seven, and at fourteen days. No significant changes were noted in peripheral blood pictures and survival rates. Another series with acute radiation injury was treated with two or more intramuscular injections of fresh femoral marrow. Blood pictures and survival rates in this series did not differ significantly from those of controls.

1292

Talbot, John M. and Ernest A. Pinson. **THE EXPERIMENTAL USE OF BONE MARROW IN ACUTE RADIATION INJURY.** Military Surgeon 108, 412-17(1951).

Studies of bone marrow homotransplants in rats whose marrows were depressed by benzene injections and by whole-body x irradiation suggest that the transplants will survive in a reasonably healthy condition for an approximate minimum of 4 weeks. Bone marrow given intramuscularly following acute, whole-body ionizing radiation injury in the lethal and sublethal ranges had no significant effects upon survival, changes in total white blood cell counts, and changes in body weights. Shielding of $\frac{1}{3}$ to $\frac{3}{4}$ of the hind limbs of rats produced significant differences in survival and weight loss as compared to the transplanted group. (NSA)

Vitamin Studies

1293

Adams, William S. and John S. Lawrence. **THE NEGATIVE EFFECT OF FOLIC ACID ON IRRADIATION LEUKOPENIA IN THE CAT.** Am. J. Med. Sci. 216, 656-60 (1948).

The prophylactic and therapeutic administration of folic acid to cats did not alter the occurrence or the magnitude of leukopenia caused by exposure to 200 r whole body irradiation. (NSA)

1294

Ames, Stanley R., J. G. Baxter, and J. Q. Griffith, Jr. **PREVENTION BY d - ALPHA -TOCOPHEROL OF INCREASED CAPILLARY FRAGILITY IN RATS FOLLOWING IRRADIATION.** Intern. Z. Vitaminforsch. 22, 401-7 (1951).

Each of 30 adult rats was given 1 cc of 200 microcuries per cc. Rn ointment intraperitoneally; 10 were controls; each of 10 was injected daily with 0.11 cc α -tocopherol concentrate containing 34.6% total tocopherols, of which 61% was α , the remainder γ and δ ; each of 10 was injected daily with 0.55 cc of a concentrate containing 72.4% total tocopherols which were 50% γ and 50% δ . At the end of 15 days, capillary fragility was determined by the positive pressure method. Both concentrates apparently offered significant protection against the increased fragility produced by Rn. However, multiple, apparently sterile, subcutaneous abscesses developed at the point of injection of the concentrate. When adult rats were given 0.5 cc of 80 microcuries per cc Rn ointment intraperitoneally, and α -tocopherol in olive oil was administered by mouth at a level of 2.5 or 10 mg daily for 10 days, the incidence of increased capillary fragility was reduced; the lower dose of tocopherol was more effective than the higher. (CA)

1295

Artom, Camillo, W. E. Cornatzer, and George T. Harrell, Jr. **THE PROTECTIVE ROLE OF PYRIDOXIN AGAINST THE TOXIC EFFECTS OF P³².** Bowman Gray School of Medicine, Wake Forest Coll. [nd] 1p. (AECU-1811)

In a continuation of our previous studies on the effects of internal radiation by P 32 as related to various dietary factors, the role of pyridoxin has now been investigated. Mice placed on various experimental diets and receiving a mixture of B vitamins without pyridoxin were injected with a single dose of radioactive phosphate (5-6 μ g). In the groups on low-protein diets (in which the vitamin deficiency was presumably slight or not yet developed) the administration of pyridoxin did not affect the survival of the animals. On the contrary a marked protection by pyridoxin was observed in experiments in which the vitamin deficiency was made more severe by adding a pyridoxin analog

(desoxypyridoxin) to the low-protein diet, or by increasing the metabolic demand for the vitamin (high-protein diets with added cystine or methionine). For instance, in the groups receiving pyridoxin together with its analog, the day of 50% deaths was shifted from the 14th to beyond the 42nd, and average time of survival from 19 to 33 days, and the proportion of survivors at the end of the 3rd week from 19 to 77%. These differences are larger than those which might result from a simple additive effect of internal radiation and vitamin deficiency. (Abstract of paper for Atlanta Meeting of Southeastern Section of the Society for Experimental Biology and Medicine, Winter, 1952.) (NSA)

1296

Carter, Robert E., Elizabeth Busch, and Verda Strang. **THE EFFECT OF VITAMIN B₁₂ ON THE LEUKOPENIA INDUCED BY RADIATION.** Blood 5, 753-7(1950). (AECU-416; LADC-694)

Crystalline vitamin B₁₂ administered via intramuscular injection, in single and in multiple doses, produced no effect on the leukopenia induced in rats by 400 r of 250 kv x-rays. (NSA)

1297

Cornatzer, W. E., Camillo Artom, George T. Harrell, Jr., and David Cayer. **BENEFICIAL EFFECTS OF VITAMIN B₁₂ AND FOLIC ACID ON RECOVERY FROM INTERNAL RADIATION BY P³².** Proc. Soc. Exptl. Biol. Med. 76, 552-4(1951).

The addition of generous amounts of folic acid, or folic acid and vitamin B₁₂, to experimental diets had no significant effect on the survival of mice injected with a dose of P³² in the higher range of the LD₅₀ (21st day). On the other hand, when sulfasuxidine was added to the diet and the mice were injected with a dose of P³² slightly below the LD₅₀ (21st day), the administration of vitamin B₁₂ and folic acid increased significantly the time of 50% deaths, the average time of survival, and the percentage of survivors at both the 21st and the 56th day. (NSA)

1298

Cronkite, Eugene P., John L. Tullis, Carl Tessmer, and F. W. Ulrich. **FAILURE OF FOLIC ACID TO INFLUENCE LETHAL RADIATION ILLNESS IN SWINE.** Proc. Soc. Exptl. Biol. Med. 73, 496-7(1950).

Eight swine were exposed to 400 r total body radiation. Four were treated with intramuscular injections of 45 mg of folic acid per day. The clinical and hematological courses were observed and postmortem examinations were performed. No differences were observed in the responses of the treated and untreated swine. 11 references. (NSA)

1299

Goldfeder, Anna, Lionel Cohen, Charlotte Miller, and Margaret Singer. **AGENTS INFLUENCING EXPERIMENTAL RADIATION INJURY. EFFECTS OF FOLIC ACID AND PYRIDOXINE.** Proc. Soc. Exptl. Biol. Med. 67, 272-8(1948).

White mice, exposed to x-radiation, were given a medium dose of 350 r in a single exposure. Folic acid and pyridoxine hydrochloride were used as possible protective agents. No appreciable effect of these drugs on the hemopoietic system was noted. On the other hand, it was found that 15 γ of folic acid injected daily during a period of seven days prior to radiation and 15 days after radiation prolonged significantly the survival time of the irradiated mice. Similar observations were made with pyridoxine hydrochloride. Thus, irradiated mice injected with 50 γ of pyridoxine hydrochloride intramuscularly daily seven days prior to radiation and 13 days post-radiation, extended significantly the life of the irradiated mice, as compared with the irradiated, unmedicated mice. (GPR)

1300

Herve, A. CONSIDERATIONS OF RADIATION SICKNESS AND ITS THERAPY. *Bruxelles med.* 29, 445-50(1949).

Observations of 210 cases receiving radiation delivered at 151 to 200 kv and 59 to 400 kv show that 34.4% and 16.9% developed radiation symptoms at low and high tensions, respectively. The author concludes that higher voltages are better tolerated for the same dose than the lower voltages, but that other physical factors and specific radiation sensitivity must also be taken into consideration. Vitamin B complex therapy gave good or favorable results in 46 out of 62 cases, showing an initial remission of gastrointestinal symptoms. (NSA)

1301

Herve, A. and J. Lecomte. ACTION OF THE SEMI-CARBAZONE OF ADENOCROME ON PETECHIAE CAUSED BY X-RADIATION. *Arch. intern. pharmacodynamie* 79, 109-12(1949).

Experiments are described which indicate that the administration of the semi-carbazone of adenochrome (adrenoxyl-1) greatly reduces the cutaneous purpura produced by x-radiation in mice of the A.K.A. strain although the length of survival-time is not significantly augmented. One hundred and forty mice of the pure strains A.K.A., C and C₅₇ received daily, 400 r x-ray doses for four consecutive days. Half of the experimental animals had previously received 200 µc of the adrenoxyl by intraperitoneal injection in a 0.2 cc volume, whereas the other half, serving as controls, were similarly injected with 0.2 cc of physiological serum. The skins of the animals, which were sacrificed six days after the irradiation was begun, were detached. Examination of the internal surfaces of the skins indicated that while the control animals showed petechiae (purpuric eruptions) and hemorrhages, particularly in the sacral regions, the adrenoxyl-injected group did not show any capillary hemorrhage and few purpuric eruptions. It is noted that preliminary experiments have shown that x-radiation does not always produce petechiae in mice and that C₅₇ mice sometimes die from irradiation before they show signs of petechiae. (NSA)

1302

Huant, E. EFFECT OF NICOTINAMIDE ON LOCAL TOLERANCE OF THE SKIN AND DEEP TISSUES TO X-RAYS. RESULTS OF INCREASING THE DOSAGE. *Gaz. hôpitaux (Paris)* 120, 313-14(1947).

This work is based on observation of 110 cases receiving radiotherapy for various conditions. During periods of radiation treatment, nicotinamide was administered preferably by intramuscular injection and sometimes by mouth with an average dose of 40 to 60 cg. In 70% of the cases the skin tolerance dose could be increased by 50 to 75% and doubled in 20% of the cases. If nicotinamide should serve to protect the deeper tissues such as nerve, vessels, and bone from harmful effects of radiation, larger x-ray doses may be used, especially in the treatment of tumors of the cervix, larynx and mediastinum which are in highly innervated and vascularized areas. A case is presented of a skin ulcer with muco-hemorrhagic exudation following x-ray therapy of a mixed tumor of the parotid with complete healing after 18 days of nicotinamide administered locally and IM. (EM)

1303

Imler, A. E. and H. Wammock. VITAMIN B₁ IN IRRADIATION SICKNESS. *Am. J. Roentgenol. Radium Therapy* 43, 243-8 (1940).

The authors employed large doses of vitamin B₁ in 21 cases of irradiation sickness with good results. In most cases the subcutaneous injection of 3,000 IU daily gave

rapid and complete relief. In a few cases recurrence of symptoms necessitated a temporary, or permanent, increase in dosage. Marked anorexia, nausea, and giddiness could generally be controlled by 3,000 IU daily, given by mouth, but nausea, anorexia, and vomiting required 6,000 IU or more daily. With the oral route also relief of symptoms did not occur before 24 or 48 hours whereas with subcutaneous injection relief occurred within 1 to 3 hours. Treatment was continued for periods varying from 3 to 20 days. (BEMP)

1304

Jacobson, Leon O., S. Phyllis Stearner, Eric L. Simmons, and Mathew H. Block. THE EFFECT OF FOLIC ACID ON THE RESPONSE OF THE PERIPHERAL BLOOD AND BLOOD-FORMING TISSUE OF THE RAT TO PARENTERALLY ADMINISTERED STRONTIUM⁹⁰. Argonne National Lab. Mar. 15, 1948. 6p. (AECD-2013; ANL-4125)

Female white rats from the Sprague-Dawley farms were injected intraperitoneally with 4.2 µc/g Sr⁹⁰ and were treated with daily injections of 15 µg folic acid. Hematological studies were made of the peripheral blood before injection and at 3, 6, and 8 weeks after the Sr⁹⁰ injection. The experiment was then terminated and all surviving animals autopsied for histological study of the blood-forming tissues. Folic acid had no observable effect on the macrocytic anemia and leucopenia that developed after the administration of Sr⁹⁰. When given daily from the start of the experiment, folic acid did not prevent the appearance of the effects of Sr⁹⁰ on the peripheral blood; when it was given after the appearance of radiation effects, no improvement was observed. Although the reason is not clear, survival appeared to be poorer in the groups that received folic acid and Sr⁹⁰ than in the group that received Sr⁹⁰ alone. Histological study showed that Sr⁹⁰ produced damage to bone marrow and lymphatic tissue. Very little evidence of regeneration was apparent at the time of autopsy. Bone marrow damage was largely compensated for by increased ectopic myelopoiesis in the spleen. Sr⁹⁰ animals that received folic acid showed no more active regeneration in hemopoietic or lymphatic tissue than rats that had received only Sr⁹⁰. The macrocytic anemia observed in the peripheral blood of strontium-injected animals was not accompanied by a megaloblastosis in the blood-forming tissue. (ADD)

1305

Lessa, Z. T. NICOTINIC ACID IN TREATMENT OF IRRADIATION SICKNESS. *Rev. paulista med.* 26, 135-50 (1945).

The author administered a daily dose of 25-50 mg of nicotinic acid orally to prevent the development of "radiation sickness" in 65 patients receiving roentgen therapy for different conditions. He reports that more than 3/4 of the patients did not show any general effects of radiation. In a few cases, cutaneous reactions, tenesmus, and diarrhea developed as a consequence of the administration of the drug. (R)

1306

MacFarland, M. L., M. V. Peters, R. M. Ballantyne, and E. W. McHenry. PYRIDOXINE AND EXPERIMENTAL X-RADIATION INJURY IN RATS. *Am. J. Physiol.* 163, 394-9(1950).

To investigate a possible relationship between pyridoxine insufficiency and x-ray injury, the effects of total-body irradiation on pyridoxine-deficient rats and on rats receiving this factor were compared. Pyridoxine deprivation was not found to increase the susceptibility of rats to x-ray damage and irradiation did not affect the concentration of

total vitamin B₆ in the livers of either deficient or control animals. (NSA)

1307

Maxfield, J. R., Jr., A. J. McIlwain, and J. E. Robertson. TREATMENT OF RADIATION SICKNESS WITH VITAMIN B₆ (PYRIDOXINE HYDROCHLORIDE). *Radiology* 41, 383-8(1943).

The authors state that the use of vitamin B₆ (pyridoxine hydrochloride) intravenously has given them the best single method of control of radiation sickness to date. The drug is simple to administer, safe to use, and has no contraindications. It should supplement and not replace other methods used for the control of radiation sickness. Reports on three cases of particular interest are given. (S.V.S.)

1308

Oppenheim, A. and B. Lih. PERORAL ADMINISTRATION OF VITAMIN B-6 (PYRIDOXINE HYDROCHLORIDE) IN THE TREATMENT OF RADIATION SICKNESS. *Radiology* 47, 381-5(1946).

A total of 50 patients received 75-100 mg of pyridoxine one-half hour before meals, 3-4 times a day. In 30 cases (60%) the results were excellent, in six cases (12%) good, in eight cases (16%) fair, and no results in six cases (12%). Symptoms of radiation sickness were aggravated in one patient following therapy. In one patient a scaly and follicular type of eruption developed, which disappeared on withdrawal and reappeared on readministration of the drug. (BA)

1309

Reeves, R. J. TREATMENT OF ROENTGEN SICKNESS WITH ORAL ADMINISTRATION OF PYRIDOXINE HYDROCHLORIDE (VITAMIN B₆). *Southern Med. J.* 39, 405-7(1946).

A daily dose of 100 mg of pyridoxine hydrochloride was found to be a most effective drug in the treatment of irradiation sickness. Because of its ease of administration and effectiveness, oral administration is advocated with reliance on intravenous injection in those cases which fail to respond. (BA)

1310

Rovello, F. and L. Ferri. TREATMENT OF LEUCOPENIA DUE TO IRRADIATION WITH VITAMIN B₆. *Haematologica* 32, 319-22(1948).

In 10 patients treated with roentgen rays for different types of tumours, the decrease in the number of leucocytes was controlled by the administration of pyridoxine (vitamin B₆), 100 mg daily. (EM)

1311

Scott, G. M. EFFECT OF EXTRA VITAMIN B FEEDING ON RATS EXPOSED TO WEAK GAMMA RADIATION. *Brit. J. Radiol.* 19, 329-32(1946).

Rats were exposed to gamma radiation in doses varying from approximately 60 to 85 r per week for a period of four months. Studies were made on the effect of weight gain and fertility with and without feeding extra vitamin B. Rats receiving extra vitamin B showed greater weight gain than the controls and their coats were in better condition. Rats receiving radiation but no extra vitamin gained less than the controls. Both female and male irradiated rats were mated with unirradiated. The irradiated females became pregnant as often as normal, but there were many cases of abortion, some died in parturition, and few of the litters were reared. These effects were not as pronounced in the rats receiving extra vitamin B. No offspring resulted from matings with irradiated male rats. (R)

1312

Scott, L. D. and G. J. Tarleton. PYRIDOXINE HYDROCHLORIDE (VITAMIN B-6) IN THE CONTROL OF RADIATION SICKNESS: PRELIMINARY REPORT. *Radiology* 47, 386-91(1946).

In twenty patients irradiated for various forms of malignant tumors who received 25 mg of pyridoxine IV, none developed nausea or vomiting. (BA)

1313

Shorvon, L. M. PYRIDOXINE IN TREATMENT OF RADIATION SICKNESS. *Brit. J. Radiol.* 19, 369-70(1946).

This article begins with a short exposition of radiation sickness varying in intensity with the part of the body treated and the area of exposure. The author reports 24 cases treated by pyridoxine and claims good results in 22 as regards the radiation sickness. The beneficial effect on the leucocytes is also stressed. Young (*Am. J. Roentgenol.* 35, 681, 1936) strongly recommended injections of liver extract. Pyridoxine is a member of the vitamin B₂ group occurring principally in liver and yeast, which Shorvon finds superior in effect to other remedies. Among the 24 cases reported, a patient suffering from Hodgkin's disease is quoted as much distressed by radiotherapy and benefitted by pyridoxine. In another case, "a female aged 60 with a large abdominal mass and secondaries in lungs from ? carcinoma of the tongue previously treated by radium and x-rays also suffered from radiation sickness but was promptly relieved by pyridoxine." (AWM)

1314

Shorvon, L. M. A FURTHER SURVEY OF RADIATION SICKNESS WITH PARTICULAR REFERENCE TO ITS TREATMENT BY PYRIDOXINE. *Brit. J. Radiol.* 22, 49-55(1949).

The theories advanced to explain the causation of radiation sickness and the remedies recommended are briefly reviewed. The results of the use of pyridoxine in 69 cases are analyzed. It is shown to be a reliable, though not infallible, drug in the treatment of radiation sickness. It has also a beneficial effect on x-ray leucopenia and the additional merit of conferring on some patients a sense of general well-being. (NSA)

1315

Stearner, S. Phyllis. EFFECTS OF FOLIC ACID ON THE ANEMIA INDUCED BY X-IRRADIATION. *Proc. Soc. Exptl. Biol. Med.* 69, 518-21(1948).

In this experiment, the number of animals observed was not large and the results obtained showed only small differences. For these reasons no definite claim can be made concerning the therapeutic effect of folic acid on the damage resulting from x-irradiation. The results can only be considered to be suggestive of a positive effect. Jacobson, however, stated that in patients treated with irradiations or nitrogen mustards, folic acid has not been shown to produce any but equivocal results. Further work is necessary to establish more definitely the possible effectiveness of folic acid in alleviating the leucopenia and anemia that follow irradiation. (NSA)

1316

Stearner, S. Phyllis and Leon O. Jacobson. THE EFFECT OF FOLIC ACID ON THE RESPONSE TO THE PERIPHERAL BLOOD OF THE RAT TO STRONTIUM⁹⁰. Argonne National Lab. June 1, 1947. 13p. (MDDC-1418-B)

Folic acid had no effect on the macrocytic anemia that followed the administration of Sr⁹⁰. At least in the case of radioactive strontium, the injury is probably exerted di-

rectly on the bone marrow and is not caused indirectly by any damage to the gastrointestinal tract or to the liver. The action of folic acid has been reported to be similar to that of liver extract and it therefore should correct any deficiency resulting from radiation damage to liver or stomach and subsequent failure to form an anti-anemic factor. Folic acid was equally ineffective in alleviating the effect of irradiation on the number of circulating leucocytes. This failure to affect the leucopenia that followed the administration of Sr^{90} does not substantiate the suggestion by Watson that folic acid may be effective as a treatment for the leucopenia following exposure to radiations. It is concluded that folic acid is ineffective as a treatment for the hematological effects of internal radiations and probably by implication, for those of external radiations as well. Since total body irradiation is more likely to damage visceral organs, however, the latter question is being investigated. (ADD)

1317

Van Haltern, H. L. THE USE OF PYRIDOXINE HYDROCHLORIDE IN RADIATION SICKNESS. *Radiology* **47**, 377-80(1946).

A total of 81 patients received 25-50 mg pyridoxine intravenously. Excellent results were obtained in 44 cases (54%), good results in 28 cases (35%) and in 9 cases (11%) vomiting was not entirely relieved and a troublesome degree of nausea remained. (BA)

1318

Wallace, W. S. STUDIES IN RADIATION SICKNESS: VITAMINS B₁ AND C AND SMALL INTESTINAL CHANGE IN RADIATION SICKNESS. *Southern Med. J.* **34**, 170-3(1941).

Following heavy roentgen irradiation of the pelvis, small intestine changes similar to those seen in vitamin deficiency are found. The roentgen changes, in the ileum are segmentation of the barium stream, flattening of the mucosal pattern, diminution in motility, and narrowing of the lumen. Avitaminosis B and C are already present in advanced carcinoma of the uterine cervix. With these facts in mind, five patients with previously untreated cervical carcinoma were given daily intramuscular injection of 10 mg thiamin chloride along with routine pelvic irradiation, while five others received daily doses of 50 mg sodium ascorbutic acid (Lilly's cevalin). The irradiation was intensive, reaching 600 r daily, with either 400 kv with a HVL of 5 mm Cu or 200 kv with a HVL of 2 mm Cu. Each of six portals received 2,000 to 2,200 r total dosage and eight patients received 2,500 to 5,000 r supplementary intravaginal radiation at 200 kv. As a result of this study the author concludes that vitamins B and C administered during heavy pelvic irradiation fails to diminish the occurrence or severity of diarrhea or to alter the radiographic changes in the ileum resulting from the irradiation. The ileal changes are apparently not due to lack of vitamin B or C. Severe nausea and vomiting were, however, almost entirely eliminated by the vitamin B and C administered. (R)

1319

Whitmore, W. H. THE PREVENTION OF IRRADIATION SICKNESS. USE OF VITAMIN B₁ IN ROENTGEN THERAPY. *Am. J. Roentgenol. Radium Therapy* **49**, 83-98 (1943).

On the basis of the similarity of symptoms of vitamin B₁ deficiency and those of radiation sickness, thiamin chloride was administered to patients undergoing radiation therapy. Radiation sickness is usually prevented by the administration of 6-9 mg daily during therapy; if symptoms of the sickness develop, the dose of thiamin may be increased. (BA)

Miscellaneous Treatment

1320

Baclesse, F. and J. Loiseleur. CHANGE IN CUTANEOUS SENSITIVITY TO X-RAYS DURING EXPERIMENTAL HYPERGLUCEMIA IN RABBITS. *Compt. rend. soc. biol.* **141**, 743-5(1947).

Intramuscular injection of a near-lethal dose of glucose 45 minutes previously to X-ray irradiation reduced the sensitivity of the skin to x-rays. (NSA)

1321

Bacq, Z. M. and A. Herve. PROTECTIVE ACTION OF METHYLAMINE AGAINST X-IRRADIATION. *Nature* **168**, 1126(1951).

Pure-bred C57 black mice 4 to 6 months old were irradiated with 250 kv x rays at the rate of 90 r/min following intraperitoneal injection of 2 mg of methylamine neutralized in water solution. Forty controls received either 700 or 850 r. All the mice irradiated with 700 r died between the 5th and the 10th day after irradiation; those which had received 850 r died between the 4th and the 8th day. In a group of 50 animals injected and irradiated with 700 r, the mortality (from the 5th to the 12th day) was small; 73% of the animals survived. The mice injected with methylamine and irradiated with 850 r died between the 4th and 11th day, later generally than the controls; only 7% survived. An injection of 2 or 2.5 mg of methylamine did not protect any animal against a dose of x rays greater than 850 r. A dose of 2 mg of methylamine injected 5 or 15 min. after the end of irradiation (700 r) shifted the mortality curve slightly to the right. (NSA)

1322

Betz, H. and H. van Cauwenberge. EFFECT OF SODIUM SALICYLATE ON RESISTANCE OF MICE IRRADIATED WITH X RAYS. *Compt. rend. soc. biol.* **145**, 1910-13 (1951).

Adult C57 mice were injected intraperitoneally with 12 daily doses of 400, 500, or 600 mg of Na salicylate/kg, then were irradiated with 700 r of 250-kv x rays. Survival rates were 25, 55, and 50%, respectively, compared to zero for controls. Injection with 500 mg/kg daily following a 700-r irradiation resulted in much more rapid death than among the controls, all dying within 6 and 12 days, respectively. A stimulating action of Na salicylate on the adrenal cortex is suggested to explain these results. (NSA)

1323

Blair, Henry A. EXTERNAL RADIATION—TOLERANCE AND THERAPY, p.46-55 of QUARTERLY TECHNICAL REPORT JULY 1, 1951, THRU SEPTEMBER 30, 1951. University of Rochester. Oct. 25, 1951. 9p. (UR-189 (p.46-55))

From an investigation of the effect of spleen shielding on x-irradiation mortality in dogs it is concluded that lead shielding of the exteriorized spleen during x irradiation is an effective means of reducing mortality. Preliminary hematological studies based upon peripheral white-blood-cell counts and hematocrits also indicate an early recovery of the hematopoietic tissue in spleen-shielded dogs. A preliminary report of a study of the effect of aureomycin and whole blood, singly and in combination, on x-irradiated dogs shows the group treated with aureomycin and whole blood to have a lower mortality rate than those treated only with blood or aureomycin. An increased incidence of severe pulmonary hemorrhage in the groups receiving blood transfusions appeared to be significant. (NSA)

1324

Boys, F. and I. D. Harris. THE EFFECT OF HEPARINIZATION ON EXPERIMENTAL POST-IRRADIATION TISSUE CHANGES IN THE LUNG. *Am. J. Roentgenol. Radium Therapy* **50**, 1-8(1943).

Rabbits were heparinized to keep the coagulation time above 20 minutes and the entire thorax irradiated to a total of 4,200-4,900 r in two weeks. Lung damage was less than in non-heparinized animals receiving the same irradiation. (BA)

1325

Brues, Austin M., ed. **RADIATION SICKNESS**, p.14-20, 41-54, 57, 60-3, 125-41, 152-4 of **QUARTERLY REPORT, FEBRUARY, MARCH, APRIL, 1951, DIVISION OF BIOLOGICAL AND MEDICAL RESEARCH**. Argonne National Lab. [nd] 46p. (ANL-4625(p.14-20, 41-54, 57, 60-3, 125-41, 152-4))

Survival was enhanced significantly in groups of LAF₁ mice injected intravenously or intraperitoneally with bone-marrow suspensions within 10 to 15 min following a single total-body exposure to 900 r of x radiation. Spleen brei injections did not afford any protection. Only a small amount of bone marrow (1.5 mg) gave nearly complete protection. Data on survival and hemopoietic recovery of mice exposed to a 1025-r total-body x irradiation with protection of the spleen and other organs and of spleen-shielded mice exposed to repeated 1025-r doses are tabulated. Peritoneal implantation of four spleens from baby mice enhanced survival of previously 1025-r x-irradiated mice, whereas a two-spleen implant had no effect. Leaving a blood vessel at the distal tip of the spleen unsevered during exteriorization and shielding greatly enhanced survival. Intraperitoneal injection of minced mouse embryos following a 1025-r x irradiation resulted in ~35% survival of mice. Combinations of spleen shielding, cysteine, and estrogen resulted in an enhancement of survival greater than the sum of individual protective values. Additional data indicating the failure of postirradiation cysteine and ascorbic acid treatment to influence radiation mortality are given. The beneficial effect of head shielding on survival of dogs exposed to 450 r of x radiation are shown. The effect of cyanide in increasing the radiosensitivity of mouse tumor fragments was not obtained in the absence of O₂ and was not caused by destruction of tumor cells. Young rats were implanted subcutaneously with the Hall mouse carcinoma 1 to 2 hr after 100-, 200-, or 300-r total-body x irradiation; organ weight and histological studies show that a growing heterologous tumor is able to evoke significant hyperplasia of proximal lymph nodes and spleen in counteraction of the effect of irradiation; in reduction of the thymus, tumor and radiation have an additive effect. Administration to 2- to 4-day chicks of 25 mg/kg of Benemid immediately prior to a 1000-r x irradiation did not increase survival or alter renal function. (NSA)

1326

Caffaratti, Enrico. **SOME SUBSTANCES WITH REDUCING ACTION (CYSTEINE, THIOGLYCOLIC ACID, ASCORBIC ACID, COMBINED CYSTEINE AND ASCORBIC ACID) AS PROTECTIVE AGENTS IN BIOCHEMICAL X-RAY INJURIES**. *Radioterapia radiobiol. e fis. med.* 4, 378-84(1951).

Mice, weight 20 g, age 30 to 35 days, were injected intravenously with 500 mg of cysteine/kg, 540 mg of thioglycolic acid/kg, 100 mg of ascorbic acid/kg, or 500 mg of cysteine + 100 mg of ascorbic acid/kg 5 min before irradiation with 800 r (5-week LD₅₀) of 180-kv x rays. The mutual protective action of the cysteine and ascorbic acid was marked, 94% of the mice so treated being alive 3 weeks after irradiation, in contrast to 45, 80, 50, and 50%, respectively, of control and cysteine-, thioglycolic acid-, and ascorbic acid-treated mice. (NSA)

1327

Campbell, Ira L. and Mary H. Ross. **PROTECTION EXPERIMENTS AGAINST RADIATION INJURY WITH**

LYMPHOCYTES. Oak Ridge National Lab. [nd] 7p. (ORNL-1193)

This experiment was undertaken to determine whether the injection of lymphocytes into irradiated animals would offer protection against the effects of radiation. The experiments were so designed as to obtain living lymphocytes in their natural medium and introduce them into genetically compatible hosts. The results were essentially negative and are presented in some detail. (NSA)

1328

Cole, L. J., V. P. Bond, and M. C. Fishler. **PRE-PROTECTION OF MICE AGAINST X-IRRADIATION MORTALITY BY SODIUM NITRITE**. Naval Radiological Defense Lab. Sept. 21, 1951. 14p. (AD-331(B); Technical Objective AW-6)

The mortality of mice receiving 600- or 750-r single dose whole-body x irradiation was reduced markedly following preirradiation intraperitoneal injection of NaNO₂ (100 to 125 mg/kg). Definite, but less marked, protection was also observed with a nitrite dose of 62 mg/kg. The decrease in radiosensitivity afforded by NaNO₂ administration was reflected in the minimal postirradiation body-weight losses observed in the nitrite-treated groups, as compared with the control animals. The possibility that nitrite protection is mediated via its effect on catalase activity is discussed. (NSA)

1329

de Carlos, R. **LEUCOPENIA DUE TO X-RAYS. PROPHYLAXIS AND THERAPY WITH VITAMIN C (ASCORBIN)**. *Gazz. sanit.* 18, 92-7(1947).

In view of the reported good effects of vitamin C in leucopenia and benign agranulocytosis the author tried its effect in 30 patients (15 men and 15 women) receiving x-ray therapy for cancer of various organs, including cancer of the prostate 3, of the lung 2, of the intestine 4, of the bladder 2, and of the marrow 2; and in the women, cancer of the cervix 9, of the breast 6. Irradiation therapy was carried out daily with a dose of 240 r. Vitamin C was given daily in 50 mg doses IM or IV. In six patients, this administration was begun some five days before the x-ray therapy, in eight on the same day, and in 16 about a week after the beginning of x-ray therapy. In the first group the leucocyte count rose (on an average by 80%) before and fell to normal levels during x-ray therapy. The rise was mainly due to a lymphocytosis, which was followed by a lymphopenia. In the second group patients with a slight initial leucopenia showed a rise in the wbc; in those with initial leucocytosis the count returned to normal, while normal counts did not vary. In two patients a slight leucopenia was unchanged. There was little change in the differential counts in this group. In the third group an initial leucopenia was followed by a transient rise to normal levels and then by a more lasting leucopenia, mainly due to a fall in lymphocytes. With the Vitamin C the leucocyte count rose to a normal level again and then fell slightly, but remained above the minimal level attained after beginning the x-ray therapy. No effect was observed in three cases. The author concludes that vitamin C has prophylactic and curative value in leucopenia due to x-ray treatment. Detailed counts are not given except by graphs for three of the cases. The author does not report any control observations. (AWM)

1330

Fulton, John D., Anna C. Arnold, Roland B. Mitchell. **THE ANTIBODY RESPONSE OF ANIMALS EXPOSED TO X-RADIATION. III. THE PROTECTIVE EFFECT OF CHEMOTHERAPEUTIC AGENTS ON A SPECIFIC IMMUNE STATUS OF X-RADIATED MICE**. USAF School of Aviation Med., Randolph Field, Texas. 15p. (Project No. 21-47-002, Report No. 3)

A study was made to determine if treatment with adrenal cortical extract, thiourea, glutathione, Reticulose, and chloromycetin, either alone or in combination, would increase the survival time of mice immunized against *Salmonella typhimurium*, x-radiated, and subsequently infected with virulent *S. typhimurium* organisms. Under the conditions of the experiment it was observed that pre-radiation treatment with glutathione alone and post-radiation dosages of chloromycetin alone increased the survival time of immunized, x-radiated, and infected mice. The combination of pre-radiation glutathione and post-radiation chloromycetin increased the survival time considerably more than did either of the agents when administered alone. Administration of adrenal cortical extract, Reticulose, and thiourea immediately prior to x-radiation did not alter significantly the survival time of the infected experimental animals. (Authors)

1331

Hall, B. V. PROTECTION OF MICE FROM LETHAL EFFECTS OF X-RADIATION WITH INTRAVENOUS INJECTION OF METHYLENE BLUE. *Federation Proc.* **10**, 58(1951).

The report is reproduced here in its entirety.

In 12 independent experiments, over 600 male and female mice were given varied x-ray doses of 500-900 r (200 kv, hvl 0.98 mm Cu, target distance 11 inches, dose rate 104 r/min.). Half of the mice were injected intravenously 2-8 min. before irradiation with methylene blue solutions whose dye content varied from 2.5 to 10.0 mg/cc. Dosages of 25, 37.5, and 50 µg of dye/gm mouse were used. Varying the amount of dye injected had little effect on protection, yet it appears that the concentration of the dye solution is a factor influencing survival after irradiation. Excellent protection was found consistently in 8 experiments employing solutions of 0.25-0.5%, whereas only 1 of 4 experiments using 1% solutions yielded statistically significant protection. The maximum protection obtained was 50-60% differential between the percentage with methylene blue 30-day survival of dye protected and control mice. Mice injected with methylene blue after irradiation were not protected. The percentage of 303 dye-pre-treated mice surviving 30 days after irradiation was nearly double that of 310 dye-free irradiated controls. The methylene blue protection may possibly result from the formation of methemoglobin which induces hypoxia of the tissues sufficient to ameliorate the lethal action of irradiation, or methylene blue may have a more direct action on tissues affording protection. Experiments are being continued which may help answer these questions.

1332

Henry, J. A. TOTAL X-IRRADIATION OF RATS UNDER URETHANE ANAESTHESIA. *Nature* **163**, 134-5(1949).

Albino rats were injected intraperitoneally with 1 cc of 10% urethane solution per 100 g body weight. A part of the group were irradiated with 600 r, and a part with 500 r, as were two groups of unanesthetized control rats. Irradiation with a 500 r dose killed about 20% of the animals within 14 days, both controls and anesthetized. The 600 r irradiation, however, killed 50% of the controls within 14 days, but killed 90% of the anesthetized rats within the same period. The effect may be one of cumulative action, or of sensitization to x-rays by the urethane. (V.E.)

1333

Herve, A. SEMICARBAZONE OF ADRENOCROME AND X-RAYS. *Arch. intern. pharmacodynamie* **85**, 242-4(1951).

The semicarbazone of adrenochrome (adrenoxyl) given by mouth reduces the purpura produced in mice by x-rays, but does not prolong the survival time. (CA)

1334

Herve, A. and Z. M. Bacq. SULFOCYANATE, TOCOPHEROL AND X-RAYS. *Compt. rend. soc. biol.* **143**, 1158-9(1949).

In the present report the authors offer an interpretation of the protective action of cyanide against the effects of strong whole-body irradiation in mice. The protective action was not demonstrated by sodium sulfocyanate, and the authors have searched for other substances which would inhibit the lethal effect of x-radiations, but which would be less toxic than the cyanide, an inhibitor of metabolism. The authors suggest that the cyanide acts either by hindering the formation of the peroxides or by diminishing the reaction of formed peroxides with reducing groups such as the -SE group. This hypothesis was tested by using vitamin E (α tocopherol), an excellent inhibitor of peroxide formation by the action of x-rays on lipids. It was found that the mice withstood the dose of x-rays administered (400 r) much better (30% mortality to 60% mortality) than mice not treated with two 10-mg intravenous injections of the α tocopherol at 24-hour intervals before the irradiation. It is concluded that the protection by cyanide against the effects of x-rays in mice is due to the action of the CN-ion; the protection is limited in the sense that it is weak if the dose of x-rays is increased, and is very weak if the injection is made as late as 15 minutes after irradiation. (NSA)

1335

Herve, A. and Z. M. Bacq. PROTECTIVE ACTION OF SODIUM NITRIDE AGAINST LETHALITY PRODUCED BY X RAYS IN MICE. *Compt. rend. soc. biol.* **144**, 1124-5(1950).

It has been reported in former notes that an injection of 0.1 mg of NaCN immediately before a 700-r irradiation of mice reduced the lethality by 70% (*Compt. rend. Soc. biol.* **143**, 881 (1949); Betz and Herve, *ibid.* **144**, 1015 (1950)). An analogous series of experiments is described here using Na_3N , whose biochemical properties (inhibitions of enzyme functions) are similar to those of NaCN. An injection of 0.1 to 0.2 mg of Na_3N in aqueous solution in mice before the administration of 700 r of x rays reduced the lethality by 60%. (NSA)

1336

Herve, A. and J. Lecomte. ADRENOXYL AND X-RAYS. *Arch. intern. pharmacodynamie* **79**, 109-12(1949).

Mice injected intraperitoneally with adrenoxyl before irradiation do not show petechial hemorrhages in the skin such as are seen in control animals. (CA)

1337

Hohl, K. APPLICATION OF THE SODIUM SALT OF ALPHA-OXYBENZYLPHOSPHINIC ACID IN LONG IRRADIATION WITH X-RAYS. *Praxis (Bern)* **38**, 568-9 (1949).

Phoselit (Na salt of α -oxybenzylphosphinic acid) inhibited toxic side effects of x-ray irradiation; body weight restoration was especially accelerated by this drug. Phoselit increased glycogenesis acting as a H-donor in the oxidation-reduction process. (NSA)

1338

Holmes, B. E. SERUM CHOLESTEROL AND IRRADIATION SICKNESS. *Brit. Med. J.* **1**, 314(1941).

This article briefly but effectively presents a worthy effort on the part of the author to clarify the elusive situation of radiation sickness. The data presented were obtained by serum analysis in 11 cases under x-ray therapy. The findings are incomplete but information is available which points to the conclusion that patients who suffer no post-irradiation discomfort have a rise in cholesterol

serum content and that those who have a typical gastric upset following irradiation fail to show this rise. The natural deduction is that cholesterol administered in susceptible cases will prevent radiation sickness. This treatment was effectively tried by Levy-Dorn and Bergheim. (R)

1339

Jenkinson, E. L. and W. H. Brown. IRRADIATION SICKNESS. A HYPOTHESIS CONCERNING THE BASIC MECHANISM AND A STUDY OF THE THERAPEUTIC EFFECT OF AMPHETAMINE AND DEXTRODESOXYEPHEDRINE. *Am. J. Roentgenol. Radium Therapy* **51**, 496-503(1944).

Of 69 cases of irradiation sickness, 21 were well controlled by amphetamine and 34 by dextro-desoxyephedrine. Evaluation of relative effectiveness of the two was not attempted. A hypothesis is suggested to explain the basic mechanism of irradiation sickness as an increased capillary permeability. This results in disturbance of intracellular and extracellular equilibrium of electrolytes and fluids, which is followed by local congestion, edema, and stasis of circulating blood. A vicious cycle is set in motion by reduced blood volume and tissue anoxia. The above drugs apparently act by their ability to maintain peripheral circulating blood volume and prevent visceral stasis. Detailed suggestions are given for the management of irradiation sickness. (BA)

1340

Kahn, J. B. Jr. MODIFICATION OF SENSITIVITY TO X RADIATION BY MORPHINE SULFATE. *Proc. Soc. Exptl. Biol. Med.* **78**, 486-9(1951).

Morphine sulfate, injected intramuscularly into ZBC male mice 30 min before exposure to total-body x radiation, raises the LD₅₀ of the radiation from 609 to 830 r. Possible mechanisms of this effect are discussed. (NSA)

1341

Kohn, Henry I. ON THE MODIFICATION OF THE TOXICITY OF X-RAYS BY IMMUNIZATION. Oak Ridge National Lab. Oct. 27, 1949. 9p. (AECU-610; ORNL-386)

Following injection with sheep erythrocytes, the Sprague-Dawley and Osborn-Mendel strains of rat showed a rise of about 50-75 r in the LD-50% of 250 kv x-rays. The Holtzman strain showed a fall of about 25 r. The injection of sheep cells prevented the rise in albumin-globulin ratio which invariably occurs after irradiation in nonimmunized rats. (NSA)

1342

Lambert, G., J. Maisin, M. Mandart, M. Meersseman, G. Podio, and E. Plugers. THE INFLUENCE OF CERTAIN METALLIC IONS ON THE SURVIVAL OF RATS RECEIVING A LETHAL DOSE OF X-RAYS. *Compt. rend. soc. biol.* **144**, 444-8(1950).

Rats received a total body x-ray dose of 600 r (180 kv) for approximately 13 minutes. Subcutaneous injections of barium chloride, lithium lactate, or mercuric chloride were administered to some of them either before or after irradiation. The barium and lithium ions hastened death, while mercuric ions seemed to retard it and diminish the percentage of the rats which succumbed. (NSA)

1343

Lavik, Paul, Jack R. Leonards, G. Warren Buckaloo, Charles Heisler, and Hymer L. Friedell. IN VIVO DIALYSIS OF BLOOD AS A MEANS OF INFLUENCING THE SURVIVAL OF X-IRRADIATED DOGS. New York Operations Office, AEC. Dec. 15, 1951. 21p. (NYO-1637)

By means of an "artificial kidney," dogs given a lethal dose of x irradiation were subjected to an *in vivo* dialysis of their blood either during or at some time after the ir-

radiation. No beneficial effects of the dialysis procedure were observed in the irradiated animals, even though the "artificial kidney" was shown to be highly efficient in removing a dialyzable substance from the extracellular fluid of dogs. While *in vivo* dialysis was not detrimental to non-irradiated controls or dogs dialyzed at the time of irradiation, sudden death occurred following dialysis in about 50% of the animals that had been irradiated 12 or more hours earlier. The latter effect of dialysis can be attributed to the removal of some essential factor(s) from the blood, for it could not be demonstrated in irradiated dogs subjected to a "sham-dialysis" procedure. Peritoneal lavage was without significant effect upon the survival of x-irradiated dogs. (NSA)

1344

Mole, R. H. PROTECTION FROM WHOLE-BODY IRRADIATION BY CHEMICAL MEANS. *J. chim. phys.* **48**, 258-61(1951).

The chemical protection afforded mice against radiation injury, following whole-body x irradiation, by injected doses of thiourea, sodium ethane-di-thiophosphate, glycerol, sodium thiosulfate, and sodium dithionate was studied. Of these, thiourea was the only chemical giving a definite protective effect (equivalent to a reduction in the effectiveness of radiation by about 10 or 15%) and this only when given immediately before irradiation. (NSA)

1345

Molomut, Norman, Milton Friedman, Irene Jacob Ryby, and Alvin Harber. EFFECTS OF ANTISPLENIC TISSUE SERUM ON ROENTGEN-RAY DAMAGE (WHOLE BODY IRRADIATION). *Am. J. Roentgenol. Radium Therapy* **66**, 245-7(1951).

The effect of antispleen serum upon recovery of mice from damage to the reticulo-endothelial system caused by whole-body x irradiation was investigated. Under the conditions used, antispleen serum did not affect the increased susceptibility of x-irradiated mice to infection with Rickettsia pox. (NSA)

1346

Parker, James Preston, Paul I. Ewing, and G. A. Emerson. LACK OF ANTAGONISM OF MALONONITRILE AND DESOXYRIBONUCLEIC ACID TO TRYPANOSOMIASIS, ALLOXAN DIABETES, AND LETHAL EFFECTS OF X-IRRADIATION. *Texas Repts. Biol. and Med.* **8**, 257-61(1950).

The authors demonstrate that neither malononitrile nor desoxyribonucleic acid, in massive repeated doses, has appreciable effects on experimental trypanosomiasis, alloxan diabetes, or lethal effects of x-irradiation in mice. (NSA)

1347

Paterson, Edith and Joyce J. Matthews. PROTECTIVE ACTION OF ETHYL ALCOHOL ON IRRADIATED MICE. *Nature* **168**, 1126-7(1951).

Pure-bred "A" strain mice 6 to 8 weeks old were given two 1-ml doses orally of ethyl alcohol (10% by volume in saline) 80 and 20 min before a 700 x-irradiation. Mortality was 63% compared with 100% for controls. A rise in the LD₅₀ radiation dose from 554 to 625 r and an extension of the life of nonsurvivors were noted with the alcohol treatment. No protection was obtained when the alcohol was given after the irradiation. The difference in protective value between 5 and 10% alcohol was not significant. Intravenous cysteine, 20 mg/mouse, gave greater protective effect than the alcohol in the doses used. Protection by alcohol was unrelated to its anesthetic effect. Intravenous nembutal, 1.3 mg/mouse, and intraperitoneal ethyl carbamate, 20 mg/mouse, did not change the LD₅₀. (NSA)

1348

Rekers, Paul E., Molly P. Coulter, and Stafford L. Warren. EFFECT OF TRANSPLANTATION OF BONE MARROW INTO IRRADIATED ANIMALS Arch. Surg. 60, 635-67(1950).

The results of the transplantation of marrow suspensions, bone and marrow and ribs, are presented; in some cases bone slivers were transplanted to the anterior chamber of the eye, or the liver or spleen, but usually the material removed from a normal dog was transplanted to the same location in an irradiated dog. A single dose of 350 r of whole body irradiation was given to the test dogs before the transplantation; similar experiments were performed on rabbits. It was found that the transplantation of the normal marrow to intramedullary marrow sites was without appreciable benefit to the irradiated animals. The transplantation of bone and marrow resulted in the death and replacement of the graft; transplantation of the normal marrow to normal or irradiated spleen or liver was also without benefit. Other results are outlined. (NSA)

1349

Revict, Emanuel. INFLUENCE OF VARIOUS LIPIDS UPON THE HEALING PROCESS OF EXPERIMENTAL RADIATION BURNS, p.175 of INTERNATIONAL CONGRESS OF RADIOLOGY, 6th Congress, London. 1950.

The author describes the technique used in order to obtain comparable radiation burns in rats, using 10 mg. radium needles. The lipids studied are divided into two classes, according to the nature of their polar groups.

The influence exerted seems to be opposite, according to the presence of a carboxyl or a hydroxyl, as polar group of the lipid. The lipids with carboxyl polar groups administered to the animals presenting radium burns have appeared to interfere with the healing process, increasing the extent and the duration of the ulceration. On the contrary, the lipids with a hydroxyl radical, promote rapid healing.

1350

Salisbury, Peter F., Paul E. Rekers, Joseph H. Miller, and Norman F. Marti. EFFECT OF EARLY CROSS TRANSFUSION ON X-IRRADIATION DISEASE. Science 113, 6-7(1951).

An examination of possible protective and regulatory factors of cross transfusion in the reduction of x-radiation toxicity is reported. A summary of some of the data obtained with the use of a cross-transfusion apparatus (Salisbury, Proc. Soc. Exptl. Biol. Med. 71, 604(1949); Salisbury and Miller, *ibid.* 74, 16(1950)) is presented. Twenty-five adult mongrel dogs were used. The control group consisted of 19 dogs, and the treated group of 6. The latter underwent a single cross transfusion for approximately 2 hr within 4 hr after an irradiation of 450 r. A quantity of blood equal to the body weight of the recipient was exchanged between each pair of animals. Peripheral blood studies showed a depression of the total leukocytes to a mean value of 400 cells/mm³ or less in the control group, whereas the cross-transfused group manifested a depression to only 1800 cells/mm³ during a corresponding period after irradiation. The reticulocyte response in the control group was 0.2% or less in the entire postirradiation period, whereas the cross-transfused dogs showed a response between 1 and 2% by the 15th day after irradiation (NSA)

1351

Simmons, Eric L., Leon O. Jacobson, N. Pearlman, and C. L. Prosser. THE EFFECTIVENESS OF DRUGS IN PREVENTING OR ALLEVIATING X-RAY DAMAGE. Argonne National Lab. Oct. 1946 68p. (MDDC-1277; CH-3329)

The protective and ameliorative properties of a variety of substances following irradiation were investigated in rabbits and mice. Four main groups of chemicals were studied: (1) Physiological saline, (2) substances capable of altering the oxidation-reduction equilibrium of the body, (3) hemopoietic stimulants, and (4) enzyme precursors and activators. None of the substances tested prevented the drastic immediate fall in leucocyte level that resulted in rabbits after 600 r total body x-irradiation. Physiological saline proved to be the most effective stimulant following irradiation. Ascorbic acid was next in effectiveness, followed by pentnucleotide, although the results with these drugs were not as significant. Many substances produced marked temporary elevations in heterophils during the late recovery period, but these were not maintained and, in fact, were frequently followed by returns to the control level. Lymphocytes, in general, were less responsive to drug stimulation than heterophils. In no case had lymphocyte counts returned to their pre-irradiation level of 37 days. (ADD)

1352

Storer, John B. and Julius M. Coon. PROTECTIVE EFFECT OF PARA-AMINOPROPIOPHENONE AGAINST LETHAL DOSES OF X-RADIATION. Proc. Soc. Exptl. Biol. Med. 74, 202-4(1950).

Para-aminopropiophenone (PAPP) when injected intraperitoneally in mice produces a maximum methemoglobinemia in 30 minutes with only a slight decrease in the methemoglobin level after 60 minutes. Of 180 mice given a single exposure of 800 r total-body x-radiation, 100% of 60 controls died within 30 days. Pre-treatment of groups of the remaining 120 mice with PAPP in doses of 20, 30, 40, and 50 mg/kg, 30 minutes before x-ray exposure resulted in 30-day survival rates of 45, 50, 60, and 72.5%, respectively. Injection of 50 mg/kg of PAPP after irradiation did not affect mortality. In a preliminary test pre-treatment with PAPP also reduced the 30-day mortality in rats exposed to x-radiation (Authors' Summary)

1353

Swisher, S. N. and F. W. Furth. THE EFFECT OF EARLY SMALL EXCHANGE TRANSFUSION ON THE X-IRRADIATED DOG. Proc. Soc. Exptl. Biol. Med. 78, 226-9(1951) (UR-186)

Immediate removal of 250 cc of blood and replacement with an equal volume of normal compatible whole blood in 20-lb dogs given 550 r whole body irradiation (expected LD₅₀) results in a marked delay in onset of radiation syndrome and mortality. There is a suggestive decrease in ultimate mortality as well. No differences in average leucocyte count, platelet count, or hematocrit in transfused dogs and in control dogs were observed, nor were there differences in clinical or postmortem anatomical findings (NSA)

V MECHANISM OF RADIATION EFFECTS

General Theoretical Considerations

1354

Allen, A. O. EFFECTS OF RADIATION ON MATERIALS, p.207-22 of THE SCIENCE AND ENGINEERING OF NUCLEAR POWER, Chap. 13, Vol. II, Clark Goodman, ed. Addison-Wesley Press Incorp., Cambridge, Mass. 1949.

Study of changes in chemical constitution and physical properties by high energy radiation is important to nuclear engineering because (a) use of materials around pile structures is limited by radiation damage suffered; (b) the study of chemical effects of radiation are important in the inter-

pretation of biological effects. The types of radiation and their interactions with matter are summarized. Subjects briefly discussed include effects of radiation on the different types of chemical bonds, simple gases, organic compounds, water and aqueous solutions, metallic corrosion, and solids. (M.F.)

1355

Allsopp, C. B. THEORIES OF THE BIOLOGICAL ACTIONS OF IONIZING RADIATIONS. *Brit. J. Radiol.* **21**, 72-4 (1948).

The two basic theories of the mode of action of ionizing radiation the target theory and the "poison" theory are examined critically. The present complete ascendancy of the target theory based on the work of Lea and Crowther are challenged. The author believes that the poison theory should not be rejected entirely and points to the formation of the free hydroxyl and hydrogen radicals when ionizing radiations pass through aqueous solutions. The possibility exists therefore that there can be a poisoning effect by OH radicals by breaking chromosomes chemically. This hypothesis does not entail a rejection of the target theory where the chromosome is destroyed by a "direct hit" by an ionizing particle, but rather may supplement this theory. (NSA)

1356

Atwood, K. C. and A. Morman. ON THE INTERPRETATION OF MULTI-HIT SURVIVAL CURVES. *Proc. Natl. Acad. Sci. U. S.* **35**, 696(1949).

It is proposed that sigmoid survival curves can be interpreted profitably on a multi-unit, single hit per unit of hypothesis, and some consequences of this hypothesis are examined. An aid to the analysis of experimental data is given and its use is illustrated. Reasons are given for preferring the multi-unit hypothesis to the usual multi-hit hypothesis. Some data on the ultra-violet irradiation of *Neurospora crassa* conidia are analyzed. (Author's Summary)

1357

Bacq, Z. M. THE INDIRECT ACTION OF X-AND ULTRA-VIOLET RADIATION. *Experientia* **7**, 11-19(1951).

Recent literature and the author's experiments favor strongly the general idea that the action of ultraviolet and x-rays on enzymes, cells, and organisms is not entirely a direct one, that chemical substances (peroxides in the case of ultraviolet rays, oxidizing short-lived free radicals in the case of x-rays) resulting mainly from the action of rays on water molecules, are really the responsible agents. The greatest part of the action of ultraviolet or x-rays is indirect. It is possible by injection of cyanide, azide, cysteine, glutathione, thiourea, etc., to decrease very significantly the death rate of rats or mice irradiated with x-rays, but only if the substance is injected before irradiation; so far, the biochemical lesion of x-irradiation has been found irreversible. (NSA)

1358

Bojanowsky, Rudolph. QUANTUM PHYSICS AND BIOLOGY. *Verhandl. naturforsch. Ver. Brünn* **73**, Vorträge viii-x (1941).

Subatomic aspects of biology are discussed. The killing of a population of single-celled organisms (*Euglena*, *Escherichia coli*) by means of ultraviolet light, or Röntgen, cathode, or α -radiation has an exponential course which is a function of the time of exposure of surviving cells, $n = e^{-KIt}$, where n is the number of surviving cells, t is the time of exposure, I is the intensity of radiation and K is a constant. A cell of *Euglena* must receive 8,000 quanta before being killed. Apparently a very small vital portion of the cell must be hit, perhaps a single atom or atom group

in the nucleus. Direct radiation of the nucleus or of the cytoplasm of fern spores, gave 95% of the effect only in the nucleus. Production of mutation in multi-celled organisms follows the same law. The possible number of atoms in a gene is discussed. Poisoning with compounds such as $HgCl_2$ or the action of a hormone follows the same law. (CA)

1359

Burton, Milton. ELEMENTARY CHEMICAL PROCESSES IN RADIOBIOLOGICAL REACTIONS. Univ. of Notre Dame. [nd] 28p. (AECU-889)

The elementary chemical processes of radiobiology are the elementary chemical effects of high energy radiation on aqueous solutions containing oxygen, on pure organic matter, and on organic matter suspended in aqueous solution. In the aqueous layer the important primary physical process is ionization; in the organic portion both ionization and excitation must be considered. In biological systems the active particles in the aqueous layer are principally OH and HO_2 . The presence of the latter particle increases the volume of the effective aqueous layer around the biological particle. The effectiveness of a hit in the organic material is determined in part by the properties of the surrounding cage and depends, among other factors, on the size of the biological particle. The effect of a hit may be propagated by ionization transfer, by free radical diffusion, by a chain reaction, or by change in local pH. Furthermore, free H and resultant HO_2 are formed in the ambient liquid even when the hit is in the particle itself. In view of these elementary processes, the biological particle cannot be uniformly sensitive to radiation over its entire volume, the target of "target theory" is not to be identified with the biological particle, a single ionization act is not necessarily lethal, nor is the target dimension simply related to the true size of the biological particle. 28 references. (NSA)

1360

Claranfi, E. THE BIOLOGICAL ACTION OF RADIATIONS IN RELATION WITH CERTAIN PROBLEMS OF EXPERIMENTAL PATHOLOGY. *Quaderni sez. perugina soc. ital. biol. sper.* **2**, 35p. (1949).

A clear review, including a critical investigation of the mechanism of action of radiations on elementary biological indicators (virus, bacteria, protozoa) and on higher organisms, as well as an examination of the effects of radiations on cells. The theory of mutations is discussed with reference to the genesis of tumors. (EM)

1361

Dufresene, O. ROENTGENTHERAPY OF PAIN. *Can. Med. Assoc. J.* **60**, 227-9(1949).

Several theories have been advanced to explain the sedative action of x-rays. They may be classified in two categories: those implicating a direct action of x-rays on the nervous elements, and those producing an indirect action on the nervous elements, by humoral modification. As striking results from direct action of x-rays on the nervous elements, the following may be mentioned: diminution of the excitability of nerve endings, and modification of the conductivity of nerves by a photo-electronic effect. Among the theories of the second category is the one advanced by Gilbert that x-rays, by destroying white cells, could produce the liberation of triphosphate of adenosine. He thought also that nucleo-protein where it is liberated should provoke the vaso-dilatation of capillaries, modifying the nutrition of the sensory receptors and consequently should relieve pain. Whatever the way by which the x-rays act on the pain, be it direct or indirect action, or by a combination of both, or even by the simple destruction of inflammation compressing nerves, there are chemical facts that x-rays relieve pain. (S.V.S.)

1362

Dustin, Pierre Jr. **MITOTIC POISONS AND THE METHOD OF ACTION OF IONIZING RADIATIONS IN BIOLOGY.** Euclides (Madrid) 9, 188-95(1949).

A review with 64 references. (CA)

1363

Ellinger, Fredrick. **THE PROBLEM OF RECOVERY FROM RADIATION EFFECTS.** Radiology 40, 62-71(1943).

The problem of recovery from effects of radiation is discussed from the point of view of cellular physiology, photochemistry, and clinical application. To clarify the problem of recovery, "true recovery" is designated as the complete morphologic and functional restoration of single cells, while the term "pseudo-recovery" is suggested for the restoration of organ function arising from growth of cells which have escaped radiation injury. "Pseudo-recovery" therefore, is the expression of the regenerative power of the tissue in question. "Clinical recovery" means restoration of organ structure and function and may include "true recovery" as well as "pseudo-recovery." An evaluation of experimental and clinical observations on recovery of single cells, tissues, and organs shows the difficulties in determining "true recovery" and demonstrates that most of the known facts are easily explainable by "pseudo-recovery." (BA)

1364

Failla, G. **SOME ASPECTS OF THE BIOLOGICAL ACTION OF IONIZING RADIATIONS (JANEWAY LECTURE 1939).** Am. J. Roentgenol. Radium Therapy 44, 649-64(1940).

Experiments by Sugiura are analyzed in an attempt to explain some aspects of the effect of ionizing radiation. S. irradiated mouse sarcomata in vivo and subsequently transplanted them into other mice where they were inactivated by about half as much x irradiation than when irradiated in vitro. In addition to the direct effect of the rays on the tumor cells, there is an indirect one exerted by the host and the tumor bed as a whole. In other experiments of S. fragments of sarcomata were irradiated with 1,500 r, then kept in distilled water, hypotonic, isothonic or hypertonic Locke-Ringer solutions; hypotonic solution, and distilled water enhanced the radiation effects, the others had no influence. All experiments suggest that radiation effects are effected by shift in osmotic pressure. Certain considerations in radiation therapy, such as varying radiosensitivities of similar tumors in different locations in the body, the determination of the value of pre-operative irradiation, and the proper interval between such irradiation and surgery, are discussed in the light of these findings. (TIS)

1365

Forssberg, Arne. **THE BEARING OF RADIATION CHEMISTRY ON THE MODE OF ACTION OF RADIATION,** p.48 of INTERNATIONAL CONGRESS OF RADIOLOGY, 6th Congress, London. 1950.

Irradiation of aqueous solutions, especially of enzymes, has shown that a marked inactivation may result from quite moderate doses but that the presence of other substances in the solutions may fundamentally alter the result. If a similar action on high molecular substances, e.g., enzymes, also takes place in vivo, we should expect to observe secondary metabolic effects in the organism. The radioactive tracer technique has yielded important results in the study of these problems, leading to the conclusion that even after moderate doses (<1,000 r.) the turnover of different intracellular substances, including not only nucleic acids but also proteins, fats and carbohydrates, is markedly and rapidly influenced. We are not in a position so far to judge the biological meaning of these metabolic changes; presumably,

however, they may be of radiobiological significance. The mechanism of "protecting" an organism against harmful action of X-rays by the injection of certain substances has also been studied with this tracer technique.

1366

Friedman, Milton. **THE RELATION OF TISSUE RECOVERY AND THE HEALING PROCESS TO THE PERIODICITY OF RADIATION EFFECTS.** Radiology 33, 633-43(1939).

The phenomena resulting from protracted fractionated radiation may be divided into two phases, the destructive phase and the healing phase. Each phase has specific characteristics and is modified to varying degrees by the quality of the radiation, the size of the daily dose, individual susceptibility, the daily exposure time, and the continuity of the treatment. The healing process itself does not function at a constant rate. Its fluctuating prowess determines whether destructive or healing phenomena dominate the clinical picture. It is this cyclic alteration of destructive phase with healing phase that can be termed periodicity. The extent to which the character of the skin and mucosal reactions are reflected in the tumor probably depends upon the latter's degree of differentiation and consequently its morphologic and physiologic resemblance to the parent tissue. During the healing phase, residual tumor cells have usually been matured by irradiation and they too have adapted themselves to radiation effects. It is, therefore, recommended that during a prolonged course of radiation no treatment be given during the healing phase. (Author's Summary)

1367

Gerstner, Herbert B. and Oskar L. Ritter. **THE BIOLOGICAL AND MEDICAL ASPECTS OF IONIZING RADIATION, I. THE EFFECT OF X-RADIATION ON THE POTENTIAL DIFFERENCE ACROSS ISOLATED FROG'S SKIN,** USAF School of Aviation Medicine. 6p. (Report No. 1)

For living membranes or tissue slides an electrode has been developed which enables the determination of resting potential, electrical impedance, permeability to tracer isotopes, and the simultaneous exposure to ionizing radiation. By means of this electrode, isolated frog's skin was exposed to an intensity of x-rays of 10,000 r per minute. Two main observations were made: first, x-radiation affects the skin potential without delay; second, x-radiation destroys the processes essential for the maintenance of the potential. The technique employed should prove useful in studying the mechanics of tissue damage and the effectiveness of protective agents. (auth)

1368

Glucksmann, A. **CYTOLOGICAL ASPECTS OF PROTECTION FROM IONIZING RADIATIONS.** Brit. J. Radiol. 23, 41-5(1950).

A review is presented concerning the cytological aspects of protection from radiation. The two main concepts of the mechanism of radiation action on cells and the radiation effects on germ cells and somatic cells are briefly discussed. The target theory of the biological action of ionizing radiations explains the radiation effect on the assumption that ionization occurs in or in the immediate neighborhood of certain molecules which constitute a vital target. A hit on this target is assumed to produce changes such as cell death in bacteria and viruses, gene mutations, or simple chromosome breaks. The "intracellular poison" concept holds that radiation effects such as inhibition of mitosis are brought about by radiation chemical changes almost anywhere within the cell. Localization of radiation effects is secondary and due to a specific sensitivity of some cell constituent to radiation chemical products. The poison concept accounts for effects known to depend on the rate and fractionation of the

radiation dosage. The mechanisms for the production of genetic effects are gene mutations and chromosome structural changes. The direct and indirect carcinogenic effects of ionizing radiations are described. It is concluded that until more fundamental information is available we can do no more than hazard guesses at the maximum permissible doses of radiation; our knowledge of cytological radiation effects is incomplete and further research is required, particularly with regard to the effects of chronic exposure to irradiation and to the mechanism of tumor induction by radiation. (NSA)

1369

Gray, L. H. THE INFLUENCE OF RADIATION QUALITY ON RADIOBIOLOGICAL RESPONSE, p.48-9 of INTERNATIONAL CONGRESS OF RADIOLOGY, 6th Congress, London. 1950.

The following types of radiobiological lesion may be distinguished: That in which the damage inflicted on individual cells appears to result from the integrated effect of the ionisation produced by a considerable number of particles. That in which the primary damage is caused by a single ionising particle or even by a single ion pair or cluster. Each class of radiobiological damage will have a characteristic dependence on the type of ionising radiation employed, determined by the distribution in both space and time of the primary acts of ionisation and excitation.

1370

Howard, A. REPORT OF SYMPOSIUM ON MODE OF ACTION OF IONIZING RADIATIONS. *Nucleonics* 7, 26-30(1950) Dec.

Summary of papers dealing with the mechanism of the biological action of ionizing radiations, presented at the Sixth International Congress of Radiology, London, July 1950. (PA)

1371

Latarjet, R. PRIMARY BIOLOGICAL EFFECTS OF RADIATIONS OBSERVED IN THE STRUCTURE OF MICRO-ORGANISMS. *Rev. can. biol.* 5, 9-47(1946).

The primary effect of radiation on a cell or a micro-organism is to initiate a chain of reactions leading to an observable injury, and must be considered photochemical, affecting a limited number of absorbing molecules. Two such physically different absorption processes as ionization and molecular ionization can induce the same chemical changes in the same sensitive cellular zone. This zone uses an equal amount of energy in both cases, the effect of low energy photons accumulating to give the same effects as ionization. The energy of a single photon (4-5 electron-volts) is sufficient to produce a chemical change in nucleoproteins. A single photon may inactivate bacteriophage. The zone which governs the division of the dysentery bacillus is of a nucleoprotein nature. Its diameter is greater than or equal to 60 m μ . In yeast, division is governed by two distinct formations similar to those in bacteria. The bacteriophages contain a radiosensitive nucleoprotein which supports the specific lytic power. The disappearance of lytic power results from the alteration of a single molecule. In some viruses, particles observed with the electron microscope and measured by filtration or centrifugation seem to consist of "minimal units." The organization of the viruses seems to become complicated in proportion to their size. (BA)

1372

Layne, D. A. THE PRODUCTION OF RADIOACTIVITY IN ANIMAL TISSUES BY HIGH ENERGY X-RAYS, p.180 of INTERNATIONAL CONGRESS OF RADIOLOGY, 6th Congress, London. 1950.

The main object of the experiments to be described was to investigate the production of radioactivity in tissues by

exposing rat tissue to beams of X-rays from the Royal Cancer Hospital 30 Mev synchrotron. Activities having half-lives less than about one minute or more than a few hours would not be detected in our experiments, but within these limits, oxygen and carbon appear to be the elements mainly responsible. Attempts have been made to calibrate the experimental counting equipment and to calculate the number of quanta above threshold energy level falling on the tissue per unit time. From these the cross-sections for the photo-nuclear reactions have been estimated and are of the order of magnitude estimated for other γ -n reactions. The biological significance may be calculated by considering the absorption of energy in tissue from the X-ray beam and from the disintegrations. It seems that, unless there are strong short-lived reactions and high resonances, the absorption of energy in tissues from disintegrations will not contribute significantly to the biological effects of high energy X-rays in them.

1373

Lea, D. E., R. B. Haines, and E. Bretcher. THE BACTERICIDAL ACTION OF X-RAYS, NEUTRONS, AND RADIO-ACTIVE RADIATIONS. *J. Hyg.* 41, 1-16(1941).

It is suggested that the lethal effect of these rays on bacteria is due to the ionization of vital areas or sensitive chem. regions in the cells. Perhaps these "targets" are genes. Many ionizing particles could pass through a cell without striking such a structure. About 100 particles must pass through a colon bacillus to cause death. The effect was independent of the time required for them to pass through. The lethal effect was independent of temperature or the concentration of the ionizing rays. (CA)

1374

Lea, D. E., K. M. Smith, B. Holmes, and R. Markham. DIRECT AND INDIRECT ACTIONS OF RADIATION ON VIRUSES AND ENZYMES. *Parasitology* 36, 110-18(1944).

The inactivation dose for tobacco mosaic virus of gamma rays is independent of concentration when the virus is irradiated dry or at high concentrations. At low concentrations the inactivation dose reaches a const. but lower value. Over the intermediate range, the inactivation dose increases with concentration. When the virus is irradiated dry or at high concentrations, the inactivation is direct and is due to ionization produced inside of the virus mol. At lower concentrations the inactivation is largely indirect and due to ionization of water. Addition of gelatin to virus solutions protects against the indirect action. Dry, powdered preparations of ribonuclease and adenylypyrophosphatase are inactivated by radiation with 3.4×10^4 and 5.5×10^6 r, respectively. On the assumption that a single ionization in an enzyme molecule leads to its inactivation, measurement of the inactivation dose gives a method of estimating the molecule weight of the enzyme. There appears to be no fundamental difference in the mechanism of radiation-inactivation of viruses and enzymes. (CA)

1375

Minder, W. A NEW THEORY OF THE MECHANISM OF IRRADIATION EFFECTS. *Radiologia Clin.* 16, 73-81 (1947).

Continuing his previous work, the author gives mathematical proof of his theory of the effects of radiation based on experiments and the laws of chemical reactions. This theory expresses at least formally all the four types of the action of radiation in relation to dosage, namely: (1) proportional course of the curves of action; (2) "delayed" linear course; (3) exponential course; and (4) "delayed" exponential course. The time-factor of the effect of radiation is also consistent with this theory. (BA)

1376

Minder, W. ON THE EXPONENTIAL LAW OF THE RADIATION EFFECT. *Radiologia Clin.* 18, 300-4(1949).

As is known, the exponential shape of the dose curve is explained by the "target" (or "hit") theory of the radiation effect on living cells by considering this effect as due to quantized events whose probability is expressed by certain volumes, the "target volumes" of the effect under consideration. In the light of recent investigations of chemical reactions produced under the action of x-rays (oxidation of H_2O , reduction of $KMnO_4$, formation of HCl from CCl_4), the author shows that the exponential law of these processes can easily be explained with the aid of such mechanisms as reversible reactions, secondary reactions, or inhibitory effects of compounds present; the work of these mechanisms is governed by certain probabilities, each expressed by a volume, the "reverse action volume"; the latter's absolute dimensions vary within the same limits (100 to 400 Å linear dimension) that characterize the "target volume" of the radiobiological theory (e.g., the inactivation of various bacteriophagic microorganisms by x-ray action). These analogies cannot be accidental and should motivate a re-shaping of the target theory. That the concepts involved have a deeper physicochemical meaning than that accepted by the biological theory is corroborated by the fact that for many chemical reactions, induced by x-rays, there exist diluting upper limits below which a radiochemical reaction does not depend on the concentration; at those limits the distances between molecules involved reach the same values, 100 to 400 Å, mentioned above. A concept which describes this phenomenon, and which evidently underlies all the others surveyed above, is that of energy transportation without loss, performed along a characteristic elementary distance. (NSA)

1377

Morowitz, Harold J. ABSORPTION EFFECTS IN VOLUME IRRADIATION OF MICROORGANISMS. *Science* 111, 229-30(1950).

From target theory a relation has been derived which gives the percentage of organisms, suspended in a medium, which survive irradiation of a given dosage (see Pollard and Forro, *Science*, 109: 374, 1949). This derivation is strictly valid only if the suspending medium does not absorb the radiation, or if the organisms are spread out in a negligible thickness of the suspending material (surface irradiation). The author derives a corresponding expression for absorbing suspending materials, for the two cases in which the organisms are fixed in the suspending material, and for the case in which the organisms are constantly stirred. (NSA)

1378

Neu, Ladislaus. THEORETICAL AND EXPERIMENTAL INVESTIGATIONS OF CELL MEMBRANE PERMEABILITY. *Strahlentherapie* 79, 141-63(1949).

By applying the laws of classical mechanics, the author attempts to explain and coordinate certain features of cell membrane permeability, such as its periodicity and its change under the influence of radiation. It is found that the membrane permeability can be considered a phenomenon which is propagated through the organism in wave form, the phase velocity of the wave being of the order of magnitude of the velocity of conduction of nerve impulses. This leads to the assumption that the medium in which the waves are propagated is the nervous system. Special attention is paid to the changes of cell membrane permeability after irradiation with x-rays, and to the periodicity of biological radiation effects in general. (NSA)

1379

Neu, L. and V. Neu. THE THEORY OF THE BIOLOGICAL EFFECT OF X-RAYS. *Med. Woman's J.* 54, 17-23(1947).

The permeability of cell membranes is increased after X-ray irradiation; unstable cell membranes have an increased sensitivity to X-rays. A hypothesis is advanced showing a close connection between the periodic behavior of the permeability of cell membranes and the recurring X-rays effect erythema. The conc. of ions in a cell increases with irradiation time; the primary effect of X-rays is an irreversible poisoning of the living cell. (NSA)

1380

Opatowski, I. THE PROBABILISTIC APPROACH TO THE EFFECTS OF RADIATIONS AND VARIABILITY OF SENSITIVITY. *Bull. Math. Biophys.* 8, 101-19(1946).

The calculation of the size of the "sensitive volume" or "control center" in biologic effects of radiations is discussed from the viewpoint of the probabilistic theory of these phenomena based on the concept of random "effective events." On the basis of that theory, the resistivity of a microorganism to radiation is defined as its "mean life" under a radiation of one r/min. This means is calculated for processes with and without recovery. The case of variable sensitivity, as it occurs, for instance, during mitosis, is discussed in detail. Methods are given to calculate this variability from survival curves or similar exptl. data. The theory is applied to expts. of A. Zuppinger on irradiation of *Ascaris* eggs with X-rays. (BA)

1381

Opatowski, I. DETERMINATION OF THE SENSITIVE VOLUME BY IRRADIATION AND THE IONIZATION DENSITY. *Bull. Math. Biophys.* 13, 263-71(1951).

Lea's formula for the determination of size of the sensitive volume is corrected and applied to experiments on inactivation of the tobacco mosaic virus using three different wave lengths of x rays. The purely geometric concept of the sensitive volume is not sufficient for explaining the known dependence of the inactivation of this virus on wave length. The concept of transfer of energy around the ionizing particles is discussed in this connection in a manner similar to that suggested by Pollard and Forro for the inactivation of the T-1 phage, and results similar to those given by these authors are obtained from an analysis of the inactivation data of J. W. Gowen (tobacco mosaic virus). Differences of interpretation of these two sets of experiments carried out with different types of radiation are pointed out. (auth)

1382

Opatowski, I. and F. R. Tangherlini. DIFFUSION AND RECOMBINATION OF PRODUCTS OF IONIZING RADIATIONS. *Bull. Math. Biophys.* 13, 273-88(1951).

The relative importance of diffusion and recombination of the products of ionizing radiations is examined in several typical cases and methods for the solution of the differential equation of columnar ionization are discussed. It is shown that Jaffé's method is not applicable to radiobiological or purely radiochemical processes in which no external electric fields are acting. A method based on a recent suggestion of Kramers appears to be particularly good when recombination is strong. (auth)

1383

Osgood, E. E. IS THE ACTION OF ROENTGEN RAYS DIRECT OR INDIRECT, (AN INVESTIGATION OF THIS QUESTION BY THE METHOD OF HUMAN MARROW CULTURE). *Am. J. Roentgenol. Radium Therapy* 48, 214-20(1942).

Ten cc of human marrow obtained by sternal puncture was mixed with 25 cc of citrated balanced salt soln. After manipulations to eliminate most of the non-nucleated red cells, the final culture consisted of about 100,000,000 nucleated marrow cells suspended in 50 cc of culture medium. With this material, 3 types of irradiation were done, -cells

and medium, cells alone, and medium alone. When the medium alone was irradiated, and then added to non-irradiated cells, there was no effect on the cells, whereas increasing cell destruction with increasing amounts of radiation was observed in the specimens in which both cells and medium, or cells alone, were irradiated. (BA)

1384

Pinney, Edmund. ON A MATHEMATICAL THEORY OF THE REACTION OF CELLS TO X-RAY IRRADIATION. *Bull. Math. Biophys.* **12**, 199-206(1950).

To describe the variation of concentration of certain substances in cells subjected to x-rays for a finite length of time, R. M. Sievert (*Acta Radiol.* **22**, 237-51(1941)) has given an equation of mixed differences involving time-lag and having discontinuous coefficients. In the present paper, Laplace transform methods are applied to solve this equation in terms of a series valid for all values of time. In particular, the conditions previously given that the concentration approaches a constant value are confirmed; otherwise, steady oscillations in concentration may be expected, or oscillations appear whose amplitude steadily increases until the cell is destroyed or the assumed mathematical model otherwise fails to apply. (NSA)

1385

Pollard, E. IONIZING RADIATION AS A TEST OF MOLECULAR ORGANIZATION. *Am. Scientist* **39**, 99(1951).

The nature of the effect in a large molecule of energy release due to ionizing radiation has been studied. Results show that where precise molecular organization is necessary for the action of a molecule such as, for example, in the action of an enzyme on a substrate, the enzyme organization is destroyed over a large region by the action of primary ionization. Rough figures for molecular weights can be obtained by these methods, and some conclusions about enzyme structure can be drawn. The present study includes the results of many investigators. (NSA)

1386

Pollard, E. C. and F. Forro, Jr. EXAMINATION OF THE TARGET THEORY BY DEUTERON BOMBARDMENT OF T-1 PHAGE. *Science* **109**, 374-5(1949).

The authors investigate the target theory of biological action, according to which a localized sensitive volume of definite size exists and within which there must be considerable liberation of energy for biological action to take place. Although Lea has examined the theory (*Brit. J. Radiol.*, Suppl. 1, p.35 (1947)), according to his views a specimen irradiated in high concentration, and in the presence of a high concentration of large molecules, should have a low efficiency for indirect action and the direct, target-type action should predominate. Since there is some question as to whether direct action ever occurs, the target theory has been investigated in deuteron bombardments in which it should certainly be valid; these were made using T-1 bacteriophage. Tabulated data on the percentage survival as a function of the number of deuterons per unit area are given for beam energies of 1.5, 2.5, and 3.5 Mev. Tabulated data on the temperature inactivation of the same phage are given; these data suggest that Lea's theory should be modified to include the possibility of inactivation caused by secondary radiation reaching the target from an ion path which does not go through the target. This is developed mathematically and the results obtained indicate that the data are consistent with the following hypotheses: 1) a target of 28 ± 4 m μ exists which is much smaller than the phage itself, and 2) the measured target size is greater than the true target size owing to the fact that radiation from the path of a deuteron which misses the target can inactivate the phage. (NSA)

1387

Read, John. THE LATERAL DISTRIBUTION OF IONS ACROSS THE TRACK OF AN IONIZING PARTICLE. PART I. THE PRESENT PICTURE AND ITS IMPLICATIONS. *Brit. J. Radiol.* **22**, 366-74(1949).

If Lea's (*Brit. J. Radiol.* (Supplement 1), **59**, 1947) picture of the lateral distributions of positive and negative ions across the track of an ionizing particle is correct, then the separation of charge must lead to a radical electric field. Expressions are deduced for this field, the corresponding potential differences, and the energy per ion pair stored in the field. Numerical values are obtained for an ion density of 1,000 ions per micron in water, hexane, and a chromosome thread. The field is of the order of 10^5 v/cm at relatively large distances from the axis of the track. An approximate expression is derived for the distribution of the positive and negative ions when in thermal equilibrium. Small ion densities can be in equilibrium with quite large separation of charge, but in the case of ion densities of 1,000 ions per micron Lea's distributions are far from equilibrium, and the electrons would return to the positive core unless captured. If, when an ionizing particle passes radially across a chromosome, this separation of charge occurs, and the electrons become attached to the fabric of the chromosome, then tensions of the order 10^5 dynes/cm² would be produced normal to circles of radius comparable with that of the chromosome. A tension wave would travel in both directions away from the point of intersection of track and chromosome. If the chromosome has weak points, e.g., between genes, breaks might be produced here, and the minute deletions might be due to the two tension waves each producing a break. Reference is made to the work of Jaffe (*Ann. Phys.* **42**, 303, 1913). (NSA)

1388

Read, John. THE EFFECT OF NITROGEN MUSTARD ON THE GROWTH OF THE BROAD BEAN ROOT (*VICIA FABA*). *Brit. J. Radiol.* **23**, 504-5(1950).

Nitrogen mustard is said to be radiometric because it produces effects apparently similar to some produced by ionizing radiations. Experiments show that oxygen does not enhance the effect of NM under conditions which greatly augment the effect of x-rays. Alternative hypotheses are (1) oxygen increases radiosensitivity by changing the metabolic state, (2) the oxygen reacts with the products of ionization (H atoms) to produce an increase in some toxic product (HO_2 , H_2O_2 , O). This experiment does not prove that hypothesis (2) is correct but is one which might have disproved it and has not. (M.F.)

1389

Read, John. PHYSICAL ASPECTS OF THE BIOLOGICAL ACTION OF IONIZING RADIATIONS. *Brit. J. Applied Phys.* **2**, 337-45(1951).

The influence of such physical factors as the linear ion density created by different radiations, the presence of dissolved oxygen or certain other molecules, and the dose rate, on the production of biological effects by ionizing radiations is discussed. Certain radiochemical experiments are outlined which show similarities with radiobiological experiments. Hypotheses are suggested which attempt to correlate and explain some of the biological observations. (NSA)

1390

Reid, A. T. and H. G. Landau. A SUGGESTED CHAIN PROCESS FOR RADIATION DAMAGE. *Bull. Math. Biophys.* **13**, 153-61(1951).

A mechanism by which transmission of the initial radiation damage, causing ionization in a sensitive volume due to absorption of radiation quanta, may take place, and a finite Markov chain model applicable to this transmission

are postulated and discussed. This mechanism is assumed to be the depolymerization of essential chain molecules which are connected to some "central group" associated with the sensitive volume. The depolymerization of the macromolecules following a hit in the sensitive volume is postulated to be determined by a chain mechanism, which acts in a manner inverse to the mechanism controlling the polymerization process. A mathematical study of this problem is made, using the theory of Markov chains. The probability of complete degradation of the chain macromolecule and the probability of recombination of the units to give the intact chain were determined, assuming that the probability of successive steps in the degradation increases linearly from the intact state to that of complete breakdown. (NSA)

1391

Ross, W. C. J. BIOLOGICAL ACTION OF X-RAYS, NITROGEN MUSTARDS, DIEPOXIDES, AND PEROXIDES. *Nature* **165**, 808-9(1950).

Organic peroxides are mutagenic, and induce chromosome abnormalities in *Vicia faba*. Similarity of the effects produced by N mustards and diepoxides, which react by a carbonium-ion mechanism, and those of x-rays and peroxides, which react by a free radical mechanism, suggest similarities in their mode of action. The nucleophilic center of the original system is changed to a highly reactive electrophilic center. The new electrophilic center could react further with a nucleophilic group on the same surface or with a group on a different surface. Mustards, diepoxides, and peroxides appear to produce breakage of the long chromosomes of *Vicia faba* at specific regions while ionizing radiations produce more random breakage. (CA)

1392

Rossi, Harald H. THE BIOLOGICAL SIGNIFICANCE OF THE TISSUE DOSE OF IONIZING RADIATIONS. *Trans. N. Y. Acad. Sci.* **2**, 270-5(1949).

A general discussion of ionizing radiations is given, with special reference to the problem of a quantitative measurement of radiation and the question as to how far the result of such measurements serves to define the conditions under which a radiobiological experiment is performed. Spatial and temporal considerations of dosimetry in connection with ionization and induced electromagnetic fields are qualitatively discussed; the author suggests the further collaboration of physicists with biologists for more exact dosimetry measurements and for discussion of the complex theoretical problems which arise in treatment of biological material. (NSA)

1393

Sacher, G. PRELIMINARY REPORT: A COMPARATIVE STUDY OF RADIATION LETHALITY IN SEVERAL SPECIES OF EXPERIMENTAL ANIMALS IRRADIATED FOR THE DURATION-OF-LIFE, p.105-22 of DIVISION OF BIOLOGICAL AND MEDICAL RESEARCH; QUARTERLY REPORT, May, June, July, 1950. Argonne National Lab. July 1950. 149p. (ANL-4488(p.105-22))

An analysis of radiation lethality in metazoan forms has been developed on the basis that (1) many or all aspects of physiological function are affected by radiations, (2) the responses of physiological systems to irradiation, and the interactions between systems, are linear, (3) a lethal process arises which is a weighted sum of the injuries to the constituent systems, (4) death occurs when this process intersects with a lethal bound of injury, and (5) when aging is a significant factor, the effects of the aging process and the radiation process combine additively. The further approximation is made that the behavior of a population is described by a representative animal, taken to be the mean or median animal. This latter approximation permits the

interpretation of data from small groups of animals, which is carried out in the present paper. The data analyzed were mean survival times at various daily exposures. Data for several species were available. By using the above hypothesis, it has been possible to deduce for each species a cumulant lethality function and an impulse lethality function which describe the course physiological injury would follow consequent to continuous and to single exposures, respectively, if the species behaved according to the hypothesis. No internal test of consistency is possible, but determination can be made as to whether the derived lethality functions are consistent with other kinds of information. At least semiquantitative consistency was obtained for several types of comparison. 20 references. (NSA)

1394

Sanden, Kurt von. TARGET-THEORETICAL INTERPRETATION OF THE RELATION BETWEEN THE STEEPNESS OF THE DOSAGE-EFFECT CURVE AND THE IONIZATION DENSITY. *Z. Naturforsch.* **4b**, 257-62(1949).

A statistical theory is developed which describes the effect of a given dosage of ionizing radiation on a set of biological objects distributed at random in the space filled by the radiation. It is assumed that an elementary target area must suffer simultaneous multiple hits to be affected by the radiation. The ionization density enters from the beginning into the formulation of the statistical problem, with the result that the steepness of the dosage-effect curve decreases with increasing ionization density. (NSA)

1395

Schon, M., B. Rajewsky, K. Sommermeyer, and H. Friedrich-Freksa. QUANTUM PHYSICS AND STATISTICS IN BIOLOGY. In *FIAT Review of German Science, 1939-1946: Biophysics, Part I*, p.1-49.

This review article is primarily a guide to the literature of quantum physics and statistics in biology. Approximately 150 references are given. Separate sections deal with quantumtheoretical features of biological problems; foundations of the target theory of the biological effect of radiation; further development of target theoretical concepts; energy migration in molecule complexes and structural units; forces which play a role in the composition of biological structural units. (NSA)

1396

Schubert, G. ANALYSIS BY RADIATION OF BIOLOGICAL ELEMENTARY STRUCTURES. *Strahlentherapie* **80**, 1-16(1949).

This is a review article, written primarily from the standpoint of the target theory, on the effect of radiation on elementary biological structures such as genes, bacteriophages and viruses. In particular, the number of hits on a target necessary for biological effects, the role of energy migration in the elementary structure, and the possible size of the elementary target regions as deduced from irradiation experiments are discussed in some detail. (NSA)

1397

Scott, C. M. SOME QUANTITATIVE ASPECTS OF THE BIOLOGICAL ACTION OF X AND GAMMA RAYS. *Med. Research Council (Brit.) Spec. Rept. Ser.* No. 223, 1-99 (1937).

In Part I (pp 1-71) the literature bearing on the mechanism of action of the rays is briefly and critically surveyed. Part II (pp. 71-99) reports experimental work 100,000 r of x-rays (80 kv, 5 ma, distance 12 cm, filter 0.1 mm Al, intensity 550 r/min) produced no change in the rate rhythm or amplitude of contraction of the isolated heart of *Rana esculenta*; 16,500 r had no effect upon the heart's respiration or upon its conversion of carbohydrate to lactic acid. The contraction of isolated auricles was unaffected by several days' continuous exposure to the β and γ rays from 5

mg Ra element (distance 2 mm, filter 0.5 mm soda glass). When the hatching of eggs of *Coliphora erythrocephala* was inhibited by x-rays (80 kv, 5 ma, distance 47 cm, filter 0.1 mm Al) the Bunsen-Roscoe law was valid for intensities ranging from 13 to 100 r/min. The dose required to kill 50% depended upon age and ranged from 50 to 340 r. The radiosensitivity of the eggs was increased by chloroform, ethyl ether and petroleum ether, but was unaltered by nitrous oxide. When x-ray was superimposed upon injury by low temp., the results indicated that the two injuries were unrelated in mechanism but that in general the individual eggs which were sensitive to cold were also sensitive to x-rays. Similar results were obtained when asphyxia or CO₂ was substituted for low temperatures. (BA)

1398

Sommermeier, K. **THE THEORY OF RADIO-BIOLOGICAL SATURATION EFFECT.** *Naturwissenschaften* **30**, 104-5 (1942).

In detg. the satn. factor of biol. radiation effects the no. of active ionizations per unit vol. count. The satn. factor is proportional to $pr^3 L$ with p the activity probability, r the vol., L the distance of successive ionizations. It is stressed that only the no. of active ionizations counts. (CA)

1399

Sommermeier, K. **ON THE EFFECTIVE CROSS SECTION OF PROTONS AND ALPHA-RAYS, AS COMPARED WITH THE RADIATION-SENSITIVE VOLUME, IN ELEMENTARY RADIO-BIOLOGICAL REACTIONS.** *Z. Naturforsch.* **36**, 57-9(1948).

In a previous work (*Naturwissenschaften* **31**; 172 (1943)) the author has shown that some radiobiological phenomena cannot be interpreted as due to a saturation effect if the total cross section of the ionizing proton is considered effective. This is confirmed by the findings of Lea (*Actions of Radiations in Living Cells*, Cambridge 1946) who has shown that, for many processes, the saturation hypothesis explains very well the quantitative data if the biologically effective cross sections of protons and α -rays are disregarded as against the dimensions of the radio-sensitive volume. However, the author objects to the interpretation of this situation offered by Lea, and suggests, as a mechanism of the elementary biophysical reaction involved, a capture of a secondary electron by a complex organic molecule. (NSA)

1400

Sommermeier, K. **RESULTS AND PROBLEMS OF THE TARGET THEORY IN RADIOBIOLOGY.** *Naturwissenschaften* **38**, 289-98(1951).

The only assumption made by the target theory is that radiation absorption in biology follows the laws of the quantum theory, the aim of which is to find the relationships between the primary reactions of the ionization radiation with the biological target and the ultimate total biological effect. Statistical experiments serve as fundamental application of the theory. Examples given of experiments with high-energy radiation show dependence of target numbers on dosage and ionization distance (from primary reaction to ultimate path in the radiosensitive medium). Experiments with primary biological structures such as viruses, phages, genes, and chromosomes are reviewed; dependence of radiation effects on the size of these bodies is shown; radiation effects (inactivation, chromosome aberrations) decrease with bodies of increasing size under the same strength of radiation. The biochemical foundations of these reactions are analyzed in detail. Reviews of target-number computations for ionization-radiation effects on higher organisms are given for bean seedlings and eggs of *Drosophila*. The relationship of radiosensitive volume and indirect ionization-radiation reactions, the safety in using exponential

curves resulting from experiments in target number computations, and the energy distribution of the primary ionizations and their dependence on the energy of the ionized particles are discussed. Experiment with the kapazitron investigate the ionization-radiation effectiveness of particles of various energies on primary biological structures of larger size. (NSA)

1401

Stewart, L. N. and Jean Bouchard. **RECENT ADVANCES IN KNOWLEDGE OF THE BIOLOGIC EFFECT OF RADIATION.** *J. Can. Assoc. Radiol.* **1**, 12-15(1950).

Irradiation can induce changes in biological materials through an intermediate product (probably OH) derived from the solvent. The stage of prophase remains the critical period in radiosensitivity of the cell and nuclear changes depend on radiosensitization of a target molecule in the vicinity. Biological reaction is determined by linear ion density. (CA)

1402

Timoféev-Ressovskii, N. W. and K. G. Zimmer. **THE TARGET PRINCIPLE IN BIOLOGY.** Hirzel, Berlin. 1947.

Among the subjects covered are: The historical development and formal statement of the target theory; the target theory with relation to biological variability, analysis of release of gene and chromosome mutation thru radiation; biophysical analysis of bactericidal effects of radiation; mechanism of energy migration in an ordered system; static ultramicroscopy with ionizing radiations. (M.F.)

1403

Tobias, Cornelius A. **MECHANISMS OF BIOLOGICAL EFFECTS OF PENETRATING RADIATION.** *Federation Proc.* **10**, 595-601(1951).

Brief descriptions are given of the mechanism of interaction of radiation with matter, various biological effects of breakdown of macromolecules by direct action of ionizing radiation, and examples of recent experimental approaches to indirect action of radiation. The effects of radiations at the cellular level were studied in haploid and diploid yeast cells. The 5 times greater resistance of diploid cells against radiation injury is explained as due to the presence of paired genes and chromosomes in the diploid cells, controlling the cell mechanisms from a number of mutually independent pairs of sites, whereas the one set of chromosomes in haploid cells results in each site being represented only once. Radiation effects on mammals and new modes of therapy of radiation injuries are reviewed. (NSA)

1404

Van der Werff, J. T. **FURTHER DEVELOPMENT OF THE THEORY OF BIOLOGICAL REACTIONS CAUSED BY ROENTGEN-RAYS.** *Acta radiol.* **28**, 168-84(1947).

The author maintains that each theory on a biologic problem should take the existing metabolism into account. In 1942, he based a mathematical theory of the biologic reactions caused by Roentgen-rays upon the principle and in this paper he described a further development of this theory. If some "biogenic" substance, in the steady state before irradiation, is influenced by X-rays, a change not only in the rate of breaking down but also of the rate of building-up of that substance may occur. With the aid of some assumptions it becomes possible to construct an "equation of metabolism." In order to test his theory, the author makes use of A. Forssberg's studies on the influence of X-rays upon the growth rate of the fungus-cell *Phycomyces blakesleeianus*. With the aid of the proposed equation, a full explanation of these experiments can be given. The theory can also be applied with equal success to the phenomena of excitation of nerves and so covers two large fields of biologic reactions. (BA)

1405

Warren, S. **MECHANISM OF RADIATION EFFECTS AGAINST MALIGNANT TUMORS.** *J. Am. Med. Assoc.* **133**, 462-3(1947).

A brief discussion of current theories on the effect of x-rays and radioactive radiations upon normal and diseased tissues. (BA)

1406

Watson, J. D. **INACTIVATING MUTATIONS PRODUCED BY X-RAYS IN BACTERIOPHAGES.** *Genetics* **33**, 633-4 (1948).

Luria reported in 1947 that reactivation by multiple infection, such as he discovered for ultraviolet inactivated bacteriophages, could not be detected after X-ray inactivation. In reinvestigating this problem, we found that X-rays, besides inactivating phage, also suppress the ability of phage to infect bacteria, one "adsorption suppressing" hit occurring on the average for every three inactivating hits. Because of this, reactivation is difficult to detect by the multiple-infection technique. We tested for it by infecting individual bacteria with one particle T2r⁺ inactivated by X-rays and one particle T2r inactivated by ultraviolet. A significant proportion of these bacteria liberate a mixture of active T2r⁺ and active T2r, which proves that X-rayed phage can participate in genetic recombination and reactivation. Similar conclusion was reached by infecting bacteria with one active particle T2r⁺ and one X-rayed particle T2r. Finally, reactivation was also detected by mixed infection with one particle each of X-ray inactivated T2r⁺ and T2r. Quantitatively, we found that for equal numbers of inactivating hits, the contribution of an X-ray inactivated particle to reactivation is lower than that of an ultraviolet inactivated one. The relative contribution of X-ray and ultraviolet inactivated particles is constant in all types of experiments listed above. This result is considered as evidence that one X-ray hit produces on the average more lethal mutations than one ultraviolet hit, thus giving the first experimental evidence for an actual difference in the spatial domain within which the genetic effects of one hit of each type can be exerted. (G)

1407

Watson, James Dewey. **THE PROPERTIES OF X-RAY-INACTIVATED BACTERIOPHAGE. I. INACTIVATION BY DIRECT EFFECT.** *J. Bacteriol.* **60**, 697-718(1950).

The inactivation by x rays of bacteriophages of the T group suspended in broth has been investigated, and the properties of the inactive viruses have been studied. Inactivation is a simple exponential function of the dose, indicating a one-hit inactivating mechanism. All the inactive particles are able to adsorb on sensitive bacteria, but only a fraction of them retain the ability to kill bacteria or to exclude another phage type. The ability to inhibit lysis or to lyse bacteria from without is not lost when the ability to kill bacteria is destroyed. Multiplicity reactivation and photo-reactivation of x-ray-inactivated phage are observed in slight amounts. The results have been used to distinguish two stages in the early period of phage reproduction, the first stage being called "adsorption," the second "invasion." (NSA)

1408

Weiss, J. **ASPECTS OF THE CHEMICAL AND BIOLOGICAL ACTION OF RADIATIONS.** *Trans. Faraday Soc.* **43**, 314-24(1947).

The general principles involved in the chem. and biol. action of radiation (x-rays, γ rays, α -particles, neutrons) are examined. In penetrating radiations the absorption of radiation energy is not specific and is approx. proportional to the mass but practically independent of the chem. linkage.

The direct and indirect action of radiations, the formation, action, and the implications of free radicals, and the relation to the phys. "hit" theory have been discussed in detail. It is found that the recombination process following the primary formation of the radicals is of considerable importance. If recombination can be neglected, the effects are approx. independent of the nature and wave length of the radiation and depend only on the total dose, while this is no longer the case if the recombination process plays a part. The extension into space of reaction chains can assume significant proportions and may be of considerable importance in the biological effects. (CA)

1409

Wijsman, R. A. **ON THE INTERPRETATION OF THE DOSE-FREQUENCY CURVE IN RADIOGENETICS.** *Genetics* **36**, 478-87(1951).

Comparison of curves of multiple-event models with the curve for a single-event model supports the theory that a linear relationship between mutation frequency and radiation dose is caused by a single event. An exception has to be made for the possibility that some events may occur with much higher probability than any of the others, in which case a multiple-event model could give rise to a single-event type curve; this case is physically unlikely. Opatowski's curve (*Bull. Math. Biophys.* **12**, 19-26(1950)) is shown to represent a one-event mechanism, and his conclusion that a many-event theory can give rise to a linear curve is unjustified. (NSA)

1410

Zirkle, Raymond E. **RELATIONSHIPS BETWEEN CHEMICAL AND BIOLOGICAL EFFECTS OF IONIZING RADIATIONS.** *Radiology* **52**, 846-55(1949).

A discussion is presented of the nature of the connecting events occurring in the "latent period" which intervenes between the energy absorption in ionizing radiation conditions and the biological effects produced by these radiations. The author assumes that the formation of new combinations which produce the biological effects is brought about by chemical reactions. Two phases of the chemical reactions are discussed, the nature of chemical reactions and the manner in which they lead to the biological effect. Early relevant reactions may occur in the cell medium, and later ones at the cell surface or within the cell itself, due to the absorption of some chemical product. The possibility of the ionization of water by the radiations and the production of changes of many products in this medium *in vivo* are discussed. Three steps are proposed to study relevance of chemical reactions: a specific radio-chemical reaction must be suspected of relevance to a given biological effect; second, if the reaction is only known to occur *in vitro* it must be proved to occur in the intact and irradiated cell; third, if the reaction passes the foregoing preliminary tests, it must be connected to the biological effect by a definite procedure. An indirect method of substantiating the third step by correlation of the variations in biological effects with variations in the radiations is outlined. The author concludes by stressing the importance of chemists in the radio-biological field and the need for further knowledge of the mechanisms of radio-biological reactions. (NSA)

General Biochemical Studies

1411

Altman, K., J. Richmond, and K. Salomon. **A NOTE ON THE SYNTHESIS OF FATTY ACIDS IN BONE MARROW HOMOGENATES AS AFFECTED BY X-RADIATION.** *Biochim. et biophys. acta* **7**, 460-5(1951) (UR-169)

The synthesis of saturated and unsaturated fatty acids in bone marrow homogenates from untreated and x-irradiated

rabbits has been studied with α - C^{14} -acetate as a precursor. Two- and three-fold increases, respectively, over pre-irradiation levels in saturated and unsaturated fatty acid synthesis were observed immediately after irradiation. Whereas saturated fatty acid synthesis, which approached control values at 48 hr after irradiation, again increased $3\frac{1}{2}$ times at 72 hr, unsaturated fatty acid synthesis had fallen to 18% of the preirradiation value. At 158 hr the relationship was reversed since unsaturated fatty acid synthesis had risen to 283% and saturated fatty acid synthesis had dropped to 58% of the preirradiation value. Oxygen uptake and $C^{14}O_2$ production increased immediately after irradiation, dropping to preirradiation values 48 hr after exposure, $C^{14}O_2$ evolution decreased steadily throughout the experimental period while oxygen uptake was unchanged 158 hr after exposure. (NSA)

1412

Anderson, C. T., H. Blaschko, J. H. Burn, and R. H. Mole. **THE PRESSOR AMINES IN THE ADRENAL MEDULLA AFTER IRRADIATION.** *Brit. J. Pharmacol.* **6**, 342-50 (1951).

Pyridoxine hydrochloride seems to protect against radiation sickness and to reduce mortality of mice given total-body x irradiation. The relation of pyridoxine and the enzyme dopa-decarboxylase to the formation of pressor amines (noradrenaline and adrenaline) has been investigated. Beginning 48 hr after lethal total x irradiation the content of pressor amines in the adrenal gland was progressively reduced. Dopa-decarboxylase activity in the liver, reduced after irradiation to some extent, was restored by adding pyridoxine to the diet; this did not influence the fall in pressor amines. Effect of insulin injection was investigated. Hypertrophy of adrenal glands following irradiation was observed. (NSA)

1413

Bancroft, Geo. H. and Victor E. Kinsey. **THE EFFECT OF X-RAYS UPON THE METABOLISM OF TUMOR TISSUE.** *Biochem. J.* **31**, 974-9(1937).

A definite lowering of the R.Q. of rat sarcoma in vivo was produced by x-rays. A parallel increase in the aerobic acid production, due mostly to lactic acid, indicated that the lowered R.Q. was not due to incomplete oxidation with the formation of acids other than lactic. Under the same conditions x-rays did not affect the metabolism of rat kidney slices. Since irradiated tumor and kidney slices metabolize pyruvic acid normally, x-rays probably attack the carbohydrate oxidation before the pyruvic acid stage is reached. (CA)

1414

Barron, E. S. G., Veronica Bonzell, Betty Gasvoda, and Louise Seki. **THE RESPIRATION AND ACETATE OXIDATION RATE OF X-IRRADIATED BACTERIA (MYCOBACTERIUM CREATINOVORANS)** p.97-8 of **BIOLOGICAL AND MEDICAL DIVISIONS; QUARTERLY REPORT, FEBRUARY, MARCH, APRIL, 1950.** Argonne National Lab. [nd] 2p. (ANL-4451(p.97-8))

It was shown previously (ANL-4291) that x irradiation of *Mycobacterium creatinovorans* with doses varying from 1000 to 10,000 r, caused an increasing inhibition of respiration of the bacteria irradiated in the culture media containing acetate. On irradiation of three-times washed bacteria the residual respiration was unaffected by 6000 r while respiration in the presence of acetate was 30% inhibited. To determine whether permanent changes could be produced in bacteria by continuous irradiation with relatively small doses of x rays, liquid cultures of *M. creatinovorans* (in acetate medium) were irradiated with 1000 r. One-day-old cultures were irradiated in test tubes with 1000 r (effective irradiation about 800 r); the

cultures were transplanted 8 hr later into another test tube which was irradiated on the following morning. The total amount of effective radiation was 11,200 r. The residual respiration, as well as the oxidation rate of acetate, was depressed in the x-irradiated bacteria. Pigment formation in the x-irradiated bacteria was also less than in the control samples. The x-ray dose received daily, 800 r, when given in a single dose had no effect either on multiplication of bacteria or on respiration. (NSA)

1415

Barron, E. S. G. and Veronica Flood. **THE EFFECT OF X-IRRADIATION ON THE METABOLISM OF THE SMALL INTESTINE OF THE RAT**, p.157-61 of **BIOLOGICAL AND MEDICAL DIVISIONS; QUARTERLY REPORT, NOVEMBER, DECEMBER, JANUARY, 1948-1949.** Argonne National Lab. Feb. 1, 1949. 5p. (ANL-4253(p.157-61))

Sprague-Dawley rats, weighing 200 g each, were given total-body x-radiation at different dosages ranging from 50 to 500 r. The animals were sacrificed at different intervals and the metabolism of strips of the small intestine were determined. The O_2 uptake of the strips of tissue from x-irradiated rats was always below normal when measured soon after irradiation. When the rats were irradiated with 50 r, respiration returned to normal values five hours later. Anaerobic glycolysis was not affected when measurements were made soon after irradiation. (ACD)

1416

Barron, E. S. Guzman and Veronica Flood. **STUDIES ON THE MECHANISM OF ACTION OF IONIZING RADIATIONS. VI. OXIDATION OF THIOLS BY IONIZING RADIATIONS.** *J. Gen. Physiol.* **33**, 229-41(1950).

The SH groups play a very important role in the processes of cell division and of cell growth. It was found previously that enzymes requiring SH groups for activity were reversibly inhibited by ionizing radiations, which indicates that the SH groups belong to proteins. In this study various thiols (glutathione, 2,3-dimercaptopropanol, propane-1, 3-dithiol, and N-phenylaminopropanedithiol) are shown to be easily oxidized in aqueous solution by ionizing radiations (x-rays, β -rays, and γ -rays). The mechanism probably involves decomposition of H_2O and formation of different oxidizing agents (OH , O_2H , O , H_2-O_2). The ionic yield (number of oxidized molecules divided by the number of ion pairs produced by ionization of H_2O) for the oxidation ($2RSH \rightleftharpoons RS-SR$) was 3 for x-rays or β -rays at pH 7, and 23% less for γ -rays, and this increased with a rise in pH value. In the absence of O_2 , the oxidation of thiols by ionizing radiations was only $\frac{1}{3}$ that obtained in the presence of dissolved O_2 . In the presence of dissolved O_2 , the irradiated thiol solutions were protected 17-27% from oxidation by catalase. (CA)

1417

Barron, E. S. Guzman, Betty Gasvoda, and Veronica Flood. **EFFECT OF RADIATION ON THE RESPIRATION OF SEA URCHIN SPERM**, p.148-63 of **BIOLOGICAL AND MEDICAL DIVISIONS; QUARTERLY REPORT, MAY, JUNE, JULY, 1948**, Austin M. Brues and Hermann Lisco, eds. Argonne National Lab. Aug. 1, 1948. 16p. (ANL-4205(p.148-63))

Authors reinvestigated problem of irradiation of single cells. Data are presented on the effect of x-rays on the respiration of sea urchin (*Arbacia punctulata*) sperm. Experimental procedure is described: effect of dilution on respiration of sea urchin sperm and effect of x-ray on respiration of sea urchin sperm. In summary: respiration of sea urchin sperm increased with dilution, up to a dilution of 1:200, where maximum values were found. At this

dilution the QO_2 value was 19.6 ± 3.9 . Sperm diluted 1:10 gave a QO_2 value of 1.7 and a dilution of 1:1,000 gave a QO_2 value of 2. The respiration of dilute suspensions of sea urchin sperm was inhibited by x-irradiation. A dosage of 20,000 r inhibited 60%; 10,000 r, 35%; 5,000 r, 25%; 1,000 r, 14%. There was little difference in inhibition when the dosage was decreased to 100 r. (S. V. S.)

1418

Barron, E. S. Guzman, Betty Gasvoda, and Veronica Flood. STUDIES ON THE MECHANISM OF ACTION OF IONIZING RADIATIONS. IV. EFFECT OF X-RAY IRRADIATION ON THE RESPIRATION OF SEA URCHIN SPERM. *Biol. Bull.* **97**, 44-50(1949).

The results of studies on the sea urchin (*Arbacia punctulata*) sperm respiration rate at various sperm dilutions and after dosages of x-radiations are presented. The experimental procedures and the technique are described. X-ray dosages of 100-20,000 r were administered in separate experiments at a water dilution of 1:200 and with or without added succinate or acetate. The respiration of the sea urchin sperm increased with dilution up to a dilution of 1:200, where the average maximum value of 19.6 ± 3.9 was found. When the dilution was increased to 1:1,000 the respiration dropped sharply to 2.0, and a dilution of 1:1,600 gave no measurable respiration. When a dose of 20,000 r of x-radiations was delivered to the sperm solution an inhibition of 66% in the respiration was seen, which increased during the second hour; 10,000 r produced a 30% decrease; 1,000 r, a 22% decrease; 500 r, a 14% decrease; and, 100 r, a 10% decrease. It was found that when the sperm was irradiated with 1,000 r, there was no respiration recovery for five hours; on addition of succinate and of acetate to the solution, the oxygen uptake was further inhibited. (NSA)

1419

Barron, E. S. Guzman and S. Louise Seki. CELLULAR RESPIRATION, CELL DIVISION, AND IONIZING RADIATIONS. Argonne National and Univ. of Chicago. Oct. 1951. 13p. (AECU-1821; UAC-462)

On x irradiation of the eggs and sperm of *Arbacia punctulata* there was inhibition of respiration with relatively large doses, whereas there was an increase with small doses. The dose required to produce an increase of respiration depended on the degree of sensitivity of the cell to the effect of ionizing radiation. Sperm cells were most sensitive; then came fertilized eggs; unfertilized eggs were the least sensitive. The inhibiting effect of x rays on cells division was observed even on irradiation with x-ray doses which produced an increase of respiration. These results are compared to similar effects produced by thiol reagents and are attributed to oxidation of the thiol compounds in the cell. (NSA)

1420

Barron, E. S. Guzman, W. Wolkowitz, and J. A. Muntz. THE EFFECT OF X-RAYS ON THE METABOLISM OF SMALL INTESTINE AND ITS PERMEABILITY TO GLUCOSE. Argonne National Lab. Feb. 3, 1947. 14p. (MDDC-1241; CH-3725)

The experiments presented in this paper demonstrate that x-rays produce immediate metabolic disturbances in the small intestine. All the experiments were made on rats which received total body irradiation. Four hours after irradiation, there was an abrupt drop of respiration in the small intestine, a diminished absorption of glucose, and a diminished phosphorylation of fructose. When rats were sacrificed 24 hours after irradiation, the respiration was within normal limits, although there was still inhibition of phosphorylation. Forty-eight hours after treatment, there was inhibition of respiration in some segments of the small

intestine. The inhibition increased 72 hours after treatment; the rate of phosphorylation of fructose was unimpaired. There was some inhibition of respiration 96 hours after treatment. Anaerobic glycolysis was generally normal. There was a linear relationship between the inhibition of glucose absorption and the amount of irradiation. (ADD)

1421

Barrow, Jack, John L. Tullis, and F. W. Chambers, Jr. EFFECT OF X-RADIATION AND ANTIHISTAMINE DRUGS ON THE RETICULO-ENDOTHELIAL SYSTEM MEASURED WITH COLLOIDAL RADIOGOLD. *Am. J. Physiol.* **164**, 822-3(1951).

The function of phagocytosis by the reticulo-endothelial system was studied by radiometrically determining the rate of removal of colloidal gold, radioactive in tracer amounts, injected intravenously into normal rabbits, and into rabbits variously treated with X-rays, thorotrast, antistine, pyribenzamine and histamine. Thorotrast temporarily suppressed almost completely the removal of colloidal gold from the circulation. Pretreatment of normal and x-irradiated rabbits with antihistamine drugs and/or histamine did not alter the rate of phagocytosis of the gold colloid. (CA)

1422

Baur, H. and M. Ludin. HISTAMINE CONCENTRATION AFTER IRRADIATION WITH X-RAYS. *Radiol. Clin.* **19**, 268-76(1950).

X-rays cause an increased blood histamine concn. in man and animals amounting to 5-6 times the normal values. In vitro irradiation of blood gives no increase. Expts. indicate that the histamine production is caused by irradiation of the reticulo-endothelial system or the bone marrow. (BA)

1423

Bennett, L. R., V. C. Bennett, and J. W. Howland. EFFECT OF ACUTE X-RADIATION ON DISTRIBUTION AND EXCRETION OF RADIOSODIUM IN THE RAT. *Federation Proc.* **8**, 350(1949).

Radiated rats have been shown to have an increased thiocyanate space for 2 weeks following a mid-lethal dose of x-radiation. A study of the sodium distribution and excretion of similar animals using radiosodium has been made. In rats during the first four days post radiation a marked retention of radiosodium occurs. Tissue distribution studies show a shift into the intestinal tract which may exceed that observed in control animals by as much as 2% of the total dose administered. Smaller shifts of radiosodium into the kidney and spleen are noted. There is an increased radiosodium content of the liver which appears to be definitely related to the increased serum level to which it holds a constant relationship. The serum sodium content increases, the maximum levels (up to 5-8 mEq) being observed at the end of 3-4 days after irradiation. Urinary radiosodium excretion may be reduced to one half that observed in control animals. Studies on dehydrated rats indicate that the urinary retention and elevated blood sodium level are not accounted for on the basis of dehydration alone. (Authors)

1424

Bennett, L. R., Vera C. Bennett, Alpha Shaver, and Theresa Grachus. ABSORPTION AND DISTRIBUTION OF VITAMIN A IN X-IRRADIATED RATS. *Proc. Soc. Exptl. Biol. Med.* **74**, 439-43(1950).

Young female rats were treated with 625 r whole-body irradiation. The rate of absorption of vitamin A alc. from the digestive tract was increased for a few days. Liver vitamin A was decreased and that of the carcass increased by the treatment. (CA)

1425

Bennett, Leslie R., Sarah M. Chastain, Arthur B. Decker, and James F. Mead. THE EFFECT OF ROENTGEN IRRADIATION UPON PROTEIN ABSORPTION IN THE MOUSE. *Proc. Soc. Exptl. Biol. Med.* **77**, 715-18(1951) (UCLA-137)

The rate of protein absorption was measured in normal mice with I^{131} -labeled human serum albumin and was compared with absorption in mice exposed to 600 r of whole-body x radiation. No change in the absorption rate after exposure was observed, although a change in tone and motility of the gastrointestinal tract was noted. (NSA)

1426

Berner, F. THE ACTION OF ROENTGEN RAYS ON THE MINERAL METABOLISM OF UNICELLULAR ORGANISMS WITH THE VIEW OF FINDING AN IRRADIATION RHYTHM WHICH DESTROYS THE CULTURES OF UNICELLULAR ORGANISMS IN THE SHORTEST POSSIBLE TIME WITH A SMALL TOTAL QUANTITY OF RAYS. *Strahlentherapie* **71**, 1-60(1942).

The alteration of the mineral metabolism of *Paramecium caudatum* under the action of roentgen irradiation was observed. A favorable irradiation rhythm was found. (CA)

1427

Billen, Daniel, G. E. Stapleton, and Alexander Hollaender. THE EFFECT OF X RADIATION ON THE RESPIRATION OF BACTERIAL CELLS. Oak Ridge National Lab. [nd] 1p. (AECU-1801)

Studies with x rays revealed that one effect was inhibition of the respiratory system of washed suspensions of *Escherichia coli*, although the magnitude of the inhibition varies with substrate, temperature, and strain of the organism used. It was found that a dose of 60,000 r, while decreasing the number of viable cells of a suspension of *E. coli* B/r by more than 99.95%, had no apparent effect on the initial respiratory rate of the exposed cells. However, the initial period of normal activity was followed by a marked decline in oxygen consumption rate as compared to the control cells. The period of normal activity was longer when pyruvate and succinate were used as substrates as compared to glucose utilization. A period of normal respiratory activity on glucose in contrast to an immediate inhibition of oxidative activity on pyruvate was observed with *E. coli* (Texas). Both exposed and nonexposed cells showed a respiratory quotient of one on glucose, although the former required a longer period of time to complete the oxidation of the substrate. Holding the exposed cells in buffer at 37°C for 60 min before adding substrate decreased the period of normal activity and caused a sharper decline in respiratory rate, while an exposed suspension held in buffer at 2°C for 3 hr following irradiation was as active as a suspension tested immediately after exposure. A comparison of exposed cells respiring at 37 and 26°C in the presence of glucose or pyruvate revealed an increased adverse effect of the radiation-induced inhibition of respiration at the higher temperature. (Entire report)

1428

Blokhin, N. N., B. M. Graevskaya, and R. Ya. Keilina. BIOCHEMICAL PROCESSES IN THE BRAIN IN DIRECT IRRADIATION BY X-RAYS. *Byull. Eksptl. Biol. i. Med.* **23**, 338-42(1947).

X-ray irradiation of dog brain, at 160 kv, at 23 mm distance by using 0.5 Cu-3.0 Al filter, each dog receiving a total of 5 unit skin doses of irradiation in 4 exposures with alternate irradiation of the right and the left temple area, was investigated in respect to biochem. effects by detn. of blood sugar (femoral artery and sinus venosus cerebri), spinal fluid sugar, blood serum protein, and the albumin-

globulin fractions of the latter. As the total irradiation increased, the total serum protein rose until the 90th day (after the 1st irradiation) it reached 200% of the initial value. In the same period the albumin fraction rose by only 26% for arterial and 32% for venous blood, while the globulin fraction rose 324 and 323%, respectively. The abs. amt. of protein in the spinal fluid remained within exptl. variations, but its albumin/globulin ratio gradually changed to 1.0 from 0.56. Arterial blood sugar remained normal, but it fell in the venous blood until the sugar utilization by the brain at the 90-day period was 37% of initial. Spinal fluid sugar did not increase. The changes are ascribed to a colloidal swelling of the brain cells, with decreased amount of intracellular fluids. (CA)

1429

Bowers, John Z. and Kenneth G. Scott. DISTRIBUTION AND EXCRETION OF ELECTROLYTES AFTER ACUTE WHOLE-BODY IRRADIATION INJURY. I. STUDIES WITH RADIOPOTASSIUM. *Proc. Soc. Exptl. Biol. Med.* **78**, 645-52(1951).

Radiosensitive tissues show a variety of alterations in radiosodium concentration after total-body irradiation above an LD₅₀. In several tissues there is a decrease followed by a sharp increase; the decrease occurs at the same time as a decrease in radiopotassium concentration. An increase in percentage water content may occur when there is a fall in radiosodium concentration. Percent loss of dry weight per day is in general most pronounced in radiosensitive tissues. Urinary excretion of radiosodium after total-body irradiation at levels approximating an LD₅₀ shows a complementary homeostatic decrease in response to the excessive loss of radiosodium through the gastrointestinal tract. (NSA)

1430

Bowman, M. C. and W. R. Franks. THE EFFECT OF X-IRRADIATION ON TISSUE RHODANATE. *Acta Unio. Intern. contra Cancrum* **6**, 765-7(1949).

The results of investigations to determine whether the destruction of tissue rhodanate by x-irradiation is accompanied by disturbances in the Pasteur reaction of the tissue are reported. The bodies of mice under light Nembutal anesthesia were covered with lead shields, only the heads receiving x-ray surface dosages of 10,000 r (base dosages of 7,000 r); the radiations were delivered by a 88-kv source with no filtration, at a distance of 10 cm over a period of 10 minutes. The irradiated animals were sacrificed at various intervals and estimations of the rhodanate activity, respiration, anaerobic and aerobic glycolysis of their grey brain matter were carried out. The rhodanate activity was determined by a slightly modified Lang method, which is described here. It was found that the Nembutal did not affect either the rhodanate activity or the respiration and glycolysis of the mouse brain grey matter; the x-irradiation did not inhibit the rhodanate activity in rat liver homogenate in vitro, but was lethal to the mice in 8 to 10 days. Summarizing, no significant activity changes in the rhodanate, respiration or glycolysis were detected. (NSA)

1431

Boyland, E. and S. Sargent. THE LOCAL GREYING OF HAIR IN MICE TREATED WITH X RAYS AND RADIOMIMETIC DRUGS. *Brit. J. Cancer* **5**, 433-40(1951).

The intradermal injection of nitrogen mustards or sulfur mustard into colored mice causes a permanent graying or bleaching of the hair similar to that occurring after exposure to ionizing radiations. This graying appears to be a radiomimetic effect. Similar graying of hair occurs in a proportion of cases when water is injected but never following the injection of saline. Graying of hair was pro-

duced by injection of known carcinogens, such as β -naphthyl-bis (β chloroethyl) is an example of limited toxic action, and so allied to vesication and induction of mutations and cancer. (NSA)

1432

Buchanan, D. L. and E. S. Guzman Barron. STUDIES ON THE EFFECT OF RADIATION ON PROTEINS. Argonne National Lab. June 1, 1947. 22p. (MDDC-1418-D)

Data are presented showing certain effects of ultraviolet and γ rays on the absorption spectra of solutions of crystalline egg albumin. The changes differ with the two types of irradiation, with variation in pH, and questionably with oxygen tension of the solution. The changes do not resemble those seen in heat, acid, or alkali denaturation. In an arbitrary fashion the rate of change in the solutions being irradiated was shown to have the "zero order" type of rate constant, implying the rate of formation of product to be independent of the concentration of solute within the limits of concentration studied, but giving no information as to the actual reaction rate. (ADD)

1433

Crabtree, H. G. THE DIFFERENTIAL EFFECT OF RADIUM RADIATION ON THE CARBOHYDRATE METABOLISM OF NORMAL AND TUMOR TISSUES IRRADIATED AT LOW TEMPERATURE. *Biochem. J.* **29**, 2334-43 (1935).

Ra radiation of tumor-tissue slices at 37.5° either under aerobic or anaerobic conditions or with HCN present (which made the tissue more sensitive) caused a selective lowering of respiration while glycolysis remained unaffected. Irradiation of tumor slices at 0-10° under the same conditions caused a pronounced lowering of glycolysis, and the respiration was unaffected. The irradiation of normal tissues (spleen, liver, kidney, testes) at 0-10° under identical conditions produced little or no effect on their metabolism, since their respiration was not accompanied by aerobic glycolysis. This difference in the effect of irradiation of tumor cells at 0-10° may be of clinical value. (CA)

1434

Davison, R. A., P. Koets, and W. C. Buzell. EFFECT OF ROENTGENOTHERAPY ON URINARY 17-KETOSTERID EXCRETION IN ANKYLOSING SPONDYLARTHROSIS. *J. Clin. Endocrinol.* **9**, 79-88(1949).

Urinary 17-ketosteroid excretion was found to be increased in spondylarthrosis of the ankylosing type in both male and female patients. High values continued for long periods of time and approached lower levels only when the patient reached a state of exhaustion. Roentgenotherapy seemed to provide a stimulus for increased excretion followed by a relative decrease. Following the roentgenotherapy the values returned to high levels although the symptoms and signs of the disease had abated. (NSA)

1435

Decker, Arthur B. and James F. Mead. THE RELATIONSHIP BETWEEN ESSENTIAL FATTY ACID DEFICIENCY AND RADIATION DAMAGE IN THE MOUSE. *Univ. of Calif., Los Angeles. Dec. 1, 1949. 64p. (UCLA-52)*

The production of both acute and chronic essential fatty acid deficiency in mice is described, and the importance of the chronic deficiency is discussed. Both chronic and acute essential fatty acid deficiency markedly increase the mortality rate of mice exposed to x-rays. The symptoms of essential fatty acid deficiency and radiation damage are similar in many respects, and each condition apparently aggravates the other. 57 references. (NSA)

1436

Deho, G. G. CHANGES IN THE PROTEIN CONTENT OF BLOOD AS A RESULT OF IRRADIATION OF THE SKELETON WITH X-RAYS. *Rass. fisiopatol. clin. e terap. (Pisa)* **21**, 817-28(1949).

In 10 of 14 patients with dorsolumbar arthrosis irradiation with low doses of x-rays caused an increase of the total protein content of blood (mostly from 0.65 to 1.45 g%). Albumins and globulins, especially the latter, increased. Before irradiation, the total protein content was rather high (6.08-9.29 g%). (CA)

1437

Dietz, A. A. and B. Steinberg. CHEMICAL COMPOSITION OF IRRADIATED BONE MARROW. *Arch. Biochem.* **23**, 222-8(1949).

The right forelegs of rabbits older than 4 months were treated with 3,000 r unfiltered X rays delivered in a field of 380 sq cm at the rate of 160 r/min. The rest of the body was covered by 1.5 mm of lead. The animals were killed 1-32 days after irradiation. Samples of marrow from non-irradiated areas were used as controls. There was a decrease in water, residue, non-protein sulfur fractions and total lipid and NPN and an increase in lipid. The increased amt. of water in a unit weight of residue in irradiated marrow is consistent with oedema observed in irradiated tissues. The inorganic phosphate frequently showed a decline during the first 8 days and then an increase over the control marrow. (EM)

1438

DuBois, Kenneth P., Denneth W. Cochran, and John Doull. INHIBITION OF CITRIC ACID SYNTHESIS IN VIVO BY X-IRRADIATION. *Proc. Soc. Exptl. Biol. Med.* **76**, 422-7(1951).

The technic of Potter (*Proc. Soc. Exptl. Biol. Med.* **76**, 41(1951)) for measuring the effects of toxic agents on citrate accumulation vivo was applied to studies on x irradiation. Lethal doses of x ray (800 r) markedly inhibited citrate accumulation in spleen, thymus, ileum, pancreas, and testes of fluoroacetate-treated rats but exerted no significant effect on brain and heart. Sublethal doses of x ray markedly inhibited citrate accumulation in spleen and thymus. The extent of inhibition was dependent upon the dose of x ray and was reversible after sublethal doses and irreversible when lethal doses were given. Accumulation of citrate occurred in the livers of irradiated rats following fluoroacetate treatment in contrast to the inability of livers of normal male rats to accumulate citrate following fluoroacetate treatment. (NSA)

1439

Edelmann, A. EFFECTS OF X-RADIATION ON WATER AND ELECTROLYTE METABOLISM IN THE RAT. *Federation Proc.* **8**, 39(1949).

The intakes of distilled water, 1% NaCl solution, and food and the excretion of urinary Na, K, Cl and water by male albino rats were determined daily previous to and following exposures to 100, 250, 500, 800, and 1000 r of x-rays. Polydipsia and polyuria occurred during the first and fifth 24 hour period following radiation. The urinary excretions of Na, K, and Cl were increased at these times. Following doses of 500 r or more there is a relative and absolute decrease in intake of the salt solution. This is a monophasic response reaching its minimum at about 3 days. The salt solution intake returns to previous levels at 5 days. After doses of 100 or 250 r, the 1% NaCl solution intake follows the biphasic curve of water intake. Food intake decreased for 2 days following radiation and

then returned to normal in about 2 days. Body weight changes paralleled the food consumption.

1440

Ellinger, Friedrich. **THE HISTAMINE HYPOTHESIS OF THE BIOLOGICAL EFFECTS OF RADIATION.** *Schweiz. med. Wochschr.* **81**, (2) 55-67(1951).

Correlation of local and systemic (general) effects of radiant energy in the animal and human body is attempted. Experimental and clinical evidence is adduced (56 references) to demonstrate the distribution of pharmacologically active substances which are locally formed or released from cells disintegrating under the impact of irradiation in the exposed area. The importance of histamine, acetylcholine and adenosine compounds for the explanation of radiation effects is discussed in detail. On the base of the available exptl. evidence histamine appears most readily to account for the production of local as well as systemic radiation effects. (Author)

1441

Feinstein, Robert N. and Carrie L. Butler. **EFFECT OF WHOLE BODY X-RADIATION AND OF INTRAPERITONEAL HYDROGEN PEROXIDE ON A NUCLEOPROTEIN-CONTAINING FRACTION OF RAT INTESTINE AND ON WHOLE RAT INTESTINE.** *USAF School of Aviation Medicine*, Nov. 1951. 7p. (NP-3642; U21021)

Whole body x-radiation of rats decreases the relative viscosity of alkaline blends of the intestine and decreases the percentage of the whole blend which forms tactoid. X-radiation decreases the amount of dry matter, nitrogen, and phosphorus found in the tactoid. The loss in phosphorus is derived from the nucleic acid fraction. X-radiation decreases the tactoid ash and tactoid ash aluminum to an extent that is of dubious statistical significance because of wide variation in control values. The ash sodium does decrease significantly.

In one experiment, intraperitoneal H_2O_2 appeared significantly radiomimetic. In a second experiment this was not found true, despite the "statistical significance" of the first findings. Such erratic results of H_2O_2 have been noted before on different lots of laboratory animals.

1442

Fink, K. **BLOOD CHEMISTRY STUDY IN DOGS EXPOSED TO CHRONIC X-RADIATION.** [University of Rochester] [nd] 16p. (MDDC-211)

The purpose of this study was to determine whether some of the biochemical components of the blood were affected in dogs by chronic x-radiation at 0.1, 0.5, 1.0, and 10 r per day over a long period of time. The concentrations of serum protein, plasma fibrinogen, whole blood NPN, serum cholesterol, serum chloride, and serum acid and alkaline phosphatases were not significantly altered in dogs subjected to chronic x-radiation at 0.1, 0.5, 1.0, and 10 r per day, six days a week. All the dogs in the 10 r groups and four dogs in the remaining groups succumbed before the experiment was terminated at the time of 622 exposures. There were no consistent changes even in the dogs which died as a result of the radiation. The only obvious changes observed in the dogs given 10 r per day which died were high fibrinogen concentrations in three of the dogs, two of which had high alkaline phosphatase levels. These changes did not develop until about a week before the animals died, so even had they occurred in all the dogs which died, they would have been of little practical value as an index to radiation damage. (ADD)

1443

Frankenthal, L. and A. Back. **THE EFFECT OF X-RAYS ON THE RESPIRATION OF FOWL ERYTHROCYTES.** *Biochem. J.* **38**, 351-4(1944).

The respiration of fowl erythrocytes is markedly and increasingly stimulated by x-ray doses from 500,000 to 2,000,000 r. When optimum doses of radiation are used the stimulation may last for several hours (as long as there is no hemolysis). But whereas non-irradiated erythrocytes, incubated at 39-40° and shaken, hardly undergo hemolysis, the hemolysis is progressive and proportional to the previous x-ray dose in irradiated erythrocytes. (CA)

1444

Goldfeder, A. and J. L. Fershing. **THE EFFECT OF RADIATION ON CELL RESPIRATION. I. RESPIRATION AND ANAEROBIC GLYCOLYSIS OF MOUSE KIDNEY IN VITRO FOLLOWING RADIATION.** *Radiology* **31**, 81-8 (1938).

Excised mouse kidney was irradiated in vitro at 4°C. with 200 KV x-rays. There was no change in O_2 consumption and R.Q. measured immediately after treatment with 1,800 to 30,000 r; no change in O_2 consumption or R. Q. after treatment with 375 mg-hrs. of radium at 37.5°C or at 4° with doses up to 4,164 mg. hrs. After treatment with radon (B plus γ rays), overnight doses totalling 1,180 to 6,170 mg-hrs, there is a drop in O_2 consumption but not in R. Q. Anaerobic glycolysis is decreased to a greater extent than respiration with equivalent doses. The results contradict the hypothesis that irradiation affects cell catalysts. B-rays are more effective than γ rays and have a direct effect on respiration and anaerobic glycolysis. (BA)

1445

Goldman, Douglas. **METABOLIC CHANGES OCCURRING AS THE RESULT OF DEEP ROENTGEN THERAPY. I. EFFECT OF 200 KILOVOLT ROENTGEN THERAPY.** *Am. J. Roentgenol. Radium Therapy* **50**, 381-91(1943).

The patients observed were on constant, accurately weighed diets, potentially neutral, low in purines and Ca, and in most instances minimal in chloride. Changes in the excretion of total nitrogen and its components are the most definite deviations from the control values presented by the investigations. There was, in general, an increase in the urinary output of total nitrogen either during the periods when radiation was being given or immediately following cessation of the treatment. Nitrogen loss was greater in patients with radiosensitive tumors. Both uric acid, and to a lesser degree, ammonia were found to be involved in this nitrogen increase. The total acid of the urine was definitely higher in most cases during or after roentgen therapy, probably the result of greater destruction of body protein. A slight diminution in amino-acid nitrogen excretion took place two to six days after irradiation and continued to the end of the observations. This seems to indicate a storage of nitrogen after the primary destructive effects of irradiation had worn off. No significant deviation of the Ca balance from control values was observed. Increase in the urinary output was found during or following roentgen therapy with deviation of the balance to the negative side. A small but definite increase in the urinary S and sulfate occurred following irradiation. All of the patients who became severely ill showed a definite chloride loss during the irradiation period. The chloride balance became positive shortly before or simultaneously with improvement in symptoms. NaCl by mouth is very frequently an effective therapeutic agent in irradiation sickness. In some cases its action was dramatic. There is a definite susceptibility to roentgen sickness of patients with protracted NaCl starvation. (R)

1446

Goldscheider, G. **EFFECT OF INTRA-UTERINE RADIUM THERAPY ON OVARIAN FUNCTION.** *Lancet* **1**, 521-3 (1949).

In an attempt to determine whether the amenorrhea produced by radiation is of ovarian or non-ovarian origin, the urinary excretion of follicle-stimulation hormones has been determined in 28 women before and after intra-uterine treatment with radium for menorrhagia. The results obtained were compared with those obtained for a few patients who had been castrated with X-rays or had received a combined treatment of X-rays and radium. The absence of an increase in follicle-stimulating hormone suggests that an artificial menopause had not been established and that the amenorrhea observed following radiation treatment was of non-ovarian origin. It is suggested that the destruction of the uterine glands could be the cause of the observed amenorrhea. Artificial menopause occurred only in women of menopausal age in whom small doses may influence ovarian function. (NSA)

1447

Gounaris, I. EXPERIMENTS ON THE ACTION OF X-RAYS ON THE RETICULO-ENDOTHELIAL SYSTEM. p.173 of INTERNATIONAL CONGRESS OF RADIOLOGY, 6th Congress, London. 1950.

The fact that alcohol is metabolised by reticulo-endothelial cells led us to study the action of X-rays on this interesting cellular system in respect of alcohol metabolism in dogs and sheep before and after a given dose of radiation. The following are some of the advantages of this method:

(1) Observations are made on the same animal so that a separate control, which might show a different biological action, is not needed.

(2) The technique can be applied to human beings, and

(3) It is possible to follow the cellular reaction during the administration of the radiation.

We have reached the following conclusions:—

(1) Small doses have an inhibiting action during the first 24 hours following irradiation, and a stimulating action about 24 hours and 48 hours after irradiation.

(2) Larger doses have an inhibiting action even 48 hours after irradiation. The stimulating action under these conditions appears 4 days after irradiation.

(3) Alcohol metabolism returns almost to normal one month after irradiation.

(4) If it is desired to "reactivate" the reticuloendothelial system further irradiation must not be given until at least 48 hours have elapsed.

(5) The radiation effect is not a result of increased resistance or of oxidation due to enzymes liberated by cellular autolysis.

1448

Gros, Charles and Paul Mandel. VARIATIONS IN THE MINIMUM ENDOGENEOUS NITROGEN EXCRETION AS AN EFFECT OF TOTAL-BODY X-IRRADIATION. *Compt. rend.* 231, 631-3(1950).

After rats on a protein-free diet had reached the minimum of their endogenous nitrogen excretion, they were irradiated with 400 r of 190-kv x rays. Determinations of the total-nitrogen, allantoin, and creatinine excretions before and 6 or more days after irradiation showed an average increase in the total endogenous excretion of 36% with a maximum of 56%. The excretion of allantoin, which is remarkably constant normally, increased by 44% on the average and 62% in the limiting case. In contrast, no variation was found in creatinine elimination. Several possible interpretations of these results are discussed briefly. (NSA)

1449

Hauschildt, James D. and Helen Supplee. THE EFFECT OF WHOLE BODY X-IRRADIATION UPON THE TOTAL NITROGEN, TOTAL PROTEIN AND REFRACTIVE INDEX

OF RAT PLASMA; INTERIM REPORT. Naval Radiological Defense Lab. June 13, 1949. 11p. (AD-131(B))

A preliminary investigation has been made upon the changes of plasma refractive index, plasma protein, and plasma nitrogen of rats which had received 650 r total body x-irradiation. A marked decrease was found to occur in all cases in the 2 to 4-day post-irradiation period. Refractive index changes paralleled those of protein and total nitrogen in plasma. (NSA)

1450

Hevesy, Georg von. EFFECT OF X-RAYS ON THE RATE OF TURNOVER OF PHOSPHATIDES. *Nature* 158, 268 (1946).

The effect of x-rays on the turnover of phosphatides of the cell nuclei and on the total tissue of the Jensen sarcoma and the liver of the rat is tabulated. The rate of turnover of the phosphatides in the nuclei is markedly diminished under the effect of x-rays and that in the cytoplasm is also diminished. In the nuclei of the liver the rate of renewal of phosphatides lags behind the rapid turnover in the cytoplasm. (CA)

1451

Hevesy, Georg von. EFFECT OF X-RAYS ON THE INCORPORATION OF C^{14} INTO ANIMAL TISSUE. *Nature* 164, 269(1949).

Rapidly growing rats irradiated with x-rays showed a significant increase in the incorporation of C^{14} in the body tissues. Since the basal metabolism of irradiated rats is decreased, it is suggested that the resulting higher activity level in the organism causes an increased incorporation of C^{14} into organic processes. (CA)

1452

Hevesy, Georg von and K. Zerahn. THE EFFECT OF ROENTGEN RAYS AND U. V. RADIATION ON THE PERMEABILITY OF YEAST. *Acta Radiol.* 27, 316-27(1946).

Irradiation with a dose of 30,000 r, sufficient to kill about 10% of the yeast cells, influenced the amount of free radio-phosphorus and radio-potassium (P^{32} and K^{42} , respectively) migrating daily from the yeast cells into the nutrient solution, and thus the cell permeability, but only to a very slight extent. The amount of migrating P^{32} , but not however of K^{42} , was greatly increased after irradiation with a sublethal dose of u.v. radiation. Irradiation does not increase the free phosphate content of yeast cells. The phase boundary is thus influenced by the effect of the radiation. The migration of intracellular P^{32} into the nutrient solution is not an interchange process, as the same percentage of P^{32} migrates into a phosphate-containing as into a phosphate-free solution. When the yeast cells were shaken with a nutrient solution containing arsenate, the amount of immigrating free P^{32} and K^{42} was found to be reduced to about half their normal values. (BA)

1453

Hewitt, John E., Thomas L. Hayes, John W. Gofman, Hardin B. Jones, and Frank T. Pierce. EFFECTS OF TOTAL BODY IRRADIATION UPON LIPOPROTEIN METABOLISM. Radiation Lab., Univ. of Calif. [nd] 27p. (UCRL-1549)

An investigation was made of the lipid metabolic derangement produced in rabbits as a result of irradiation. A correlation was found to exist between the high level of total lipoprotein 30 hr after irradiation and subsequent death of the animal. Serum opalescence was associated with low-density lipoprotein only and not with total lipoprotein level. Changes observed in the lipoprotein levels after irradiation were found to be consistent with the theory of conversion of low-density lipoprotein to higher density components. The injection of heparin after irradiation

hastened the return of lipoprotein levels to normal values. Injection of toluidine blue, protamine sulfate, or quinine produced changes in the lipoprotein pattern similar to those shown after irradiation. (NSA)

1454

Higinbotham, Noe, Edward S. Mika, and Robert B. Withrew. **THE EFFECT OF X-RAYS ON UPTAKE AND LOSS OF IONS BY DISCS OF POTATO TUBER TISSUE**, p.111-14 of **BIOLOGICAL AND MEDICAL DIVISIONS; QUARTERLY REPORT, FEBRUARY, MARCH, APRIL, 1948**, Austin M. Brues and Hermann Lisco, eds. Argonne National Lab. May 1, 1948. 4p. (ANL-4163(p.111-14))

This report concerns the preliminary results of a study on the effect of ionizing radiations on the capacity of various types of plant tissues to exchange ions with the environment. The present data show the effects of x-rays on uptake of radioactive rubidium ions from an external solution by discs of potato tuber tissue. Effect of x-rays on the outward diffusion of ions into distilled water was studied by means of the electrical conductance method. Data are presented in Table 10. Results show that higher doses of x-rays appreciably increase tissue permeability. (S.V.S.)

1455

Holmes, B. E. **PHYSICAL, BIOCHEMICAL, AND THERAPEUTIC ASPECTS OF VOLUME DOSE. III. BIOCHEMICAL ASPECTS OF VOLUME DOSE**. *Brit. J. Radiol.* **18**, 238-40 (1945).

General discussion by the author on biochemical aspects of volume dose: includes discussion of cholesterol in the blood, liberation of histamine after x-radiation, etc. Read before General Meeting of the British Institute of Radiology, November 16, 1944. (S.V.S.)

1456

Hornykiewytch, Th. **THE INFLUENCE OF X-RAYS ON HYDROGEN ION CONCENTRATION IN TISSUES UNDER VARIOUS EXPERIMENTAL CONDITIONS**, p.166-7 of **INTERNATIONAL CONGRESS OF RADIOLOGY**, 6th Congress, London. 1950.

A short review of methods of pH measurement with a glass-needle electrode is given. The following experimental results are reported: -The measurement of pH in the subcutaneous tissues of the thigh of the rat after a single irradiation with 4,000 r. After an initial acidity, there follows an alkalinity, 24 hours after irradiation, which lasts approximately 3 days and then falls in value. This is followed by four further alkaline "waves" at intervals of 5-6 days which, however, have no connection with erythema. Fluctuations in pH of a similarly periodic character occur throughout the body after irradiation of the thigh. Irradiation of inflamed tissue with 500-1,000 r causes a slight "relative alkalinity" in the tissue, which lasts 2 days. This is preceded by small acid waves which are not periodic but depend on the number and the time of the irradiations. The pH measurements of X-ray ulcers at varying periods of development show a distinct alkaline reaction in the ulcerated area. Changes in pH also occur after irradiation (200 r) of the whole body of mice. An initial acid phase is followed by an alkaline phase lasting 3-4 days. The initial (normal) values are reached again 7-8 days after irradiation. The physico-chemical changes which may produce pH fluctuations are discussed, and a comparison is made between the influence of X-rays and ultrasonic treatment on tissue reactions.

1457

Jarvis, J. L. and D. Cayer. **EFFECTS OF RADIATION THERAPY ON THE URINARY EXCRETION OF NIACIN AND RIBOFLAVIN IN PATIENTS WITH MALIGNANT**

DISEASES. RELATIONSHIP TO RADIATION SICKNESS. *Radiology* **52**, 574-8(1949).

Experiments to determine whether malnutrition predisposes radiation sickness are presented in which the urinary excretion of niacin and riboflavin in a group of patients with malignant disease was measured before and after x-ray therapy. Of the 30 patients studied, 21 received total radiation doses of 1,800-8,120 r. Four patients received radium doses of 3,600-4,800 mg-hr and five patients received a combination of the two types of therapy. The excretion levels of niacin and riboflavin are given in a table included in this paper. Seven patients who had nausea and vomiting show significantly lower vitamin excretion levels than those without these symptoms. Good results have been obtained by the use of vitamins of the B complex for radiation disease therapy. (NSA)

1458

Kirschner, Leonard B., C. Ladd Prosser, and Henry Quastler. **INCREASED METABOLIC RATE IN RATS AFTER X-IRRADIATION**. *Proc. Soc. Exptl. Biol. Med.* **71**, 463-7(1949).

In order to verify the hypothesis that catabolism is increased by irradiation, the basal metabolism of albino rats was measured after total body exposure to x-rays. The rats were irradiated, two or three at a time, from a 200-kv source with no filter and at a target distance of 55.5 cm, one-half of the dose being delivered from above, and one-half from below the animals; the average tissue dose rate was 40.5 r/min. Twelve rats received 800-972 r, six of which developed severe diarrhea, showed an oxygen consumption elevation of 35% in 24 hours, lost weight rapidly, and died in 3-5 days. The remaining six rats died 9-10 days after irradiation, and two out of eight irradiated with 648 r also died at this time; all showed an oxygen elevation of about 58%. The six rats which survived the 648 r irradiation, showed an average increase in oxygen consumption of 32% during the first seven days, and a less pronounced increase over a period of 16 days after the irradiation. Doses of 54-432 r were given to other groups of rats and caused an average increase of about 8.5%. In all of the experiments, the increased metabolism did not coincide with weight loss either in time course or in dose dependence. (NSA)

1459

Koch, R. and A. Bohländer. **EXPERIMENTAL INVESTIGATION ON EFFECTS OF VITAMINS ON LIVER METABOLISM IN ANIMALS SUFFERING FROM RADIATION INJURIES**. *Strahlentherapie* **85**, 331-41(1951).

Total-body x radiation in white mice resulted in a reduction of the liver glycogen to 27% of its original value. In homogeneous and heterogeneous animal material, the distribution of the liver glycogen corresponds to that of the normal Gaussian distribution. No quantitative changes of the total N content of the liver were found. (NSA)

1460

Koch, Ruprecht, and Adam Bohlander. **EXPERIMENTAL INVESTIGATIONS OF VITAMIN EFFECTS ON LIVER METABOLISM AFTER RADIATION INJURY. II. EFFECT OF LACTOFLAVIN AND PYRIDOXIN ON GLYCOGEN AND TOTAL NITROGEN OF THE LIVER IN TOTAL BODY IRRADIATED ANIMALS**. *Strahlentherapie* **85**, 599-605(1951).

Mice were subjected to total-body x irradiations of 350 to 400 r each on 5 consecutive days, while 0.5 mg lactoflavin or 2.5 mg pyridoxin were given by subcutaneous injection 6 days before the first irradiation and after each irradiation except the last one. The animals were killed and investigated chemically several hours after the last

irradiation. Irradiation did not change the N content of the liver, and vitamin treatment had no effect. The glycogen content of the liver dropped to 27% normal after irradiation; lactoflavin treatment decreased the loss of glycogen to 55% normal, and pyridoxin treatment decreased it to 51% normal. (NSA)

1461

Kretzschmar, C. H. and F. Ellis. THE EFFECT OF X-RAYS ON ASCORBIC ACID CONCENTRATION IN PLASMA AND IN TISSUES. *Brit. J. Radiol.* **20**, 94-9(1947).

"An adequate daily dose of ascorbic acid can prevent or minimize the fall of white blood cells which follows x-ray exposure. It diminishes the risk of x-ray sickness. There is however no uniformity in the result." Vogt, quoted by the authors, does not believe that exposure to x-rays has any relation to the excretion of ascorbic acid in the urine, but he considers that the marked deficiency of ascorbic acid in malignant patients is purely due to the disease, whether cancer or lymphadenoma. The authors estimated the ascorbic acid in plasma of patients under x-ray treatment, and in most cases it was found to be below the initial level before exposure. After x-ray exposure of normal rabbits estimation of ascorbic acid was made and a fall in the level was found for some time after exposure. The ascorbic acid content of muscle and kidney tissue from rats exposed in vivo to x-rays was also found to be lower than normal. (AWM)

1462

Krizek, H., I. Silverbach, and S. Schwartz. THE EFFECT OF LETHAL DOSE OF TOTAL BODY X-RAY ON URIC ACID AND ALLANTOIN EXCRETION IN DOGS. *Univ. of Chicago*. June 15, 1946. Decl. Jan. 15, 1948. 28p. (MDDC-1647; CH-3851)

In five dogs given single lethal doses of total body x-ray, urinary excretion of uric acid increased 3 to 6-1/2 days before death; allantoin excretion showed no significant change. Uricolytic indices, therefore, dropped during the terminal period. Uric acid excretion was determined in one dog given 12.5 r daily total body x-ray, and in one given a slowly lethal dose of plutonium, and showed a similar terminal increase. These changes are probably due to liver dysfunction. In all dogs studied excretion of substances giving a color with the uric acid reagent but not destroyed by incubation with uricase showed no consistent change after irradiation. Rabbits appeared to be poorly suited for study of purine metabolism. (ADD)

1463

Latarjet, R. and J. Loiseleur. FIXATION OF OXYGEN IN RADIOBIOLOGY. *Compt. rend. soc. phys. hist. nat. Genève* **57**, 234-5(1942); *Compt. rend. soc. biol.* **136**, 60-3(1942).

X-rays ionize the dissolved O and numerous organic compounds present in the tissues then act as acceptors. (CA)

1464

Lavik, Paul S. and Helen Harrington. SOME BIOCHEMICAL EFFECTS OF RADIATION ON LYMPHATIC TISSUE. *Western Reserve Univ. School of Medicine*. July 15, 1951. 30p. (NYO-1626)

The effect of a toxic dose of P³² or whole-body x irradiation on the P composition and P³² incorporation of thymus, spleen, and normal and regenerating liver has been studied in adult rats. The changes observed in chemical composition have been related to the histological irradiation damage. The radiosensitive lymphatic tissues, thymus and spleen, showed a marked decrease in desoxyribonucleic acid P as a result of irradiation, whereas the P composition of normal and regenerating liver, nonlym-

phatic tissues, did not change significantly. Radiation caused an inhibition of the P³² incorporation of into the desoxyribonucleic acid fraction of all tissues but normal liver, which had a very low P³² uptake into this fraction in both normal and irradiated rats. Adrenalectomy did not prevent the changes occurring in thymus after irradiation. The relation of inhibition of desoxyribonucleic acid synthesis to the chemical and histopathological changes which occur is discussed. (NSA)

1465

Lawrence, Geo. H. THE EFFECT OF TOTAL-BODY X-RADIATION ON 17 KETOSTEROID EXCRETION IN DOGS. *Endocrinology* **45**, 383-8(1949).

The urinary excretion of 17-Ketosteroids was followed in 11 dogs after exposure to a minimum lethal dose of total-body x-radiation. Significant increases in steroid excretion occurred in all animals between the 5th and 12th day after treatment. The excretion then fell to normal or subnormal levels, then showed a trend toward normal levels by the 30th to 40th day. The changes in excretion are interpreted as alteration of adrenal cortical and/or testicular activity in these animals, and are similar to those reported in adaptation to other stimuli. (CA)

1466

Loofbouroow, John R., Mary Elizabeth Englert, and Cecelia Marie Dwyer. INCREASED YIELD OF NUCLEIC ACID-LIKE SUBSTANCES FROM IRRADIATED YEAST. *Nature* **148**, 113-14(1941).

A comparison of nucleic acid present in irradiated and non-irradiated yeast (*Saccharomyces cerevisiae*) showed a higher per cent in the former as well as greater proliferation-promoting activity. (BA)

1467

Lourau, Marguerite and Odette Lartigue. MODIFICATIONS OF GLYCEMIA UNDER THE INFLUENCE OF TOTAL X-RAY RADIATION. *Compt. rend.* **230**, 1426-8(1950).

In previous work (*Experientia* **6**, 25, 1950) it was shown that total body x-irradiation causes modifications of glucose metabolism; this paper is a presentation of the results of experiments to determine the extent of the modifications with fasting and with high saccharose intake. Two groups composed of 13 guinea pigs each, were irradiated in one dose calculated to deliver 500 r/animal; the blood glucose levels were determined at varying intervals for periods up to 35 days. It was shown that the hyperglycemia occurring after the ingestion of saccharose by animals, after 14 and 48 hours fasts, is significantly increased by the radiation dose given, and that there is a large decrease in glucose tolerance due to the irradiation, since it was found that the hyperglycemia was much more extreme in the animals irradiated 12 and 14 days before a dose of 1 g of saccharose than in nonirradiated animals. The authors conclude that the importance of the two effects is not equal although they apparently arise from the same phenomena. (NSA)

1468

Lourau, Marguerite and Odette Lartigue. HEPATIC GLYCOGENESIS IN WHOLE-BODY X-IRRADIATED ANIMALS. *Compt. rend.* **232**, 1144-6(1950).

Glycogenesis in the guinea pig is diminished following sublethal x irradiation. This is not due to the inability of the hepatic cell to synthesize glycogen but to the absence of substrate, the glucose in the circulation probably having been abnormally metabolized to a substance incapable of entering into glycogen synthesis. (NSA)

1469

Lourau, M. and O. Lartigue. EFFECT OF WHOLE-BODY X-IRRADIATION OF THE GUINEA PIG ON UTILIZATION

OF GLUCOSE BY THE LIVER. *J. physiol. (Paris)* **43**, 593-603(1951).

Male guinea pigs weighing 400 to 500 g were irradiated sublethally with 500 r of 180-kv x radiation. Hepatic glycogenesis was observed to be deficient. This deficiency was manifested less by a diminution in the quantity of glycogen formed in the course of glucose absorption than by the impossibility of preserving the stocks of glycogen during the period following absorption. The authors hypothesize that irradiation does not affect the direct synthesis of glycogen from alimentary glucides, but impedes synthesis from small molecules. (NSA)

1470

Ludewig, Stephan and Alfred Chanutin. EFFECT OF WHOLE BODY X-IRRADIATION ON THE STORAGE OF IRON IN LIVER, SPLEEN, AND KIDNEY OF RATS. *Am. J. Physiol.* **166**, 384-6(1951).

The iron contents of the liver, spleen, and kidneys of rats were determined at varying intervals after whole body exposure to x-ray doses of 500 r. The values for the liver and spleen increased steadily during the first two weeks and decreased during the third week following irradiation. Small increases were noted in the kidneys during the second post-radiation week. Unusually high iron values were observed in the liver and spleen of anemic irradiated rats. A derangement in iron metabolism follows x-irradiation and is manifested by the storage of excess iron in tissues. (NSA)

1471

Marinelli, L. D. and J. M. Kenney. THE ABSORPTION OF RADIOPHOSPHORUS IN IRRADIATED AND NON-IRRADIATED MICE. *Radiology* **37**, 691-7(1941).

Experiments were undertaken to investigate the effect of roentgen irradiation on gross phosphorus metabolism in some animal tissues. Albino mice more than 12 months of age were used. All animals were given tracer doses of P^{32} intraperitoneally as Na_2HPO_4 immediately after irradiation and sacrificed at different intervals. Comparative quantitative studies were made of skin, muscle, and bone removed from both the treated and untreated extremity of the same animal. There was no difference in the P^{32} content per g of tissue in either the muscle or skin of the 2 legs. In the bone, however, the P^{32} content of the irradiated bone was higher than in the untreated extremity. (BA)

1472

Markees, S., O. Käser, and R. Lanz. PYRUVATE METABOLISM IN NORMAL AND PATHOLOGICAL PREGNANCY IN NARCOSIS, AND X-RAY IRRADIATION. *Schweiz. med. Wochschr.* **80**, 1079-81(1950).

The following average values in $mg\%$ were obtained for blood pyruvate levels: normal 0.8; after the 20th week of pregnancy 1.3; nephropathy and preeclampsia; 1.5; eclampsia 3.7; 6-8 hours after narcosis, 2.1. The increase in blood pyruvate concentration after x-ray treatments paralleled the symptoms of radiation sickness. (CA)

1473

Mead, James F., Arthur B. Decker, and Leslie R. Bennett. THE EFFECT OF X-IRRADIATION UPON FAT ABSORPTION IN THE MOUSE. *J. Nutrition* **43**, 485-500(1951). (UCLA-90)

Fat absorption in mice was followed using methyl oleate containing 10% of the spectrophotometrically active methyl octadecadienoate as a tracer. The rate of absorption of this mixture was shown to be nearly constant. Mice which had received 600 to 700 r whole-body x-irradiation showed a tendency toward increased tone and motility of the gastro-intestinal tract, resulting in retention of oil in the stomach or rapid passage past the absorbing surface. De-

spite these changes, fat absorption per se appeared to be about normal. A post-irradiation increase in fecal fat was shown not to be due to lowered absorption since it occurred in animals on a fat-free diet. It is concluded that there is no evidence for post-irradiation impairment of fat absorption. (NSA)

1474

Milne, John and Abraham White. EFFECT OF ADRENAL CORTICAL EXTRACT AND OF X-RAY IRRADIATION ON SERUM PROTEINS OF MICE. *Proc. Soc. Exptl. Biol. Med.* **72**, 424-8(1949).

Normal mice and mice bearing a transplantable lymphosarcoma were given single injections of adrenocortical extract or exposed to a single total body x-ray dose of 200 r. Examination 3 - 6 hr after the x-ray treatment revealed a marked increase in total serum proteins, but electrophoretic tests showed no significant alteration in the relative distribution of the serum proteins. (CA)

1475

Muntz, A. A., E. S. Guzman Barron, and C. L. Prosser. MECHANISM OF ACTION OF IONIZING RADIATIONS. III. PLASMA PROTEIN OF DOGS AFTER X-RAY IRRADIATION. *Arch. Biochem.* **23**, 434-45(1949).

Lethal doses of x-rays were given to mongrel dogs as a total body dose. For one week following, the electrophoretic patterns of their plasma proteins showed no change, but from the seventh day until death, albumin decreased steadily. Three to 5 days before death, fever ensued, and this was accompanied by a striking increase in $\alpha_3 + \alpha_4$ -globulins, with some increase in β -globulin fibrogen. Extraction of lipids did not decrease the amounts of $\alpha_3 + \alpha_4$ -globulins as determined electrophoretically. A single injection of bovine albumin equal to one half the total normal plasma albumin caused no effect other than a temporary rise in plasma albumin. In the terminal period, blood volume and total protein increased. Death occurred 12 to 18 days after exposure. (CA)

1476

Nizet, R. E., C. Heusghem, and A. Herve. CHANGES IN THE ADRENAL CORTEX AFTER X-RAY IRRADIATION OF A DISTANT PART OF THE BODY OF THE RABBIT. *Compt. rend. soc. biol.* **143**, 876-7(1949).

With the abdominal region shielded, the hind legs were subjected to a single dose of 2000 r. The adrenal cortex showed large decreases in total lipides and cholesterol within 3 hr. Recovery occurred within 48 hr. Urinary excretion of 17-ketosteroids remained within the normal range (125-300 γ /24 hr). (CA)

1477

North, N. and L. F. Nims. TIME-DOSE STUDY OF BIOCHEMICAL RESPONSES OF RATS TO X-RADIATION. *Federation Proc.* **8**, 119-20(1949).

A time-dose study of biochemical responses of the adrenal-pituitary system in fasted rats following whole-body x-radiation indicate a pattern of changes comparable to that following other stresses. Male albino rats were subjected to radiation doses of 500 to 2000 r at a rate of 50 r per minute and sacrificed at periods of time ranging from 3 to 48 hours following exposure. Analyses of tissue constituents show an immediate and progressive increase in liver glycogen and no change in testis glycogen. There is a simultaneous decrease in the adrenal and liver cholesterol but little change in the testis cholesterol and a late increase in the plasma cholesterol. The adrenals also show an initial decrease in ascorbic acid content with a subsequent return to normal, while little variation from the unirradiated controls is seen in pituitary, liver or testis ascorbic acid. There are no evident effects of radiation on

total body, adrenal, or pituitary weights in fasted animals. (NSA)

1478

Orlov, S. M. PHOSPHORUS-CALCIUM METABOLISM IN EXPERIMENTAL RICKETS AND THE EFFECT OF IRRADIATION BY X-RAYS. *Voprosy Pediat. i Okhrany Materinstva i Detsva* 18, No. 5, 10-14(1950).

Initiation of rickets in young dogs depends not only on deficiency of Vitamin D, but also on severe disproportionate Ca and P content in food (such as Ca/P of $\frac{1}{4}$). Reestablishment of nearly normal Ca/P ratio in the diet rapidly normalizes the assimilation of these elements, while mere addition of vitamin D (125,000 units in 3 days) is insufficient. Irradiation of vegetative nervous centers (360-725 r) of the medulla leads to a sharp temporary improvement of assimilation of Ca from the intestinal tract, as well as a significant improvement of P assimilation. (CA)

1479

Painter, Elizabeth E. and E. W. Pullman. WATER AND ELECTROLYTE CHANGES IN RAT INTESTINE AFTER TOTAL BODY X-RADIATION. *Federation Proc.* 9, 97 (1950).

Preliminary experiments carried out on the small intestine of 220 gm male rats before and after a single dose of total body x-radiation (LD 70) indicate that increases in sodium content can be correlated with decreases in potassium and with increases in chloride and water content in the first few days after radiation. These increases in sodium content of the intestine have been confirmed by radioactive sodium studies reported earlier by us. That increase in sodium is in part related to the exchange of sodium for potassium in gut cells appears to be a valid conclusion from our results. (Authors)

1480

Peterson, Ruth D., Clarissa H. Beatty, and Edward S. West. EFFECT OF TOTAL BODY X-IRRADIATION ON GLUTATHIONE LEVELS IN RATS. *Proc. Soc. Exptl. Biol. Med.* 77, 747-9(1951).

A study has been made of blood and liver glutathione in rats after 500 r total body x irradiation. The data show, first, that irradiation generally causes a decrease in blood glutathione; and second, in some cases, a decrease in liver glutathione. (NSA)

1481

Pietra, R. URINARY ELIMINATION OF 17-KETO STEROIDS AFTER IRRADIATION OF THE HYPOPHYSIS. *Folia Endocrinol. (Pisa)* 3, 209-23(1950).

Human beings showed no substantial changes from normal elimination. (CA)

1482

Plasencia, H. T. ACTION OF SPREAD OUT AND FRACTIONATED RADIATIONS ON SOME CHEMICAL EQUILIBRIA OF THE BLOOD. CONTRIBUTION TO THE STUDY OF THE GENERAL BIOLOGICAL ACTION OF RADIATION. *Acta Unio. Intern. contra. Cancerum* 4, 333-58(1939).

Due to the destruction of cells there is a hydremia, a decline in the albumin:globulin ratio and a decrease in the amount of chloride in the red cells and in the plasma. The disturbances in the interrelations between the endocrine organs and in the nervous regulations are followed by a diminished alkali reserve, by diverse changes in the proportion of anions to cations, by an increase in the amount of acetone bodies and in the circulating glutathione, by a fall in blood sugar, and by hypocholesterinamia. These as well as the clinical symptoms depend upon the intensity of the daily irradiations. (BA)

1483

Ragan, C., C. P. Donlan, J. A. Coss, Jr., and A. F. Grubin. EFFECTS OF X-RAY IRRADIATION ON VISCOSITY OF SYNOVIAL FLUID. *Proc. Soc. Exptl. Biol. Med.* 66, 170-2(1947).

In vitro reduction in viscosity of synovial fluid when exposed to X-ray irradiation was noted. Reduction in viscosity varied directly with the amount of irradiation. The hyaluronic acid content did not change and the hyaluronic acid was still susceptible to enzymatic hydrolysis after exposure to X-rays. Reduction in viscosity of pure Na hyaluronate solutions was noted as well but to a lesser degree. It is suggested that the effect of X-rays may be a breaking of secondary valences present in synovial fluid hyaluronic acid without a profound change in the hyaluronic acid molecule. The physiologic implications are discussed in light of the widespread presence of this and similar acid mucopolysaccharides throughout the connective tissue of the organism. (BA)

1484

Richmond, Jonas E., Kurt I. Altman, and Kurt Salomon. THE RELATION OF OXYGEN UPTAKE TO HEMOGLOBIN SYNTHESIS. *Science* 113, 404-5(1951).

Bone marrows of normal rabbits and of rabbits exposed to 800 r of x rays were removed at varying time periods after exposure to radiation. Homogenates were prepared from these marrows and incubated at 38°C in the presence of α -C¹⁴-glycine as a hemoglobin precursor. O₂ consumption of the homogenates and the amount of hemin and globin synthesized was determined. The results a difference in the time relation between O₂ consumption and the synthesis of hemin and globin, respectively. Hemin synthesis as well as O₂ consumption increases considerably in homogenates from bone marrows removed immediately after irradiation. Furthermore, O₂ consumption and hemin synthesis appear to reach a minimum about 1 week after exposure to radiation at a time when marked degenerative changes prevail in the marrow. Globin synthesis also increases after radiation, but, in contrast to hemin synthesis, it reaches a maximum 48 hr after radiation at a time when O₂ consumption already approaches a minimum value. However, the decay curve of globin resembles in its shape that of O₂ consumption and hemin synthesis. Recovery of all three functions begins 2 to 3 weeks after radiation, which agrees well with histological findings. (NSA)

1485

Richmond, Jonas E., Kurt I. Altman, and Kurt Salomon. THE EFFECT OF X-RADIATION ON THE BIOSYNTHESIS OF HEMOGLOBIN. *J. Biol. Chem.* 190, 817-25(1951).

Hemoglobin synthesis was studied in bone marrow and spleen homogenates of rabbits exposed to 800 r of x radiation at a rate of 26 to 27 r/min with C¹⁴ labeling of specific precursors for hemin and globin. Hemin and globin synthesis are differently affected by radiation, both evidently going on at different rates. A new term, W, as an expression of the hemin- and globin-forming capacity of the organ systems is introduced and its value calculated for bone marrow and spleen homogenates. (NSA)

1486

Riley, Richard F. and Esther Richter. PAPER CHROMATOGRAPHIC STUDY OF FREE AMINO ACIDS OF YOLK OF DEVELOPING NORMAL AND X-IRRADIATED CHICK EMBRYOS. *Univ. of Calif., Los Angeles.* Nov. 26, 1951. 8p. (UCLA-171)

The free amino acids of yolk of fertile chick embryos between the 5th and 20th day were examined by paper chro-

matography after removal of proteins by alcohol precipitation and lipids by petroleum ether and ethyl ether extraction. α -Alanine, arginine, glutamic acid, glutamine, leucine(s), lysine, and tyrosine were found consistently, and cysteine acid, glycine, methionine, proline, and serine, threonine, and valine were also found in most extracts. Appreciable amounts of peptides were absent. 500 r of x irradiation ($\sim$ LD₅₀) administered on the 10th day did not alter this picture appreciably. (NSA)

1487

Robertson, James E. METABOLIC CHANGES OCCURRING AS THE RESULT OF DEEP ROENTGEN THERAPY: II. EFFECT OF 1000 KILOVOLT ROENTGEN THERAPY. *Am. J. Roentgenol. Radium Therapy* **50**, 392-9(1943).

Seven patients were subjected to a careful study of nitrogen and chloride metabolism before, during and after 1,000-kv roentgen therapy. The results proved to be similar to the results of the study conducted in the same laboratories on the effect of 200-kv roentgen therapy. Supervoltage roentgen radiation was shown to produce an increased excretion of nitrogen, uric acid, and chloride in some of the patients, just as does radiation of lower voltage. That the negative N balance results entirely from tissue destruction is strongly indicated by its restriction to cases in which large tumors disappear under the influence of roentgen radiation. In all cases in which study was sufficiently prolonged, a period of N storage followed that of N loss. Chloride metabolism changes in the nature of a negative chloride balance were demonstrated but less frequently in the patients receiving the 1,000—than the 200-kv therapy. Though the chloride change seems to be correlated with the degree of nausea and vomiting, this study suggests that it is a secondary result of a disturbance in water balance rather than the precipitating cause of the roentgen sickness. Roentgen sickness was observed much less frequently under million-volt roentgen therapy than under 200,000-kv roentgen therapy. No significant differences in changes in metabolism induced by irradiation with 200 kv and 1,000 kv roentgen rays were demonstrated. (R)

1488

Ross, M. H. and J. O. Ely. NEUTRON AND ROENTGEN-RAY EFFECTS ON PROTEIN CONTENT OF RAT INTESTINE. *Am. J. Roentgenol. Radium Therapy* **62**, 718-22(1949).

The present investigations are extensions of previous studies on the effects of penetrating radiations on the chemical constituents of the cells of the crypts of Lieberkuhn. White rats of the Brooklyn strain were used for the estimation of total protein; 10 rats received 600 r of roentgen radiation, 9 received 56 n of neutron radiation, 10 received 100 n of neutron radiation, and 10 received 200 n of neutron radiation. Each irradiated rat was paired with a control rat of the same weight and all the rats were killed 24 hours after the completion of the irradiation; sections of the duodenum of each rat were fixed in alcohol-acetic acid, embedded and sectioned, and the sections were photographed with an ultraviolet microscope for tyrosine, tryptophane and arginine determinations. In a second experiment to determine the effects of irradiation on the nitrogen content of the intestinal cells, two groups of 10 white rats were irradiated with 200 n of neutron radiation and killed 24 and 48 hours after the treatment; the entire small intestine was extracted and the total dry weight of the mucosa was determined. It was found that there was a significant decrease in the mucosa weight 24 hours after irradiation and a greater decrease 48 hours after irradiation; a slight decrease in the percentage of nitrogen was also noted after irradiation. Decreases in the tyrosine and tryptophane contents of crypts were noted after 600 r roent-

gen irradiation, but not after 56 n total body neutron irradiation; decreases were also noted after irradiation with 100 and 200 n neutron irradiation; the arginine contents were found to decrease 24 hours after 600 r or 200 n irradiation. (NSA)

1489

Ross, M. H. and J. O. Ely. RADIATION EFFECTS ON LIVER GLYCOGEN IN THE RAT. *J. Cellular Comp. Physiol.* **37**, 163-71(1951).

A total of 830 rats were irradiated with x rays or neutrons in a study of the x effects of irradiation on the amount of hepatic glycogen in the liver. Glycogen deposits were found after irradiation in the liver cells of rats fasted prior to and after irradiation. Glycogen deposits were also found in fasted irradiated rats after shielding various portions of the body. From these results it was deduced that the effect of radiation on glycogen deposition is not a primary one. (NSA)

1490

Salomon, K., K. I. Altman, G. W. Casarett, and T. R. Noonan. EFFECT OF X-RAY RADIATION AND OF STARVATION ON HEMOGLOBIN SYNTHESIS IN THE RAT. *Federation Proc.* **8**, 247(1949).

After whole body radiation and in acute starvation erythropoiesis is depressed. Information concerning the anabolism of the circulating hemoglobin under these conditions seems desirable. Since the alpha-carbon atom of glycine has been shown to be incorporated in hemin and globin, methylene labeled glycine was used in this investigation. Glycine (1 or 2 microcuries) was administered to radiated and to starved rats. All animals were killed 24 hours later. Hemoglobin, hemin and globin were isolated from their blood and the C-14 content of these compounds determined. The C-14 activity ratio of hemin to globin on a gram to gram basis was found to range from 4-13 in all control animals. The ratio of C-14 activity of hemin to globin isolated from rats injected with glycine immediately after radiation with 600 r varied from 25 to 32. Hemin synthesis was increased in all these rats. On the other hand, when glycine was injected 6 days after exposure to 600 r no measurable hemin synthesis occurred, and the activity ratio was found to be zero. The activity ratio after 5 days starvation was 64; hemin synthesis in these rats was increased whereas globin formation was depressed. In 7 days starvation the activity ratio was zero, hemin synthesis was not measurable, globin formation was depressed. In both radiated and starved animals the ratio of C-14 activity of hemin to that of globin deviates considerably from control values.

1491

Sanigar, E. B., L. E. Krejci, and E. O. Kraemer. THE EFFECT OF ULTRAVIOLET RADIATION AND SOFT X-RAYS ON THE SEDIMENTATION AND LIGHT ABSORPTION OF PURIFIED HUMAN SERUM ALBUMIN. *Biochem. J.* **33**, 1-16(1939).

The sedimentation constant of the unaggregated protein in the irradiated solutions remained essentially that of native albumin. Three hours irradiation with soft x-rays (29,000 r.u.) caused no detectable change in the sedimentation behavior or the absorption spectrum. (Part of Authors' Summary)

1492

Scartozzi, Cesare and Giovanni Silvestri. ACTION OF X-IRRADIATION OF THE SPLEEN ON EASILY EXTRACTABLE IRON. *Pathol. sper.* **36**, 65-80(1948).

Three days' irradiation of rabbits at the spleen with the exciting irradiation, 3 min with 21 r or 4 min with 28 r, caused increase in easily isolated Fe of blood, which be-

came normal again after 15-25 days. After an interval of 140 days the same rabbits were subjected to inhibiting irradiation, 15 min at 110 r, and after 3 days showed no difference in easily isolated Fe, but after 8 days diminution of easily isolated Fe from original values of the order of 1.500-1.600 down to 0.560-0.580 mg/100 ml blood the values remained low for 45 days and returned to normal only at 65 days. When liver and muscle were similarly irradiated, labile Fe values were either affected, although a slight rise was noted in the case of inhibiting irradiation of the liver. (CA)

1493

Shacter, Bernard and M. C. Fishler. DECREASE IN THE SULFHYDRYL CONTENT OF RAT PLASMA FOLLOWING X-IRRADIATION. Naval Radiological Defense Lab. Apr. 26, 1950. 10p. (AD-214(B))

Exposure of rats to 750 r total body x-radiation is followed after several days by a marked decrease in the sulfhydryl content of the blood plasma. (NSA)

1494

Shacter, Bernard, Helen Supplee, and Cecil Entenman. EFFECT OF X-RADIATION, RADIOMIMETIC SUBSTANCES AND SURGICAL TRAUMA ON THE SULFHYDRYL CONTENT OF PLASMA, FINAL REPORT. Naval Radiological Defense Lab. Nov. 27, 1951. 22p. (AD-333(B); Technical Objective AW-6; U20409)

Plasma sulfhydryl concentrations (SC) were determined for 3- to 6-month-old rats of both sexes. Determinations were performed by amperometric titration with a rotating Pt electrode (TIP U16692); SC was estimated on both a protein and unit-volume basis. A Westinghouse x-ray-therapy unit was employed at 250 kvp and 25 r/min. Animals subjected to 700 r total-body x irradiation in a single exposure showed an SC decrease 2 days following irradiation. Lowest values were obtained 6 to 8 days after exposure when SC approximated 60% of control concentrations. By the twelfth day, SC values approached normal levels. A similarly delayed decrease, of lesser magnitude, was observed after intraperitoneal administration of N mustard and triethylene triazine at a dose rate of 1 mg/kg body weight. Lowest values were obtained on the fifth day. No well-defined changes in SC were detected during a 6-day starvation period or after a single exposure to 300 r total-body x irradiation. Surgical trauma induced by laparotomy produced a significant SC decrease at 24 hr after injury, followed by a linear return to normal concentrations over a 12-day period. No significant changes occurred in the first 12 hr subsequent to laparotomy; no sex differences were observed. It is suggested that decreases in SC following tissue injury may be indicative of a markedly increased rate of utilization of sulfhydryl groups by regenerating tissue. (Presented in part at a meeting of the American Association for Cancer Research, Inc., April 1951.) (NRS abst.) (NSA)

1495

Shacter, Bernard, Helen Supplee, and Cecil Entenman. EFFECT OF X-RADIATION AND LAPAROTOMY ON THE POLYSACCHARIDE CONTENT OF PLASMA; RELATIONSHIP TO PLASMA SULFHYDRYL CHANGES, FINAL REPORT. Naval Radiological Defense Lab. Nov. 27, 1951. 11p. (AD-334(B); Technical Objective AW-6; U20432)

The nonglucosamine polysaccharide content (PC) of rat plasma was determined colorimetrically by the tryptophane method of Shetlar and others (*Proc. Soc. Exptl. Biol. Med.* 67, 125(1948)). Blood was collected in syringes moistened with 20% K oxalate. Male rats subjected to 700-r total-body x irradiation in a single exposure showed no PC change during the first 5 postirradiation days. PC levels

rose significantly on the sixth day, remained elevated for a few days, and returned to normal by the twelfth day. Exposure to 300-r total-body x radiation had no effect on PC. Laparotomy resulted in a significant PC increase in 24 hr. Highest values, which were attained 1 to 2 days following laparotomy, returned gradually to normal. PC was consistently greater for male control and laparotomized rats than for the corresponding female animals. In general, sulfhydryl changes (TIP U20409) were detected sooner and lasted longer than the polysaccharide changes. It was tentatively concluded that the same conditions produce the 2 changes; however, the polysaccharide elevations may be less detectable by the methods employed. (NRS abst.) (NSA)

1496

Schoenberg, Melvin D., Robert E. Brooks, John J. Hall, and Herman Schneiderman. EFFECT OF X-IRRADIATION ON THE HYALURONIDASE-HYALURONIC ACID SYSTEM. *Arch. Biochem.* 30, 333-40(1951).

X-irradiation caused a reduction in viscosity of vitreous and umbilical-cord hyaluronate solutions, and a continuing loss in viscosity after cessation of the irradiation, and markedly decreased the average molecular weight. The half-time values for irradiated hyaluronate were greater than for nonirradiated. There was a decrease in the activity of x-irradiated hyaluronidase solutions. (CA)

1497

Schwartz, Samuel. SOME BIOCHEMICAL EFFECTS OF IONIZING RADIATIONS. *Bull. Univ. Minn. Hosp. Minn. Med. Found.* 20, 617-54(1949).

From experimental studies and from a survey of the literature, the following conclusions have been drawn: The most striking biochemical changes found after excessive radiation exposure in humans were (1) an increase in urine "corticosteroid-like substances in all of the five individuals studied, (2) a prolonged increase in the "adenosine triphosphate" phosphorus in the peripheral white blood cells of a patient given total body x-ray for the treatment of a metastasizing parotid tumor, (3) pronounced terminal increases in urinary coproporphyrin excretion in three patients who died within a few weeks after heavy exposure to external radiations, and (4) increased excretions of "uroseoin fraction" pigments in severely ill patients given large doses of total body x-irradiation. Other changes found included a shift to the left in the Arneth count, and an increase in erythrocyte sedimentation rate. The chief changes found in experimental animals include the following: (1) a drop in urinary coproporphyrin excretion followed by a terminal rise, (2) an increased excretion of fecal urobilinogen, indicative of increased red cell destruction, (3) an increased terminal excretion of kynurenic acid, (4) an increased excretion of uric acid and a decreased uricolytic index, and (5) terminal increases in excretion of urinary urobilinogen. More fundamental information is needed on the nature of both early and late biochemical effects of radiation. Studies of physiologically important oxidation-reduction phenomena, and protein and enzyme effects seem especially promising. (NSA)

1498

Schwartz, Samuel. STUDIES OF LIVER FUNCTION IN EXPERIMENTAL ANIMALS WITH SPECIAL REFERENCE TO RADIATION AND METAL EXPOSURE. *Univ. of Chicago Metallurgical Lab.* July 31, 1947. Decl. May 12, 1948. 37p. (AECD-2020; CH-3855)

Total-body x-radiation was administered, with a 200 kv x-ray machine operated at 15 ma. Radiation was delivered at the rate of about 6 r/minute. One-half mm copper and one mm aluminum filters were used. Plutonium and strontium⁹⁰ were administered intravenously or intramuscularly. The various (nonradioactive) metals studied

were injected subcutaneously in the thigh. These metals included beryllium, lead, uranium, thorium, mercury, arsenic, and lanthanum. Relatively extensive studies of liver function were made only with beryllium. In addition, the effect of BAL was studied in relation to the use of this substance in the treatment of metal poisoning. The metal salts used were dissolved in water and generally brought to pH 5-6 by the addition of sodium hydroxide. Chief emphasis was given to the excretion of urinary urobilinogen. This test, employing Watson's method, was chosen. Three tests for liver function were investigated: the cephalin flocculation test of Hanger, the colloidal gold test of Gray, and the thymol turbidity test of MacLagen. Most complete studies were made of the first of these tests in dogs, rabbits, and rats, as well as in human subjects. Occasional analyses of serum bilirubin were also made. Venous blood was used in the dog studies. Cardiac blood was drawn from rabbits and rats. In the present work only urine studies were done routinely in the rabbits; both urinary and fecal excretion of porphyrin was followed in many of the irradiated dogs. It is apparent from the data presented that liver function, as reflected in urinary excretion of urobilinogen, was not profoundly affected, except terminally, in animals exposed to lethal amounts of radiation. Furthermore, any changes in serum proteins produced by radiation were not associated with significant changes in the serum tests of liver function used. These results are in agreement with the general consensus of opinion in the literature. (ADD)

1499

Schwartz, Samuel. STUDIES OF PORPHYRIN METABOLISM. IV. THE EFFECT OF IRRADIATION ON COPROPORPHYRIN EXCRETION. Univ. of Chicago Metallurgical Lab. Nov. 25, 1946. Decl. Aug. 8, 1948. 28p. (MDFC-1221; CH-3719)

The effect of irradiation exposure on coproporphyrin excretion has been studied in 38 dogs. A diminished excretion of this porphyrin in urine and feces was found to follow the administration of lethal or nearly lethal doses of total body x-ray, strontium⁹⁰, and plutonium. In most instances, a sharp increase in porphyrin excretion occurred during the terminal period. Preliminary studies showed no significant change in the ratio of the two coproporphyrin isomers (I and III) following irradiation. (ADD)

1500

Setälä, Kai. PRELIMINARY OBSERVATIONS ON THE EFFECTS OF IRRADIATION UPON THE CHYLOMICRONS IN HUMAN BLOOD. Radiology 50, 803-9(1948).

An attempt was made to determine the effects of roentgen or radium rays on the mobile visible lipids in human blood following administration of a fatty meal and before the lipids were deposited in the tissues. As a method of investigation, instead of quantitative chemical determinations, which are subject to considerable error, chylomicron counts were obtained at half-hour intervals. Observations were made on 32 individuals, and every precaution was taken to avoid the possibility of error. It was found that irradiation regularly produced changes in the amount and metabolism of the visible blood lipids. Further it was found that, to produce changes, the irradiation must be done within a given time interval after the ingestion of the fatty food. It appeared, also, that irradiation of certain regions of the body, as the abdomen, the pelvis and the bifurcation of the common carotid was followed by a particularly marked effect. With the histamine theory in mind, the effect of intramuscular injections of histamine acid phosphate was also investigated. Such injections, suitably timed in relation to the fatty meal, effected changes in the lipid metabolism comparable to those following irradiation. In persons with symptoms of radiation sickness, the

changes in the blood lipids were particularly severe. It is assumed that the decrease and/or disappearance of the mobile visible lipids observed in these studies in an effect of hemoconcentration due to increased permeability of the capillaries caused by irradiation or histamine administration. (NSA)

1501

Setälä, K. and P. Ermala. ON IRRADIATION SICKNESS. Ann. Chir. Gynaecol. Fenniae 37, Suppl. 1, 1-59(1948).

The relationship between irradiation sickness and mobile visible blood lipids is discussed in this report based on 65 cases. The cases uniformly demonstrated a marked decrease in the chylomicron count during radiation sickness, which was not present in irradiated cases not developing the sickness; the degree of sickness was proportional to the degree of depression in the count. Irradiation in excess of 350 r over the abdomen, pelvis, and the bifurcation of the common carotid produced radiation sickness with changes in chylomicron count, while corresponding irradiation over extremities produced no sickness or changes in count. The administration of histamine acid phosphate caused changes in chylomicron counts similar to those found in radiation sickness. The authors suggest that their work corroborates that of others who found that irradiation liberates a "histamine-like substance" (not in all effects similar to histamine, and unresponsive to antihistaminics); paraganglionic elements may be affected either directly by the irradiation or by a toxin resulting from irradiation. (NSA)

1502

Smith, D. E., E. B. Tyree, H. M. Patt, and E. M. Jackson. THE EFFECT OF WHOLE-BODY X-IRRADIATION ON THE METABOLISM OF THE RAT. Proc. Soc. Exptl. Biol. Med. 78, 774-7(1951) (AECU-1253; UAC-367)

Determinations have been made of the influence of whole-body x irradiation upon the rate of weight loss of the starving rat and upon the level of basal O₂ consumption of both the starved and the fed rat. Since irradiation was without effect upon these quantities it was concluded that single, whole-body exposures to irradiation do not bring about increased metabolism. The discrepancies between these and the previous data which supported the hypothesis of a radiation-induced increase in metabolism are discussed. 11 references. (NSA)

1503

Smith, Falconer and Willie W. Smith. EXERCISE EFFECTS ON TOLERANCE TO RADIATION. Am. J. Physiol. 165, 662-6(1951).

As a whole, the effect of moderate exercise for 8 hr consecutively a day, or for 12 hr a day in equally spaced periods of 3 hr, was to decrease slightly, if at all, the tolerance of mice to whole-body irradiation. After a radiation dose which was 100% lethal, 7 out of 30 mice failed to tolerate 3 consecutive days of exercise for 8 hr/day. Those surviving the exercise period showed no difference in survival time from their irradiated controls. Phenobarbital sedation after irradiation failed to increase the radiation tolerance of mice. It is concluded that radiation lethality does not parallel the rate of O₂ utilization under the conditions of these experiments. (NSA)

1504

Stearner, S. Phyllis., E. J. B. Christian, and Austin M. Brues. EFFECTS OF X-IRRADIATION ON RENAL FUNCTION IN NEWLY-HATCHED CHICKS. Proc. Soc. Exptl. Biol. Med. 78, 676-9(1951).

Young chicks were exposed to 1000 r x-radiation at dose rates of 6 or 43 r per min. Detns. of excretion rate of urate and phenol red and of blood urate levels indicated that death in the initial period (within 8-24 hours) following

high rate exposures was preceded by renal failure and a rapidly developing azotemia. Individuals that survived 24 hours or more after exposure, whatever the dose rate, continued to excrete at the normal rate. Phenol red retention invariably accompanied failure of urate excretory function. (BA)

1505

Thompson, H. E. and L. T. Steadman. THE EFFECTS OF WHOLE BODY X-IRRADIATION ON THE BLOOD GLUCOSE LEVELS IN RABBITS, p.13-33 of QUARTERLY TECHNICAL REPORT, OCTOBER 1, 1950 THRU DECEMBER 31, 1950. University of Rochester. Feb. 1, 1951. 20p. (UR-152(p.13-33))

Rabbits were irradiated under light anesthesia with 200 krp x radiation, half-value layer of 1.6-mm Cu. With doses of 500 r and greater, temporary elevations in plasma and red blood cell glucose were observed with a maximum increase at 2 to 4 hr from the start of the irradiation and with a return to normal within 24 hr. The rise in the glucose level increased with the dose and for 1000 r the maximum elevation in the plasma was about 90% and in the red cells about 80%. Animals which were irradiated with a second dose of 500 r between 7 and 33 weeks after the first irradiation showed glucose increase comparable to those receiving a single dose of 1000 r. (NSA)

1506

Trudova, R. G. MEASUREMENT OF ISOELECTRIC POINT OF CELL COLLOIDS IN PLANTS UNDER THE ACTION OF X-RAYS. Doklady Akad. Nauk S.S.S.R. 72, 197-9(1950).

Irradiation of oat rootlet tips with 250 r. (in 1-min. exposure) gave only a temporary growth retardation; at 500 r. the effect was more definite, and at 13000 r. mitosis was essentially stopped. A shift of isoelectric point of colloids of the plasma and nucleus occurs simultaneously but returns to normal within 24 hrs. even at 13000 r. dosage; this maximum shift is to 2.8-3.4 pH for plasma (2.4-2.6 normal) and 3.4-4.2 pH for nucleus (2.8-3.0 normal) taken 15 minutes after x-ray exposure. The individual spread of values is greater after irradiation than in controls. (CA)

1507

Uchimura, T. THE EFFECT OF ULTRAVIOLET AND ROENTGEN RAYS ON THE REDOX-POTENTIAL OF THE FROG MUSCLE IN VIVO. J. Biochem. 25, 207-17 (1937).

The redox-potential of normal frog muscle is nearly +230 mv E h. Irradiation with ultraviolet or roentgen rays causes the increase of the reduction-potential, which is highest at the dosage of 10 min. exposure with uv-rays and at 135 r with Roentgen-rays. At larger doses this increase was rather inhibited. With uv-rays the rise of the reduction-potential took place soon after the irradiation, but with Röntgen-rays it happened after certain intervals. This observed change in potential took place only when each component of the reducing system is muscle (dehydrogenase +H₂-donator) are all present. The recovery of the potential to the initial value took place earlier in the case of uv-rays than in the case of Röntgen rays. There exists an optimal dosage of irradiation for the increase of the reduced glutathione. By applying excess it was rather inhibited. It is proposed that the biological effect of light might be partially sought in the activation of the reducing agents in the tissue. (Author's Summary)

1508

Venters, K. D. and Elizabeth E. Painter. SENSITIVITY OF X-RAYED ANIMALS TO INFUSION OF HISTAMINE, ADENOSINE, AND TRYPSIN. Federation Proc. 9, 129-30(1950).

Control and x-rayed rabbits and dogs given an LD-50 dosage have been infused in the manner described previously (Fed. Proc. 7:90, 1948) and "threshold values" have been established for exogenous histamine, adenosine, and trypsin. It appears that sensitivity of rabbits to adenosine is not increased after radiation, but sensitivity to histamine increases markedly. Maximal changes in sensitivity are directly correlated with other physiological findings occurring at the same time after radiation and must be a function of damage to tissue. Marked susceptibility of x-rayed rabbits to trypsin has made it impossible to record changes with this substance. It is apparent from the table below that dogs show their maximal increase in sensitivity to all 3 substances (approximately 50% change) at 2-2½ hours after x-radiation. These findings are correlated exactly in time with the main clinical sign of vomiting in the dog. Our studies suggest that more than one breakdown product may be involved in the early biochemical disturbance to account for the symptoms of radiation sickness.

Threshold Values for Maintaining 5-8 mm Hg Drop in Blood Pressure

Control Rabbits	Post-radiation in hours					
	1	1½	2	2½	3	
Histamine 6.7 (14)	7.0	3.1	2.0	2.2	2.7	
Adenosine 111.2 (12)	119.0	192.0	208.0	281.0	188.0	
Trypsin 107.0 (10)	No threshold could be established after radiation					

Control Dogs	Post-radiation mgm/kg/min					
	1	1½	2	2½	3	
Histamine 1.2 (17)	1.0	0.6	0.5	0.4	1.1	
Adenosine 120.4 (21)	94.0	81.2	81.4	93.0	118.0	
Trypsin 113.2 (16)	96.0	89.0	55.3	49.3	73.0	

1509

Wattenberg, L. RADIATIONS-INDUCED CHANGES IN ULTRAVIOLET ABSORPTION SPECTRA OF URINE: II. QUANTITATIVE SPECTROPHOTOMETRIC STUDIES. Argonne National Lab. Jan. 14, 1947. 30p. (MDDC-701; CH-3661)

Methods are described for the quantitative estimation of kynurenic acid in dog urine. These are based on analysis of the ultraviolet absorption spectrum either of unpurified diluted urine or of purified urine extracts. Urine kynurenic acid excretion has been studied in 13 mongrel dogs administered lethal amounts of x-ray in either single or multiple doses. Twelve of the animals showed an increase in urine kynurenic acid concentration at some time shortly before death. This increase is best seen in the urine ultraviolet absorption spectrum as a plateau or actual maximum at about 245 mμ. Because of diminished terminal per diem urine volume in several dogs, the per diem excretion of kynurenic acid rose significantly in only 10 animals, with questionable increases in two of the others. Two dogs injected with plutonium were also studied. One, which died after 90 days, showed a terminal increase in urine kynurenic acid excretion. The other, which died 234 days after receiving the plutonium excreted very little kynurenic acid throughout its course. This dog showed the most evidence of liver damage of any of the dogs studied. Data are insufficient to interpret the findings adequately. Some of the factors that may be involved in kynurenic acid excretion are discussed. (ADD)

1510

Wattenberg, L. and Samuel Schwartz. RADIATION-INDUCED CHANGES IN ULTRAVIOLET ABSORPTION ON

SPECTRA OF URINE: I. GENERAL EFFECTS. Argonne National Lab. July 25, 1946. 21p. (MDDC-700; CH-3541)

Several hundred ultraviolet absorption spectra (Beckman spectrophotometer) have been prepared from urine of control and irradiated dogs receiving either external or internal radiation. Unless death occurs too soon (i.e., within less than two weeks) there is a consistent increase in absorption in the regions of 245, 310, and/or 270 m μ in acid solution. The 235 and 310 m μ increases are shown to be due to kynurenic acid, a metabolic derivative of tryptophane. The 270 m μ increase is shown to be due to uric acid. The effect on the spectra of variations in pH are described. (ADD)

1511

Weber, R. P. and F. R. Steggerda. **HISTAMINE IN RAT PLASMA: CORRELATION WITH BLOOD PRESSURE CHANGES FOLLOWING X-IRRADIATION.** Proc. Soc. Exptl. Biol. Med. **70**, 261-3(1949).

Rats, after x-irradiation with mid-lethal dosage (600 r) show assayable histamine in concentrations of 1 to 2 γ per 2 cc of blood plasma at two hour and five day intervals following the irradiation. Rats irradiated similarly to those used in the histamine assay experiments show a fall in blood pressure that correlates with the appearance of histamine in blood plasma and strongly suggests that histamine is responsible for the lowered blood pressure. Rats, from four to six days after a mid-lethal dosage of irradiation, show a loss in appetite and weight, and a critical fall in blood pressure from which only 50% will recover. The rest died within 9 or 10 days after the irradiation was given. (NSA)

1512

Whilden, R. M., Enzmann, E. V., and C. P. Haskins. **THE INFLUENCE OF ROENTGEN RAYS UPON THE NITROGEN FIXATION BY AZETOBACTER.** J. Gen. Physiol. **24**, 789-96(1941).

N fixation decreases approximately linearly with increasing doses of x-rays. Respiration is affected indirectly by some inhibition of cell multiplication. Small doses of x-rays often produce a slight, transient increase in rate of O uptake. (CA)

1513

Woodward, G. E. **GLUTATHIONE AND ASCORBIC ACID IN THE TISSUES OF NORMAL AND TUMOR-BEARING ALBINO RATS.** Biochem. J. **29**, 2405-12(1935).

Walker No. 256 carcinoma and Philadelphia No. 1 sarcoma were found to contain glutathione (I) in amounts comparable to those of other tissues and ascorbic acid-like material (II) in amounts higher than in any tissue except the adrenal. I and II were found only in the growing part of the tumors. The ratio of I to II in sarcoma was under 1.4 and in carcinoma over 1.6. Corresponding tissues from normal and tumor-bearing rats showed no differences in the amounts of I and II. Long-continued injections of ascorbic acid, mannose, glucose or oxidation-reduction dyes caused no changes in the amounts of I or II in tumors and the tumor growth was unaffected. Treatment of tumors with x-rays decreased the values of I, if the x-rays retarded the tumor growth. The value of II was decreased only in the sarcoma by x-ray treatment, x-ray resistant tumors showed no decrease in the amounts of I and II. (CA)

1514

Zahl, Paul A. and Harry G. Albaum. **ADENOSINE TRIPHOSPHATE LEVELS IN MOUSE BLOOD AFTER WHOLE-BODY IRRADIATION AND DURING TUMOR GROWTH.** Proc. Soc. Exptl. Biol. Med. **77**, 388-93(1951).

No changes were observed in the blood levels of total nucleotide or of adenylic acid, adenosine diphosphate, or adenosine triphosphate during the wasting period following whole-body x irradiation of mice. Massive injected doses of adenosine triphosphate (ATP) failed to induce overt symptoms of shock in mice. In mice with implanted tumors there was found a continuous decrease in blood ATP until about the 10th postimplantation day, followed by a rise of ATP. The decrease paralleled the increase in tumor weight. No significant changes were observed in total nucleotide values for blood during tumor growth, nor was the adenylic acid or the adenosine triphosphate picture different from that for normal mice. (NSA)

Studies on Nucleoproteins and Nucleic Acids

1515

Abrams, Richard. **EFFECT OF X-RAYS ON NUCLEIC ACID AND PROTEIN SYNTHESIS.** Arch. Biochem. **30**, 90-9(1951).

Rats and rabbits were irradiated with 500 r and 800 r, respectively. They were injected intraperitoneally immediately, and at intervals up to 24 hrs with isotopically labeled glycine. Purines were fractionated from the intestines of the animals and the adenine and guanine contents measured isotopically. The rates of synthesis of desoxyribonucleic acid and ribonucleic acid was markedly reduced by x-rays, but the synthesis of protein was relatively unaffected. (CA)

1516

Ahlstrom, Lucie H., Hans v. Euler, and Georg v. Hevesy. **ACTION OF X-RAYS ON NUCLEIC ACID METABOLISM IN RAT ORGANS.** Arkiv. Kemi. Mineral. Geol. A **19**, No. 9, 16p. (1944).

Nucleic acid (I) metabolism in liver, spleen and intestinal mucosa of adult rats was inhibited $\frac{1}{3}$ to $\frac{1}{2}$ during the 2 hr immediately after irradiation of the animals with 1,500-3,000 r. This result was similar to that obtained in previous studies on Jensen sarcoma. In the liver and spleen of rats $3\frac{1}{2}$ days old the percentage of newly formed I mols. was 2 and 10, resp., which was 20 and 4 times as great as in the corresponding organs of adult animals. The daily wt. increase of the liver of rats $3\frac{1}{2}$ - $4\frac{1}{2}$ days old was 10.2%, and studies with radioactive P as an indicator showed that the content of new I mols. was twice as great as that which would parallel the increase in wt. The formation of each 3 new I mols. was accordingly linked with the disappearance of 1 old I mol.; this result was also similar to that observed with Jensen sarcoma. The percentage decrease of I metabolism in the organs of rats 3-4 days old under the influence of x-rays was about the same as that in the organs of adult rats. If the irradiation dose mentioned above was spread over 2 hr, the effect was more pronounced: during this period, I metabolism in the liver of rapidly growing rats fell from 2% to 0.2%, that in the spleen from 10% to 2%. A considerable portion ($\frac{1}{6}$ with liver) of the inhibitory action of x-rays therefore appears to disappear during the first 2 hr after radiation. During irradiation of rats 3-4 days old with 15 r per min. addnl. formation of I and liver growth practically ceased. (CA)

1517

Ahlstrom, Lucie H., Georg v. Hevesy, and K. Zerahn. **ATTEMPTS TO FIND PRODUCTS BLOCKING NUCLEIC ACID FORMATION IN THE CIRCULATION OF AN IRRADIATED ORGANISM.** Arkiv. Kemi Mineral. Geol. **23A**, 1-6 (1947).

Several rabbits four weeks old were irradiated with 7,500-10,000 r. Blood transfusions of 9-23 ml. were made

from these animals to paired litter-mates which had not been irradiated. Radioactive phosphate (20 microcuries) was administered subcutaneously to the nonirradiated rabbits and after two hours the specific activity of the desoxyribonucleic acid phosphorus extended from the kidneys, liver, and intestinal mucosa was compared with the free phosphate extended from the corresponding organisms and from the plasma. Control experiments were carried out on rabbits transfused with blood from nonirradiated litter-mate rabbits. As the result of the transfused, irradiated blood the formation of labeled desoxyribose nucleic acid is definitely slower in the kidney, probably slower in the liver, but unaffected in the intestinal mucosa. (BA)

1518

Butler, G. C. EFFECT OF X-AND GAMMA-RAYS ON AQUEOUS SOLUTIONS OF SODIUM THYMONUCLEATE. *Can. J. Research* **27B**, 972-87(1949).

The changes in viscosity of highly polymerized Na thymonucleate solutions upon irradiation with x- and γ -rays was investigated. It was found impossible to correlate absolute viscosity values with particle size and shape. The relations of change produced to total dosage, to the presence of protective agents, to concentration of solution and to dosage rate indicate that the radiations act through the mediation of activated water molecules. Direct ionization, on the other hand, in the nucleate molecules has by comparison a negligible effect. (CA)

1519

Butler, J. A. V. and B. E. Conway. ACTION OF IONIZING RADIATIONS AND OF RADIOMIMETIC SUBSTANCES ON DESOXYRIBONUCLEIC ACID. II. EFFECT OF OXYGEN ON THE DEGRADATION OF THE NUCLEIC ACID BY X-RAYS. *J. Chem. Soc.* **1950**, 3411-18(1950).

Irradiation of 0.1% solutions of thymus nucleic acid at the rate of 206 r/min gave a fairly large and a complete loss in viscosity after 7,000 and 40,000 r, respectively. The loss of viscosity ceased at the end of irradiation of O-free solutions but continued with O-saturated solutions. The after effect was ascribed to a product of molecular O_2 , which, however, was not H_2O_2 . (CA)

1520

Butler, J. A. V., L. A. Gilbert, and K. A. Smith. RADIO-MIMETIC ACTION OF SULFUR AND NITROGEN MUSTARDS ON DESOXYRIBONUCLEIC ACID. *Nature* **165**, 714-6(1950).

Methyl bis-B-chloroethylamine and B-dichloroethylsulfide, but not chlorodiethyldimethylamine destroy the structural viscosity of thymus desoxyribonucleic acid. The original structural viscosity, relative viscosity used with decreasing ratio of flow, is gradually converted to a viscosity similar to water, independent of pressure, and showing no streaming birefringence. X-ray irradiation of 22,000 r also produces an effect in the structural viscosity of nucleic acid which is quantitatively similar to that of 2 mg of N mustards. This ratio of effectiveness is similar to that observed in rats and mice for total body x-ray irradiation and oral dose of N-mustard. (CA)

1521

Conway, B. E., L. Gilbert, and J. A. V. Butler. ACTION OF IONIZING RADIATIONS AND OF RADIOMIMETIC SUBSTANCES ON DESOXYRIBONUCLEIC ACID. III. MOLECULAR WEIGHTS OF DESOXYRIBONUCLEIC ACID DEGRADED BY X-RAYS AND BY TREATMENT WITH A NITROGEN MUSTARD. *J. Chem. Soc.* **1950**, 3421-5(1950).

Irradiation with 40,000 r (O present) caused a decrease in the molecular weight of thymus nucleic acid from approximately 1.5×10^6 to 5.3×10^5 . Reaction of 10 mg

($ClCH_2CH_2$) $_2$ NCH $_3$ for 5 days decreased the molecular weight to 4.5×10^5 . The degraded substances showed a considerable degree of polydispersity. (CA)

1522

de Nicola, Marina. EFFECTS OF X-RAYS ON THE CELL DURING ACTIVE METABOLISM OF NUCLEIC ACIDS. *Publ. staz. zool. Napoli* **22**, 283-93(1950).

The effect of X rays on nucleic acid metabolism in germinal and secretory cells was studied on the testis of *Asellus aquaticus* during spermatogenesis. Doses of 250 to 5000 r with intensity 1330 r/min at a distance of 5 cm from the ventral side without filters were used. The fundamental effect of X rays in various doses is always the same: 'all the desoxyribonucleic acid (I) gradually disappears and is transformed into ribonucleic acid (II) which is expelled from the cell until this, completely deprived of nucleic acids, dies. The gonad appears poorer and poorer in germinal and to lower degree in theca cells; after 2 months' treatment the gonad still exists but with a greatly reduced number of cells. It is believed that the cells whose function is essentially to metabolize nucleic acids, for their own and external use, are particularly radiosensitive. (EM)

1523

de Nicola, Marina. ACTION OF X RAYS ON THE METABOLISM OF NUCLEIC ACIDS IN PROLIFERATIVE AND SECRETORY CELLS. *Experientia* **6**, 432-3(1950).

The action of x rays on the metabolism of nucleic acids in proliferative and secretory nonproliferative cells has been investigated. X rays cause a stoppage of desoxyribonucleic acid synthesis and a conversion of desoxyribonucleic acid into ribonucleic acid. All germ cells, including spermatozoa, show this effect, and the same is true for the follicular secretory cells. The germ cells are blocked at different stages of mitosis or meiosis. On the contrary, the follicular cells continue their characteristic secretory cycle, until they are entirely deprived of both nucleic acids and eventually die. The conclusion is drawn that the action of x rays is essentially specific for the nucleic acids as such, and not for some intermediate substance of their metabolism, and that stickiness, metaphasic block, and chromosome abnormalities are probably a secondary effect of this action. (NSA)

1524

Ely, J. O. and M. H. Ross. NUCLEIC ACID CONTENT IN INTESTINES OF RATS AFTER X-RADIATION. *Cancer Research* **8**, 285-94(1948).

The effects of total-body x-radiation (600 r) of rats on the crypts of Lieberkühn were studied by ultraviolet-light-absorption and other methods. It was found that x-radiation caused a decrease in the amount of ultraviolet-light-absorbing material in the crypts of Lieberkühn of rats at various levels along the intestinal tract; the decrease in the amount was found at various periods of time ranging from 4 hours to 17 days. Involved in the decreased absorption of ultraviolet light were desoxyribonucleic acid, ribonucleic acid and the structural framework of the tissue, all of which were found to be reduced. The amount of inorganic ash also was found to be reduced. (NSA)

1525

Ely, J. O. and M. H. Ross. NUCLEIC ACID CONTENT IN INTESTINES OF RATS AFTER NEUTRON RADIATION. *Cancer Research* **8**, 607-12(1948).

It was reported in a previous paper (*Cancer Research*, **8**, 285, 1948) that whole-body x-radiation of rats resulted in decreased amounts of desoxyribonucleic acid, ribonucleic acid, structural proteins, and non-volatile ash in the cells of the crypts of Lieberkühn in the intestines. Studies on the effects of whole-body neutron irradiation of rats on the

crypts of Lieberkühn have been made using ultraviolet absorption and chemical staining methods. It was found that neutron radiation caused a decreased ultraviolet light absorption in the crypts of Lieberkühn in the duodenum of rats; the decrease was found at various periods of time ranging from 4 to 48 hours after irradiation. The effects produced increased with the dosage and the decreased ultraviolet absorption has been linked with ribonucleic acid and deoxyribonucleic acid. It was also found that the amount of inorganic ash was reduced. These effects of neutron radiation are similar to those previously found after whole-body exposure to x-rays. (NSA)

1526

Errera, M. IN VITRO AND IN SITU ACTION OF IONIZING RADIATIONS ON NUCLEO-PROTEINS OF THE CELL NUCLEUS. Cold Spring Harbor Symposia Quant. Biol. 12, 60(1947).

Radiation effects on the nucleoprotein complex of the cell nucleus have been studied. Experiments *in vitro* showed an indirect action of the radiation while experiments *in situ* evidenced a direct effect of irradiation. Nucleoprotein complexes of the nucleus were shown to be strongly affected when irradiated *in situ*. (CA)

1527

Feinstein, Robert N. EFFECT OF IRRADIATION AND OF VARIOUS REAGENTS ON VISCOSITY OF NUCLEOPROTEIN SOLUTIONS. Proc. Soc. Exptl. Biol. Med. 76, 646-9 (1951).

Cysteine, glutathione, cyanide, and thiocyanate greatly increase the viscosity of alkaline solutions of nucleoprotein (thymus chromosomes), while urea, uracil, thiourea, thio-uracil, cystine, and BAL do not do so. Ascorbic acid increases the viscosity only after prolonged incubation. H_2O_2 is without effect on the viscosity. If cysteine is added to the alkaline nucleoprotein solution before x irradiation, the expected reduction in viscosity is largely prevented. If the cysteine is added after x irradiation, it is much less effective in this respect. The suggestion is made that these phenomena may be relevant to the question of the mechanism of cysteine and some other agents in increasing resistance of organisms to x-ray lethality. (NSA)

1528

Harrington, Helen and Paul S. Lavik. THE EFFECT OF IONIZING RADIATION ON THE DESOXYRIBONUCLEIC ACID CONTENT OF RAT THYMUS NUCLEI. Western Reserve University, School of Medicine. Sept. 27, 1951. 16p. (NYO-1627)

The DNA phosphorus content per nucleus has been determined in thymus cells of normal and irradiated rats, and it has been found that irradiation causes no significant change in this value. Since there is a decrease in the DNA phosphorus concentration of thymus tissue following irradiation, several mechanisms of radiation action which could cause a decrease in DNA phosphorus concentration while allowing the DNA phosphorus per nucleus to remain unchanged are discussed. It has been suggested that an inhibition of DNA synthesis, resulting in a decreased new cell production, followed by the elimination of old lymphocytes from the thymus could account for both experimental findings. (NSA)

1529

Harrington, Nyra J. and Robert W. Koza. EFFECT OF X-RADIATION ON THE DESOXYRIBONUCLEIC ACID AND ON THE SIZE OF GRASSHOPPER EMBRYONIC NUCLEI. Biol. Bull. 101, 138-50(1951).

Cytological and cytochemical studies were made on embryonic nuclei of the grasshopper, *Chortophaga viridifasciata*, after x-ray doses of 4000, 10,000 and 12,500 r. The changes induced were photometrically measured by using (1) the Feulgen reaction to determine relative changes

in the DNA desoxypentose, and (2) the methyl green stain to indicate the degree of polymerization of the nucleic acid. X-radiation was found to cause swelling of the nuclei. When correction was made for this, the Feulgen-stained nuclei showed no significant loss of DNA after irradiation, but the nuclei stained with methyl green disclosed a highly significant loss of stainability. This is interpreted to indicate that x rays do not destroy the DNA but induce depolymerization of the nucleic acid. This study has shown that it is not safe to make quantitative estimates of DNA (stained by Feulgen or methyl green) from microscopic observations and photographs. The visually apparent loss of Feulgen-stainability after irradiation is probably not due to a decrease in the DNA desoxypentose but rather to the increased dispersion of the DNA in nuclei that have undergone x-ray-induced enlargement. (NSA)

1530

Bevesy, Georg v. ON THE EFFECT OF ROENTGEN RAYS ON CELLULAR DIVISION. Revs. Mod. Phys. 17, 102-11 (1945).

While mitotic counts give important data on the effect of Röntgen rays on growing tissue, this method fails in the investigation of behavior of full-grown tissue. The effect of ionizing irradiation on all types of tissue can be studied by detg. the amt. of newly formed desoxyribonucleic acid before and after irradiation. The newly formed nucleic acid is detd. by using radioactive P as an indicator. Therapeutic and larger doses of Röntgen rays inhibit the formation of desoxyribonucleic acid in the growing and full-grown tissues to about the same extent. A large percentage (about $\frac{3}{4}$) of the inhibiting action disappears within 2 hrs, after irradiation. The difference between growing and grown tissues is interpreted by assuming that a far longer time elapses for an av. full-grown tissue cell to reach the mitotic stage and thus to have a greater chance to regenerate from the damaging influence of the irradiation. The problem of direct and indirect action of Röntgen rays on cell division is discussed. (CA)

1531

Bevesy, Georg v. EFFECT OF X-RAYS ON THE INCORPORATION OF C^{14} INTO DESOXYRIBONUCLEIC ACID. Nature 163, 869-70(1949).

To determine whether the rate of formation of desoxyribonucleic acid is reduced by the effect of ionizing radiations, C^{14} was incorporated into the purines of desoxyribonucleic acid in the organs of rapidly growing rats after x-radiations. About 5 mc of C^{14} incorporated into the carbonoxyl group of sodium acetate were injected subcutaneously in each of 91 one- to three-week old rats. The rats were killed after a lapse of six hours, and the desoxyribonucleotides were separated from the proteins by extraction with trichloroacetic acid; the purines obtained were precipitated and their radioactivity ascertained. Half of the rats had been previously radiated with a dose of 950 r. The amount of labelled purines obtained from the irradiated rats was about half that obtained from the controls. The rate of incorporation of C^{14} into the proteins was not reduced by irradiation; so it is concluded that the rate of formation of desoxyribonucleic acid is reduced by the radiations. This rate reduction of one of the main constituents of cell nuclei may help to explain the blocking effect of irradiation on cell division and the formation of anomalous mitotic products in the irradiated tissue. (NSA)

1532

Holmes, Barbara E. THE INHIBITION OF RIBO- AND THYMO-NUCLEIC ACID SYNTHESIS IN TUMOR TISSUE BY IRRADIATION WITH X-RAYS. Brit. J. Radiol. 20, 450-3(1947).

Using P-32 as a tracer, the uptake of this element in the thymonucleic acid fraction in rat tumor tissue (Jensen rat

sarcoma) is markedly inhibited by x-rays, while the ribonucleic acid fraction is inhibited to a smaller extent. Nembutal as a sedative inhibits the uptake of P-32 in both these fractions and should not be used. There is confirmation of Hevesy's observation that irradiation of one tumor can effect the nucleic acid metabolism of another tumor in the same animal. (BA)

1533

Holmes, Barbara E. THE INDIRECT EFFECT OF X-RAYS ON THE SYNTHESIS OF NUCLEIC ACID IN VIVO. *Brit. J. Radiol.* **22**, 487-91(1949).

The synthesis of thymo- and ribo-nucleic acid (in the Jensen rat sarcoma) was studied in irradiated tumors and in other tumors in an irradiated animal which were themselves not receiving irradiation. The directly irradiated tumors received a dose of 2,000 r, which was sufficient to produce regression in many cases. Radioactive phosphorus, P³², was introduced intraperitoneally to measure the radiation effect on the nucleic acid synthesis as demonstrated by the inhibition of the uptake of P³². The details and results of the various experiments undertaken are presented. Thymonucleic acid synthesis was reduced to about 25% of the normal in the screened tumor; the ribonucleic acid renewal was affected similarly, but to a much smaller extent. In animals killed one hour after irradiation, the direct and indirect effects of the radiations were large. When P³² was injected about 2 hours after irradiation and the animal killed one hour later, the ribo-nucleic renewal was nearly normal in all tumors; the thymonucleic synthesis of the screened tumor was nearly normal, and in the irradiated tumor was about 60% of normal. When injected at four hours after irradiation and killed one hour later, the thymonucleic synthesis was found to be proceeding at a normal rate. Counts indicate that the dose of x-radiation used produces a considerable amount of abnormal mitosis, while no normal mitosis is taking place five hours after irradiation. (NSA)

1534

Jungner, Ingmar. DIELECTRIC DETERMINATIONS OF MOLECULAR WEIGHT AND DIPOLE MOMENT OF SODIUM THYMONUCLEATE, THE INFLUENCE OF X-RAYS. *Acta Physiol. Scand. Suppl.* **20**, 69(1950).

Studies of x-irradiated aqueous solutions of DNA show that x-rays mainly have a depolymerizing effect. Only after very large doses (100,000 r to a 0.05 per cent solution) does the specific polarity fall considerably whereas the molecular weight remains relatively constant at about 30,000. The effect of the x-rays on stronger concentrations of DNA (0.625 per cent) is smaller but essentially similar.

No after-effect of the x-rays on the dielectric properties can be noted within 12-48 hours of irradiation. (Author's Summary)

1535

Kamen, M. D. APPLICATION OF RADIOACTIVE ISOTOPES TO THE STUDY OF RADIATION EFFECTS IN CELLS. *Radiology* **49**, 223-30(1947).

Metabolizing cells which are not actively synthesizing new protein do not transfer phosphate from the "nucleoprotein" fraction. Synthesis of new protein or enzyme is associated with transfer of phosphate from the "nucleoprotein" fraction. Agents which prevent enzyme formation and protein synthesis also stop flow of phosphate from the "nucleoprotein" fraction. It would be premature to suggest that disturbances in nucleoprotein metabolism are the central factor in induction of the pathological manifestations observed to result from irradiation of cells. There does appear to be sufficient evidence available to indicate that investigation of cellular responses to a wide variety of

chemical agents may clarify many aspects of the radiation problem, particularly in conjunction with isotope studies. (GPR)

1536

Kelly, Lola S. and Hardin B. Jones. EFFECTS OF IRRADIATION ON NUCLEIC ACID FORMATION. *Proc. Soc. Exptl. Biol. Med.* **74**, 493-7(1950).

Mice of the A strain bearing bilateral transplants of mammary carcinoma were used to demonstrate an indirect effect of irradiation on the desoxypentose nucleic acid turnover rate. In two experiments the animals were irradiated by means of radioyttrium (Y⁹⁰) colloids which localize in the liver when injected intravenously and remain at the site of injection when given intramuscularly. The nucleic acid turnover rate was measured by giving a tracer dose of radioactive sodium phosphate (P³²), sacrificing the animals after two hours, and isolating the desoxypentose nucleic acid from their tumors and livers. The specific activity of the nucleic acid phosphorus was measured and considered to be an index of the turnover rate. It was found necessary to purify the nucleic acid much more carefully than is done in standard methods in order to obtain a constant specific activity upon successive reprecipitations. The animals whose livers were irradiated with 4.25×10^5 ergs showed only 66% of the tumor nucleic acid specific activity of the control group. The animals whose muscles were irradiated with 4.25×10^5 ergs showed only 84% of the tumor nucleic acid specific activity of the control group. Both these experiments definitely confirm the existence of an indirect effect of radiation on the desoxypentose nucleic acid turnover rate. One group of animals received 60 r (1.4×10^5 ergs) total body x-irradiation with 180 kv x-rays and both the tumors and livers showed a significant depression in the turnover rate. (NSA)

1537

Lawrence, J. H. and H. B. Jones. THE BIOLOGICAL EFFECTS OF RADIATION: PROGRESS REPORT FOR THE PERIOD JANUARY 1947 TO JUNE 1947. University of California. June 30, 1947. 6p. (NP-516)

Two growth inhibiting factors, dibenzanthracene and a folic acid derivative, were found not to inhibit desoxyribose nucleic acid metabolism as does ionizing radiations. It was possible to irradiate bone marrow effectively using a radioactive colloid which is highly concentrated in bone marrow. The depression of bone marrow nucleic acid metabolism did not seem to be as sensitive to irradiation, relative to its general radiosensitivity, as compared to liver. The enzymatic systems responsible for the synthesis of thyroxine were extremely resistant to irradiation in contrast to nucleic acid metabolism. Techniques have been worked out to test the effects of irradiation on various organic metabolic processes using radioactive carbon. (NSA)

1538

Limperos, George. ROENTGEN IRRADIATION OF DESOXYRIBONUCLEIC ACID. III. THE RELATION OF DOSE TO DEGREE OF DEPOLYMERIZATION IN VIVO AND THE INFLUENCE OF OXYGEN TENSION. *Cancer Research* **11**, 325-9(1951).

The degree of depolymerization of DNA extracted from rat thymus 24 hr after roentgen irradiation in vivo, as measured by the structural viscosity and streaming birefringence of the solutions, was found to be directly proportional to x-ray doses of 250 to 1000 r. A reduced oxygen tension (10%) was found to inhibit the depolymerization of DNA, whereas an increased oxygen tension (100%) was found to be relatively ineffective in increasing the depolymerization. A 10% oxygen tension was found to be less effective than thiourea in preventing the involution of rat thymus tissue induced by roentgen irradiation. (NSA)

1539

Limperos, G. and W. A. Mosher. ROENTGEN IRRADIATION OF DESOXYRIBOSENUCLEIC ACID. I. MECHANISM OF THE ACTION OF IRRADIATION IN AQUEOUS SOLUTION. *Am. J. Roentgenol. Radium Therapy* **63**, 681-90 (1950).

Desoxyribose nucleic acid (DNA) in water solution was irradiated with various doses of x-rays from a 120-kv source, at the rate of 1700 r/min; the DNA was placed in petri dishes (10 ml in each dish) and covered with a sheet of duralumin 0.001 in. thick before the irradiation. The DNA was found to be depolymerized in aqueous solution by the x-rays as well as by chemically generated free radicals; thiourea inhibited depolymerization by both means. These results were interpreted as evidence that the mechanism of action of x-rays on the DNA in water solution is indirect, mediated through the production of free radicals from the solvent; additional evidence of the indirect action was obtained by the inability of x-rays to depolymerize the DNA in a dry state, in ethylene glycol, or in frozen aqueous solution. The presence of NaCl and desoxyribonuclease was found neither to inhibit nor increase the depolymerization. There was evidence of hydrogen bonding in the DNA. 20 references. (NSA)

1540

Limperos, G. and W. A. Mosher. ROENTGEN IRRADIATION OF DESOXYRIBOSENUCLEIC ACID. II. PHYSICO-CHEMICAL PROPERTIES OF DESOXYRIBOSENUCLEIC ACID FROM IRRADIATED RATS. *Am. J. Roentgenol. Radium Therapy* **63**, 691-700(1950).

Male albino rats were irradiated from a 120 kv source in groups of 10 in a circular copper cage through a 0.75-mm Cu filter, with a total of 1000 to 2000 r, with or without prior injection with thiourea. The thymus glands were removed immediately or 24 hr later and extracted for DNA. The irradiation of the DNA in vivo produced two effects: (1) when the animals were sacrificed immediately after irradiation, the DNA extracted from the thymus was low in N (due to a splitting off of purine bases); (2) when the animals were sacrificed 24 hr after irradiation, the DNA was almost completely depolymerized. Thiourea injected before irradiation did not inhibit the splitting off of the purine bases from the DNA but did inhibit the depolymerization to some extent. Possible mechanisms for these reactions are suggested. (NSA)

1541

Loofbourov, J. R., A. Oppenheim-Errera, Dorothea G. Loffbourov, and Constance A. Yeats. RELEASE OF NUCLEOTIDES AND NUCLEOSIDES BY DAMAGED LIVING CELLS. *Biochem. J. (London)* **41**, 122-9(1947).

An investigation was made of the role of nucleotides and nucleosides in the increased proliferation-promoting activity of cell-free suspension fluids from cells slowly damaged by lethal radiation (I) as compared with similar fluids from undamaged cells (II). The nucleotide-N and nucleoside- and free purine-N contents of I were respectively about 34 and 5 times those of II. Nucleotides isolated from I, when combined with amino-acids and B-factors found in I, duplicated the proliferation-promoting effect of I. The nucleotide and nucleoside fractions consisted principally of adenine and guanine derivatives. Spectroscopic evidence indicated a synthesis of materials absorbing at 2600 Å, within the living, injured cells during the course of injury. (BA)

1542

Mitchell, J. S. DISTURBANCE OF NUCLEIC ACID METABOLISM PRODUCED BY THERAPEUTIC DOSES OF X- AND GAMMA RADIATIONS. PART I. METHODS OF INVESTIGATION. PART II. ACCUMULATION OF PENTOSE

NUCLEOTIDES IN CYTOPLASM AFTER IRRADIATION. PART III. INHIBITION OF SYNTHESIS OF THYMONUCLEIC ACID BY RADIATION. *Brit. J. Exptl. Pathol.* **23**, 285-313(1942).

The experimental methods are described. Ultraviolet photomicrography was mainly used, but measurements of ultraviolet absorption and fluorescence spectra, and histochemical tests, were also made. Unirradiated and irradiated fixed, unstained biopsy specimens were photographed on the same microscopic field, and the degree of blackening at any point was measured photometrically. Maximum "optical staining" was obtained by use of the wave length 2,537 Å. From these data the effective concentration of the nucleic acids was deduced. (CR)

1543

Moses, M. J., R. DuBow, and A. H. Sparrow. THE EFFECTS OF X-RAYS ON DESOXYRIBOSENUCLEIC ACID IN SITU; QUANTITATIVE CYTOCHEMICAL STUDIES ON TRILLIUM. Brookhaven National Lab. [nd] 1p. (AECU-1162)

X rays are known to reduce the viscosity of solutions of desoxyribose nucleic acid (DNA). This has been interpreted as a depolymerization of the DNA molecule. However, this effect has only been observed on extracted DNA, and it is not known that depolymerization actually occurs in the intact cell. Such evidence has been sought cytochemically, utilizing quantitatively the methyl green reaction for polymerized DNA and the Feulgen reaction for total DNA. Moreover, a modification of the latter reaction involving prolonged 1N HCl hydrolysis measures the rate at which acid degradation occurs and yields further information on the state of the molecule. Living buds of *Trillium erectum* undergoing meiosis were irradiated at 50, 200, and 20,000 r, the latter dose being sufficient to markedly reduce viscosity of DNA solutions. Methyl green and Feulgen reactions were carried out on sections of the Carnoy-fixed anthers. Microphotometric measurements were made of the dye content of pollen mother cell nuclei. In no case did irradiation produce the anticipated decrease in methyl green content. In one experiment, pachytene nuclei, irradiated at 20,000 r showed a 20% increase in methyl green content over controls. The Feulgen reaction (optimal hydrolysis) was not affected, indicating no change in total DNA. However, the degradation of DNA (loss of thymic acid) through prolonged hydrolysis was markedly inhibited after heavy irradiation. From the methyl green results it cannot properly be said that depolymerization of DNA, such as is caused by treatment with hot water or the enzyme DNase, has been induced by irradiation. Indeed, it would seem that the net result has been to increase the stability of the DNA molecule rather than to decrease it.

1544

Paoletti, Mario. EFFECT OF X RAYS ON THE METABOLISM OF THE NUCLEIC ACIDS. *Radioterapia radiobiol. e fis. med.* **4**, 225-36(1951).

The effect of 100 to 200 r of x radiation on nuclear staining of epidermal cells of the guinea pig was investigated. A decrease in nucleic acids, particularly thymonucleic and ribonucleic acids, is suggested. (NSA)

1545

Rubin, B. A. THE RELATION OF NUCLEIC ACID METABOLISM TO THE GENETIC EFFECT OF RADIATION IN BACTERIA. Brookhaven National Lab. [nd] 1p. (AECU-1436)

The report is reproduced here in its entirety.

Levels of continuous radiation (x rays or β rays) which rapidly kill resting bacteria (*E. coli* B/r) permit the growth of metabolizing organisms. When resting cells are inoculated into a fresh medium the inception of growth

(lag) is delayed as a direct function of the radiation dose rate; but when multiplication begins, the rate of increase of cell mass during continuous radiation is equal to that in unirradiated controls and the same final culture densities are reached. Average cell size increases with the number of generations that have occurred during irradiation, but this accounts for only a fraction of the cell mass, the logarithmic increase in viable count makes up the rest. An examination of the mutant population (resistant to streptomycin) in cultures which have grown from 0 (resting) to 14 generations during irradiation indicates that the mutation rate is affected by the radiation dose, but not by the number of genetic reduplications during irradiation. Under the same conditions, changes in nucleic acid metabolism appear which are related to the extent of synthesis that has occurred during the irradiation.

1546

Scholes, George, Gabriel Stein, and Joseph Weiss. ACTION OF X-RAYS ON NUCLEIC ACIDS. *Nature* **164**, 709-10(1949).

The chemical effect of large doses, e.g., 2 to 4×10^6 r units on Na thymonucleate and Na ribonucleate were studied. The irradiation was conducted on 100 ml. solutions containing up to 2% of Na thymonucleate or Na ribonucleate. In every case deamination was caused by the x-rays yielding NH_3 . The production of NH_3 is of the order of 0.1 millimole per 10^8 g-r. In the presence of atmospheric oxygen the yield is greater. Van Slyke amino N determinations indicate a ring opening in the purine or pyrimidine bases. At the same time there is an increase in the amount of titratable acid as determined by titration with phenolphthalein and alkali; the yield is of the order of 0.3 mg equivalents of titratable acid groups per dose of 4×10^6 r. For the separation and identification of any lower molecular fragments formed, x-ray-treated thymonucleate or ribonucleate solutions were electrodyalyzed at room temperature for 40-50 hrs. An increase in dialyzable phosphate and also in inorganic phosphate was observed in the positive pole section. From the negative pole of the dialyzer bases were obtained which could be precipitated by AgNO_3 in acid solution and which were afterwards isolated as a mixture of the picrates. Preliminary experiments have shown that one of these bases is ademine. A second Ag salt was obtained in alkaline solution which after hydrolysis gave a positive pentose test and also gave a small amount of the bases in the form of picrates. This evidence indicates the presence of a small amount of nucleosides. The action of OH radicals produced chemically by means of H_2O_2 and Fe^{++} on thymonucleate and ribonucleate in aqueous solutions at room temperature was studied. From this reaction mixtures of urea and guanidine were isolated from ribonucleate and urea was isolated from thymonucleate. (CA)

1547

Scholes, George and Joseph Weiss. CHEMICAL ACTION OF IONIZING RADIATIONS ON NUCLEIC ACIDS IN AQUEOUS SYSTEMS. *Nature* **166**, 640-2(1950).

Samples of yeast ribonucleic acid and thymus desoxyribonucleic acid are irradiated with x-radiation ranging in intensity from 30,000 to 90,000 r units. The yields of ammonia and inorganic phosphate produced during irradiation are measured with the sample in air, in vacuum, and H_2 . The yields of NH_3 decrease from air to vacuum to H_2 . It is concluded that the attack on the bases in the nucleic acid is predominantly by an oxidative radical, e.g., hydroxyl. Determination of the inorganic phosphate formed under similar conditions shows an increase in yield from air to vacuum to H_2 ; this leads to the conclusion that the H atoms

(produced along with OH from H_2O by the radiation) may also play some part in the degradation of the nucleic acid. (CA)

1548

Skipper, Howard E. and Jack H. Mitchell, Jr. EFFECT OF ROENTGEN-RAY RADIATION ON THE BIOSYNTHESIS OF NUCLEIC ACIDS AND NUCLEIC ACID PURINES. *Cancer* **4**, 363-6(1951).

Roentgen-ray radiation (950 r) has been shown to inhibit the incorporation of radioactive carbon from bicarbonate and formate into viscera nucleic acids and nucleic acid purines over a period of 6 hr. Under similar conditions, fixation of carbon from these compounds into viscera homogenate appeared to be increased somewhat following roentgen-ray radiation. Glutathione had no apparent effect on the radiation-induced nucleic acid inhibition. (NSA)

1549

Sparrow, Arnold H., Montrose J. Moses, and Robert Steele. SENSITIVITY OF CHROMOSOMES TO BREAKAGE BY X-RAYS AND ITS RELATIONSHIP TO THE NUCLEIC ACID CYCLE IN DIVIDING CELLS. Brookhaven National Lab. [nd] 1p. (AECU-790)

The document is in abstract form; it is reproduced below in its entirety.

The number of chromosome breaks produced after irradiation by 50 r of 160 kv x-rays at various stages of the mitotic nuclear cycles have been studied in *Trillium erectum*. Sensitivity, as determined by counting the number of chromosome fragments, shows at least a 50-fold change. It is highest at late prophase and first metaphase and lowest at early postmitotic interphase. Since production of acentric fragments leads to cellular dysfunction and death, it is reasonable to assume that our sensitivity curve is a measure of the ability of the cell to recover from radiation damage.

The experimental modification of the sensitivity of dividing cells (e.g., tumor cells) to x-ray damage would be facilitated by an understanding of the biochemical systems immediately involved. In hopes of delineating some of the factors which determine either high or low sensitivity of the chromosomes to breakage and since metabolism of the nucleic acids has been shown to be easily upset by x- and ultraviolet irradiation, an attempt was made to correlate changes in PNA and DNA during mitosis with sensitivity of the chromosomes to breakage. Microchemical analyses of the DNA and PNA content of *Trillium* pollen mother cells (PMC) at different mitotic stages show no significant change in amount of either DNA or PNA per PMC throughout divisions. The significance of these results in terms of changes in nucleic acid concentration, synthesis, "target" size, and physical effects will be briefly discussed.

1550

Sparrow, A. H. and Florence M. Rosenfeld. X-RAY INDUCED DEPOLYMERIZATION OF THYMONUCLEOHISTONE AND SODIUM THYMONUCLEATE. *Science* **104**, 245-6(1946).

Solutions of 0.2% Na thymonucleate in water and 0.4% thymonucleohistone in 1 M NaCl were irradiated with x-rays. Streaming birefringence, present in both solutions before x-raying, was considerably decreased by 120,000 r and the loss was much greater for the nucleate than for the histone. These changes probably represent a degradation or partial depolymerization of high mol. wt. particles into shorter, more symmetrical chains or segments. These may (1) represent the initial step in the production of gene mutations and chromosomal breaks, and (2) be instrumental in causing a breakdown of the normal nucleic acid metabolism of the cell. (BA)

1551

Taylor, Babette, Jesse P. Greenstein, and Alexander Hollaender. **EFFECTS OF X-RADIATION ON THYMUS NUCLEIC ACID.** *Science* **105**, 263-4(1947).

The effects of x-radiation up to 56,000 r on dialyzed solns. of sodium thymus nucleate (TNA) were studied. Two phenomena were observed: (1) a decrease in viscosity of TNA proportional to dosage of x-rays and independent of temperature, and (2) a progressive and presumably indirect effect manifest at higher temps. and not detected at 0°. Chem. and enzymatic studies indicated that whatever the way in which the particles had been damaged by x-radiation it did not involve a splitting of primary linkages or a rearrangement of spatial configurations necessary for its susceptibility to enzymatic attack. (CA)

1552

Taylor, Babette, Jesse P. Greenstein, and Alexander Hollaender. **EFFECTS OF X-RADIATION ON SODIUM THYMUS NUCLEATE.** *Arch Biochem.* **16**, 19-31(1948).

The effect of X-rays on aqueous solutions of sodium thymus nucleate is apparently to break up the long, fibrous particle into shorter fragments of variable dimensions. The passage from a state of monodispersion to a state of wide polydispersion continues, after the actual irradiation has stopped, for several hours until a new equilibrium is reached. The extent of the change, or the level of that new equilibrium depends on the dose of roentgens delivered and is independent of the time over which that dose is given. The chemical properties and susceptibility to desoxyribonuclease— Mg^{++} of sodium thymus nucleate are essentially independent of the state of polymerization or dispersion as altered by X-rays. (NSA)

1553

Euler, Hans von and L. Hahn. **INFLUENCE OF ROENTGEN RAYS ON ISOLATED CELL NUCLEI.** *Acta radiol.* **27**, 268-80(1946).

Nuclei carefully isolated from calf thymus at pH 4-6 were irradiated with 25,000 and 65,000 r to compare the physiological state of isolated cell nuclei with their state in a living tissue. Nucleoproteins were prepared from the irradiated nuclei and characterized by analysis, and by viscosity, dialysis and adsorption measurements. A study of the properties of the nucleoproteins showed no significant changes due to the irradiation. This result is not interpreted as meaning that the nuclei have totally lost their biological activity. (NSA)

1554

Euler, Hans von and Georg v. Hevesy. **EFFECT OF X-RAYS ON THE NUCLEIC ACID EXCHANGE IN JENSEN SARCOMA TISSUE.** *Kgl. Danske Videnskab. Selskab. Biol. Medd.* **17**, 3-38(1942).

A radioactive phosphate solution was injected into rats with Jensen sarcomas and after 2 hours the nucleic acid of the sarcoma tissue was isolated. In the 2-hour period 2-3% of the nucleic acid P had been replaced from the injected material. The sarcoma tissue contained 9 mg/g of nucleic acid P. Irradiation of the sarcomas with 450 r of X-rays usually caused a 35-50% decrease in nucleic acid formation but some sarcomas were irradiation-resistant and showed no decrease. No significant changes in the free phosphate contents of plasma and liver were produced by the irradiation. In necrotic sarcoma tissue the nucleic acid exchange was 25-50% of that in nonnecrotic tissue. The phosphate P of the sarcoma tissue was exchanged rapidly with that of the blood plasma. X-ray irradiation of 2000 r had no appreciable influence on the rate of renewal of the acid soluble P compounds of the sarcoma. (CA)

1555

Euler, Hans von and Georg v. Hevesy. **ACTION OF X-RAYS ON NUCLEIC ACID METABOLISM IN JENSEN SARCOMA.** *Arkiv. Kemi Mineral. Geol.* **17A**, 60p. (1944).

Experiments in which phosphorus 32 is injected into rats having Jensen sarcoma show that x-radiation inhibits mitosis and, possibly earlier, decreases production of desoxyribonucleic acid in the growing sarcoma, the effect decreasing when the interval between the irradiation and the injection is increased from a few min. to several days. The production is not appreciably affected by fasting. New production of nucleic acid is accompanied by simultaneous degradation of previously formed nucleic acid and, in a degenerating sarcoma, degradation counterbalances or more than counterbalances new production. The contents of free P in the liver and plasma of rats are 58 and 6.5 mg% respectively, and the free and total P contents of the sarcoma are 49 and 298 mg% respectively; these values being unaffected by irradiation. (CA)

Enzyme Studies

1556

Abderhalden, R. **FURTHER STUDIES ON THE APPEARANCE OF KNOWN ORGANIC SPECIFIC PROTEINASES IN URINE AFTER ROENTGEN-RAY TREATMENT.** *Fermentforschung* **16**, 215-20(1939).

The specific known proteinases appearing in the urine after x-ray irradiation of the brain and liver can be detected 6-6½ hrs after the x-rays. The enzyme possesses not only organ but also species specificity. The magnitude of the dose which causes the appearance of cell proteinases of the irradiated organ in the urine amounts to 330 r for the liver, 247.5 r for the brain and 165 r for the hypophysis in the dog. (CA)

1557

Arvy, L., J. A. Boiffard, and M. Gabe. **EFFECT OF LARGE DOSES OF X-RAYS ON THE DISTRIBUTION OF ALKALINE PHOSPHATASES IN SOME ORGANS OF THE MOUSE.** *Compt. rend. soc. biol.* **143**, 233-4(1949).

Histological changes are described in adult white mice given whole body radiation of 2,000 r. The Gomori technique showed characteristic shifts in alkaline phosphatase in the cells of the spleen, intestine, and kidney. (NSA)

1558

Baldini, Mario. **ACTION OF X-RAYS AND SHORT WAVES ON THE URICASE OF PIG LIVER.** *Atti accad. fisicocrit. Siena, Sez. Med.-fis.* **18**, 202-11(1950).

The activity of pig liver uricase extracts, obtained by shaking powdered pig liver with a Na borate solution at pH 9.3 for 3-4 hours, was found not to be substantially influenced by either X-ray or short wave irradiation. (CA)

1559

Barnard, R. D. **A NOTE ON THE DEPRESSION OF BLOOD CHOLINESTERASE LEVEL FOLLOWING X-RAY THERAPY AND ITS BEARING ON THE MECHANISM OF RADIATION SICKNESS.** *Med. Record* **161**, 350-52(1948).

The blood cholinesterase concn. is reduced by x-ray therapy. This change affords an explanation of the cholinergic symptoms of radiation sickness. (CA)

1560

Barron, E. S. Guzman. **EFFECTS OF X-RAYS ON TISSUE METABOLISM.** *Argonne National Lab.* Oct. 29, 1946. 63p. (AECD-2316; CH-3654)

The effect of x-rays, given in a single dose of total body radiation at doses varying from 900 r to 100 r, on the

metabolism of tissues has been studied. Litter-mate rats of the Sprague-Dawley strain were treated with x-rays and sacrificed at different intervals. The metabolism of the following tissues was studied: spleen, liver, kidney, thymus, adrenals, testis, and submaxillary glands. Whenever possible measurements were made of the O_2 uptake in the presence of oxidizable substrates requiring sulfhydryl enzymes for oxidation, as these enzymes, were previously found more susceptible to the action of x-rays. In general, the respiration of all tissues and the oxidation of substrates requiring sulfhydryl enzymes was diminished immediately after irradiation, with thymus as the only exception. Oxidation of pyruvate, of succinate, of d-amino acids and of 1 (+) glutamate—all requiring sulfhydryl enzymes—was inhibited in the different tissues examined. (NSA)

1561

Barron, E. S. Guzman. THE EFFECT OF IONIZING RADIATIONS ON THE ACTIVITY OF ENZYMES, p.10-16 of CONFERENCE ON BIOLOGICAL APPLICATIONS OF NUCLEAR PHYSICS, JULY 12-27, 1948. Brookhaven National Lab. July 1948. 7p. (BNL-C-4(p.10-16))

Results indicate that the biological action of ionizing radiations is due mainly to the products of the irradiation of water. When irradiation is used in small doses this effect may be limited to the oxidation of the sulfhydryl groups present in the cell, either the fixed -SH groups of the protein moiety of enzymes or the soluble -SH groups. Oxidation of the first will produce inhibition of the sulfhydryl enzymes; oxidation of the second group will produce inhibition of cellular division and cellular growth. When irradiation is used in larger doses it will produce protein denaturation by a series of mechanisms still unknown. The first effects are reversible; the last are irreversible and the extent of recovery will be determined by the rate of protein synthesis. (Author's Summary)

1562

Barron, E. S. Guzman and S. Dickman. STUDIES ON THE MECHANISM OF ACTION OF IONIZING RADIATIONS. II. INHIBITION OF SULFHYDRYL ENZYMES BY ALPHA-, BETA-, AND GAMMA-RAYS. J. Gen. Physiol. 32, 595-605(1949).

Two crystalline SH enzymes, phosphoglyceraldehyde dehydrogenase and urease, were used to study inactivation by ionizing radiations. Po in citrate buffer served as a source of α -radiation; a solution of $Sr^{90}Cl_2$ was the source of β -radiation; and Ra enclosed in a brass tube was the source of γ -rays. The SH enzymes were inhibited by these radiations through the oxidation of -SH groups essential for their activity. When the -SH groups were protected from oxidation by conversion to mercaptides, a usually inhibiting dose of γ -rays was without effect and the enzyme could be completely reactivated with glutathione. The mechanism of inhibition by ionizing radiation is through H_2O_2 , and partial protection can be obtained by small amounts of catalase. The oxidation of -SH groups by H_2O_2 which causes inhibition is variable. In α -radiation oxidation by H_2O_2 contributes 30% of the inhibition, but in radiation by β -rays this proportion is much greater. Ionizing radiations affect proteins either by oxidation of their -SH groups, which is a reversible phenomenon, or by denaturation and destruction of molecules, which is an irreversible phenomenon. The first requires fewer ionizing radiations. (CA)

1563

Barron, E. S. Guzman, Sherman Dickman, John A. Muntz, and Thomas P. Singer. STUDIES ON THE MECHANISM OF ACTION OF IONIZING RADIATIONS. I. INHIBITION OF ENZYMES BY X-RAYS. J. Gen. Physiol. 32, 537-51 (1949).

Dilute solutions of sulfhydryl enzymes (phosphoglyceraldehyde dehydrogenase, adenosinetriphosphatase, succinoxidase) showed reduced activity on irradiation by small amounts of x-rays. When the inhibition was partial the enzyme was reactivated on addition of glutathione. When the inhibition was more complete, reactivation was only partial. These observations are interpreted as being due to oxidation of the -SH groups of the protein by the products of water irradiation, the radicals OH and O_2H , and H_2O_2 and atomic oxygen. The mechanism of the oxidation is best explained by Weiss's theory (Nature, 153, 748, 1944; 157, 584, 1946). The irreversible inhibition which occurs when the dose of x-rays is increased is attributed to protein denaturation. Inhibition of the non-sulfhydryl enzymes trypsin, catalase, and ribonuclease, which required larger amounts of x-rays, is attributed to protein denaturation. These experiments are further evidence that inhibition of enzymes by ionizing radiations is due to the indirect action of the products of irradiated water rather than to direct ionization of the enzyme through collision with ionizing radiation. (NSA)

1564

Barron, E. S. Guzman, Sherman Dickman, Thomas P. Singer, and John A. Muntz. THE EFFECT OF X-RAYS ON THE ACTIVITY OF ENZYMES. University of Chicago, Metallurgical Lab. Aug. 1946. 44p. (MDDC-1131; CH-3806)

Moderate amounts of x-rays produce inhibition of enzymes requiring the presence of -SH groups for activity. This inhibition is due to oxidation of the -SH groups to the inactive disulfide as shown by enzyme reactivation with glutathione. Inhibition and reactivation were performed on phosphoglyceraldehyde dehydrogenase, adenosinetriphosphatase, and succinoxidase. Besides this oxidation of -SH groups, X-rays have been shown to irreversibly inhibit the activity of enzymes. This inhibition has been attributed to protein denaturation. A number of crystalline enzymes—trypsin, catalase, lactic dehydrogenase, ribonuclease—when tested under the conditions of our experiments (with the enzyme, the rate-limiting step in the reaction) were not inhibited by moderate amounts of x-rays. However, inhibition was produced on diminishing the amount of enzyme. These inhibitions are produced by nonspecific protein denaturation produced by large amounts of irradiation. (ADD)

1565

Barron, E. S. Guzman and Veronica Flood. THE EFFECT OF X IRRADIATION ON CYTOCHROME C, p.167 of BIOLOGICAL AND MEDICAL DIVISIONS QUARTERLY REPORT, NOVEMBER, DECEMBER, JANUARY, 1949-50, Austin M. Brues, ed. Argonne National Lab. [nd] 1p. (ANL-4401(p.167))

Reduced cytochrome C was easily oxidized on irradiation with hard x rays (200 kv), the oxidation being proportional to the intensity of irradiation. The oxidation produced by 10,000 r was completely reversed on addition of a suitable reducing agent. The ionic yield was 0.55. It seems that this oxidation is produced only by the OH radicals given off on irradiation of water. H_2O_2 had no effect at all since the addition of catalase did not diminish the extent of oxidation. O_2H radicals (presumably formed on reduction of O_2 dissolved in water) seem also to have no effect because the extent of oxidation was not diminished on irradiation in the absence of dissolved O_2 . On irradiation of ferricytochrome C in neutral, acid, and alkaline solutions with x-ray intensities of 50,000 and 100,000 r, it was found that cytochrome dissolved in acid solution was more susceptible to the destructive effect of ionizing radiations. On irradiation with 100,000 r in 0.005M HCl there was almost complete disappearance of the big Soret band of the porphyrin nucleus and of the band at 5300 A of ferricytochrome.

1566

Bier, M. and F. F. Nord. THE EFFECT OF CERTAIN IONS AND OF RADIATION ON CRYSTALLINE TRYPSIN. Arch. Biochem. and Biophys. **31**, 335-6(1951).

Ca ions decrease the rate of autodigestion of trypsin; Mn ions also have a stabilizing effect but other ions are without effect. Electrophoresis showed that the active enzyme had a mobile boundary. Ca had no effect on proteolysis of other proteins. The sensitivity of the enzyme to radiation (high-intensity electron bursts of about 1 μ sec from a 3-mev capacitron) is higher at pH 2.6 than at pH 8. Frozen buffered solutions of trypsin were less sensitive to radiation than liquid preparations. (CA)

1567

Billen, Daniel and Herman C. Lichstein. THE EFFECT OF X RADIATION ON THE ADAPTIVE FORMATION OF FORMIC HYDROGENLYASE IN ESCHERICHIA COLI.

Oak Ridge National Lab. [nd] 1p. (AECU-1705)

The report is reproduced here in its entirety.

During studies on the mechanism of X radiation effects on microorganisms carried out in this laboratory, the adaptive formation of formic hydrogenlyase in resting cell suspensions of *Escherichia coli* was investigated. The data show that X irradiation of resting cell suspensions of *E. coli*, in doses of 60,000 r or greater, prevents completely the ability to synthesize formic hydrogenlyase, while having no effect on preformed hydrogenlyase activity. (NSA)

1568

Brandt, C. L., P. J. Freeman, and P. A. Swenson. THE EFFECT OF RADIATIONS ON GALACTOZYMASE FORMATION IN YEAST. Science **113**, 383-4(1951).

Galactozymase formations in yeast have been subjected to radiation of ultraviolet light, visible light, and x radiation, resulting in a different reaction to each. Photodynamic action of visible light seems to be confined to the surface whereas ultraviolet light appears to strike deeper and prevents galactozymase synthesis. X rays appear to prevent division but have no effect on galactozymase formations. (NSA)

1569

Brooks, Robert E. and Herman Schneiderman. STUDIES IN THE HYALURONIDASE-HYALURONIC ACID SYSTEM. II. THE REACTION OF X-IRRADIATED HYALURONATE WITH HYALURONIDASE. University of California Los Angeles. July 14, 1949. 22p. (AECU-425; UCLA-36)

It has been reported (AECU-170) that x-irradiation of bovine vitreous humor potassium hyaluronate results in a loss in viscosity due to irradiation, and a continuing loss for about five hours after irradiation. In this report, the interaction of the irradiated hyaluronate with hyaluronidase and the effect of x-irradiation on the enzyme are considered. The previously reported loss in viscosity has been confirmed experimentally with bovine vitreous humor and human umbilical cord hyaluronate. The viscosity dilution curve for irradiated and nonirradiated hyaluronate is similar in the range of concentrations used. For a similar initial relative viscosity, the reaction of hyaluronidase with irradiated hyaluronate is much slower than with nonirradiated hyaluronate. Suggestions are made as to the mechanisms of these effects and their relation to radiation damage. Results suggest that any damage resulting from x-irradiation of the hyaluronidase-hyaluronic acid system is due more to the reduction in viscosity of the hyaluronic acid than to the action of x-rays on the enzyme. (NSA)

1570

Carter, C. E. THE EFFECT OF TOTAL BODY X-RADIATION ON THE ACTIVITY OF SEVERAL ENZYMATIC SYSTEMS OF RAT SPLEEN. Oak Ridge National Lab. Apr. 26, 1949. 24p. (AECU-231)

Because of the sensitivity of mammalian hematopoietic tissue to damage from ionizing radiation, rat spleen has been assayed for enzymatic activity catalyzing the degradation of benzoyl-L-arginineamide, glycyl-L-leucine, leucyl-glycylglycine, and glycyldehydroalanine, substrates for intracellular proteolytic enzymes; the phosphate activated desamidation of glutamine; and the degradation of ribonucleic and desoxyribonucleic acid in spleens from normal animals and from animals exposed to x-radiation. The late effects of whole body x-radiation on the several enzyme systems of rat spleen are described. Of the enzymes studied, ribonuclease shows the most striking alteration of activity following radiation, depressions of activity being found 24 hours following exposure to doses as low as 100 r. In rats exposed to 500 r, ribonuclease activity in spleen is severely depressed and no evidence of recovery was found in periods up to 12 days following radiation. (NSA)

1571

Collinson, E., F. S. Dainton, and B. Holmes. INACTIVATION OF RIBONUCLEASES IN DILUTE AQUEOUS SOLUTIONS BY HYDROXYL RADICALS. Nature **165**, 267-9 (1950).

Hydroxyl radicals (OH) were prepared in aqueous solution in 3 ways, (a) $\text{Fe}^{++} + \text{h}\nu$; (b) $\text{Fe}^{++} + \text{H}_2\text{O}_2$; (c) $\text{H}_2\text{O}_2 + \text{h}\nu$. In every case it was shown, with suitable control expts. that (OH) was responsible for the inactivation of ribonuclease. It was also shown that the inactivated enzyme competes effectively with the active enzyme for (OH). These results suggest that the effects produced by absorption of nuclear radiations in living tissues may, in some cases, be due to the action of free radicals. (CA)

1572

Dale, Walter M. THE EFFECT OF X-RAYS ON ENZYMES. Biochem. J. (London) **34**, 1367-73(1940).

Irradiation of crystalline carboxypeptidase and of partly purified polyphenoloxidase by x-rays leads to the destruction of a constant amount of enzyme by a given dose of x-rays independent of the concentration of the enzyme. In consequence the per cent destruction of the enzyme increases with decreasing concentration. This is shown for a wide range of x-ray doses and concentration of the enzymes, very small doses of x-rays acting in the same way as big doses. When carboxypeptidase is irradiated while mixed with its substrate, no destruction occurs. Enzymes apparently play an important part in explaining the effect of radiation on living tissue. Their concentration and state during irradiation will determine the biological effect of radiation in those cases where they are a limiting factor in cell metabolism. (BA)

1573

Dale, W. M. THE EFFECT OF X-RAYS ON THE CONJUGATED PROTEIN D-AMINO-ACID OXIDASE. Biochem. J. (London) **36**, 80-5(1942).

The enzyme d-amino-acid oxidase can be split into alloxazine adeninedinucleotide (prosthetic group) and a highly specific protein. The high chemical activity of these components allows the measurement of the effect of x-rays on them in concns. as low as they occur in living matter. The radiosensitivity of these 2 substances is greatest when they are irradiated separately. When irradiated as a mixture, however, the inactivation is almost entirely due to the inactivation of the protein since the dinucleotide is "protected" by the presence of the protein. (BA)

1574

Dale, W. M., J. V. Davies, and W. J. Meredith. FURTHER OBSERVATIONS ON THE PROTECTION EFFECT IN RADIATION CHEMISTRY. Brit. J. Cancer **3**, 31-41(1949).

Solutions of carboxypeptidase and of alloxazine-adenine dinucleotide were irradiated with x-rays. The constancy of

the ionic yield was verified. The protective power of various substances (e.g. glucose, urea, dimethylurea, thiourea, dimethyl-thiourea, egg albumin, colloidal S, and $\text{Na}_2\text{S}_2\text{O}_3$) was determined. Compounds containing S had a very high protective power. With certain substances the protective power diminished as the concentration increased. This was observed only with carboxypeptidase. (CA)

1575

Dale, W. M., L. H. Gray, and W. J. Meredith. THE IN-ACTIVATION OF AN ENZYME (CARBOXYPEPTIDASE) BY X- AND ALPHA-RADIATION. *Phil. Trans. Roy. Soc. (London)* **242**, 33-62(1949).

The inactivation of aqueous solutions of pure crystalline carboxypeptidase by x-radiation and α -radiation has been studied. It is concluded that in each case the enzyme molecules are inactivated by collision with a labile product resulting from the ionization of the water. The x-ray ionic yield is approximately constant and equal to about 0.18 enzyme molecules inactivated per ion pair of water at all enzyme concentrations between about 2×10^{-4} and 2×10^{-2} g enzyme/ml. At lower concentrations a smaller x-ray ionic yield was observed. At an enzyme concentration of 3×10^{-5} g/ml the results are not affected by the absence of dissolved oxygen. The α -ray ionic yield is only about one-twentieth of the x-ray ionic yield, that is, 0.01 molecules of enzyme inactivated per ion pair of water, and appears to increase about twofold over the concentration range 5×10^{-6} to 5×10^{-3} g enzyme/ml. An attempt is made to correlate the x-ray and α -ray ionic yields with what is known concerning the spatial distribution of the ions. It is concluded that the extremely high concentration of positive ions which forms the core of the α -ray track probably plays a very significant role in the general radiochemistry of α -radiation. The small inactivation of carboxypeptidase brought about by exposure to α -rays could be ascribed to the secondary electrons (δ -rays) which travel clear of the α -ray track and it is not certain that any inactivation of enzyme is brought about by the primary α -ray ionization. (NSA)

1576

da Silveria, Marieta and M. Deodata Azevedo. PROTECTION OF AN ENZYME AGAINST THE DESTRUCTIVE ACTION OF NEUTRONS. *Arch. portugaises sci. biol. Suppl.* **10**, 114-16(1951).

The presence of Na_2SO_3 prevented inactivation of aqueous fumaric hydratase by a Ra-Be neutron source, whereas the presence of L-cysteine had no protective effect. The Na_2SO_3 increased the enzymatic power of the hydratase both before and after irradiation. (NSA)

1577

Dinning, James S., I. Meschan, Cecilia K. Keith, and Paul L. Day. EFFECTS OF X-IRRADIATION AND URETHANE TREATMENT ON CHICKEN BONE MARROW ENZYMES. *Proc. Soc. Exptl. Biol. Med.* **74**, 776-7(1950).

Mature hens were given a single whole-body x-irradiation of 300 r. This treatment markedly reduced the bone marrow endogenous respiration, choline oxidase, and succinoxidase. The intraperitoneal injection of urethane also reduced marrow choline oxidase, and reduced succinoxidase but to a lesser degree. Both x-irradiation and urethane treatment rendered the chickens leucopenic. (NSA)

1578

Doherty, David G. PROTECTION OF ALPHA-CHYMOTRYPSIN AGAINST GAMMA RADIATION. Oak Ridge National Lab. [nd] 1p. (AECU-1794)

Electrophoretically homogeneous α -chymotrypsin was prepared from bovine pancreas by the usual procedures, lyophilized, and utilized for all the radiation experiments.

Enzymatic activity was determined by following the rate of hydrolysis of glycyl-L-tyrosine amide with a potentiometric formol titration. Dilute chymotrypsin solutions were exposed to γ -ray dosages from 1000 to 120,000 r from a cobalt source at the rate of 140 r/min; maximum inactivation of 30% was obtained at the 40,000-r level. Dry chymotrypsin irradiated at dosages from 500,000 to 10,000,000 r gave essentially similar results although shifted to a higher dosage level. The K_m remained unchanged from all the irradiated enzyme, indicating that there had been no alteration in the active centers of the enzyme molecule. This was substantiated by binding studies with a radioactive tagged substrate by the procedure of Doherty and Vaslow (*J. Am. Chem. Soc.*, (1952) Jan.). Since substrates protect enzymes against radiation damage it might be expected that competitive inhibitors would show the same effect. Adjustment of concentrations might yield conditions which would give protection but very little inhibition. Thus chymotrypsin was irradiated with 20,000 r in the presence of several inhibitors, i.e., acetyl-L-tyrosine, 4-p-hydroxyphenyl-3-acetamino-butanone-2, p-hydroxyphenyllactic acid, and phenyllactic acid. Inhibition varied from 2 to 50% while, with the exception of phenyllactic acid, which gave 50% protection, the other inhibitors afforded complete protection to the enzyme. Different inhibitors are being investigated in an effort to gain some insight into the structural part of the enzyme damaged by radiation. (Entire report)

1579

Doyle, William L. THE DISTRIBUTION OF PHOSPHATASES IN THE RABBIT APPENDIX AFTER X-IRRADIATION. *Am. J. Anat.* **87**, 79-117(1950).

Staining reactions and quantitative determinations of the acid and alkaline phosphatase content of the cells of the rabbit appendix at various levels from the mucosa to the muscularis are presented for the normal animal and for rabbits irradiated with a total-body dose of 625 r of penetrating x-rays. 29 figures. 12 references. (NSA)

1580

Feinstein, Robert N., Carrie L. Butler, and Daniel D. Hendley. EFFECT OF WHOLE-BODY X-IRRADIATION AND INTRAPERITONEAL HYDROGEN PEROXIDE ON MOUSE LIVER CATALASE. *Science* **111**, 149-50(1950).

Whole-body x-irradiation (17 r/min, total 800 r) reduces liver catalase progressively from 9% (2 min after irradiation) to 82% (1 week), with no later data available. Twenty milliequivalents H_2O_2 , injected as 4% solution, decreases the same activity 32% after 2 min, 41% after 2 hr, showing a slow irregular recovery from the 4th day on with 10% activity decrease at the end of 4 weeks. Agreement with in vitro experiments is discussed. (CA)

1581

Forssberg, Arne. ACTION OF ROENTGEN RAYS ON THE ENZYME CATALASE. *Acta radiol.* **27**, 281-93(1946).

The mode of action of roentgen rays on living organisms is discussed and the variation in sensitivity of the cells of different organs, tissues, and species is noted in relation to the conditions under which radiation is administered. To study the problem of whether the action of radiation is direct, the hit theory, or indirect, a "radiochemical" action, the author has investigated the effect upon the enzyme catalase using a solution of the purified crystalline substance. By varying the catalase concentration of the solution, the intensity of irradiation, and the gas concentration of the solution, results were obtained which indicate a complicated interaction of the irradiation products formed in the solvent with the enzyme, as well as some direct action upon the enzyme molecules. Results obtained when

the enzyme solution was frozen seems to indicate that the reaction is predominantly in the immediate vicinity of the enzyme molecule. (R)

1582

Forssberg, A. MECHANISM OF THE ACTION OF X-RAYS ON ENZYMES IN WATER-SOLUTION. *Nature* 159, 308-9 (1947).

Pure crystalline catalase was diluted to 3.7×10^{-6} g per ml at pH 7.4 and exposed in the absence of oxygen to a dose of 1.24×10^4 r of x-rays at 275 r/min.; 54% of the enzyme was inactivated. The effect of adding various organic compounds in 0.1 to 0.2 millimol concentration was tested. Unsaturated acids (fumaric and maleic) partly protected the enzyme against inactivation by x-rays. Related saturated acids (malonic and succinic) had no effect. Cysteine increased and cystine decreased the percentage of enzyme inactivated; similarly glutathione increased and oxidized glutathione decreased the percentage inactivated. If Weiss's view that the action of x-rays on aqueous solutions is due to free H atoms and OH radicals is accepted, and it is assumed that the H atoms inactivate catalase, these results can be explained by involving the reactions $2\text{RSH} + \text{OH} \cdot \rightarrow \text{RSSR} + \text{H}_2\text{O} + \text{H} \cdot$. A 10^{-5} to 10^{-3} molar concentration of iodide ions protects catalase against inactivation by x-rays. (AWM)

1583

Frederic, J. HISTOLOGICAL AND HISTOCHEMICAL STUDY OF THE SKIN OF THE GUINEA PIG TREATED WITH X-RAYS. *Arch. biol. (Liège)* 60, 79-101(1949).

A study was made of morphological changes produced by x-rays in the epidermis, and, in particular, in the histological elements containing substances with -SH groups (sulfhydryles). The skin of the paws of 32 guinea pigs was irradiated with 3,000, 2,000, and 1,500 r. The histological and histochemical evolution is shown on nine microphotographs. (NSA)

1584

Gierlach, Z. S. and A. T. Krebs. THE TETRAZOLES AS INDICATORS OF RADIATION DAMAGE. *Army Medical Department*. Jan. 3, 1950. 14p. (NP-1419)

Plant seeds irradiated with x-rays and then treated with tetrazolium salts show that the irradiation effect can be detected by changes in the reducing power of the enzyme systems and can be measured by the amount of colored formazan formed. The relation between dose and irradiation effect on the reducing systems can be written in exponential functions with a constant characteristic for the proper enzyme systems. The environment is of great importance. The radiation effect is altered when seeds are irradiated in the wet or dry states, when different pH values are used, or upon pre- or post-treatment with various chemicals, etc. The tetrazolium salts used were 2,3,5 triphenyl tetrazolium chloride, 2,3 diphenyl-5-methyl tetrazolium chloride, and neotetrazolium. 29 references. (NSA)

1585

Holle, Fritz. SERUM CHOLINESTERASE ACTIVITY DURING INFLAMMATION AND X-IRRADIATION. *Z. ges. exptl. Med.* 115, 107-26(1949).

Cholinesterase (I) was determined by titration according to Hall-Lucas. The normal range of total serum I was equivalent to 3.0-4.8 ml 0.01 N NaOH. It was constant for an individual. After inflammation induced by bacteria, there was a short initial increase in I followed by a prolonged decrease, with a rise to normal values after 8-10 days. X-irradiation or a combination of irradiation and inflammation resulted in a decrease lasting for 36-48 hr.

I was probably bound to the plasma colloids of the albumin fraction. The causes for the variation of I are discussed. (CA)

1586

Holmes, B. INACTIVATION OF RIBONUCLEASE IN DILUTE AQUEOUS SOLUTIONS. *Nature* 165, 266-9(1950).

Enzymes in aqueous solution are inactivated by x-rays. However, certain other materials in this solution can protect the enzymes. Thus very little destruction of the enzyme occurred while sufficient glutathione was present to give a definite nitroprusside test for reduced glutathione at the end of the irradiation. Oxidized glutathione also had some protective action. In the case of ribonuclease and probably of other enzymes not containing essential SH groups, there is no evidence that dissolved O_2 or the formation of H_2O_2 plays any essential part in the effects produced by x-rays. (CA)

1587

Jacobsohn, Kurt and Marieta da Silveira. ACTION OF RADIUM AND NEUTRON-SOURCE RADIATIONS ON ENZYMATIC ACTIVITY. *Arch. portugaises sci. biol. Suppl.* 10, 105-6(1950).

Fumaric hydratase in liver extract was not inactivated by prolonged Ra or x radiations but was completely inactivated by a 5-day exposure to an unmoderated Ra-Be neutron source. Thiaminase in fern-leaf extract was not inactivated by either Ra or neutron source. (NSA)

1588

Jacobsohn, Kurt and Marieta de Silveira. ACTION OF NEUTRONS ON ENZYMATIC ACTIVITY. *Arch. portugaises sci. biol. Suppl.* 10, 110-11(1950).

Aqueous fumaric hydratase was not inactivated by exposure to a Ra-Be neutron source moderated by 10 cm of paraffin. It is concluded that only fast neutrons decrease enzymatic activity. Exposure to the unmoderated source slowly inactivated alkaline serum phosphatase and serum cholinesterase. (NSA)

1589

Jacobsohn, Kurt and Marieta da Silveira. INVESTIGATION OF THE MECHANISM OF ENZYMATIC INACTIVATION BY NEUTRONS. *Arch. portugaises sci. biol. Suppl.* 10, 112-13(1950).

Dry fumaric hydratase, prepared by precipitating liver extract with acetone and ether, was not inactivated by irradiation with fast neutrons for the same period of time that completely inactivated the aqueous enzyme. A secondary inactivation effect is attributed to the irradiation products of water. (NSA)

1590

Jacobsohn, Kurt P. and Marieta da Silveira. ON THE MECHANISM OF FERMENTATION INACTIVATION BY NEUTRONS. *Bull. soc. chim. biol.* 33, No. 7, 673-80(1951).

The enzymes fumaric hydratase, urease, alkaline serum phosphatase, serum cholinesterase, and thiaminase, either dry or in various aqueous substrates, were irradiated with x-ray, Ra, and Ra-Be sources. The fumaric hydratase, in particular, undergoes a sudden and total inactivation on irradiation by fast neutrons in aqueous fermentative extracts; no effect is noted when dry or when irradiated by slow neutrons, γ rays, or x rays. The conclusion that the destruction of the fermentation system is caused by products of neutron-induced decomposition of water is discussed. (NSA)

1591

LeMay, Marjorie. THE ABSENCE OF INHIBITION OF -SH ENZYMES BY MODERATE AMOUNTS OF X RADIATION, p.92 of DIVISION OF BIOLOGICAL AND MEDICAL

RESEARCH QUARTERLY REPORT, MAY, JUNE, JULY, 1950. Argonne National Lab. July 1950. 1p. (ANL-4488(p.92))

An experiment has been designed to determine whether the reduced O_2 uptake by rat tissues following irradiation is due to (1) inhibition of $-SH$ enzymes and not to inhibition of other enzymes concerned with complete oxidation of substrates, or (2) failure of the substrate to diffuse as easily in irradiated tissue as in normal tissue. Results of this experiment indicate that x-ray doses that are high enough to cause hematological changes and death in rats do not cause measurable effects in the metabolism of rat kidney slices nor in the enzyme systems studied, including succinic dehydrogenase. (NSA)

1592

LeMay, Marjorie. EFFECT OF X-RADIATION UPON SUCCINOXIDASE OF RAT KIDNEY. (18772). *Proc. Soc. Exptl. Biol. Med.* **77**, 337-9(1951).

The succinoxidase system, as well as its component enzymes, the $-SH$ enzyme succinic dehydrogenase, and cytochrome oxidase, were determined in rat kidney homogenates within 2 hr after rats were x-irradiated with 400 or 800 r. No inhibition of any of the enzymes was found. The metabolism of kidney slices from rats given the foregoing amounts of x radiation was studied manometrically with sodium succinate and lithium pyruvate substrates. No statistically significant differences were obtained between the oxidative activities of the kidney slices from the control and irradiated animals. The lack of correlation between certain of the in vivo and in vitro effects of irradiation upon enzyme systems is discussed. (NSA)

1593

Ludewig, Stephan and Alfred Chanutin. EFFECT OF X-RAY IRRADIATION ON THE ALKALINE PHOSPHATASE OF THE PLASMA AND TISSUES OF RATS. *Am. J. Physiol.* **163**, 648-54(1950).

The activity of plasma alkaline phosphatase of rats was determined after single and multiple doses of x rays at varying periods after total-body x irradiation. Relatively small decreases in phosphatase activity were found after exposure to 300 r. More marked and prolonged decreases were obtained after 500- and 800-r doses in both fed and fasted animals. Multiple daily radiation with small doses also causes a decrease in plasma enzyme activity. The alkaline phosphatase activity of the thymus is markedly increased during the first two days following irradiation. Small increases are observed in the spleen. Practically no change in enzyme activity is seen in the livers and kidneys of irradiated rats. The changes in the weights of the thymus, spleen, and liver after irradiation are presented. (NSA)

1594

Ludewig, Stephan and Alfred Chanutin. DISTRIBUTION OF ENZYMES IN THE LIVER OF CONTROL AND X-IRRADIATED RATS. *Arch. Biochem.* **29**, 441-5(1950).

The activities and percentage distributions of nonmercapto enzymes (catalase, esterase, arginase, rhodanese, and alkaline phosphatase) in rat liver homogenate and liver connective tissue are presented. The alkaline phosphatase is the only enzyme whose activity is greater in connective tissue than in liver homogenate. The activities of these enzymes in the nuclei, mitochondria, submicroscopic particles, and supernatant fluid of liver homogenates are presented. Total-body exposure of rats to a dose of 500 r of x rays has no effect on the activity of nonmercapto enzymes. (NSA)

1595

Manoïlov, S. E. and L. F. Semenov. INACTIVATION OF DESOXYRIBONUCLEIC ACID DEPOLYMERASE BY X RAYS. *Doklady Akad. Nauk S.S.S.R.* **71**, 359-60(1950).

Irradiation with 250-11, 400 r of X-rays (no specifications of frequency range) of the enzyme preparations (made according to Mac Carthy) in distilled H_2O and examination of the activity of the product on polymerized nucleic acid, prepared by numerous techniques and used with 0.15 M $MgCl_2$ activator, showed that 1000 r dosage lowers the activity very significantly and total inactivation results with 11,400 r dosage (93.6%). No action was noted at 250 r level. (CA)

1596

Mazia, Daniel. EFFECTS OF RADIATION ON ENZYME SYSTEMS, p.7-9 of CONFERENCE ON BIOLOGICAL APPLICATIONS ON NUCLEAR PHYSICS. Brookhaven National Lab. July 1948. 154p. (BNL-C-4(p.7-9))

The aim of this investigation was to set up a system adapted to the study, at a biochemical level, of the special problems of chromosomal effects of radiation. The system studied has been an enzyme-substrate system incorporated into a monomolecular film. The enzyme-substrate films have an expectedly high sensitivity to radiation. Calculations suggest that in such a "solid phase" system the effects of a single ionization or ionization product may spread over a considerable area of the film. The sensitivity of an enzyme-substrate system may depend on its physical organization. The films described are more sensitive to x-rays than comparable solution. The sensitivity varies with the compression of the film. These findings are discussed in relation to the problem of intrinsic sensitivity. (S.V.S.)

1597

Mazia, Daniel and Gertrude Blumenthal. INACTIVATION OF ENZYME-SUBSTRATE FILMS BY SMALL DOSES OF X-RAYS. *Proc. Natl. Acad. Sci. U. S. A.* **34**, 328-36(1948).

Pepsin-albumin films may be inactivated by small doses of X-rays. Doses of about 100 r produce about 50 per cent inactivation. The sensitivity to radiation depends on the physical configuration of the molecules. It may be varied by surface compression. Calculations suggest that the effects of a single radiation event (ionization or radical production) may be spread to include a large number of enzyme molecules. (NSA)

1598

Mazia, Daniel and Gertrude Blumenthal. INACTIVATION OF ENZYME-SUBSTRATE FILM BY SMALL DOSES OF X-RAYS. *J. Cellular Comp. Physiol. Suppl.* **1**, **35**, 171-86 (1950).

It has been shown that one may, using an enzyme-substrate film, set up in a biochemical system which has a sufficiently high sensitivity to radiation to permit comparisons with more complex biological systems and which is adapted to the study of some of the variables, particularly structural variables, with which radiation biologists are concerned. The radiation sensitivity of the system depends on its structure and may be varied by physical manipulation so that some of the factors involved in intrinsic sensitivity may be investigated. The evidence that the high radiation sensitivity of this system may depend on an intermolecular spreading, over considerable distances, of the effects of a single primary radiation event is discussed. (NSA)

1599

Petrakis, N. L., F. M. Ashler, and R. L. Ferkel.

HISTOCHEMICAL STUDIES ON THE EFFECT OF TOTAL BODY X-IRRADIATION ON THE ALKALINE PHOSPHATASE, RIBO- AND DESOXYRIBONUCLEIC ACID CONTENT OF RAT LIVER CELLS. Naval Radiological Defense Laboratory. June 2, 1949. 18p. (AD-126(B))

The quantitative histochemical changes in alkaline phosphatase, ribo- and desoxyribonucleic acid were studied in rat liver epithelium for a six-day period after 600 r and 1,500 r total body x-irradiation. With the 600 r exposure, a temporary decrease in phosphatase occurred in the nuclei and cytoplasm of these cells during the first six hours. This was followed by an increase above normal at the one, two, and six day time intervals studied. A temporary increase in ribonucleic acid concentration occurred during the first 24 hours, followed by a decrease below normal at the two- and six-day interval. The concentration of nuclear desoxyribonucleic acid was decreased at the two- and at the six-day intervals. An immediate increase in all three of the above substances was found during the first 24 hours after 1,500 r x-irradiation. All observations indicate that the rat liver epithelium is histochemically sensitive to these levels of x-irradiation. (NSA)

1600

Ross, M. H. and J. O. Ely. **NEUTRON EFFECTS ON ALKALINE PHOSPHATASE OF RAT INTESTINE.** Am. J. Roentgenol. Radium Therapy **62**, 723-5(1949).

The effect of neutron irradiation of 200 n on the alkaline phosphatase concentration of the rat duodenum was investigated in 10 albino rats of the Brooklyn strain. An increase in alkaline phosphatase activity at pH 9.0 was found in the nuclei and nucleoli in the cells of the crypts of Lieberkühn when β -glycerophosphate, desoxyribonucleic acid, ribonucleic acid, adenylic acid, guanylic acid, or diphenyl phosphate was used as the source of organic phosphorus. No difference could be observed between the phosphatase activity of the cells in the villi of the duodenum from irradiated and from nonirradiated animals. No difference in phosphatase activity at pH 7.0 was noted in any of the parts of the duodenum of irradiated and nonirradiated animals with any of these substrates. (NSA)

1601

Setlow, R. B. **THE INACTIVATION OF CATALASE BY DEUTERONS AND HEAT.** Arch. Biochem. Biophys. **34**, 396-408(1951).

The inactivation of beef red-cell catalase by fast deuterons, heat, and a combination of the two has been reported. The data have been analyzed quantitatively in terms of the target theory of ionizing radiation and the theory of absolute reaction rates. Evidence for the existence of at least two forms of stable catalase has been presented. The data are shown to indicate two possible alternative molecular weights (about 250,000 and 130,000) for catalase. (NSA)

1602

Sherman, Frederick G. and Herman B. Chase. **EFFECTS OF IONIZING RADIATIONS ON ENZYME ACTIVITIES OF YEAST CELLS. I. RELATION BETWEEN ANAEROBIC CARBON DIOXIDE PRODUCTION AND COLONY PRODUCTION AT INTERVALS AFTER X-RADIATION.** J. Cellular Comp. Physiol. **33**, 17-25(1949).

Saccharomyces cerevisiae, grown in Reader's solution was irradiated 30 minutes with 3,000 r per minute. The maximum effect of approximately 30% inhibition of CO₂ production occurred in 2-4 hours after starting irradiation and remained constant for 24 hours. At the same time approximately 85% of cells were unable to form visible colonies on solid medium. Between 12 and 24 hours after irradiation anaerobic CO₂ production on a per cell basis declined progressively. Colony-producing cells which re-

mained after irradiation proliferated more rapidly than nonirradiated cells, presumably under the influence of substances released from damaged cells. (CA)

1603

Sherman, Frederick G. and Herman B. Chase. **EFFECTS OF IONIZING RADIATIONS ON ENZYME ACTIVITIES OF YEAST CELLS. II. INFLUENCE OF DILUTION ON X-RAY-INDUCED INHIBITION OF ANAEROBIC CARBON DIOXIDE PRODUCTION AND COLONY FORMATION.** J. Cellular Comp. Physiol. **34**, 207-19(1949).

Yeast grown in a synthetic (I) and a nonsynthetic (II) medium was irradiated with 90,000 r in 30 minutes. Dilution of the cell suspension increased the effect of irradiation on anaerobic CO₂ production of yeast grown in I but CO₂ production was not affected much in yeast grown in II. Dilution gave only a small increase in the effect of radiation on colony formation in yeast grown in I but did not change the effect of yeast grown in II. When non-irradiated cells were mixed with irradiated buffer or irradiated cells were mixed with nonirradiated buffer the amount of CO₂ was reduced at lower concentrations of cells but the effect of radiation became nil at higher cell concentrations. Inhibition of colony formation occurred only at low cell concentrations when irradiated buffer was remixed with non-irradiated cells. X-rays exert effects on cell division and enzymes associated with anaerobic CO₂ production through different mechanisms. (CA)

1604

Sonnenblick, B. P. **REDUCTION OF NEOTETRAZOLIUM CHLORIDE BY X-RADIATED ROOT TIP CELLS OF ALLIUM.** Biol. Bull. **101**, 230(1951).

Reports by several investigators (Antopol, Glaubach, Goldman, Narahaia, Sonnenblick) indicate that the enzyme systems responsible for the reduction of neotetrazolium chloride (NT) are present in many living tissues. The faintly yellow salt undergoes a progressive series of color changes and is finally converted to an insoluble purple-black granular compound located characteristically in the cytoplasm about the nuclear membrane. Studies on the mechanism of NT reduction show that active -SH groups play a significant role in the process. Since reports exist indicating that moderate amounts of x-rays effect inhibition of sulfhydryl enzymes in vivo and in vitro, it was decided to study the reduction of NT by x-radiated root tip cells. Dormant bulbs and actively growing roots were irradiated and excised roots subsequently tested at various periods following exposure. Roots were given 300, 600, or 900 r, while bulbs were exposed to 300, 1200, or 2400 r. Tests indicate that cells given treatments causing a moderate frequency of chromosomal aberrations show no inhibition in the speed and intensity of NT reduction. With dosages causing severe nuclear damage, the results are variable, but even after such exposures NT reduction can proceed as well as in control material. To interpret these results the following must be considered: (1) the greater sensitivity of dilute aqueous solution of enzymes to irradiation than when accorded the protection of other substances within cells, (2) the possibility of unequal inhibition of different sulfhydryl enzymes by x-rays, and (3) the role played by other than -SH enzymes in NT reduction. Very recently LeMay of Cambridge Univ. reported no inhibition of the -SH enzyme succinic dehydrogenase in rat kidney slices and homogenates following 400 r or 800 r of total body x-radiation, a result in vivo contrasting markedly to the effect in vitro of x-rays on dilute solutions of that enzyme.

1605

Tahmisian, T. N. and D. M. Adamson. **OXIDASE IN-**

CREASE IN MELANOPLUS DIFFERENTIALIS EGGS CAUSED BY X-IRRADIATION. J. Exptl. Zool. 115, 379-97(1950). (ANL-4401)

When diapause eggs of *Melanoplus differentialis* are x-irradiated (200 kv, 15 ma) with dosages ranging from 25,000 r to 200,000 r, the hydroquinone oxidase activity in the eggs is decreased immediately after the exposure. The enzyme activity increases with time so that the highest activity is obtained approximately eight days after exposure. Oxidase activity after irradiation varies in the following sequence: 25,000 r > 50,000 r > 100,000 r > 200,000 r > control. The oxidase is inhibited by cyanide, carbon monoxide, and heat. Its activity is not affected by azide, phenylthiourea, nor diethyldithiocarbamate. The oxidase is specific for hydroquinone, and in addition, it appears to have some effect on p-phenylenediamine. It does not oxidize the -SH group in glutathione nor cysteine. Resorcinol or tyramine hydrochloride are also not oxidized by the enzyme. The nitroprusside test reveals that the native -SH groups are not oxidized as long as 124 hours after x-irradiation. However, by 18 days practically all -SH groups are absent. The increase in hydroquinone oxidase may be due either to the abolition of check mechanisms that normally repress oxidation or to an increase in the oxidase itself resulting from the breakdown of zymogens in the egg. (Authors)

1606

Woodard, Helen Quincey. **SOME EFFECTS OF RADIATION ON LIVING BONE**, p.161-2 of **INTERNATIONAL CONGRESS OF RADIOLOGY**, 6th Congress, London. 1950.

Preliminary work indicated that the bones of young adult mice contain sufficient alkaline phosphatase for quantitative measurement. As the phosphatase activity diminishes markedly after moderate doses of roentgen rays, the bones are suitable test objects for the quantitative study of the effects of irradiation in vivo. Accordingly about 1.5 cm. of one hind leg of each of a series of male albino mice of about 20 gms. body weight was irradiated, the remainder of the body being shielded. At intervals of 4 to 50 days after irradiation the mice were killed, and the alkaline phosphatase activities of irradiated and control legs were compared. The majority of the experiments were performed with 185 kv roentgen rays with a half value layer of 0.8 mm. copper and a dosage rate of 160 r/min. With doses of 900 r to 1,500 r a depression of phosphatase activity was apparent in the irradiated bones in 4 to 7 days, with a minimum value after 10 to 20 days. This was followed by partial recovery, but, even after a dose of 900 r, recovery was not complete in 50 days. In some cases there was indication of a secondary depression beginning at about 35 days. After doses of 3,000 r phosphatase activity was almost abolished, and there was no evidence of recovery in periods up to 45 days. A study was also made of the effects of roentgen rays with half value layers of 6 mm. of aluminium and of 4 mm. of lead.

H₂O₂ Problem

1607

Alper, Tikvah. **HYDROGEN PEROXIDE AND THE INDIRECT EFFECT OF IONIZING RADIATIONS. Nature 162, 615-16(1948).**

Experiments undertaken on bacteriophage S 13 in vitro apparently have shown that when the phage is in dilute solution the hydrogen peroxide formed by ionizing radiations will inactivate it. And in experiments on "indirect effect" of ionizing radiations on this phage the ratio of ionic yield for direct action only to ionic yield in dilute

solution is of importance for gaining an insight into the "active radical" mechanism. (NSA)

1608

Barron, E. S. Guzman, Veronica Flood, and Betty Gasvoda. **STUDIES ON THE MECHANISM OF ACTION OF IONIZING RADIATIONS. V. THE EFFECT OF HYDROGEN PEROXIDE AND OF X-RAY IRRADIATED SEA WATER ON THE RESPIRATION OF SEA URCHIN SPERM AND EGGS. Biol. Bull. 97, 51-5(1949).**

The results of experiments on the sea urchin sperm respiration rate after the addition of hydrogen peroxide to the medium and after x-irradiation of the medium are presented. The hydrogen peroxide was used at concentrations of 0.01 - 0.0001 M in a 1:200 sperm solution; x-ray dosages of 50,000 - 200,000 r were given. Total inhibition by hydrogen peroxide occurred at 0.001 M concentration; the inhibition decreased with peroxide concentration and approached zero at 0.0005 M. When sea water was irradiated with 200,000 r, a 60% sperm inhibition occurred; 50,000 r produced a 10% inhibition, while the addition of catalase, previous to the sperm addition and after irradiation, had no effect on the inhibition. Since the sea water irradiated with 200,000 r gave no positive test for hydrogen peroxide it is postulated that inhibition is not due to the action of H₂O₂ but to stable organic peroxides. (NSA)

1609

Barron, E. S. Guzman and Betty Gasvoda. **PRELIMINARY REPORT; HYDROGEN PEROXIDE FORMATION ON X IRRADIATION OF WATER WITH HARD AND SOFT X RAYS, p.164-6 of BIOLOGICAL AND MEDICAL DIVISIONS; QUARTERLY REPORT, NOVEMBER, DECEMBER, JANUARY, 1949-50, Austin M. Brues, ed. Argonne National Lab. [nd] 3p. (ANL-4401(p.164-6))**

Hydrogen peroxide formation on irradiation of distilled water by hard x rays (200 kv) and by soft x rays (50 kv, 40 ma) was measured by colorimetric determination at the end of irradiation. On irradiation with an intensity of 100,000 r there was formation of 4 µg/cc with hard x rays, and of 1.3 µg with soft x rays. There was a small increase on irradiation with soft x rays when the water was stirred with a magnetic stirrer. (NSA)

1610

Barron, E. S. Guzman and Betty Redfield. **PROGRESS REPORT: STUDIES ON THE MECHANISM OF ACTION OF IRRADIATED WATER ON CELL METABOLISM, p.78-81 of DIVISION OF BIOLOGICAL AND MEDICAL RESEARCH QUARTERLY REPORT, MAY, JUNE, JULY, 1950, Austin M. Brues, ed. Argonne National Lab. [nd] 4p. (ANL-4488(p.78-81))**

It was shown previously (Barron et al., Biol. Bull. 97, 51-6(1949)) that the respiration of sea-urchin sperm was inhibited when the cells were suspended in x-irradiated sea water or artificial sea water. The mechanism of this inhibition is still unknown. Possibility of ClOH formation was tested, but none was detected. Consideration of the influence of electrolytes on H₂O₂ formation in x-irradiated water and of effects of x-irradiated water on sperm respiration gave indeterminate results. (NSA)

1611

Barron, E. S. Guzman and L. Seik. **BIOCHEMISTRY AND PHYSIOLOGICAL CHEMISTRY, p.101-5 of DIVISION OF BIOLOGICAL AND MEDICAL RESEARCH; QUARTERLY REPORT, AUGUST, SEPTEMBER, OCTOBER, 1951, Austin M. Brues, ed. Argonne National Lab. [nd] 5p. (ANL-4713(p.101-5))**

The role of H₂O₂ in the biological effects of ionizing radiation was investigated by determination of the amount of H₂O₂ produced after x irradiation of H₂O, the effect of

H_2O_2 on the metabolism of bacteria and yeast, the respiration of marine eggs and sperm, and the oxidation of glutathione and dihydrodiphosphopyridine nucleotide. From these experiments it was concluded that the role of H_2O_2 in the effects of ionizing radiation on the substances and biological processes mentioned is negligible. Specific activity was determined for some of the contents of an aquarium that was seeded with C^{14} -containing *Scenedesmus* 3 yr ago and sealed. Results of the analyses appear to approximate the true isotope effect, which seems to be about 8% or less between mixed organic and inorganic carbonate. (NSA)

1612

Bonet-Maury, P. THE FORMATION OF HYDROGEN PEROXIDE IN WATER EXPOSED TO IONIZING RADIATIONS, p. 42 of INTERNATIONAL CONGRESS OF RADIOLOGY, 6th Congress, London. 1950.

It seems that hydrogen peroxide is formed by different mechanisms under the action of X-rays (from H radicals and dissolved oxygen) and of α rays (from OH radicals). Interpreting these facts in the light of recent theories leads to the consideration of irradiated water as an oxy-reduction system (a solution of H and OH radicals) in which action on the dissolved material depends not only on such physico-chemical factors as temperature, concentration of the dissolved material, pH, energy of activation, etc., but still more on the nature and intensity of the radiation conditioning the initial geometrical distribution of the radicals in the liquid. This geometrical factor constitutes an essential characteristic of the chemistry of ionizing radiations.

1613

Bonet-Maury, P. and M. LeFort. THE FORMATION OF H_2O_2 IN WATER IRRADIATED WITH X-RAYS AND ALPHA RAYS. *Compt. rend.* 226, 1363(1948).

Water was irradiated with x-rays of wavelength 0.9 Å and with α -rays from Rn and Po. The amount of H_2O_2 formed with x-rays at 20° was greatly dependent on the concentration of dissolved O_2 in the water. No H_2O_2 was formed in water completely freed of dissolved O_2 . With α -rays at 20° it was observed that the yield of H_2O_2 was independent of the amount of dissolved O_2 and linearly dependent on the amount of irradiation. (CA)

1614

Dustin, P., Jr. and C. Gompel. ACTION OF HYDROGEN PEROXIDE ON CELL MITOSIS IN THE MOUSE INTES-TINE. *Compt. rend. soc. biol.* 143, 874-5(1949).

Dilute solutions of H_2O_2 were injected intraperitoneally in adult mice. A few hr later the intestinal wall showed a decrease in number of normal mitotic figures, and the presence of numerous pycnecrotic nuclei similar to those seen after X-ray irradiation. Similar nuclear lesions appeared in the thymus. (CA)

1615

Evans, T. C. EFFECTS OF HYDROGEN PEROXIDE PRODUCED IN THE MEDIUM BY RADIATION ON SPERM-ATOZOA OF *ARBACIA PUNCTULATA*. *Biol. Bull.* 92, 99-107(1947).

Heavily irradiated water (over 100,000 r) was found to have deleterious effects on sperm placed therein. These effects were reduction of survival time and delay in first cleavage when such treated sperm were used to inseminate fertile eggs. The injury became more pronounced the greater the irradiation dose and the longer the sperm remained in the irradiated water. The chief, if not the only, agent responsible for these effects of irradiated water was hydrogen peroxide. This was shown by chemical test, by similarity of its action with that of hydrogen peroxide, and by removing the toxicity with catalase extract. The effects of hydrogen peroxide on fertility and subsequent cleavage

time are discussed regarding possible interpretations of similar reactions of the sperm to more direct effects of roentgen radiation. (auth)

1616

Wagner, R. P., C. H. Haddox, R. Fuerst, and W. S. Stone. THE EFFECT OF IRRADIATED MEDIUM, PEROXIDE AND CYANIDE ON THE MUTATION RATE IN *NEUROSPORA*. *Genetics* 35, 137-8(1950).

Biochemical mutations have been induced in *Neurospora crassa* at a rate significantly higher than the control rate by treating the conidia with nutrient broth which had previously irradiated with ultra-violet light, and also by treating the conidia with hydrogen peroxide and with potassium cyanide. The mutations were detected after having been passed through the sex cycle. The rates induced by these various agents are not significantly different from one another, but are significantly lower than the rate induced by direct irradiation with ultra-violet. The types of biochemical mutants produced, as far as they have been identified, do not seem to be any different from those induced by direct irradiation. These results with *Neurospora* fully confirm in all important respects the results obtained by Stone et al. (1947, 1948) and Wyss et al. (1948) using bacteria, and definitely establish the production of mutants by indirect irradiation, as well as by hydrogen peroxide which has been postulated to be one of the mutagenic agents formed as a result of irradiation. (G)

1617

Weiss, Joseph. ACTION OF IONIZING RADIATIONS ON AQUEOUS SOLUTIONS. *J. chim. phys.* 46, 593-6(1949).

In a lecture delivered in Paris, the author outlined his views on the action of ionizing radiations on aqueous solutions. Unlike photochemical agents, for which water is transparent and the primary action is localized in the dissolved substance, the ionizing agents act primarily upon water molecules. Electron transfers lead to the formation of ions H_2O^+ and H_2O^- which decompose into ($H^+ + OH$) and ($OH^- + H$) respectively, thus producing neutral fragments OH and H, capable of various interactions with a number of dissolved substances. Several examples of such reactions and their physico-chemical characteristics are given. The importance of these studies in the field of radiobiology is shown by certain transformations of organic compounds obtained by the author and explained according to his views, (irradiation of phenols, amino acids, etc.). (NSA)

1618

Wyss, O., J. B. Clark, F. Haas, and W. S. Stone. THE ROLE OF PEROXIDE IN THE BIOLOGICAL EFFECTS OF IRRADIATED BROTH. *J. Bact.* 58, 151-7(1948).

There is a marked similarity between certain biological effects produced by ultraviolet irradiation of nutrient broth and by the addn. of H_2O_2 to broth. The effects of either can be negated by catalase. Because the direct action of peroxide on the cells in the absence of an org. substrated failed to increase the mutation rate, it is probable that the results are due to the interference of an org. peroxide in some metabolic function. Whether the catalase reacts with the org. peroxide (or some oxidized mol.) or only with the H_2O_2 in equil. with it, is not known. In either case, since the cells studied contain active catalase, it is necessary to postulate that some reaction must occur such as the union of the labile substance with an anabolic enzyme which protects the mutating mol. from the catalase of the cell. (CA)

Low Temperature Studies

1619

Allen, Bennet M., Ole Arne Schjeide, and Lynette B. Hochwald. THE INFLUENCE OF TEMPERATURE UPON

THE DESTRUCTION OF X-RAYED HEMATOPOIETIC CELLS OF TADPOLES. J. Cellular Comp. Physiol. **38**, 69-82(1951). (UCLA-93)

The object of this work is to determine the influence of temperature upon the destruction of the hematopoietic cells of tadpoles of *Rana catesbiana* exposed to a dosage of 500 r hard x rays. Counts in 426 tadpoles were made and the percentage of destroyed cells was determined. Temperatures continuously maintained at different levels from 0 to 11°C hold destruction evenly to a very low percentage which increases rapidly from 13 up to 33.5°C—the highest temperature tolerated. Experiments at temperatures up to 23°C are upon a basis of 24 hr. The destruction and rapid resorption reaches a maximum at 33.5°C. Low temperatures applied immediately after x-ray treatment are as effective as if applied during and after irradiation, and the rate of destruction increases proportionally to subsequent temperature increase. The destruction rises very slowly in x-rayed tadpoles kept at 4.5 and 10°C through a period of 10 days. Visible destruction of x-rayed hematopoietic cells of tadpoles is due to destructive reactions subsequent to irradiation conditioned by the temperature at which they are reared. (NSA)

1620

Allen, Bennet M., Ole Arne Schjeide, and Lynette B. Hochwald. **RELATION OF LOW TEMPERATURES TO X-RAY INJURY OF HEMATOPOIETIC TISSUE OF TADPOLES.** Proc. Soc. Exptl. Biol. Med. **73**, 60-2(1950).

The hematopoietic cells of tadpoles occur in the caudal portion of the kidneys and undergo extensive mitotic division. They are destroyed by hard X-rays with a dosage of 500 r, leaving very few remaining after the lapse of 7 days. 196 tadpoles of *Rana catesbiana* were used in these expts. A study of cell destruction in tadpoles refrigerated at 0–5.5°C showed that these low temps. preserve all but a very small per cent during the 24 hr of refrigeration. The ratio of destruction in the refrigerated compared with that at normal temps (averaging 18.9°C) ranged from 1:6 to 1:33. In one series of 58, tadpoles refrigerated for 4 days showed extremely little cell destruction, while those removed at the end of 2 days and maintained for 1 day or 2 days at normal temp. showed a very great amount of destruction. Refrigeration before and during X-ray treatment did not give results appreciably different from those produced by refrigeration after irradiation. Thus, refrigeration prevents the degeneration of x-rayed hematopoietic cells but does not prevent the primary injury that leads to their degeneration at normal temps. (BA)

1621

Bachofer, C. S., C. F. Ehret, and S. Mayer. **PRELIMINARY REPORT; EFFECT OF TEMPERATURE ON INACTIVATION OF BACTERIOPHAGE BY X RAYS**, p.170 of BIOLOGICAL AND MEDICAL DIVISIONS; QUARTERLY REPORT; NOVEMBER, DECEMBER, JANUARY, 1949–50, Austin M. Brues, ed. Argonne National Lab. [nd] 1p. (ANL-4401(p.170))

Procedures have been established to determine the rate of inactivation by x rays of T-1 coliphage in broth and in chemically defined media, for liquid, dried, and lyophilized states. Equipment has been designed for irradiation in vacuo at different temperatures with simultaneous registering of temperature. The effect of temperature on x-ray inactivation has been investigated at various points from 77 to 310°K. It has been established that lower temperatures decrease the rate of x-ray inactivation. (NSA)

1622

Cook, Evelyn Vanderwilt. **INFLUENCE OF LOW TEMPERATURE ON RECOVERY FROM ROENTGEN RAYS.** Radiology **32**, 289-93(1939).

Eggs of *Ascaris equorum* (megalocephalia) variety *univalens*, were irradiated at room temp. with 5,000 r and transferred to 5°C and 25°C. Cleavage is delayed from 2 to 5 hr by the irradiation at 25°C but is not completely inhibited. At 5°C the delay in cleavage by x-rays is the same as at 25°C. Eggs irradiated and kept at 25°C show 1–2% normal embryos, but those kept at 5°C show a greater % (maximum 45%) which increases with increase in length of time of storage at 5°C. Storage at 5°C without irradiation produces no injurious effects. Recovery from x-ray injury may occur in the absence of appreciable metabolism. (BA)

1623

Evans, T. C., J. P. Goodrich, and J. C. Slaughter. **RADIOSENSITIVITY OF SKIN OF NEW-BORN RATS. III. SENSITIVITY AT DIFFERENT TEMPERATURES.** Proc. Soc. Exptl. Biol. Med. **47**, 434-7(1941).

New-born rats were irradiated (2010 r) at different temperatures (0–40°C.) and the skin sensitivity increased as the temperature was raised. The rate of heart-beat and O₂ consumption responded to temperature in much the same manner as the radiosensitivity. It is possible that temperature exerts its effect on radiosensitivity through its control of such metabolic processes as these. (BA)

1624

Evans, T. C., J. P. Goodrich, and J. C. Slaughter. **TEMPERATURE AND RADIOSENSITIVITY OF SKIN OF NEW-BORN RATS. IV. EFFECTS OF DECREASED CIRCULATION AND BREATHING DURING IRRADIATION.** Radiology **38**, 201-6(1942).

New-born rats were irradiated under conditions in which the metabolic rate was lowered. In all cases, an increased radio-resistance of the skin toward roentgen ray occurred. (BA)

1625

Evans, T. C., W. A. Robbie, J. P. Goodrich, and J. C. Slaughter. **LOW TEMPERATURE AND RADIOSENSITIVITY OF SKIN OF NEW-BORN RATS. II. RESISTANCE AT DIFFERENT DOSAGES.** Proc. Soc. Exptl. Biol. Med. **46**, 662-4(1941).

Lowering the temperature (0–8°C.) of newborn rats during irradiation increased the resistance of the skin to roentgen irradiation. A dosage increase of 1200–1700 r was required to produce an injury comparable to that of animals rayed at room temperature. The ratio of dosage required at low temperature to the dosage at room temperature decreases from 5 (at 1500 r–cold) to 2.2 (3300 r–cold). (BA)

1626

Hempelmann, Louis H., Theodore T. Trujillo, and Norman P. Knowlton, Jr. **THE EFFECT OF LETHAL DOSES OF X-RAYS ON CHILLED AND THYROIDECTOMIZED ANIMALS.** Los Alamos Scientific Lab. [nd] 15p. (AECU-239; LADC-663)

New-born rats chilled to 2–5°C before exposure to lethal amounts of X-ray irradiation showed an increased survival rate as compared to unchilled control rats. The lowering of the environmental temperature of adult mice exposed to 675 r of x-ray decreased the 30 day survival rate. Adult rats and mice showed no significant increase in the 30-day survival rate when chilled after, or before and after irradiation. Adult rats were not protected from the lethal effects of x-radiation by thyroidectomy. (NSA)

1627

Kempton, J. H. and Louis R. Maxwell. **EFFECT OF TEMPERATURE DURING IRRADIATION ON THE X-RAY SENSITIVITY OF MAIZE SEED.** J. Agr. Research **62**, 603-18(1941).

Repeated expts. show that the x-ray sensitivity of air-dry (8% moisture) seeds of maize depends upon their temp.

during irradiation. Temps. used ranged from -187° to 66°C . Maximum sensitivity occurred for the temp. range 0°C to room temp. Increases or decreases of seed temp. from these values resulted in a reduction of the x-ray sensitivity. (BA)

1628

Lamarque, P. and C. Gros. NEW EXPERIMENTS ON THE RESTORATION FACTOR OF RADIOBIOLOGY. *J. radiol. électrol.* 30, 539-42(1949).

In previous experiments the authors have demonstrated (*Acad. Med.* 1 (1944) Nov.; *J. Radiol. Electrol.* 26, 129 (1944-1945)) that the eggs of *Bombyx mori* exhibit certain restorative properties after being subjected to irradiation, and that refrigeration suspends this restoration. In the present paper, reports are given of three types of experiments: (1) the eggs were irradiated in single doses and incubated immediately afterwards; (2) the radiation was of the fractionated type, consisting of equal dosages 48 hr apart (the eggs were incubated between the treatments); and (3) the eggs were irradiated as in experiment 2 but they were placed in a refrigerator between the first and second, and between the second and third irradiations. Total doses ranged from 300 to 3,000 r for all groups of experiments. In group 1 it was seen that the threshold of efficacy lies at about 1350 r; in order to prevent 50% of the eggs from hatching, it was necessary to use 1500 r. The eggs of group 2 exhibited more restorative power than those of group 1, probably because they were able to restore themselves partially between irradiations. Results of the third group of experiments were identical with those of group 1. This illustrates that the refrigeration serves to suspend the restoration. (NSA)

1629

Latarjet, Raymond. EFFECT OF COLD ON THE RESTORATION OF A YEAST AND A BACTERIUM DAMAGED BY RADIATION. *Compt. rend.* 217, 186-8(1943).

Saccharomyces ellipsoideus, if kept at 5°C . remains metabolically active and is able to inhibit the damage of x-rays. In *Bacillus "paradysenterial Y"* at 5°C . the primary lesion remains latent and develops on rise of temperature. This is because the bacteria are unable to repair the primary damage since there is simultaneous stopping of metabolism at 5°C . Yeast resembles the behavior of *Ascaris ova* studied by E. V. Cook (*Radiology* 32: 289 (1939)). A table states the exposure to x-rays used and also to ultraviolet light. (BA)

1630

Maxwell, Louis R., J. H. Kempton, and Vernon M. Mosley. EFFECT OF TEMPERATURE ON THE X-RAY SENSITIVITY OF MAIZE SEEDS. *J. Wash. Acad. Sci.* 32, 18-24 (1942).

Air-dry seeds were subject to 35 kr (kilo-roentgens; 1000 r) x-rays at 45 kv. The seeds were heated or cooled before, during or after irradiation. To decrease x-ray sensitivity by hot or cold treatments the high or low temperatures must prevail during irradiation. There is a general but varying amount of recovery with time elapsing between x-raying and planting for all the treatments used. (BA)

1631

Patt, Harvey M. and Marguerite N. Swift. INFLUENCE OF TEMPERATURE ON THE RESPONSE OF FROGS TO X-IRRADIATION. *Am. J. Physiol.* 155, 388-93(1948).

The authors found that frog survival was not influenced by altering body temperature during and/or for the first 24 hr after total-body irradiation with 1,000 and 3,000 r. Survival was greatly enhanced when animals were kept in the cold ($5-6^{\circ}\text{C}$.) continuously after exposure. This altered

sensitivity was thought to result from decrease in rate of development of radiation damage (prolongation of the latent period) rather than to any appreciable recovery. When animals were removed from the cold after 60-130 days, there was no change in absolute survival or any clear difference in the time course of deaths from that observed in irradiated animals maintained at 23°C . (YBR)

1632

Patt, Harvey M., Marguerite N. Swift, and Ella B. Tyree. INFLUENCE OF TEMPERATURE ON RADIO-SENSITIVITY IN THE FROG (*RANA PIPIENS*). *Federation Proc.* 7, 90-1(1948).

Influence of temperature on survival after X-irradiation was studied in frogs. In preliminary experiments animals were given total body x-radiation at 23°C and were kept at different temperatures after irradiation. Survival of experimental animals was corrected for the small mortality observed among non-irradiated controls. Results are tabulated. Prolonged survival with low temperature treatment is clearly evident. Some 80-90% of animals kept at 5°C for periods of 3 to 4 months after irradiation have survived a dose which is lethal to animals at 22°C within 3 to 6 weeks. Experiments are in progress to determine whether the altered radio-sensitivity is accomplished merely by a decrease in the rate at which degenerative changes occur or by a more rapid and complete recovery from the effects of irradiation. (FP)

1633

Smith, Wille W., Benjamin J. Highman, J. R. Mitchell, and Henry C. Blount, Jr. EFFECT OF ENVIRONMENTAL TEMPERATURE ON THE RESPONSE OF MICE TO WHOLE BODY ROENTGEN RADIATION. *Proc. Soc. Exptl. Biol. Med.* 71, 489-501(1949).

Young male mice were irradiated in groups of 10 with approximately 500 r delivered by a 170-kv machine at a focal distance of 50 cm and a dose rate of 56-64 r per minute, the radiations being screened through 0.55 mm of Al and 0.25 mm of Cu. In the first six experiments, approximately half of the animals were previously acclimatized to the temperature conditions to which they were subjected after the radiations; in the 30°C . environment, 46% of those acclimatized died compared to 63% of those not acclimatized, while in the 10°C . environment, 52% of those acclimatized died in comparison to 71% of those not acclimatized. Leucocyte counts made on the first and fourth days after irradiation showed no difference attributable to the temperature. In the last three experiments, when the mice were caged singly and thus were unable to huddle together, 69% in the 10°C . room died compared with 39% in the 30°C . room. The results show that the net effect of a sufficiently cold environment is to lower the resistance of mice to the lethal action of x-rays; subjection to the environment previous to the irradiation favors survival. It was also noted that mice kept in a 30°C . environment, which die following irradiation, frequently show fatty changes in the liver. (NSA)

1634

Suguira, K. THE EFFECT OF HIGH AND LOW BODY TEMPERATURES UPON THE GROWTH OF IRRADIATED MOUSE SARCOMA 180. *Radiology* 37, 85-93(1941).

X irradiation of 500, 750, and 100 r was given in vivo to 7 days old (5-8 mm) sarcomas. Within 2 hr after x-ray treatment the animals were exposed to ultra short radio waves at a potential of 17 or 18 volts for 5 to 30 min; the short wave treatment was repeated on 5 for 6 successive days. X-ray treatment of 500 r alone caused 3% regressions, when combined with heat 20% regressions; with 750 r x-rays alone 15% regressions and combined with

heat 45% regressions resulted; with 1000 r alone 50% and in combination with heat 75%. Transplants of sarcoma 180 were made into mice kept for 1 to 3 days in a refrigerator at 3–5°C, they were then returned to the low temperature environment for 4 weeks. Tumor growth was retarded during the 1st week but simulated that of the controls thereafter. Takes occurred in 100% of the animals. When tumors were removed from refrigerated animals and transplanted to normal mice at 1, 2, and 3 weeks, takes were similar to the controls. Mice bearing 7-day old sarcoma 180 were refrigerated at –10°C. and after death were kept at 3°C, for 48–72 hr. The tumors were then transplanted to normal mice; except for a 1 week delay in growth transmissibility was not affected. Growth capacity of the sarcoma was completely destroyed if the host was sacrificed by a blow or anesthesia and the body kept at 22°C. for 18 hr. Tumors, 7-day old, were inordinated with dosages of 500 r, 750 r, and 1000 r and within 3 hr the animals were placed in 3 to 5°C refrigerators and kept there for 4 weeks. With 500 r no tumor regressions occurred although there were 3% in the controls. With 750 r alone there were 15% and with refrigeration, 12%; with 1000 r alone 50% regressed and with refrigeration only 27%. Small fragments of tumor weighing approx. 6 mg were placed upon filter paper moistened with Locke-Ringer soln. wrapped in parafilm and placed in thermos bottles with solid CO₂, removed at varying intervals (1–168 hr) thawed to room temperature and inoculated into normal mice. Growth was only slightly inhibited, the takes numbering 80 to 90%. (BA)

1635

Suskind, S. R. RESUSCITATION OF HEAT-INACTIVATED SEEDS BY X-RADIATION. *J. Heredity* **41**, 97-102(1950).

Previously reported resuscitation of heat-inactivated seeds by x-radiation was not confirmed. Changes in humidity and subsequent changes in the moisture content of the seeds caused considerable variation in lethal temperature. A refined technique using a modified Abderhalden drying apparatus and constant boiling liquids, proved to be an accurate and versatile method for the heat treatment of biol. materials. (auth)

1636

Trudova, R. G. EFFECT OF TEMPERATURE ON THE SENSITIVITY OF WHEAT GERMINATION TO X RADIATION. *Doklady Akad. Nauk. S.S.S.R.* **79**, No. 2, 353-6 (1951).

Effects on the mitotic activity of the root-tip meristem of wheat of 500 r of x radiation prior to exposure at 0, 20, and 36°C and of 250, 500, 1000, and 2000 r following exposure to these temperatures are presented graphically. (NSA)

Radiation Chemistry of Aqueous Solutions

1637

Allen, Alexander J., Robert E. Steiger, Mary A. Magill and Rachel G. Franklin. AMINO ACIDS, ACYLAMINO ACIDS, DIPEPTIDES, OCYL DIPEPTIDES AND DERIVATIVES OF THESE COMPOUNDS. II. EFFECTS OF IRRADIATION WITH CATHODE RAYS AND ULTRAVIOLET LIGHT. *Biochem. J.* **31**, 195-204(1937).

Solutions of several amino acids and a large number of derivatives of amino acids and dipeptides were submitted to the action of cathode rays and ultraviolet light. In every case the compounds underwent a change and NH₃ was liberated. The absorption after irradiation was usually shifted toward the longer wave lengths. Possible reaction mechanisms are given. (CA)

1638

Allen, A. O. RADIATION CHEMISTRY OF AQUEOUS SOLUTIONS. *J. Phys. & Colloid Chem.* **52**, 479-90(1948).

Water irradiated by 1 mev cathode rays or x-rays decomposes to H and H₂O₂, the latter subsequently decomposing to yield O. The decomp. is reversible and comes to a standstill when the H pressure over the water reaches 1 or 2 cm. Previous claims that water is stable to x-rays resulted from failure to detect the very small concn. of decomp. products present at the steady state. More densely ionizing radiations yield higher steady state H pressures; β -rays from tritium (av. energy 5 kv) give 10 cm or more, cyclotron deuterons (8 mev), pile radiation (mixed γ -rays and fast neutrons) give 1 atm. or more, and γ rays apparently give a still higher value. All types of radiation break up H₂O to free radicals H and OH. The products, mol. H and H₂O₂, form by dimerization of these radicals in regions where they are produced in relatively high concn. Radicals that escape by diffusion into the main body of water react with the products, reducing or oxidizing them back to H₂O by a chain reaction process analogous to the gas-phase combination of H and Cl mols. The fraction of radicals that escape is smaller the more densely ionizing the radiation; hence the steady-state concn. of H for fast-electron or pile radiation was found to be greatly increased by the presence of solutes that react with solute. Two possible theories are suggested for the regular increase of initial yield with ionization. (CA)

1639

Anderson, R. S. and B. Harrison. THE QUANTITATIVE EFFECT OF X-RAYS ON ASCORBIC ACID IN SIMPLE SOLUTION AND IN MIXTURES OF NATURALLY OCCURRING COMPOUNDS. *J. Gen. Physiol.* **27**, 69-75(1943).

Data are presented on the disappearance of ascorbic acid in inorganic soln. under irradiation with x-rays. The presence of serum albumin or plasma does not materially affect the reaction, but in the presence of rat muscle this is considerably smaller. (CA)

1640

Barron, E. S. Guzman and Veronica Flood. THE OXIDATION OF SULFHYDRYL-CONTAINING SUBSTANCES BY IONIZING RADIATIONS, p. 116-40 of MEDICAL AND BIOLOGICAL DIVISIONS QUARTERLY REPORT, FEBRUARY, MARCH, APRIL, 1948, Austin M. Brues and Hermann Lisco, eds. Argonne National Lab. May 1, 1948. 25p. (ANL-4163(p.116-140))

The oxidation of the sulfhydryl groups of glutathione, 2,3-dimercaptopropanol, and propane 1,3-dithiol, under the action of ionizing radiations produced by x-rays and γ rays, has been studied. X-ray dose varied from 500-5,000 r, and γ radiation from 270 to 1,380 r. In mildly acid solutions (pH 5 or below) glutathione was not appreciably oxidized by 500 r. At pH values above 6, oxidation was readily measurable. The amount of oxidation, at constant pH values and constant -SH content was proportional to the amount of radiation. Oxidized glutathione was not reduced by the ionizing radiations produced by x-rays or γ rays. A micromethod for the colorimetric determination of sulfhydryl groups is presented. The biological significance of these experiments is discussed. (auth)

1641

Bonet-Maury, P. and M. Frilley. PRODUCTION OF H₂O₂ IN WATER UNDER THE ACTION OF X-RAYS. *Compt. rend.* **218**, 400-2(1944).

An exptl. detn. of the ratio of the quantity of H₂O₂ produced under definite conditions to the energy absorbed by the water. The peroxide is titrated photocolormetrically.

The energy absorbed is calculated as the no. (N) of pairs of ions per cc in terms of the number of roentgens measured at the surfaces of the water, the absorption coeff. of the water, and the thickness of the water irradiated. The concn. in H_2O_2 increases with N. It is independent of the wave length and the time of irradiation. The method is therefore applicable to the detn. of the absorbed energy regardless of the kind of ionizing radiation employed. It is accurate to 5%. (CA)

1642

Burton, Milton. **ELEMENTARY PROCESSES IN THE RADIATION CHEMISTRY OF WATER AND IMPLICATIONS FOR RADIOBIOLOGY**, p.42-3 of **INTERNATIONAL CONGRESS OF RADIOLOGY**, 6th Congress, London. 1950.

In the radiation chemistry of aqueous systems, primary ionization processes are more important than primary excitation processes. The ionization mechanism can be divided into three stages: ionization, neutralization, decomposition (Eyring, Hirschfelder and Taylor). Slow moving "radiations" which produce a high density of ionization (e.g., protons or alpha particles) are more effective than fast-moving ones giving a low density (e.g., beta particles and electrons from absorption of X- or γ -rays). The heavy particles readily produce H_2O_2 and H_2 in pure water, but special means are required to demonstrate chemical effects from the fast moving radiations. This was achieved by Allen and Ghormley, who also showed that the difference is, in fact, one of velocity and not of mass, by demonstrating that the slow-moving electrons emitted in the radioactive decay of tritium produce chemical effects typical of high density ionization. The neutralization process has been examined by Magee and Burton. There are two mechanisms: (1) capture of an electron by a positive ion, followed by dissociation of the excited molecule produced; and (2) interaction with neighbouring molecules, from which decomposition does not necessarily result. In water, the electron primarily emitted is slowed down to thermal velocities and ultimately captured in a dissociative process yielding atomic hydrogen and the hydrated OH-ion. It is the latter which reacts with hydrated H-ion formed in the ionization column and neutralizes it. The chemical effects observed in water and biological systems are related to four elementary phenomena. (1) H and OH radicals primarily produced enter into back reactions involving H_2O_2 . Allen has explained the behaviour of radio-sensitizers (e.g., Br- or I-ion) on this basis. (2) H and OH radicals may react with reducible and oxidizable entities present in biological systems. (3) The microscopic effect of production of high local concentrations of H-ion in the column or of rather high concentrations of OH-ion in its periphery. The associated changes of pH might profoundly affect any labile molecule locally present (Franck). (4) When a hit and ensuing ionization occurs deep within an organic molecule the probability of chemical change (mutation) may be less than when the hit occurs near the surface. Per unit volume large targets may be less effective than small targets.

1643

Casati, Annibale. **UNIFIED THEORY OF THE MECHANISM OF ACTION OF X RADIATION. "REDUCING POWER" AND "SECONDARY CHEMICAL ACTION."** *Radiol. med.* **37**, 1020-4(1951).

The mechanism of decomposition of chemical substances by x rays is discussed solely in relation to the ionizing action of the radiation. The secondary chemical action is considered to be the intermediate formation of unidentifiable and unrecoverable substances which react with less radiosensitive substances to give the observed results. Thus, an aqueous solution is considered to be a mixture of

radiosensitive H_2O and insensitive solute. A discussion is given of the protective effect of a solute having great chemical affinity for the decomposition products of H_2O on the stability of the other solutes. (NSA)

1644

Dainton, F. S. **ON THE EXISTENCE OF FREE ATOMS AND RADICALS IN WATER AND AQUEOUS SOLUTIONS SUBJECTED TO IONIZING RADIATION.** *J. Phys. & Colloid Chem.* **52**, 490-517(1948).

From a consideration of the molecular structure of water, electron-impact data on water vapor, and the general mechanism of energy loss of fast charged particles passing through matter, it is concluded that the primary radiochemical act in water vapor is in part ionization, with formation of H_2O^+ , and H^+ (and OH), and OH^+ (and H), and in part excitation, probably with dissociation to H (^2S) and OH (in either the $^2\Pi$ or $^2\Sigma$ states). Charge neutralization and ion-neutral molecule reactions result in more H atoms and OH radicals being formed. Effects of radical recombination and wall adsorption on the ionic yield of water vapor and its dependence on dose rate are discussed. The kinetics of the radiolysis of pure water and of indirect action on solutes are discussed, and it is concluded that in high solute concentrations the ionic yield should be independent of both solute concentration and dose rate. At low solute concentration under conditions where only a fraction of the available radicals react with the solute, $\text{H}_2 + \text{H}_2\text{O}$ are to be expected among the primary products and the ionic yield becomes a function of the dose rate and solute concentration. Very preliminary results are presented on the X- and γ -ray induced and the hydrogen peroxide-photosensitized polymerization of acrylonitrile and show the OH group to be present. The kinetics of these reactions indicate that H atoms and OH radicals are formed by the action of X- and γ -rays on water and that these species are probably not uniformly distributed but exist in high local concentration. (auth)

1645

Dale, W. M. **ACTION OF X-RAYS ON AQUEOUS SOLUTIONS INCLUDING THE RELATIONSHIP BETWEEN RADIATION EFFECT AND CHEMICAL STRUCTURE**, p.43-4 of **INTERNATIONAL CONGRESS OF RADIOLOGY**, 6th Congress, London. 1950.

The action of ionizing radiations on substances in aqueous solution is partly direct and partly indirect, the indirect effect being preponderant at the level of concentration which occurs in tissues and cells. In certain cases the indirect effect can be proved by the fact that the ionic yield is independent of the concentration of the solute over a wide range. Only at extreme dilution is there a falling off in the efficiency of radiation. In other cases this independence does not occur even at higher concentrations, although the radiation action is still mainly indirect. Examples of this type of reaction are the deamination of amino acids and the liberation of sulphur from thiourea. The effective agent in the indirect action of radiation is generally assumed to be OH radicals and H atoms formed from the solvent (water). The presence of a second solute able to react with radicals will reduce the radiation effect on the original one by competing for these radicals. The first solute, therefore, appears to be "protected" by the second solute. The degree of protection afforded can be used as a measure of the radiosensitivity of various solutes of different molecular structure when the size of their molecules and their concentration is taken into account. Substances of low molecular weight with special atomic grouping show wide differences in response to radiation. The simple theory of sharing of radicals by solutes is not sufficient to explain fully the protection effects observed,

since the protective power per unit mass of substance is dependent on the concentration of this substance (phenomenon of the "changing quotient"). The specificity of the deamination of amino acids and their derivatives by X-rays again demonstrates the dependence of the radiation effect on the structure from which the amino group is split off.

1646

Dale, W. M. and J. V. Davies. **LIBERATION OF HYDROGEN SULFIDE BY X-RADIATION FROM CYSTEINE AND GLUTATHIONE.** *Biochem. J.* **48**, 129-32(1951).

The oxidation of the thiol of glutathione or proteins to the disulfide form is considered to be a biologically important step. These experiments reveal that apart from any reversible oxidation there are also irreversible changes produced by x-rays leading to the liberation of H_2S . However, it is not known whether this is an oxidation or reduction process. The discovery of the H_2S is due to the fact that the present method of investigation made it possible to determine accurately the thiol group within a minute fraction of 1%. Although amino acids in general are deaminated by x-radiation, with cysteine the radiation energy seems to be used for H_2S production and not for deamination. The instability of glutathione is well known, and these experiments show that glutathione responds to radiation with production of H_2S , except for a sharp depression at about pH 5.5. (CA)

1647

Dale, W. M., J. V. Davies, and C. Gilbert. **THE KINETICS AND SPECIFICITIES OF DEAMINATION OF NITROGENOUS COMPOUNDS BY X-RADIATION.** *Biochem. J.* **45**, 93(1949).

Experiments are described, showing the deamination by x-rays of some amino acids and their derivatives, polypeptides, and related nitrogenous compounds; the relationship between the ionic yield and the radiation dose had been studied in detail for glycine. The ionic yield rose from 0.3 to 2.9 for very dilute to nearly saturated solutions; the ionic yield for dry glycine was 2.96. An explanation of the high ionic yield with glycine is presented in terms of a hypothesis assuming either a chain reaction or the formation of radicals by excitation in addition to charge neutralization. The continuous rise of the ionic yield is interpreted as being caused by recombination of radicals competing with deamination even at the highest concentrations of glycine, due to a low affinity of glycine to radicals. The explanation offered, although consistent with the experiments described, is concluded to be somewhat unsatisfactory in view of the radiation effects on thiourea. The biological significance of the results is discussed. (auth)

1648

Dale, W. M., J. V. Davies and C. Gilbert. **THE DEAMINATION OF GLYCINE BY ALPHA-RADIATION FROM THE DISINTEGRATION OF BORON IN A NUCLEAR REACTOR.** *Biochem. J.* **45**, 543-6(1949).

The deamination of glycine by the densely ionizing particles from the disintegration of boron by slow neutrons in a nuclear reactor was studied; an account of the necessary technique is given and the dosimetry is fully discussed. The ionic yields for the liberation of ammonia were 0.17 and 0.56 for the 1 and 20% solutions of glycine, respectively, being 15 and 19% of that due to x-radiation. The higher efficiency of deamination by this radiation compared with the inactivation of an enzyme by α rays from radon and its products is discussed. (NSA)

1649

Dale, W. M., W. J. Meredith, and M. C. K. Tweedie. **MODE OF ACTION OF IONIZING RADIATIONS ON AQUEOUS SOLUTIONS.** *Nature* **151**, 280-1(1943).

Experiments on the x-irradiation of a wide range of concentrations of carboxypeptidase showed that the proportion of the molecules inactivated was determined by the ratio of the dose to the initial concentration and that it increased as the ratio increased. This may be written $y/y_0 = f(D/y_0)$, where y_0 and y are the concentrations before and after receiving a dose of D roentgens. It is necessary to postulate that the energy received from the radiation forms a quantized intermediate product—perhaps "activated water"—which distributes the energy between the active and inactive enzyme molecules, inactivating the former. "Protective" molecules are effective in extremely small concentrations since this transferred energy is distributed between the two or more molecular species. Protection cannot be due to direct absorption of the x-radiation, since quantities are too small to absorb the energy directly; neither can it be due to compound formation, since there are so many protecting compounds. Calculations based on the direct-hit theory also fail to account quantitatively for the results obtained. The formula presented explains results obtained with many different compounds. (CA)

1650

Dunlap, C. E. and F. C. Robbins. **THE EFFECT OF ROENTGEN RAYS, RADON, AND RADIOACTIVE PHOSPHORUS ON THIAMIN CHLORIDE.** *Am. J. Roentgenol. Radium Therapy* **50**, 641-7(1943).

Exposure to radon and to radioactive phosphorus in vitro partially destroyed the activity of aqueous solutions of thiamin chloride as tested on *Phycomyces* and *Phytophthora*. Large doses of x-rays had no effect. Exposure of thiamin to large doses of radon did not result in splitting the molecule with subsequent selective destruction of either the thiazole or pyrimidine intermediate. Heavy irradiation in vivo produced no detectable change in the thiamin content of mouse blood or liver. (BA)

1651

Efrati, E., A. Back, and L. Halberstaedter. **INFLUENCE OF THE MEDIUM ON THE INACTIVATION OF TETANUS TOXIN BY X-RAY IRRADIATION.** *Nature* **159**, 715-6 (1947).

Two types of tetanus toxin, prepared in different ways, were used to study the influence of the medium on toxin inactivation in vitro by X-rays. The medium was varied by adding a series of proteins and peptones to the toxin samples. The results of the irradiation are given. The addition of different substances to the medium diminished the x-ray effect on the toxin in varying degrees. (S.V.S.)

1652

Farmer, F. T., G. Stein, and J. Weiss. **CHEMICAL ACTIONS OF IONIZING RADIATIONS ON AQUEOUS SOLUTIONS. PART I. INTRODUCTORY REMARKS AND DESCRIPTION OF IRRADIATION ARRANGEMENTS.** *J. Chem. Soc.* 3241-5(1949).

The development of the theory of the action of ionizing radiations on aqueous solutions, leading up to the theory of formation of free radicals (Weiss, *Nature* **153**: 748 (1944)), is discussed. Apart from the intrinsic interest in the action of the radiations, these investigations are of interest because they allow the reactions of free radicals to be studied in the absence of interfering reagents and because the products of reaction are somewhat similar to those obtained in biological systems in which the same molecules are involved. Experimental arrangements for irradiations with x-rays (γ rays), neutrons, and α rays, and the radiation dosimetry, are discussed in detail. (NSA)

1653

Fricke, H. and B. W. Petersen. **THE RELATION OF CHEMICAL, COLLOIDAL, AND BIOLOGICAL EFFECTS**

OF ROENTGEN RAYS OF DIFFERENT WAVE-LENGTHS TO THE IONIZATION WHICH THEY PRODUCE IN AIR. I. OXYHEMOGLOBIN IN AQUEOUS SOLUTION. *Am. J. Roentgenol. Radium Therapy* **17**, 611-20(1927).

X-rays cause the oxidation of oxyhemoglobin to methemoglobin, and irradiating a solution with increasing doses the rate of transformation is proportional to the momentary concentration of oxyhemoglobin. The ratio of the amount of oxyhemoglobin transformed to the ionization produced in atmospheric air is found independent of the wavelength of the rays (0.25 to 0.75 A.U.) when the coefficients of mass absorption of the oxyhemoglobin solution (u_1) and of air (u_2) are equal. When KCl is added to the oxyhemoglobin solution making $u_1 > u_2$, the ratio is only constant for the longer wavelengths, the chemical action of the shorter wavelengths being comparatively too small, which effect is due to the production of Compton-electrons. (BA)

1654

Frilley, M. THE RADIOCHEMISTRY OF AQUEOUS SOLUTIONS: A SURVEY OF RECENT FRENCH RESEARCH. *Brit. J. Radiol. Suppl.* **1**, 50-5(1947).

Work performed on the production of H_2O_2 by irradiation of water is reviewed. The H_2O_2 yield is the same for both X-rays and α -rays. The role of dissolved oxygen in the production of H_2O_2 by irradiation of water is described. The H_2O_2 yield is increased in the presence of hydroquinone, cysteine ascorbic acid, and aldehydes; organic acids, however, diminish the yield of H_2O_2 . pH changes and the mechanism of the action of ionizing radiations on aqueous solutions are considered briefly. (NSA)

1655

Gray, L. H. THE PRESUMED DISTRIBUTION OF IONS AND EXCITED GROUPS IN LIQUIDS. *J. chim. phys.* **48**, 172-8(1951).

Biological effects are discussed in terms of type of ionization produced by radiation. Dense ionization as produced by α particles results in high local H_2O_2 concentrations. Some biological effects of radiation are enhanced and some are reduced in going from low ionization density to high ionization density. (CA)

1656

Grimmett, L. G. SOME ASPECTS OF THE MECHANISM OF ACTION OF IONIZING RADIATION ON LIVING CELLS. *Texas Repts. Biol. and Med.* **8**, 134-46(1950).

This article discusses some of the theories advanced to account for the effect of radiation on cells and the sensitivity of cells to varying intensities of radiation. The author emphasizes the role radiochemistry can play in explaining the mechanism of cell damage such as the production of free radicals from water by radiation. 11 references. (NSA)

1657

Kashchenko, L. A. EFFECT OF RADIANT ENERGY ON THE GONADOTROPIC FACTOR OF THE ANTERIOR LOBE OF THE HYPOPHYSIS. *Doklady Akad. Nauk S.S.S.R.* **77**, No. 1, 157-60(1951).

Anterior pituitary hormone extract was exposed to 30,000 to 1,034,000 r of x radiation, to 0.022 to 35.00 mcd of radium β radiation, or to ultraviolet light. Changes in gonadotropic activity are tabulated. Activity changes on up to 90-days storage following the 100,000-r x irradiation also are listed. (NSA)

1658

Koenig, Virgil L. and J. D. Perrings. PHYSICO-CHEMICAL EFFECTS OF RADIATION; I. EFFECT OF X-RAYS ON FIBRINOGEN AS REVEALED BY THE ULTRACENTRIFUGUE AND VISCOSITY. Los Alamos Scientific Lab. [nd] 28p. (AECU-1725; LADC-1027)

Bovine fibrinogen irradiated in the dry state and dissolved in 0.1M NaCl and 0.1M Na_2HPO_4 has been studied on the ultracentrifuge at various concentrations. Significant differences in the ultracentrifugal behavior were observed for different amounts of radiation. Significant differences in viscosity behavior of irradiated fibrinogen dissolved in 0.1M Na_2HPO_4 from the control unirradiated fibrinogen were observed. Fibrinogen irradiated in the presence of oxygen, nitrogen, and helium was studied on the ultracentrifuge. Fibrinogen irradiated in the presence of helium showed greater alteration than in either oxygen or nitrogen. Fibrinogen irradiated when dissolved in 0.1M Na_2HPO_4 showed alteration. When the radiation was increased a heavier second component appeared on the ultracentrifuge diagram. Less radiation is required in the dissolved state than in the dry state to produce comparable changes. At least 1×10^8 r is necessary in the dry state to produce a significant change in the fibrinogen. In the dissolved state 5×10^4 r is sufficient to produce a significant change. (NSA)

1659

Krenz, F. H. THE EFFECTS OF HIGH ENERGY RADIATIONS ON WATER AND AQUEOUS SYSTEMS. *Can. J. Research B*, **26**, 647-56(1948).

In order to obtain a better idea of the effect that irradiated water has when biological systems are exposed to high energy radiation, the properties of the water were investigated. Evidence was obtained for vibrationally excited "polymers" of water which result in long lived activity. It is concluded that the large "indirect effect" of water on biological systems may well be due to the properties of the "polymers." A cross section of the dilatometer used in measuring the water expansion upon gamma radiation, expansion curves and curves of lag effect in water and some aqueous solutions are presented. 35 references. (NSA)

1660

Landau, H. G. A PROBLEM IN RADIOBIOLOGY: DIFFUSION AND RECOMBINATION OF IONS. *Bull. Math. Biophys.* **12**, 27-34(1950).

The problem of the distribution of ions which are formed in the path of an ionizing particle and undergo diffusion and recombination is solved by a perturbation method. When diffusion is more important than recombination this treatment gives a more accurate distribution than previous approximations. (CA)

1661

Loiseleur, J. ELECTRONIC EXCHANGES IN WATER ACTED ON BY X-RAYS. *Compt. rend.* **214**, 76(1942).

The amount of H_2O_2 formed on irradiation with x-rays was found to increase with decreasing pH; but the pH of pure water was found to decrease on irradiation. From the second fact, it is agreed that the primary step must be disappearance of OH^- . The proposed mechanism is: $2 OH^- + O_2 = H_2O_2 + O_2^-$ followed by $O_2^- + 2 H^+ = H_2O_2$. (CA)

1662

Loiseleur, J. and C. Crovisier. INCREASE IN VISCOSITY AND REFRACTIVE INDEX OF WATER SUBJECTED TO THE ACTION OF X-RAYS. *Compt. rend. soc. biol.* **136**, 739-40(1942).

Twice-distilled water was exposed to the $K\alpha$ rays ($\lambda = 0.71\text{\AA}$) from a Mo target for long periods. The viscosity and λ increased very slightly in all cases. Small quantities of H_2O_2 were formed in water containing dissolved O_2 , but not in water freed of O_2 . (CA)

1663

Loiseleur, J. and R. Lataret. DEMONSTRATION, BY DIRECT POTENTIOMETRIC MEASUREMENT, OF THE

INTERVENTION OF OXYGEN IN THE EFFECTS OF X-RAYS. *Compt. rend. soc. biol.* **135**, 1534-7(1941).

In saturated solutions at pH 6 in water freed of air or O₂, hydroquinone is not oxidized by irradiation with K α x-rays from a Mo target. The Pt-electrode potential of the solution remains unchanged or decreases slightly. In water saturated with air, oxidation occurs and the Pt-electrode potential gradually rises as more and more quinone is formed. (CA)

1664

Luria, S. E. and F. M. Exner. **THE INACTIVATION OF BACTERIOPHAGES BY X-RAYS--INFLUENCE OF THE MEDIUM.** *Proc. Natl. Acad. Sci. U. S.* **27**, 370-5(1941).

X-rays have an "indirect" effect in water or saline suspensions of bacteriophages. Probably some agent is produced in the medium by the irradiation which oxidizes or reduces the phages. In the presence of foreign proteins bacteriophages are also inactivated by x-rays, but with reduced sensitivity. This seems to be a "direct" effect on phage itself. (BA)

1665

Mathis, Alice L., Robert E. Brooks and Herman Schneiderman. **STUDIES IN THE HYALURONIDASE-HYALURONIC ACID SYSTEM. I. THE EFFECT OF X-IRRADIATION ON HYALURONIC ACID.** University of California, Los Angeles. Feb. 11, 1949. 10p. (AECU-170; UCLA-11)

Hyaluronic acid is a mucopolysaccharide which is believed to be composed of equimolecular amounts of acetyl glucosamine and glucuronic acid. X-irradiation was found to cause a change in potassium hyaluronate solution, which manifests itself by a reduction in viscosity. After cessation of the irradiation, the viscosity decreased to some extent for period of about five hours. (NSA)

1666

Minder, W. **THE PROBLEM OF TRANSFERENCE OF ENERGY IN BIOLOGICAL IRRADIATION.** *Radiologia Clin. Suppl.* **15**, 81-5(1946).

The effects of irradiation on substances of known chemical composition in aqueous solutions are exerted in a round about way through the agency of the solvent, water. A transference of energy must take place from the H₂O molecules activated by the radiation to the dissolved substance. As a result of radiation below 25°, 35°, and 50° respectively, solutions of bromoform, ortho-dichlorobenzene and ferrous sulphate in water show no temperature coefficient of reaction. Irradiation with X rays on radium does not affect frozen (solid) solutions. This shows that the energy-transfer and therefore the radiation effect is only possible where there is freedom of molecular movement (diffusion). (NSA)

1667

Minder, W. **RADIO-CHEMISTRY OF ORGANIC HALOGEN COMPOUNDS**, p. 44 of **INTERNATIONAL CONGRESS OF RADIOLOGY**, 6th Congress, London. 1950.

The formation of halogen hydrides by irradiation of aqueous organic halogen compounds is certainly an indirect effect via the solvent molecules. The yield is independent of the concentration of the irradiated solution, and the action is completely suppressed in the frozen state. The yield is, without exception, smaller with aromatic than with aliphatic substances, and in the experiments described is of the order of 0.16 and 2.6 molecules per ion. The reaction is altered quantitatively and qualitatively by adding other substances (protection effect). From the limiting values of the independence of concentration on the one side, and the absolute values of protection on the other, the maximal distance of the diffusion of energy, free from loss, can be determined. The results give values which are in

good agreement and, according to the substance concerned, vary between 20 and 100 times the diameter of the molecule of water. Halogen hydride is also formed when halogens—containing hydrocarbons are irradiated in organic solutions (alcohol, acetone). The yield is proportional to the concentration in small concentrations, and reaches a limiting value in greater concentrations. The action of this irradiation also must be considered as an indirect effect although in the higher concentrations a direct effect is superimposed. Addition of water up to a molecular ratio 1:1 does not change the yield. The "effective volume" (ratio between ionic yield and concentration) is approximately 100 to 200 times greater than the dimension of the reacting molecules.

1668

Mosher, Wm. A. **IONS AND RADICALS IN BIOCHEMICAL PROCESSES.** *Conf. on Biol. Antioxidants, Trans. 4th Conf.* **13-44**(1949); *J. Franklin Inst.* **251**, 665-74(1951).

A discussion of free radical formation, ionic oxidation of organic compounds, and effects of x-irradiation and free radicals on nucleic acids. The x-ray is a producer of free radicals rather than a producer of ionized particles. X-rays, neutrons, ultraviolet light, and sonic vibrations have proved effective in the depolymerization of desoxyribonucleic acid in vitro. If radical chain-stopping agents, such as thiourea, are added to nucleic acid there is marked protection from the destructive effect of x-rays, chemically produced radicals, and other physical agents. This protection can be looked upon as a type of antioxidation. (CA)

1669

Mullis, A., W. Minder, A. Liechti, and F. Wegmüller. **EXPERIMENTS WITH A MODEL ON THE BIOLOGICAL PRIMARY EFFECT OF IRRADIATION.** *Radiologia Clin.* **15**, 295-312(1946).

The living cell is too complex a system for the study of the analytic effects of radiation, and therefore attempts were made to examine the "physical primary effect", of rays on artificial models of simple construction. Earlier experience has shown that halogen compounds of benzene are hydrolyzed by x-rays, with production of an acid consisting of the halogen and hydrogen. Hydrolysis was observed to be proportional to the radiation applied, while it had no relation to the concentration of the compound. The rate of hydrolysis was conditioned on the dose of radiation and on the number of chlorine atoms in the molecule of the compound. In the work presented the radiation hydrolysis of p-dichlorobenzene and of hexachlorobenzene was studied. When p-dichlorobenzene was dissolved in ether and the latter dissolved in water no hydrolysis occurred by radiation, but when a saturated aqueous solution of the compound was used, hydrolysis, production of hydrochloric acid, and a corresponding increase in the conductivity of the solution were observed. The ionic yield of the reaction was rather small (0.33 5%), indicating that only a minimal part of the substance had been converted. It is important to note that in the case of mono-chlorobenzene approximately half the amount of hydrochloric acid was produced in comparison with p-dichlorobenzene. In the fully substituted compound C₆Cl₆ no hydrolysis on irradiation was observed. Therefore it seems probable that production of hydrolysis should not be regarded as an isolated function of the chlorine atom, but that co-operation of hydrogen atoms present in the compound may have some additional and important function. The fact that hydrolysis of p-dichlorobenzene was hampered by the presence of ether is worth noting. (AWM)

1670

Pickels, E. G. and R. S. Anderson. **MOLECULAR ASSOCIATION OF HEMOCYANIN PRODUCED BY X-RAYS AS**

OBSERVED IN THE ULTRACENTRIFUGE. J. Gen. Physiol. **30**, 83-99(1946).

When normal, monodisperse hemocyanin (60.5 S) from Limulus polyphemus was irradiated in neutral buffer with X-rays, several new, more rapidly sedimenting ultracentrifugal components (86 S, 107 S, 122 S) were produced, with a corresponding loss in the amount of the unaffected protein. The amount of the effect was roughly proportional to the amount of irradiation. The new resolvable components apparently represented an association of the primary particles into aggregates of 2, 3, and 4 primary particles, respectively. The proportional amount of hemocyanin affected decreased almost to the vanishing point as the conc. of the protein was raised to high levels. The absolute effect, i.e., the total number of particles affected in a given vol., increased with the concn. of hemocyanin, at least for concns. below 15%. The presence of 33% horse serum during irradiation inhibited the effect on the hemocyanin almost completely, with hemocyanin concns. of both 0.8 and 14%. The presence of 2.8% egg albumin during irradiation lowered the effect by about 70% in the case of dilute preparations (0.8% hemocyanin) but by only about 25% in the case of 14% solutions. A lowering of the solution's oxygen tension during irradiation enhanced the effect, almost doubling it in some cases. (BA)

1671

Scholes, George and Joseph Weiss. FORMATION OF HYDROXYLAMINE FROM AMINO COMPOUNDS IN AQUEOUS SOLUTION BY IRRADIATION WITH X-RAYS. Nature **167**, 693(1951).

NH₂OH is produced upon irradiation of adenine, guanine, cytosine, alanine, lysine, ethylamine, and histamine with x-rays. No NH₂OH is obtained from hypoxanthine, uracil, uridine, and NH₃, and only small amounts are obtained from nucleic acids. Yields of NH₂OH depend on the pH. Irradiation of solutions of NH₄ salts by x-rays results in oxidation to nitrate. (CA)

1672

Stein, G. and J. Weiss. CHEMICAL EFFECTS OF IONIZING RADIATIONS. Nature **161**, 650(1948).

Simple org. compounds, e.g., benzene and benzoic acid, in dilute aqueous systems have been exposed to penetrating radiations and the reaction products studied. When benzene was irradiated by X-rays, about 0.1 millimol. of phenol was formed, also, a smaller quantity of biphenyl among other substances. In similar experiments with a neutron- γ -ray source (corresponding to 1 g Ra mixed with Be powder) benzene gave, in addition to the products mentioned above, catechol and products originating from the opening of the benzene ring. In all cases the total yield of the hydroxylated reaction products depends on the pH of the solutions. (CA)

1673

Stein, G. and J. Weiss. CHEMICAL ACTIONS OF IONIZING RADIATIONS ON AQUEOUS SOLUTIONS. IV. THE ACTION OF X-RAYS ON SOME AMINO ACIDS. J. Chem. Soc. 3256-63(1949).

Glycine (0.4 g) in H₂O (100 cc.) irradiated in vacuo with x-rays ($10^5 - 10^6$ r) gave H, NH₃ (0.1 millimole approx.) and HCHO (traces; recognized by isolation of the 2,4-dinitrophenylhydrazone). In comparable experiments alanine gave H, NH₃ and MeCHO; serine gave H, NH₃, glyoxal and glycolaldehyde. The amounts of H, NH₃, and aldehydes were a nonlinear function of the irradiation dose and both oxidative and reductive mechanisms contribute to the deamination. (CA)

1674

Svedberg, T. and S. Brohult. SPLITTING OF PROTEIN MOLECULES BY ULTRA-VIOLET LIGHT AND ALPHA RAYS. Nature **143**, 938-9(1939).

Irradiation of hemocyanin, hemoglobin, and serum albumin with uv light and α -rays, both at room temp. and at the temp. of liquid air shows that in the case of hemocyanin the splitting into half mols. is a primary reaction. In the case of hemoglobin and serum albumin the irregular breakdown is caused by secondary reactions. The amount of hemocyanin dissociated by a given no. of α -particles can be accounted for upon the assumption that each mol. struck by an α -ray is split into halves. (CA)

1675

Tchaperoff, I. C. C. DETERMINATION OF THE EFFECT OF IRRADIATION BY X-RAY ON P-AMINOBENZOIC ACID, USING CLOSTRIDIUM ACETOBUTYLICUM FOR ASSAY. Can. J. Research **24E**, 49-54(1946).

A study has been made on the effect of x-ray irradiation by producing inactivation of p-aminobenzoic acid as determined by assay with C. acetobutylicum. It has been shown that p-aminobenzoic acid in concentration of 1×10^{-4} μ gm per cc is inactivated by an X-ray dose as small as 50 r at 190 kv. The significance of the destruction of Paba in connection with the treatment of infective lesions is discussed. (auth)

1676

Weiss, Joseph. RECENT WORK ON THE ACTION OF IONISING RADIATIONS ON AQUEOUS SYSTEMS, p.165-6 of INTERNATIONAL CONGRESS OF RADIOLOGY, 6th Congress, London. 1950.

Chemical compounds of biological importance discussed are: (a) Amino-acids. The action of ionizing radiations on amino-acids leads to deamination, and the process is in certain respects similar to the biological process of deamination. Ammonia, which is formed in this process, is capable of producing mutation effects. A number of different amino-acids have been studied in detail. The simplest of these (glycine) is known to be a precursor of the blood pigment in the human body. (b) Nucleic Acids (Nucleotides and Nucleosides). The action of X-rays on different types of nucleic acids in aqueous systems has been investigated. On irradiation of these solutions ammonia is formed and from the solutions a number of low molecular products including nucleosides and free purine bases have been isolated and identified. The constituent bases are themselves also attacked as evidenced by the production of ammonia and by increase in the number of free amino-groupings. The action of X-rays on nucleotides and on some nucleosides has recently been investigated. (c) Sterols. The irradiation of cholesterol by X-rays in aqueous systems leads principally to the formation of two substances, one of which seems to be of particular interest as it has been isolated from the arteriosclerotic human aorta, from pig's spleen and testis and from ox liver, and it may be of some importance in steroid metabolism. The action of X-rays on pregnenolone and on a number of steroid hormones in aqueous systems has also been investigated.

VI GROWTH AND DEVELOPMENT

1677

U. S. Department of Agriculture. 1948 FIELD RESULTS WITH CERTAIN RADIOACTIVE MATERIALS AS PLANT

STIMULANTS; PROGRESS REPORT. May 1949. 43p. (M-4376)

Field experiments with radioactive materials as plant stimulants were conducted during the 1948 crop season by the Bureau of Plant Industry, Soils, and Agricultural Engineering, in cooperation with the State agricultural experiment stations of Arkansas, Illinois, Kentucky, Michigan, Mississippi, Montana, North Carolina, Ohio, New York, Washington, West Virginia, and the College of Agriculture, University of Georgia. Three radioactive materials were used in the field experiments: Alphasat (commercial material) at the rate of 5, 10, and 20 pounds per acre; radium (as used, contained 30 μ g of Ra per pound); and uranyl nitrate. The data from these field experiments is presented in this report in tabulated form. The general conclusion drawn from the data is that no effect of the radioactive materials was found, either beneficial or harmful. There were a few cases of differences that reached the 5% level of significance, but they were no more than would be expected from normal distributions. No comment is made with regard to the individual experiments. (S.V.S.)

1678

Alexander, Lyle T. **RADIOACTIVE MATERIALS AS PLANT STIMULANTS. FIELD RESULTS.** *Agron. J.* **42**, 252-5(1950).

Applications of alphasat, radium, and uranyl nitrate in field experiments with a number of crops showed that these materials had no effect, either beneficial or harmful. (CA)

1679

Amoroso, E. C. and A. S. Parkes. **EFFECTS ON EMBRYONIC DEVELOPMENT OF X-IRRADIATION OF RABBIT SPERMATOZOA IN VITRO.** *Proc. Roy. Soc. London, B* **134**, 57-78(1947).

Rabbits in which ovulation was induced artificially by intravenous injection of 50 I. U. chorionic gonadotrophin were inseminated with spermatozoa exposed in vitro to doses of x-rays varying from 50-100,000 r, the ova being examined grossly, under visual microscopy with hematoxylin eosin and under ultraviolet microphotography. At 250 r-1,000 r, the normal divisions dropped progressively below the normal of 80-90% down to 2% independently of intensity or type of irradiation and time of irradiation before insemination (5-17 hours). Entry of spermatozoa into ova was effected at all dose levels. Cytological damage to the spermatozoa nucleus appeared at 10,000 r, polyspermy appeared at 1,000 r. Activation occurred at all levels, but syngamy became irregular at 10,000 r with suppression of spindle fiber formation at higher dosages. Occasional haploid and triploid ova were observed at the one-cell stage, but not in divided ova, and there was no continued gynogenetic development. From 50-250 r, normal fertile young were born. At 500 r, incidence of pregnancy and litter size were reduced, young were less viable, but survivors were normally fertile. No implanted embryos, fetuses or living young were obtained from spermatozoa exposed to 1,000 r or over. (BA)

1680

Barr, J. S., J. R. Lingley, and E. A. Gall. **THE EFFECT OF ROENTGEN IRRADIATION ON EPIPHYSEAL GROWTH. I. EXPERIMENTAL STUDIES ON THE WHITE RAT.** *Am. J. Roenthenol. Radium Therapy* **49**, 104-15(1943).

Groups of 30, 90, and 180-day old albino rats were subjected to roentgen irradiation of one knee-joint, and the resulting changes studied histologically and roentgenographically. Doses of 665-1,165 r produced moderately severe changes; doses of 1,335-1800 r caused very severe damage, indicated by disruption of cartilage cell columns and destruction of chondrocytes. There was no evidence indicating stimulation and practically none of regeneration of

epiphyseal cartilage. Other tissues showed only transitory changes. No degenerative or traumatic changes were found in the irradiated joints even after 9 months' observation. The doses used all produced retardation of growth, which varied roughly in proportion to the dose. Doses in excess of 1300 r produced essentially complete arrest of growth of the treated epiphysis. (BA)

1681

Berk, Sigmund. **BIOLOGICAL EFFECTS OF IONIZING RADIATIONS FROM RADIUM AND POLONIUM ON FUNGI. PART III. THE PREVENTION OF MOLD GROWTH IN OPTICAL INSTRUMENTS SERIES.** Pitman-Dunn Labs., Frankford Arsenal. July 1951. 89p. (NP-3798; FA Report R-1016)

Constant irradiation with various 7.5- μ g sources of Ra inhibited the sporulation of *Chaetomium globosum*, *Lenzites trabea*, *Aspergillus niger*, *A. flavus*, and a species of *Penicillium* growing on potato-dextrose agar. There was an appreciable difference in radiosensitivity of the species. It was concluded that α particles were primarily responsible for the effects observed. The biological effects of the irradiation of dry *A. niger* spores with Po α particles was dependent on the dose: (a) the lowest dose showing any visible effect (114 α or 26,900 rep) interfered with the sporulation of the fungus; (b) higher doses interfered with the extent of vegetative proliferation of the fungus; (c) larger doses (1000 α or 236,000 rep) inhibited the production of a germ tube; (d) still larger doses caused abnormally swollen spores which failed to produce germ tubes, and (e) doses in excess of 25,000 α particles or 5,900,000 rep were lethal. Isolates made from *A. niger* cultures that had been bombarded with Ra α particles yielded a number of mutant strains. Some of the variants were characterized by dwarf and giant conidial heads, others by a short conidiophore and a powdery type of sporulation. (NSA)

1682

Blanc, R. and C. Villee. **DIFFERENTIAL REACTIONS OF VARIOUS SCUTE STOCKS OF DROSOPHILA MELANOGASTER TO X-RADIATION.** *Genetics* **26**, 140(1941).

In a preliminary investigation of the phenotypic effects of X-rays on the bristles of different stocks of *Drosophila melanogaster*, different members of the scute series, sc, sc⁵, sc⁶, and sc¹⁰, a wild type, Canton S, and various compounds of these were subjected, while prepupae, to 2115 r units of X-radiation. Experimental and control flies were left to hatch in Petri dishes on moist filter paper at 25°C. The imagines were recorded for bristle effects. A total of 1659 experimental and 1363 control flies were examined. The bristle effects produced were chiefly complete absence or great reduction in size, although a few bent, curved, or doubled bristles occurred. The percentages of the different bristles affected in the various stocks were compared using the effect in Canton S as a "norm." It was found that the effects of X-rays on the bristles differed in the various stocks used, so that in each case a pattern of X-ray effects specific for the stock was superimposed on the bristle pattern characteristic for that stock under control conditions. It was found that those bristles affected by the scute genotype under control conditions are more likely to be affected by X-radiation than those not. In other words, the combined effect of genotype and X-radiation is greater than would be expected on the basis of simple summation. This suggests that X-radiation and the scute genotype affect the same or closely integrated processes. (G)

1683

Bliss, C. I. and C. Packard. **STABILITY OF THE STAND-**

ARD DOSAGE-EFFECT CURVE FOR RADIATION. Am. J. Roentgenol. Radium Therapy **46**, 400-4(1941).

The standard dosage-effect curve for *Drosophila* eggs and X-irradiation was tested for statistical accuracy and possessed greater stability in both slope and position than had been generally reported in investigations of toxic effects. (BA)

1684

Blum, Harold F., J. Courtland Robinson, and Gordon M. Loos. THE LOCI OF ACTION OF ULTRA-VIOLET AND X-RADIATION, AND OF PHOTORECOVERY, IN THE EGG AND SPERM OF THE SEA URCHIN. Proc. Natl. Acad. Sci. U. S. **36**, 623-7(1950)

Given in moderate doses, both ultraviolet radiation and x-rays delay cell division (cleavage) of the eggs of the sea urchin *Arbacia punctulata*. Experiments are summarized which indicate that the locus of this action is, in both cases, associated with cell nuclei, as contrasted to cell cytoplasm. There is recovery from the effect of the radiation, as indicated by return toward the normal rate of cleavage. Following treatment with ultraviolet radiation, recovery is accelerated by illumination with "visible" radiation. This photorecovery has its locus in the cytoplasm of the egg. In the case of x-irradiation, visible radiation appears to be without effect on the recovery of cleavage rate. (NSA)

1685

Boell, E. J., O. M. Ray, and J. H. Bodine. EFFECT OF X-RAYS ON THE OXYGEN CONSUMPTION OF EMBRYONIC CELLS. Radiology **29**, 533-40(1937).

Effects of x-rays on the growth, respiration and oxidation mechanism of the eggs and embryos of the grasshopper (*Melanoplus differentialis*) have been presented. X-rays in the dosage supplied (2040, 5000 r units) do not affect the respiration (O_2 intake) of diapause or blocked embryos. The stimulating action of 3,5-dinitro-o-cresol on O intake of the diapause embryos is not interfered with by x-irradiation. Actively developing eggs and embryos are affected by x-rays as indicated by changes in growth and respiration. X-rays applied to actively developing eggs and embryos in which growth has been stopped by exposure to 10° produce no measurable effect on respiration, or stimulation of respiration by the addition of 2,4-dinitrophenol. Hatching of actively developing x-rayed eggs is greatly decreased and embryos hatching do not primarily affect the respiration mechanism of the embryonic cell but rather bring about fundamental changes in protoplasmic organization. (CA)

1686

Bonham, Kelshaw. EFFECT OF X-RAYS UPON THE FRESH-WATER SNAIL, *RADIX JAPONICA*. University of Washington Applied Fisheries Lab. May 16, 1949. 33p. (AECU-309; UWFL-21)

Radix japonica (Jay) from a creek in Richland, Washington, were x-rayed with a Coolidge tube at the approximate rates of 120 or 500 r/min. using 200 kvp and 20 ma with filters of 0.5 mm of copper and 1 mm of Al. In three experiments involving 162 adult snails and graduated series of doses up to 80,000 r, mortalities significantly higher than in the controls were observed in groups receiving 10,000 r or more. Egg masses similarly x-rayed with doses of 180 r, 1,000 r, or 10,000 r were retarded in their development as compared to the controls in the groups receiving 1,000 r and 10,000 r. Crawling activity of the newly hatched young was inhibited only in the 10,000 r group. Ratio of hatched to unhatched was inversely related to exposure. (NSA)

1687

Bonham, Kelshaw, Lauren R. Donaldson, Richard F. THE EFFECT OF X-RAY ON MORTALITY, WEIGHT, LENGTH, AND COUNTS OF ERYTHROCYTES AND HEMATOPOIETIC CELLS IN FINGERLING CHINOOK SALMON, *ONCORHYNCHUS TSCHAWYTSCHA WALBAUM*. Growth **12**, 107-21(1948).

Eight groups of fingerling chinook salmon, *Oncorhynchus tshawytscha* Walbaum, were subjected to different x-ray doses graduated from 100 r to 5,000 r, and one group was used as a control. The lowest exposure levels at which irradiated groups were significantly adversely affected 12 weeks after exposure were, in mortality 250 r, in weight 500 r, and in length 1,000 r. Group means when tested against the mean of all nine groups combined showed significant decline in number of cells in the circulating blood at exposures of 750 r and 1,250 r two and three weeks after irradiation. Concentration of hematopoietic cells in the kidney showed similar decline in the 750 r group one and two weeks after irradiation. (NSA)

1688

Brace, Kirkland C. EFFECTS OF X-RAYS ON SIZE OF YEAST CELLS. Proc. Soc. Exptl. Biol. Med. **74**, 751-5 (1950).

When yeast cells were exposed to 20,000 r of x-rays and cultured in liquid medium, they and their descendants attained a mean cell volume more than twice that of cells derived from nonirradiated controls. On the other hand, there were no corresponding differences in specific gravity and nitrogen content per unit of cell volume. It is accordingly concluded that enlargement of yeast cells after irradiation is largely a nonselective increase in cell constituents rather than a swelling due mostly to uptake of water. (NSA)

1689

Brumfield, R. T. CELL-LINEAGE STUDIES IN ROOT MERISTEMS BY MEANS OF X-RAY INDUCED CHROMOSOME REARRANGEMENTS. Genetics **27**, 135(1942).

Certain types of chromosome rearrangements induced by X-rays are passed on through subsequent cell division to all the descendants of the affected cell. Thus chromosome changes induced by X-rays offer a means of "tagging" a single cell and determining the kind and extent of tissues derived from it. This paper reports results obtained by the use of this method in studying cell lineage in root meristems.—Germinating seed of *Vicia faba* and *Crepis capillaris* were X-rayed, allowed to grow for three weeks after radiation, then primary root tips were fixed and sectioned transversely. Cytological observations revealed that many of the root meristems thus treated were chromosomal chimeras, both normal and rearranged complements (usually unequal translocations) being found in the same root. All chimeras so far observed have been sectorial ones. In most of the chimeras of both *Vicia* and *Crepis* the sector having the rearranged complement represents about one-third of the root and includes root cap, epidermis, cortex, endodermis, and central cylinder. This indicates that in these roots a single cell may give rise to all the above tissues and that the whole root develops from but few cells at the extreme tip. Sectorial chimeras would not be expected if the meristem consisted of "histogens" as described by Hanstein. (G)

1690

Bruns, K. H., W. Dittrich, W. Paul, and G. Schubert. CHANGES IN THE ROOT GROWTH OF BARLEY SEEDLINGS PRODUCED BY FAST ELECTRONS OF A 6-MEV BETATRON. Strahlentherapie **81**, 173-6(1950).

The action of fast electrons (from a 6-Mev betatron) on the growth of roots of barley seedlings was compared with that of x-rays, the dose range being 1,000 to 6,000 r. The radiobiological action was measured by the percentage decrease of the rate of growth of irradiated roots, as reflected in the root lengths 80 hr after the irradiation. A statistical treatment of the results revealed a weaker action of fast electrons as compared with that of x-rays. (NSA)

1691

Brunst, V. V. THE EFFECT OF X-RAY IRRADIATION UPON THE LUMBO-SACRAL REGION OF THE AXOLOTL (*SIREDON MEXICANUM*). *Anat. Record* **103**, 430-1(1949).

The following is an abstract and is reproduced here in its entirety.

The lumbo-sacral regions of 235 axolotls (24 and 30 days after hatching) were locally treated with doses of 100 r. to 8000 r. Forty animals served as untreated controls. In the first series of experiments, the investigation of fixed animals was made three months after treatment. The suppression of growth resulted in a more or less pronounced waist-like narrowing of the treated part of the body. In such animals, the hindlimb skeleton, pelvic girdle, and some elements of the vertebral column were completely absent. In the cases where the animal was incorrectly oriented during irradiation, a partial development of the extremities was observed. These small limbs with arrested growth showed a relatively complete differentiation of skeletal and other tissues. In the second series of experiments, the irradiated animals were fixed a variable period of time (from 4 days to 76 days after treatment, and in some cases, 6 months after treatment). The following results were obtained: A temporary inhibition of development was observed 4-5 after treatment. A primary acute reaction was observed 20-35 days after treatment. The end of the acute reaction and late secondary stimulation were observed 40-50 days after treatment. A secondary stable state was observed 60 days after irradiation. This state persisted for an unlimited period of time.

1692

Brunst, V. V. INFLUENCE OF LOCAL X-RAY TREATMENT ON THE DEVELOPMENT OF EXTREMITIES OF THE YOUNG AXOLOTL (*SIREDON MEXICANUM*). *J. Exptl. Zool.* **114**, 1-35(1950).

In this paper a detailed description of the effects of x-radiation upon the development of the extremities of the axolotl is given. This paper consists of two parts. The first part describes the effects of irradiation upon the lumbosacral region in the axolotl. The second part describes the effects of irradiation in the lumbo-sacral region upon the gradual development of the extremities of axolotls. The purpose of these experiments was to investigate the succession of changes in the irradiated parts of the axolotl body during the process of development and to determine whether it is possible to stimulate development by means of weak irradiation. The effects of the irradiation up to 63 days following irradiation are discussed. 27 references. (NSA)

1693

Brunst, V. V. THE EFFECTS OF LOCAL X-RAY IRRADIATION ON THE TAIL DEVELOPMENT OF YOUNG AXOLOTLs. *J. Morphol.* **86**, 115-41(1950).

Young axolotls were irradiated while under anesthesia with 1,000, 2,000, 3,000, or 6,000 r delivered by a 43-kv machine with no filtration at a target distance of 17 cm to localized areas in the tail region, the rest of the body being carefully shielded; of the 120 animals tested, all recovered

in water immediately after irradiation. The treated animals were photographed, described, fixed in a solution of bichloride of mercury, imbedded in paraffin, and sectioned 35 to 40 days and 85 to 100 days following irradiation. Two types of effects were noted: the primary type was characterized by inflammation, degeneration of the epithelium, notochord, and the neural tube, and inhibition of growth, in evidence 35 days after irradiation; the secondary type which followed the primary and was characterized by inhibition of growth of the irradiated portions (the tissue appearing normal but lacking the ability to divide) and the subsequent growth in many cases of a second tail (which never attained normal size and had varying anatomical characteristics). (NSA)

1694

Brunst, V. V. INFLUENCE OF X-RAYS ON LIMB REGENERATION IN URODELE AMPHIBIANS. *Quart. Rev. Biol.* **25**, 1-29(1950).

A review is presented on the mode of action of x-rays in inhibiting limb regeneration in urodele amphibians, on the source of cells for the regenerating blastema, and on the influence of x-rays on growth and differentiation in the regenerative process; the author discusses in detail the results of a number of important works on the subject, including some seldom-referred-to Russian papers. The primary reaction of the organism to the irradiation may consist in profound alterations in the cells, often seen as pathological degeneration and death; inflammation may also be the primary reaction. The surviving tissues recover their normal appearance, but not their potentialities; regeneration is lost. Postamputation irradiation causes not only an arrest of regeneration, but also a rapid decrease in the size of the treated regenerate, due to an inflammatory process; irradiation prior to amputation causes no size reduction. Suppression of cell division does not affect the differentiation process; tissue and organ differentiation in irradiated animals may be completed despite a cessation of growth. Other results are discussed. 220 references. (NSA)

1695

Brunst, V. V. and Frank H. Figge. THE DEVELOPMENT OF SECONDARY TAILS IN YOUNG AXOLOTLs AFTER LOCAL X-RAY IRRADIATION. *J. Morphol.* **89**, 111-33 (1951).

High doses of x radiation (600 to 1200 r) applied to localized areas of tails of Axolotls, 10 days after their hatching, "stimulated" the formation of secondary tails. The induced cartilaginous skeletons were at first totally independent of the normal cartilaginous elements. Growth of the normal tails may be inhibited by x-radiation. (NSA)

1696

Chase, Herman B. GREYING INDUCED BY X-RAYS IN THE MOUSE. *Genetics* **31**, 213-14(1946).

Irregularities in degree and pattern described by previous workers have been here controlled by obtaining groups of hairs at known stages of development and by using hard X-rays in a phantom to give homogeneous dosages to the whole animal. The inbred C₅₇ Black strain has been used. The threshold dosage is 250 r and about 50 percent loss of pigment occurs with 500 r. A higher dose of 1000 r using soft rays on a prepared area gives 100 percent loss of color. Plucking of hair on areas of 1.5 square centimeters is essentially the method of obtaining new hair generations. Time of X-raying relative to times of plucking makes it possible to have on same animal several areas differing as to hair age. Maximum effect on the hair itself is when hair is growing rapidly; maximum effect on loss of pigment is instead at time pre-

ceding hair growth. Effect is on the reservoir of melanophores. This standardized method on C₅₇ Black gives permanent readings within three weeks and has permitted biological assays of radiations from different sources (radium, betatron) and has been used in comparative studies on different genotypes and phenotypes. (G)

1697

Chase, Herman B. GREYING OF HAIR I. EFFECTS PRODUCED BY SINGLE DOSES OF X-RAYS ON MICE. *J. Morphol.* 84, 57-76(1949).

Local areas on C57 Black strain mice were exposed to comparatively low dosages, 31 r to 1000 r, but mostly between 200 r and 500 r at definite times before hair was plucked, at plucking, and at definite times following plucking. Plucking hair by means of the fingers from several separate areas of the coat is the method for obtaining areas in known stages of hair growth. Plucking of club-hairs from an area stimulates the follicles of that area alone to produce the next hair generation. Inactive (Telogen) follicles when x-rayed given in the succeeding hair generations the maximum greying response for the particular dose. Active follicles (Anagen) when x-rayed lose hair already present and the succeeding generations of hair are less grey for the particular dose than those from treated inactive follicles. Epilation and growth retardation and delay effects are opposite in severity to the greying effects, with respect to active or inactive follicles at the time of treatment. The threshold response for follicles treated in the inactive phase occurs with 200 r for 100 kv., 550 r/min. irradiation and with 250 r for 200 kv., 102 r/min. irradiation. There is a graded response. The greying effect is permanent; that is, persists for succeeding hair generations. A discussion of the literature is presented mainly in terms of the degree of sensitivity to greying of different animals and in terms of the irregularity of the response. Considerable regularity of response, in the mouse at least, is obtainable by controlling the stage of hair growth at the time of treatment. A tentative hypothesis is presented involving inactivation or killing of melanoblasts of the dermal reservoir in relation to a melanoblast population cycle associated with epidermal follicle development. Hair development and pigmentation are shown to be separate processes. 26 references. (NSA)

1698

Chase, Herman B. EFFECTS OF X-RAY DOSES ON THE CONTROLLED GREYING RESPONSE IN MICE. *Acta Unio Intern. contra Cancrum* 6, 768-70(1949).

The normal pigmentation process of the hair follicles in mice and the gene-controlled variations of this process were investigated through a study of the responses to x-radiations. Controlled graying response in the highly inbred C-57 Black mouse strain could be obtained by plucking hairs; radiation doses were delivered by 100 and 200-kv X-ray machines, by the 20 million volt betatron and by radium applications. It was found that age, sex, weight, and specific hair location do not influence a hair response to irradiation; the stage of development of the hair does, however, affect the nature and degree of the response, maximum graying occurring when inactive or resting follicles are irradiated. The threshold for the graying effect was found to be 250 r; at 500 r, there was a 50% response, while at 1,000 r, a 95-100% response was elicited. The graying effect was found to be permanent for succeeding hair generations. It is concluded that this type of study is especially useful for comparative studies involving different species and phenotypes, different irradiation sources, natural versus induced graying, and single versus cumulative doses. (NSA)

1699

Clark, Francis E. and C. A. I. Goring. GROWTH OF BACTERIA IN THE PRESENCE OF RADIOACTIVE PHOSPHORUS. *J. Bacteriol.* 62, 352-4(1951).

A basal soil extract broth initially containing 0.2 ppm inorganic P and 0.6 ppm organic P was enriched with 0.5% glucose, 0.2% KNO₃, 0.1% MgSO₄, and 4 ppm P³¹ as KH₂PO₄. The added phosphorus contained either 0, 0.01, 0.1, 1.0, or 5.0 mc of P³² per mg P³¹. Sterilized aliquots at each level of activity were given standard inocula of known micro-organisms. The results suggest that although P³² exerts lethal effects on many individual cells, the surviving cells continue to multiply until their growth is limited by other factors, such as accumulation of staling products or substrate exhaustion. Consequently, turbidimetric or gravimetric differences, or interference with substrate transformation as indicated by measurements of pH or of C, N, or P mineralization may not be readily apparent. Nevertheless, in view of higher viable counts at 7 days for the 0.1-mc level of activity than for the 0 level, it is believed that low levels of P³² must to some extent delay normal aging or growth cycle of cultures. Low viable counts at 5.0 mc and the cytological observations at 0.1 mc or more of activity likewise indicated a deleterious effect of such levels of P³² radioactivity. (NSA)

1700

Cottet, P. and W. Minder. THE INFLUENCE OF THE COMBINED ACTION OF LIGHT AND X-RAYS ON THE ROOT GROWTH OF VICIA FABA VULGARIS. *Schweiz. med. Wochschr.* 77, 195-7(1947).

A study was made of the influence of 3 factors on the growth of *Vicia faba vulgaris*: benzopyrene (I), light, and x-rays. I was stabilized in glycerol with serum according to Graffl. The seeds were soaked in this solution for 24 hours. During this period they absorbed twice their weight of I. This could be demonstrated by spectroscopic examination of the acetone extract of the seedlings. I accelerated root growth by 40% during the 5 days after treatment of the seeds. This effect was partially depressed in the light as the result of a photosensitizing action. The inhibiting effect of x-rays (200 roentgens) was more pronounced in those plants which had previously been treated with I. This was probably because I activated the life processes so that the tissue was rendered more sensitive to the radiation. (CA)

1701

Dent, J. N. and Robert L. Amy. DEVELOPMENTAL EFFECTS OBSERVED IN HABROBRACON AFTER EXPOSURE TO BETA RADIATION. *Growth* 14, 113-21 (1950).

Developing individuals of *H. juglandis* were exposed to various levels of beta radiation for 48-hr periods just before hatching or during the early larval period. At the highest levels of radiation used, the wasps died before hatching or in the larval stage. At intermediate levels death usually occurred during pupation with considerable degree of inverse correlation between the extent of imaginal differentiation and the amount of radiation given off. At the lowest levels it was apparent that most of the animals attained adult form. The rate of development was somewhat reduced at the highest and intermediate levels but not at the lowest levels. Pupation without cocoon formation was a frequent occurrence at the intermediate levels. Evidence which indicates that irradiated animals reaching adulthood were sterile is presented. (NSA)

1702

Dittrich, W., W. Paul, M. Riedel, and G. Schubert. BIOLOGICAL RADIATION EFFECTS OF FAST ELECTRONS

ON GERMINATING BARLEY. *Strahlentherapie* **80**, 17-34 (1949).

After 24 hours of swelling in water, barley kernels were subjected to irradiation by fast electrons of 4 Mev energy. The results were compared with nonirradiated and with x-ray-treated kernels. Measurements were made of the time it took the coleoptile to break through the soil, and the time that passed until the first leaf broke through the coleoptile-sheath, as well as the length of growth of the leaf. With increased dosages the inhibition of the germinal growth became greater and the percentage of coleoptiles breaking through the soil was smaller; the length of growth of the leaf under the same conditions became more and more retarded. Electrons with different energies (2 to 5 Mev) did not produce any different biological radiation effect if equal dosages were used. Fast electrons were less retarding and less damaging than x-ray unit dosages. Theoretical implications of this fact are discussed. Small dosages (1,600 r and less) of fast electrons had a growth-stimulating effect. (NSA)

1703

Drobkov, A. A. BIOLOGICAL EFFECTS OF NATURALLY RADIOACTIVE ELEMENTS. *Uspekhi Sovremennoi Biol.* **31**, 82-100(1951).

A review of effects of Ra, U, Th and other elements on plants. Radiophotographs are shown of sugar beets, virus-infected tobacco, tomato, and pea plants. 84 references. (CA)

1704

Emmett, John. EFFECT OF X-RADIATION ON *TRYPANOSOMA CRUZI*. *J. Parasitol.* **36**, 45-7(1950).

Virulent cultures of *Trypanosoma cruzi* in a medium were irradiated by x-ray doses of 10,000-100,000 r from a 180-kv machine using two unfiltered tubes and at a target distance of 14.8 cm; with this apparatus 10,000 r could be delivered in about 5 min. After varying exposures, 0.5 cc amounts of the cultures were immediately injected intraperitoneally into white mice weighing about 10 g; nonirradiated cultures were injected into control animals. It was found that with dosages up to 100,000 r the trypanosomes remained viable and morphologically unchanged; however, from 10,000 r upwards, a definite decrease in infective power of the organisms was induced. The earliest infection in an experimental animal was on the 5th day, but the majority of the animals did not become positive until several days later, as compared with positive control animals on the 4th to the 7th day. Subcultures from the 100,000 r cultures were allowed to grow a week, checked for motility and numbers, and injected into mice; the approximate number of organisms was somewhat decreased from controls. It is concluded that the radiosensitivity of *Trypanosoma cruzi* parallels that of *T. gambiense* and *T. brucei*, but it is noted that the *T. gambiense* organisms became noninfectious after lower irradiation (12,000 r). (NSA)

1705

Euler, H. von, L. Ahlstrom, and B. Hogberg. CHANGES PRODUCED IN YEAST CELLS BY ROENTGEN RAYS AND CHEMICAL SUBSTANCES. *Z. physiol. Chem.* **277**, 1-17; 18-25(1942).

The damage suffered by the yeast cells (brewer's yeast) exposed to the rays at a distance of 20 cm from the Roentgen tubes was estimated from the number of dead cells which ranged after 5 hours from 5% to 5000 r to 76% at 50,000 r. The surviving cells showed a reduced rate of multiplication afterward as compared with non-irradiated cells. Up to 40% of the surviving cells showed an increase in size. The content in nucleic acid of the yeast was re-

duced by approx. 20%. Large quantities of colchicine (0.5 to 1 g per 100 cc) inhibit the multiplication of yeast. The influence of 300 to 1000 γ is insignificant. Under the influence of colchicine the cells enlarge by 20 to 50%. The treated yeast is more sensitive to Roentgen rays. Doses of 15,000 r have no influence on the fermenting power of the yeast. This is not altered by pretreatment with colchicine. An extract from rat spleens added to yeast not only causes a decrease of growth but also cell degenerations. However, the fermenting effect of the yeast is increased by the spleen extract. (CA)

1706

Evans, T. C., J. C. Slaughter, E. P. Little, and G. Failla. INFLUENCE OF THE MEDIUM ON RADIATION INJURY OF SPERM. *Radiology* **39**, 663-80(1942).

The same dose of x-rays administered to sperm of *A. punctulata* in concentrated form and in sea water suspensions of increasing dilution, inactivated an increasingly larger % of the sperm the more dilute the suspension. Addition of seminal fluid, egg water, egg albumin, gelatin, germ arabic, glycylglycine (pH 8.2) and glycine (pH 8.2) produced decrease in the % of sperm inactivated by a given dose of x-rays. (BA)

1707

Forssberg, Arne. THE REACTIONS OF *PHYCOMYCES BLAKESLEEANUS* AFTER X- AND GAMMA-IRRADIATION. *Acta Radiol.* **22**, 252-9(1941).

P. blakesleeanus was irradiated with x-rays and gamma-rays over a wide range of doses and intensities. Data with regard to the methods of irradiation, and of control of extraneous factors, are promised for a later paper. The author states that a reduction in growth rate can be observed after doses as small as 0.001 r. (BA)

1708

Foster, R. F., L. R. Donaldson, A. D. Welander, K. Bonham and A. H. Seymour. SOME EFFECTS ON EMBRYO AND YOUNG RAINBOW TROUT (*SALMO GAIRDNERI* RICHARDSON) FROM EXPOSING THE PARENT FISH TO X-RAYS. *Growth* **13**, 119-42(1949).

One hundred and forty-eight rainbow trout approximately 20 months old and approaching sexual maturity were divided into a control group and seven irradiated groups. Total body irradiation doses of 50 r, 100 r, 500 r, 750 r, 1,000 r, 1,500 r, and 2,500 r were administered at a distance of 48 in. from the target of the x-ray tube, using 200 kv and 20 ma and filters of 0.5 mm of Cu and 1.0 mm of Al. The average radiation intensity received by the fish was 8.25 r/min. When the fish became mature about three months after irradiation, they were spawned and a total of 115,454 eggs were obtained from 67 females. The gametogenesis, egg development, abnormalities, fry mortality, early fingerling mortality, and growth of the fish are discussed at length and the results are tabulated. Photographs of apparatus used and development stages are furnished. Included are a series of photographs showing: the stages of development of the rainbow trout eggs; the abnormal trout eggs from parents exposed to various doses of x-radiation; abnormal rainbow trout embryos reaching various stages of development; and common types of abnormal fry found among rainbow trout fry. (NSA)

1709

Friedewald, W. F. and R. S. Anderson. THE EFFECTS OF ROENTGEN RAYS ON CELL-VIRUS ASSOCIATIONS. FINDINGS WITH VIRUS-INDUCED RABBIT PAPILLOMAS AND FIBROMAS. *J. Exptl. Med.* **78**, 285-304(1943).

The virus-induced papillomas of cottontail as well as domestic rabbits regress completely within a few weeks when exposed to 5,000 r of X-ray irradiation. The X-rays

do not immediately kill the papilloma cells, but lead to death by inhibiting cellular division and producing pathological changes in the cells which then continue to differentiate. The virus associated with the growths, however, not only persists in undiminished amount during regression, but often an increased yield of it can be obtained on extraction. The fibroma virus in crude extracts or in vivo is inactivated by far less irradiation than the papilloma virus. 10,000 r destroys 90% or more of the infectivity of the fibroma virus, whereas at least 100,000 r is required to inactivate 50% of the papilloma virus in extracts containing about the same amount of protein. No variant of the papilloma virus or fibroma virus has been encountered as a result of the irradiation. (BA)

1710

Goldfeder, Anna. FURTHER STUDIES ON THE RADIO-SENSITIVITY OF THE ANALOGOUS MOUSE MAMMARY TUMORS dbrB AND C3H. Radiology 47, 845-63(1951).

The growth rates of mammary adenocarcinomas of mice were studied before and after irradiation. Chalkley's method (J. Nat. Cancer Inst. 4, 47-53(1943-44)) was applied for quantitative evaluation of growth activity of the tumors, taking the mitotic index as the criterion. A depression in mitotic activity in the irradiated tumors was noted, the extent of which depended upon the dose of radiation applied and the lapse of time between exposure and removal of the tumors for analysis. An earlier and more pronounced return of mitotic activity was noted in the faster-growing dbrB type tumors following sublethal doses of radiation, as compared with the slower-growing C3H type. The levels of the phosphorylated intermediates in the glycolytic cycle for the two mouse mammary adenocarcinomas were determined. The more rapidly growing mammary tumor (dbrB) shows significantly higher levels of glucose-1-phosphate, adenosine triphosphate, and possibly glycogen, and a lower level of inorganic phosphorus than the slower-growing C3H tumor. These findings strongly suggest that a higher level of energy is available for vital function in the dbrB tumor. Some of the compounds encountered in the phosphorylated glycolytic cycle, particularly adenosine triphosphate, may be more readily affected by irradiation in the C3H tumor than in the dbrB tumor. The metabolic processes were operative even after such large doses as 30,000 r for the dbrB tumor and 12,000 r for the C3H, although these doses proved to be lethal for their respective growth activities. Successful application in radiotherapy and advantages of applying large doses of x rays through small portals exposing only the tumor is discussed. (NSA)

1711

Gordon, Solon A. PHYTORADIOLOGY, p.124-5 of BIOLOGICAL AND MEDICAL DIVISIONS; QUARTERLY REPORT FEBRUARY, MARCH, APRIL 1949. Austin M. Brues and Herman Lisco, eds. Argonne National Lab. [nd] 2p. (ANL-4291(p.124-5))

Inactivation of auxin by x radiation is a first order reaction until most of the auxin is destroyed, the ionic yield is 1 in contrast to a value of 25 reported by Skoog. The source of the discrepancy is being investigated. Initial results indicate that radiation interferes with the production of indole acetic acid and its precursor indoleacetaldehyde. (R.D.B.)

1712

Gordon, S. A., R. Stutz, and R. Weber. ACTION OF X RADIATION ON GROWTH BY CELLULAR ELONGATION, p.144-51 of BIOLOGICAL AND MEDICAL DIVISIONS; QUARTERLY REPORT, NOVEMBER, DECEMBER, JANUARY, 1949-50. Austin M. Brues, ed. Argonne National Lab. [nd] 8p. (ANL-4401(p.144-51))

The first shoot of the oat seedling provides a tissue whereby one phase of the growth process, cellular expansion, can be separated from cellular division and differentiation. This phase of growth is apparently resistant to ionizing radiation, inhibition being manifest at rather high dose levels of x radiation. Within relatively narrow limits of dose, growth inhibition can be reversed following irradiation by addition of growth hormone (auxin) and partly reversed by sulfhydryl activants. Such reversals could be interpreted as indicating an inactivation of the foregoing essential components of the growth process by ionizing radiation. A small quantity of C¹⁴-labeled growth hormone, indoleacetic acid, has been synthesized. Synthetic procedures employed are detailed, particularly in view of some erroneous aspects of the published method for the synthesis of this radioauxin. Initial biological experiments using radioindoleacetate show the compound to be physiologically active and to have no deleterious effect on growth due to its emission. (Authors)

1713

Gray, L. H. and M. E. Scholes. THE EFFECT OF IONIZING RADIATIONS ON THE BROAD BEAN ROOT. PART VIII. Brit. J. Radiol. 24, 82-92; 176-80; 228-36(1951).

A detailed study of the effect of x and α radiation on normal root growth of the broad bean, *Vicia faba*, has been made. The morphological and histological aspects of root growth are discussed and equations are derived correlating root growth with mitotic activity and cell elongation. Morphological observations on root growth as a function of time after irradiation are presented. Data obtained from histological studies of changes in roots exposed to 143 r of x rays are reported. The quantitative aspects of the observed cytological abnormalities are considered with particular regard to cell elongation and the correlation of root growth with mitotic activity. Abstracts of succeeding sections of this paper (Brit. J. Radiology 24, 285-91(1951) May and *ibid.*, 348-52(1951) June) appeared in Nuclear Science Abstracts as NSA 5-4317 and 5-4318, respectively. (NSA)

1714

Gray, L. H. and M. E. Scholes. THE EFFECT OF IONIZING RADIATIONS ON THE BROAD BEAN ROOT. PART VIII. Brit. J. Radiol. 24, 285-91(1951).

After exposures lasting a few min to doses of γ radiation up to 250 r, x radiation up to 140 r, and of α radiation up to 36 rep, the rate of growth of roots of *Vicia faba* falls to a minimum and then returns to normal. The γ - and x-ray growth inhibition is dependent on the duration of exposure. The α -ray inhibition is independent of exposure times between 10 min and 24 hr. The minimum value of the growth rate relative to control roots, which occurs at about the 6th day after irradiation, is exponentially related to dose for α radiation. It is also exponential for γ radiation delivered in 12 or 24 hr and tends to exponential for long-duration exposures to x radiation. The relation is sigmoid for both γ and x radiation at higher dose rates. The relative biological efficiency of α radiation compared with x radiation varies from about 4.5 to 12.5, according to the dose level and duration of exposure at which the radiations are compared. Histological changes seen in roots from 2 to 10 days after exposure to 140 r of x rays have been examined in detail. It is concluded that chromosome structural damage constitutes a major factor leading to growth inhibition by all three radiations. (NSA)

1715

Gray, L. H. and M. E. Scholes. THE EFFECT OF IONIZING RADIATIONS ON THE BROAD BEAN ROOT. VIII. Brit. J. Radiol. 24, 348-52(1951).

Two appendices to the previous articles appear. Appendix I gives a detailed description of the germination and culture of the *Vicia faba* used in the experiments, the method used to measure roots with minimum handling, and the procedure for irradiation by α particles. Appendix II includes an explanation of how the number of cells per unit volume of tissue of a particular region can be estimated, the method of estimating τ (duration of mitosis) and t (means intermitotic time at any point in the root), and a definition of resting nucleus, prophase, metaphase, and telophase. 20 references. (NSA)

1716

Handford, S. W. STUDIES ON THE EFFECT OF X-RADIATION ON MORPHOGENESIS OF AMBLYSTOMA PUNCTATUM. Anat. Record 103, 540(1949).

The following is an abstract and is presented here in its entirety.

Embryos at stages 11-12, 15-16, 20-21 and 36-37 received an air dose of 246 r. from a 200 kv therapy machine. The 300 animals treated survived from 15-30 days and all showed pronounced developmental defects. It seems clear that the earlier the stage the greater and more general are the effects. This leads to a shorter time of survival for animals at earlier developmental stages relative to more advanced animals upon which the effects are more specific and slower to become manifest. Outstanding in the individuals treated during early stages are abnormalities of the tail-bud, a general oedema which probably derives from damage of the pronephros; and the eye and gill-mound on one side only. Animals that received treatment at more advanced stages show reduction in the number of digits of the forelimb, failure of the hindlimb to develop normally, and a striking defect of jaws which disallows feeding at stage 46. No complete morphologic study of the preserved material has yet been made.

1717

Henshaw, Paul S. THE ACTION OF X-RAYS ON NUCLEATED AND NON-NUCLEATED EGG FRAGMENTS. Am. J. Cancer 33, 258-64(1938).

Experiments have been carried out to determine whether a certain radiobiological effect results from changes produced in the nucleus or some other part of the cells irradiated. Eggs of *Arbacia punctulata* were used and the effect observed was delay in cell division caused by x-rays. Nucleated and non-nucleated egg fragments were obtained by the centrifuge method, both of which will undergo fertilization and development. These were irradiated and inseminated, and the moment when 50% had divided was determined. It was found that for a given dose of radiation an appreciable delay of about the same extent was produced in whole eggs and nucleated fragments, whereas no delay was produced in the non-nucleated fragments. Thus, since there is a direct correlation between the presence of a nucleus and the manifestation of an irradiation effect and since irradiation changes occurring in parts exclusive of the nucleus produce no observable effect, it appears that the slowing in cell division brought about in *Arbacia* eggs by X-rays is due to changes produced directly in the nucleus by the radiation. (Author's Summary)

1718

Henshaw, Paul S. RESPONSES OF DROSOPHILA PUPAE TO X-RAYS. Radiology 34, 721-30(1940).

The use of *Drosophila* pupae as test objects for quantitative radiobiological work has been considered and investigated. The relation between radiosensitivity, developmental activity, and respiratory rate at various stages during the pupal period has been detd. Using as a criterion of effect, development to the stage of pigmented bristles

legs, and wings, and failure of the imago to emerge, from the puparium, it was found that during the first 18 hrs, the organisms maintain a strikingly uniform radiosensitivity, but that beyond this point their resistance increases at a rapid rate. Considering normal development alone, 3 fairly distinct phases were recognized: the first from 0 to 24 hrs, characterized mainly by destruction and removal of larval organs; the 2nd from 24 to 48 hrs, by relative quiescence, and 3rd, 48-96 hrs, by active organogenesis. The rate of O_2 uptake in these forms decreases during the 1st phase, reaches a minimum during the 2nd and increases during the 3rd, reaching a level at the time of emergence about equal to that at the beginning of the pupal stage. There was therefore, a positive correlation between the rate of O_2 uptake and developmental activity, but none between either of these and radiosensitivity. The reproducibility of the quantitative response of pupae 7 to 18 hrs old to radiation was found to be within narrow limits. The general shape of the curve showing rate of O_2 uptake during the pupal period was not changed appreciably when lethal doses of radiation were administered early in the period. Only a slight delay was manifested which probably has little significance. (BA)

1719

Henshaw, Paul S. PECULIAR GROWTH LESIONS IN FROGS INDUCED BY IRRADIATION OF SPERM CELLS WITH X-RAYS. J. Natl. Cancer Inst. 3, 409-17(1943).

The changes responsible for growth lesions occur in the nucleus of the irradiated cells, the sperm nucleus after heavy irradiation will enter the egg (as part of the sperm cell) but will not fuse with the egg nucleus, growth abnormalities are not obtained in those cases in which the sperm nucleus is not functional. The fact that the sperm cell was free-living at the time of treatment, that it has a haploid number of chromosomes and that a normal egg fertilized with a treated sperm will give rise to growth abnormalities in later development, makes it clear that growth modifications may result from injury to only half of the chromosome complement of the cell. These findings may be regarded as evidence that a radically changed pattern of multicellular growth may be set in motion by the sudden modification of nuclear substances in a single cell. (Authors conclusion) (BA)

1720

Henshaw, Paul S. and H. Turkowitz. SOME EFFECTS OF ROENTGEN RAYS ON SACCHAROMYCES CEREVISIAE. Am. J. Roentgenol. Radium Therapy 43, 93-106(1940).

Cultures of *Saccharomyces cerevisiae* were exposed to intense beams of 200 kv x-rays for varying times, and the subsequent rate of growth measured photometrically. A family of growth curves was obtained which indicated that the growth processes were delayed in some way by the irradiation, but not impaired. This delay appears to be due to organisms killed by the radiation rather than injured; the survivors appear to be as vigorous as the controls. The survival curve of the organisms tends toward the exponential form, with no sigmoid characteristic, indicating that this organism is in the "one-hit-to-kill" category. Microscopical examinations showed that cells affected lethally may undergo several divisions following exposure, but that they rarely, if ever, go beyond the 40-cell stage. (BA)

1721

Hicks, Samuel P. ACUTE NECROSIS AND MALFORMATION OF DEVELOPING MAMMALIAN BRAIN CAUSED BY X-RAY. Proc. Soc. Exptl. Biol. Med. 75, 485-9(1950). (AECU-949)

In the course of an investigation of the pathologic effects of ionizing radiation on the development of the mammalian nervous system it was found that growing central nervous tissues in fetal rats and mice could be selectively and extensively destroyed by x radiation with virtually no destructive effect on other organs. Irradiation of pregnant rats and mice with 200 and 600 r to the whole body resulted in acute necrosis of the rapidly growing parts of the brain, spinal cord, and retinas of their fetuses. This developed within a few hours, was highly selective for the central nervous system, and was often severe and extensive at 200 to 600 r. At 150 r damage was less, and was followed in two days by malformations in the neuroblastic zones. Fetuses allowed to go to term and sacrificed after days or weeks showed severe maldevelopments of corpus callosum, hippocampus, striatum, and cerebral cortex. Extraneural lesions were absent below 200 r and rare at 400 r. Below 100 r no destructive lesions occurred. (NSA)

1722

Kinkel, C. L. THE EFFECT OF ROENTGEN RAYS UPON THE GROWING LONG BONES OF ALBINO RATS. I. QUANTITATIVE STUDIES OF THE GROWTH LIMITATION FOLLOWING IRRADIATION. *Am. J. Roentgenol. Radium Therapy* **47**, 439-57(1942).

The growing epiphyseal regions of the right hind leg of albino rats of various ages were irradiated with filtered 200 kv x-rays in various doses. Growth and development of the irradiated and control (opposite) femurs were followed radiographically for 1 year. The irradiation produced quantitatively predictable degrees of stunting, ranging from temporary retardation to permanent cessation of growth, depending on the dose administered. The amount of radiation required to produce minimal stunting bears a linear relationship to the age of the animal treated; it cannot be correlated with rapidity of growth, or with skin effect. The period of temporary retardation is followed by return to the normal growth rate. Young animals recover more quickly than old, and can tolerate quantities of radiation far in excess of the minimal stunting dose. Months after irradiation with large doses there is no evidence of bony decalcification. Microscopic studies show a return to normal cartilage and bone architecture and absence of permanent marrow or blood vessel injuries. (BA)

1723

Hinkel, C. L. THE EFFECT OF ROENTGEN RAYS UPON THE GROWING LONG BONES OF ALBINO RATS. II. HISTOPATHOLOGICAL CHANGES INVOLVING ENDOCHONDRAL GROWTH CENTERS. *Am. J. Roentgenol. Radium Therapy* **49**, 321-48(1943).

Female Sherman strain albino rats of various ages were anesthetized, immobilized, and irradiated with 600-2500 r of filtered 200 kv X-rays over a field of 5 mm in diameter including the right distal femoral growth center. The left femur of each animal served as the unirradiated control. At various times after irradiation, the animals were sacrificed, the bones of the hind legs fixed, decalcified and studied histologically. Dodds classification of five zones occurring in actively growing cartilage (*Am. J. Anat.*, **55**: 139, 1938) is used as the basis for the descriptions of observed changes. Microscopic abnormalities become evident before there is appreciable interference with growth. Stunting when it occurs, is apparently the result of temporary or permanent cessation of cartilage growth in a distal direction. More lasting secondary effects are explained on the basis of injury to vessels, osteoblasts, and marrow cells. Histopathological changes, are related to dose, age, and interval after irradiation. The amount of osteoclasia

and chondroclasia found proximal to the line of advancing cartilage columns, and the degree of normal anatomical restitution are proportional to the completeness of marrow and vascular regeneration. Osteoid deposition and true osteogenesis do not take place in the absence of osteoblasts; instead a brittle "pseudo bone" is formed. There is always an increase in mineral deposition following irradiation. The metaphyseal region of bones growing after irradiation contains more mineral and more bone than normal. The power of cartilage to regenerate is retained even after large doses of X-rays (2000 r). Blood vessels are markedly reduced in number and rendered irregular in caliber and marrow cells are seriously affected by large doses. Possible mechanisms for the direct and indirect changes are discussed. (BA)

1724

Irvine, Virginia C. X-RADIATION AND GROWTH SUBSTANCES AS AFFECTING PLANT PRIMORDIAL TISSUES. *Proc. Soc. Exptl. Biol. Med.* **43**, 453-5(1940).

In sunflower, zinnia, and tomato seedlings after moderate x-ray doses the meristematic region becomes divided into 2 or 3 parts with separate groups of leaves, leading to distortion or fasciation of leaves, disturbed phyllotoxy, and stunted growth of whole plant. B-naphthoxyacetic acid applied in lanolin paste gives similar, but not identical results. (BA)

1725

Jacobson, L. and R. Overstreet. THE UPTAKE BY PLANTS OF PLUTONIUM AND SOME PRODUCTS OF NUCLEAR FISSION ADSORBED ON SOIL COLLOIDS. *Soil Sci.* **65**, 129-34(1948) (MDDC-1006)

The uptake of plutonium and the fission products Y, Ce, Sr, Te, and Zr + Cb by two species of plants, barley and dwarf pea, was examined. Studies were made using bentonite clay suspensions (barley) and a montmorillonite soil (dwarf pea). In all cases, the roots possess a marked ability to fix large proportions of the above elements even when trace amounts are initially adsorbed on clay particles. With the exception of Sr, the bulk of the activity remains in the roots. Sr is readily translocated to the tops. On the basis of greenhouse experiments, it is concluded that soil activities of the order of 0.1 microcurie per gram in the region of contact with roots will result in obvious injury to the plant. It is estimated that noticeable injury to the plant will occur at much lower levels of soil activity than 0.1 microcurie per gram. (ADD)

1726

Jornlin, Francis M. THE ATOMIC BOMB'S EFFECTS ON PLANTS AND SOILS. *Fertilizer Review* **23**, No. 4, 7-11; **14**, No. 5, 7-9, 11-13(1948).

The possible effects of radioactivity on plants and soils are discussed, together with an investigation of the claims of Mr. Takeo Furuno in Nagasaki that the crop yields after the atomic bombing were accelerated. A description is given of the heat, radiations, and blasts produced by the bombs at Hiroshima and Nagasaki, with respect to their immediate and residual influence on plants, seeds, and soil at various distances from the centers of the blasts. Seeds and other organisms below the soil surface received little irradiation; many plant abnormalities were noted in new sproutings soon after the radiations. The soil at 3,936 feet from the center of the blast showed little radioactivity two months after the bombing, and no activity one year after the bombing. The increased yields in Furuno's fields are believed to be due to large amounts of fertilizer, in the form of potash and $(\text{NH}_4)_2\text{SO}_4$, that he added to the soil. Carefully controlled research is now in progress to establish more definite facts concerning the biological effects of the bombing. (NSA)

1727

Karnofsky, David A., Priscilla A. Patterson, and Lois P. Ridgway. **THE TOXICITY OF ROENTGEN RAYS TO THE CHICK EMBRYO.** *Am. J. Roentgenol. Radium Therapy* **64**, 280-8(1950).

Roentgen rays have been found to exert both an acute and a delayed toxic effect on the chick embryo. The acute effect results in death of the embryo within 20 hours after irradiation. In embryos, eight days and older, the acute toxic effect is dependent on a dose rate above 5 to 10 r/min, and is relatively independent of a total dose above 800 r. The embryo shows an increasing sensitivity to this acute effect during the 3rd to 7th day of incubation, it is most sensitive at the 8th to 10th day, and its response is stabilized at a slightly more resistant level on the 12th day and beyond. The acute death may be avoided, and delayed deaths produced, by lowering the dose rate appropriately for the age of the embryo at the time of irradiation. The delayed effects of roentgen rays are cumulative, and the LD-50 for chick embryos of 2 to 12 days of age is in the range of 1,000 to 1,500 r, at dose rates varying from 1 to 43.4 r. The effects of roentgen rays are still cumulative to produce delayed deaths at a dose rate of 0.55 r/min. The embryos succumbing to the delayed lethal effect of roentgen rays may show vascular injury and hemorrhage, generalized edema, consisting of either a watery or gelatinous fluid, necrosis of the liver and stunting of growth. Developmental abnormalities are common, and are chiefly evident in the beak, limbs, head, and eyes. (NSA)

1728

Kersten, H. J., H. L. Miller, and G. F. Smith. **STIMULATIVE EFFECTS OF X-RAYS ON PLANTS.** *Plant Physiol.* **18**, 8-18(1943).

Investigations were made of stimulation of primary root growth in seedlings from seeds given a small dose of soft x-rays. An apparatus was constructed which permitted 2,000 seeds to be germinated in water culture under controlled conditions. Observations were limited to the first five days of germination. Data on root length and wet and dry weights of roots of seedlings from 1,000 corn seeds (Stowell's Evergreen Sweet Corn) given soft x-ray treatments at voltages ranging from 15 to 25 kv peak were compared to corresponding data obtained from seedlings from 1,000 non-irradiated corn seeds germinated at the same time under the same controlled conditions. Statistical analysis of the data indicates beyond a reasonable doubt that stimulation of primary root growth was obtained by irradiating dry seeds of corn at voltages in the neighborhood of 17.5 to 20 peak kv but not at lower or higher voltages. (BA)

1729

Koch, Wilhelm. **TISSUE DISTRIBUTION OF PETEOSTHOR AND ITS COMPONENTS THORIUM X AND PLATINUM IN THE GROWING ORGANISM AND THE INFLUENCE OF THORIUM X ON EPIPHYSEAL PLATE GROWTH IN THE YOUNG RABBIT.** *Strahlentherapie* **85**, 253-89(1951).

In the organism, ThX (Ra^{224}) and Pt deposits each, independently, favor particular organs. Due to the dysfunction of the enchondral ossification, a several weeks' ThX treatment in rabbits results in a retardation of the growth in length; an impoverishment of the bones in Ca salts; the occurrence of spontaneous fractures, a lesser weight increase and premature birth in the pregnant animal. The selective ThX deposit in the newly calcifying and ossifying tissues permits a ThX therapy in all cases where calcifications and ossifications are primarily involved. During pregnancy and in children, this treatment is contra-indicated. (NSA)

1730

Koester, M. L. **THE EFFECT OF CONTINUOUS GAMMA RADIATION UPON STARCH FORMATION IN ZEA MAYS POLLEN.** *Genetics* **36**, 559(1951). (AECU-1463)

The report is reproduced here in its entirety.

Mature pollen from corn plants was tested with 0.2 per cent solution of iodine potassium iodide to determine those grains which were not completely filled with starch and for this study classed as abnormal. Plants used in this experiment received from 0.09 to 222.2 r per day throughout the growing season. A relationship was found between dosage received and percentage of abnormal pollen produced. Pollen from plants which received dosages up to 1.3 r per day showed no increase over the control in the percentage abnormal, but for dosages above 2.6 r per day there was observed a gradual increase in the percentage of abnormal pollen grains. The highest dosage studied gave the greatest percentage of abnormal pollen, 57.0 per cent. When the log of the dose was plotted against the percentage of abnormal pollen, the data were shown to fit a portion of a sigmoid curve. (NSA)

1731

Latarjet, Raymond. **INTRACELLULAR GROWTH OF BACTERIOPHAGE STUDIED BY ROENTGEN IRRADIATION.** *J. Gen. Physiol.* **31**, 529-44(1948).

Growing *Escherichia coli* infected with bacteriophage T2 was X-rayed during the 21 minutes latent period which elapses between infection and lysis of the cells. Survival curves of the infected bacteria were determined almost from minute to minute; they disclosed the following facts which are related to the process of phage growth: During the first 7 minutes, the infective virus particle remains in the cell unique and genetically intact. The host cell synthesizes some ultraviolet-absorbing material probably devoted to building future particles. From the 7th to 9th minute the X-ray resistance of the virus particle increases, probably because of some internal change. Then, multiplication starts and is completed at about the 13th minute, when an average of 130 virulent units is present per cell, displaying an X-ray resistance twice as high as that of the extracellular virus particle. From 13 minutes to the end, the new units progressively recover the X-ray sensitivity of the extracellular virus. Nothing can be said about either the rate of multiplication between 9 and 13 minutes, or the nature of the multiplying units, except that they are more radiation-resistant (probably smaller) than the extracellular virus. The first steps of the growth process are favored by an unknown component of the lysate, different from the active particles. Several particles can grow in the same host cell. (NSA)

1732

Luce, W. M. **REDUCTION IN FACET NUMBER IN FULL-EYED (REVERTED BAR) DROSOPHILA BY X-RAYS.** *Genetics* **36**, 563(1951).

Larvae of an inbred full-eyed (reverted to full from Bar) strain of *Drosophila melanogaster*, kept at 28 degrees C., were treated with X-ray dosages ranging from 1000 to 3000 r applied at the rate of 500 r per min. The corneas of the eyes of the imagoes which developed from the treated larvae were dissected off, mounted on slides, projected, and the facets counted. The X-rays produced a reduction in facet number. The rate of reduction was approximately 0.075 facets per r. The X-rays when applied before the larvae were 54 hours old (reckoned from the time when the larvae were laid as eggs) had no effect. Larvae treated at anytime when they were from 59 to 80 hours of age responded with essentially similar rates of reduction in facet number per r applied, with some evidence that the rate was less for the lowest dosage used (1000 r). — The X-rays

prolonged larval development. The rate of prolongation, approximately 0.011 hrs. per r, appeared nearly constant for all X-ray applications within the age limits (38-80 hrs.) used in this experiment with the qualification that the 3000 r treatments had a slightly diminished effect on the rate of prolongation. (G)

1733

Modigliani, Franco. STATISTICAL ANALYSIS OF THE EXPERIMENTS ON THE INFLUENCE OF RADIOACTIVE MATERIAL ON THE GROWTH OF CROPS CONDUCTED IN THE U.S.A. IN THE YEARS 1944 TO 1946. Canadian Radium and Uranium Corp. [nd] 36p. (NP-332)

A statistical analysis has been made of 30 field and greenhouse experiments conducted over the years 1944 to 1946. Results of the calculations indicate that with radioactive material added to commercial fertilizer the odds are 19 to 1 that beneficial effect was derived by the following vegetables: pea, cucumber, tomato, lima bean, lettuce, carrot, and sweet potato. A few small-scale experiments on the effect of radioactive material on vegetable crops grown on soil treated with manure failed to reveal any significant beneficial effect resulting from treatment. A few scattered experiments, insufficient for reliable conclusions, on the effect of radioactive material added to commercial fertilizer on crops other than vegetables, namely cereals, cotton, and tobacco, generally failed to reveal any significant beneficial effect of radioactive material on the weight of crops. One experiment with tobacco indicated an increase of 50% in nicotine content. (ACD)

1734

O'Brien, John P. STUDIES ON THE CELLULAR BASIS OF REGENERATION IN *NAIS PARAGUAYENSIS* AND THE EFFECTS OF X-RAYS THEREON. *Growth* 10, 25-44 (1946).

The cellular bases of anterior and posterior regeneration in *Nais paraguayensis* has been studied. Neoblasts, a special type of regenerative cell, constitute a persistent cell stock in the adult naid; they undergo proliferation and migration, and together with the ectoderm enter actively into the regenerative process. X-radiation inhibits regeneration, anteriorly and posteriorly, by way of a selective inhibitive effect upon those cellular elements through the activity of which regeneration is normally accomplished. The neoblasts are more susceptible to irradiation than ectodermal epithelium; sufficient exposure causes their eventual disintegration. Small knobs, formed anteriorly and posteriorly in irradiated specimens, though often bearing stomodeal and proctodeal invaginations, do not represent true regenerative activity. (BA)

1735

Otis, Eileen M. INTRA-UTERINE DEATH TIME IN SEMI-STERILE MICE. *Anat. Record* 105, 533(1949).

Semi-sterile mouse pedigrees descended from males exposed to chronic x-radiation have been studied to determine intra-uterine death time of inviable zygotes. Inviability is presumably due to unbalanced chromosomes. Six pedigrees show developmental failure before the 12th day of pregnancy. Comparison of mouse and human developmental stages has been made using the literature on human development and timed. A curve has been constructed by plotting the time of appearance and differentiation of individual organs or tissues in mouse embryos against the time of corresponding structures in human embryos. From this curve, it is judged that the time span of intra-uterine failure (7-12 days of mouse pregnancy) in the present sample of semi-sterile pedigrees is probably comparable to the second to 6th week of human pregnancy.

1736

Perri, Teodoro. THE BIOLOGIC ACTION OF X-RAYS ON EMBRYOS OF AMPHIBIANS. EXPERIMENTS OF TRANSPLANTATION. *Riv. biol.* 42, 119-54(1950).

In order to analyze the behavior of the different rudimentary organs of irradiated embryos, the author has transplanted such organs on normal embryos, in order to follow their destiny even after the death of the irradiated donors. The following conclusions are listed: (1) The optic vesicle of an embryo, irradiated with certain lethal doses, if it is transplanted on a normal embryo, outlives by a long time the irradiated embryo; in fact, it is sometimes in pretty good condition at the death of the receiver. (2) The fore part of the encephalon is very susceptible, much more than the hind parts. The rudimentary olfactory organ is more resistant than the fore encephalon, but generally less than the optic vesicles. Very resistant are the dorsal cord, the myotomes and the rudimentary tail. (3) In the transplantation of the fore part of the head from irradiated to the normal embryos the disappearance of the fore parts of the encephalon causes the rudimentary olfactory organs to come in mutual contact; the same thing happens with the optic rudimentary organs. (4) The general conclusion is that the embryos irradiated with certain doses of x-rays die, evidently on account of the death of organs indispensable to life, and because those conditions fail that render possible the life of that unity of a superior order which is represented by the organism in its entirety. Some rudimentary organs, however, preserve the capacity to live and to develop themselves at least for a long time, which occurs if they are transplanted on normal embryos. (5) Experiments of transplantation from normal to irradiated embryos and from irradiated to normal embryos, have not brought into evidence that the irradiated medium is in itself hurtful to a normal rudimentary organ, or that the normal medium is itself hurtful to an irradiated rudimentary organ. 35 references. (NSA)

1737

Quastler, Henry and Marianne Baer. INHIBITION OF PLANT GROWTH BY IRRADIATION. PART I. DISCRETE STEPS OF GROWTH INHIBITION AND PATTERN OF DOSE-RESPONSE-RELATION. *J. Cellular Comp. Physiol.* 31, 213-34(1948).

Seeds of Mung beans were treated with various doses of roentgen rays and subsequently allowed to grow in test tubes. The growth of primary root, hypocotyl, and epicotyl were observed and recorded. Each of these three parts grows only for a limited period of time reaching a limited length, even in normal plants. The final length is a useful measure of growth. Irradiation inhibits growth. The relation between final length of primary root and dosage administered shows a pattern characterized by several levels, where the root length remains stable in spite of considerable changes of dosage, and intermediate zones where the root length is labile and varies with dosage. The latter correspond to relatively narrow dosage zones. The dose-response relations for hypocotyl and epicotyl are similar to but simpler than those for the root. It is assumed that the complex pattern of relations between dosage administered and growth inhibition observed corresponds to an equally or more complex hierarchy of growth mechanisms. (NSA)

1738

Quastler, Henry and Marianne Baer. INHIBITION OF PLANT GROWTH BY IRRADIATION. II. SENSITIVITY AND DEVELOPMENT. *J. Cellular Comp. Physiol.* 33, 349-63(1949).

A report is presented on the responses to x-irradiations administered to young growth bean seedlings. The concept of radiosensitivity is defined and methods for its calculation are presented in this report. The most sensitive type of response was elicited when the radiation doses were 1,500-3,500 r for the seedlings and were equivalent in their effect to 29,000-66,000 r delivered to dry seeds; the response was characterized by fully developed side roots and a stunted primary root. A series of experiments eliciting the severe reaction type, characterized by delayed primary growth arrest of the root and inhibition of the development of the side roots and the epicotyl, consisted of radiations of 2,500-5,000 r. It was concluded that the growing seedlings are more sensitive to roentgen rays than dry seeds. It was seen that with mild growth inhibition in the roots, the radiosensitivity rises rapidly, before any growth occurs, and reaches a high value; in severe reactions to the roots, the sensitivity rises to a lesser degree. The developmental rise of sensitivity for the hypocotyl and epicotyl is similar to that for the roots. (NSA)

1739

Quastler, Henry and Marianne Baer. INHIBITION OF PLANT GROWTH BY IRRADIATION. III. SUCCESSIVE RADIATION EFFECTS; HOMOLOGOUS RESPONSES. *J. Cellular Comp. Physiol.* **35**, 75-94(1950).

Growing seedlings of Mung beans (*Phaseolus aureus*) were subjected to roentgen irradiation. The resulting responses showed great diversity but they can be analyzed into a small number of distinct components, most of which are related in nature, or homologous, to some reaction found in dry seeds. Different radiation effects characterized by their timing, and this serves as an additional means of distinguishing distinct growth mechanisms by their differential response to irradiation. (BA)

1740

Quastler, Henry and Marianne Baer. INHIBITION OF PLANT GROWTH BY IRRADIATION. V. RADIATION EFFECTS ON INITIATION AND COMPLETION OF GROWTH. *Cancer Research* **10**, 604-12(1950).

The observations reported concern linear growth in Mung beans (*Phaseolus aureus*), including the growth of individual segments and of the entire hypocotyl and the first segment of the epicotyl in normal plants, after resection of various parts, and after total or partial irradiation with various doses of x radiation. Irradiation with x rays causes three distinct effects: temporary inhibition of growth completion and permanent reduction of the capacities both for initiating and completing growth. Permanent stunting is an effect of local irradiation. An analysis of dose-response relations shows that the apparatus for growth initiation is more vulnerable than the apparatus concerned with actual growth. (NSA)

1741

Rollason, G. S. X-RADIATION OF EGGS OF *RANA PIPIENS* AT VARIOUS MATURATION STAGES. *Biol. Bull.* **97**, 169-86(1949).

Eggs of *Rana pipiens* in the germinal vesicle stage (ovarian eggs), metaphase of the second maturation division (uterine eggs) and during completion of the second maturation division (eggs twenty minutes after fertilization) were irradiated with doses of roentgen units ranging from 100-41,600 r. The irradiation was carried out by means of two Coolidge-type water-cooled tubes at 180 kv, through filters of 2 mm Cu and 1 mm Al; no filtration was used with the highest dosage given, 41,600 r. Counts were made of cleaved eggs, gastrulae, neurulae, hatched embryos, and normal tadpoles. The jelly surrounding the eggs was apparently unaffected except on the ovarian eggs at the

highest irradiation doses (25,600 r and 41,600 r); damage at these doses may have been an indirect effect of the x-rays on the oviduct. The cleavage rate and pattern were not affected; the percentage of cleavage was very much lowered by the irradiation. The lower doses of x-rays had relatively little effect on the ovarian eggs; the uterine eggs were more sensitive to x-radiation than were the ovarian eggs, while the fertilized eggs were by far the most sensitive of the three groups tested; when a dose of 1000 r was administered to the fertilized eggs, only 9.6% of the animals gastrulated, 1.4% of these showed evidence of neurulation and non hatched; a dose of 41,600 r inactivated the uterine eggs, while at this latter dosage, although only a small percentage of the ovarian eggs cleaved, of those that cleaved, 87.5% gastrulated, 62.5% neurulated, and 10.71% hatched. The types of abnormalities produced by irradiation of the eggs are similar to those resulting from irradiation of the sperm of the same species. A delay of 24 hours between irradiation and fertilization of the uterine eggs, to simulate the required delay for the ovarian eggs, appeared to have no effect; there seemed to be no recovery from the effects of the x-radiation. There was no difference in the effectiveness of the different x-ray intensities used in this work as long as the total roentgen exposure remained the same. 43 references. (NSA)

1742

Rugh, Roberts. HISTOLOGICAL EFFECTS ON THE EMBRYO FOLLOWING X-RADIATION. *J. Morphol.* **85**, 683-95(1949). 27p. (AECD-2596)

Larvae of *Amblystoma punctatum* (a salamander) measuring 2.2 cm in total length were given a single dose of 15,000 x-rays for the purpose of studying the resultant histo- and cytological changes after a period of one week, when they were killed. Mitosis was abruptly inhibited in all cells which had not started the process. Those cells which were in mitosis at the time of irradiation were either able to complete the process or the nuclei and chromatin were so severely damaged that the typical intermitotic "resting cell" stage could not be achieved. The tissues most resistant to x-ray damage in the larva were cartilage and muscle, probably because they were the farther developed. There was no evidence of damage to the intercellular matrix of the cartilage or to the myoplasm or myofibrillae of the muscle. The tissue most sensitive to x-ray damage in the larva was that of the central nervous system and the related sense organs. Neuroblasts were sloughed off into the brain cavity and neurocoel, cells and nuclei were in all stages of degeneration, and there was no evidence of growth. This tissue is the most actively differentiating tissue at the time of irradiation. The larval or embryonic tissues are variously sensitive to x-ray damage in a manner quite different from the adult tissues. Discussion is included which points to the possibility that severe damage is impinged upon the so-called resting cell, as compared with the more obvious mitotic phases, since there was complete inhibition of mitoses in all non-mitotic cells. (NSA)

1743

Rugh, Roberts. SOME PRE-LETHAL EFFECTS OF *AM-BLYSTOMA OPACUM* LARVAE EXPOSED TO 25,000 r X-RADIATION. *Anat. Record* **103**, 500-1(1949).

The following is an abstract and is presented here in its entirety.

Larvae of *A. opacum* measuring from 1.7 to 2.6 cm. in total body length were irradiated at 25,000 r, single dose, and studied for morphological and physiological corollaries of irradiation-induced death during the ensuing 9 days. Neuromuscular and cardiac responses showed slight im-

mediate increase, then slow decline with partial recovery at approximately 3-day intervals. The prior ingestion of food increased slightly the peaks of initial activity. Irradiated larvae never ingested food. Chromatophore, gill, and hindlimb development were abruptly stopped as of the time of irradiation. Histological analysis indicated the total absence of mitotic figures after 1 week, with many pycnotic and fragmental nuclei. This implies radiation damage to the nuclei of so-called resting cells. Growth (cell proliferation) was stopped in all tissues. The central nervous system and related sense organs showed the greatest radiation damage. The cells of the brain and cord were disarranged, sloughed off into the neurocoel, or the nuclei extremely abnormal. The cartilage and muscle showed the least radiation damage. It is evident that the most actively proliferating tissue was the most sensitive.

1744

Rugh, Roberts. INHIBITION OF GROWTH AND THE PRODUCTION OF OEDEMA BY X IRRADIATION. *J. Exptl. Zool.* **114**, 137-57(1950).

Incidental to studies on the histopathological effects of x-rays on the early frog (*Rana pipiens*) embryo, it was discovered that at certain stages of development and certain x-ray doses, edema would develop within 24 hours in the majority of cases, and this edema would persist until the death of the embryo. This finding indicated the necessity for trying to determine the exact stage and dose necessary to reproduce the edematous conditions to the maximum extent and the possible origin of the edemas. The results of single exposures to x-irradiation doses of 10,000 to 50,000 r of tadpoles at various stages of development are discussed with respect to the inhibition or stoppage of growth and the production of lordosis (curved back), edema, and other morphological changes. (NSA)

1745

Russell, Liane Brauch. X-RAY INDUCED DEVELOPMENT ABNORMALITIES IN THE MOUSE AND THEIR USE IN THE ANALYSIS OF EMBRYOLOGICAL PATTERNS. I. EXTERNAL AND GROSS VISCERAL CHANGES. *J. Exptl. Zool.* **114**, 545-601(1950) (ORNL-595)

Four-hundred and twenty newborn mice, irradiated with 250 kvp x-rays during intrauterine life, were studied externally and by gross dissection. Treated stages differed by 24 hour intervals and ranged from day $\frac{1}{2}$ to day $13\frac{1}{2}$ after fertilization. Dosages employed were 200 r (100 r in a few cases) for a survey of all stages; 300 and 400 r for dosage comparisons at the last five stages. The irradiated embryos and controls were hybrids between two pure strains (C57 black female x Nb male) and came exclusively from second litters. Irradiation with 200 r before implantation ($\frac{1}{2}$ - $4\frac{1}{2}$ days), and with 300 r at $9\frac{1}{2}$ days increases prenatal mortality in early and late stages, respectively. The peak incidence of natal death follows irradiation on days $9\frac{1}{2}$ and $10\frac{1}{2}$. Considerable depression of birth weight occurs as a consequence of irradiation between days $8\frac{1}{2}$ and $10\frac{1}{2}$. Considerable depression of birth weights occurs as a consequence of irradiation between days $8\frac{1}{2}$ and $13\frac{1}{2}$. Birth weight curves for different doses are unimodal and roughly parallel. They indicate that maximum depression would follow irradiation at a stage intermediate between days $10\frac{1}{2}$ and $11\frac{1}{2}$. Considering two main types of effect following irradiation—namely, prenatal mortality and abnormality at birth—the intrauterine development of the mouse seems to be divisible into three broad phases: (1) days $\frac{1}{2}$ to $4\frac{1}{2}$ (possibly $5\frac{1}{2}$)—considerable incidence of probably early death but 98% (100% in external characters) normality among survivors to term; (2) days $6\frac{1}{2}$ to $13\frac{1}{2}$ —little or no prenatal death but high incidence of abnormalities at birth; (3) days $14\frac{1}{2}$ to birth (data from preliminary

experiment)—neither prenatal death nor visible abnormalities at term with doses of 300 r and below; abnormalities (cataract, hydrocephalus, skin defects) do, however, develop later in life. Irradiation during the $6\frac{1}{2}$ to $13\frac{1}{2}$ day phase reveals a definite pattern of critical periods in the formation of a variety of characters of the newborn. Externally apparent and visceral abnormalities produced with considerable incidence in consequence of treatment on a definite day (or days) and abnormalities, each of which occurred in only one animal are listed. Using the evidence of critical periods, some of the induced abnormalities have been linked with certain phases, or physical events, in the chain of processes known to lead to the formation of affected characters. Sensitivity in some cases occurs at the time of visibly fastest degree of change in a primordium (e.g., the critical period for digital reductions corresponds to the time of growth of limb buds; the second phase of susceptibility to tail reduction is coincident with early tail growth). In other cases, sensitivity is not predictable from known facts of descriptive embryology (e.g., critical period for overgrowth in feet, first phase of susceptibility to tail reduction—both occurring before appearance of visible primordia). Increase in incidence of abnormality with increase in dose indicates that, even where there is an all-or-none effect (actually rarer than graded response), animals are continuously distributed with regard to sensitivity. The sensitivities of certain processes are low and show little scatter. There are both close similarities and striking differences between radiation induced abnormalities and the effects of known genes. (NSA)

1746

Russell, Liane Brauch and W. L. Russell. CHANGES IN THE RELATIVE PROPORTIONS OF DIFFERENT AXIAL SKELETAL TYPES WITHIN INBRED STRAINS OF MICE BROUGHT ABOUT BY X-IRRADIATION AT CRITICAL STAGES IN EMBRYONIC DEVELOPMENT. *Genetics* **35**, 689(1950).

This paper is reproduced here in its entirety.

An extensive study on the effects of single doses of x rays on (C57 x NB) F_1 hybrid mouse embryos, at stages ranging from days $\frac{1}{2}$ to $13\frac{1}{2}$ after fertilization, revealed that the critical period for a posterior shift in the thoracolumbar border was from days $7\frac{1}{2}$ to $9\frac{1}{2}$, with day $8\frac{1}{2}$ exhibiting peak sensitivity. Two strains, one (129) showing considerable natural variability in number of presacral vertebrae and the other (B alb C) showing natural variability in this and in the thoracolumbar border, were chosen, as being probably more sensitive than the specified uniform hybrids, for an extensive dosage-comparison study. Almost 600 newborn mice irradiated during the critical period with doses of 25, 50, 100, or 200 r and 647 controls have been obtained. In the B alb C, an increase in fourteenth-rib development occurs with 25 r on day $8\frac{1}{2}$, is greater with 50 r, and complete with 100 or 200 r. (Number of sternbrae and number of ribs articulating with the sternum are also increased, but correlation with the thoracolumbar shift is incomplete.) Both B alb C's and 129's, whose normal presacral complement is 26-or-27 and 25-or-26, respectively, are shifted toward the higher number by irradiation on day $8\frac{1}{2}$ (50 and, possibly, even 25 r) and, less markedly, on days $7\frac{1}{2}$ and $9\frac{1}{2}$. As had been anticipated, in strains where there is no natural variability, characters are considerably more resistant to radiation-induced shift. This is true of the position of the thoracolumbar border in strain 129 and of the presacral number in the (C57 x NB) F_1 hybrid.

1747

Russell, Liane Brauch and W. L. Russell. THE EFFECTS

OF RADIATION ON THE PREIMPLANTATION STAGES OF THE MOUSE EMBRYO. Anat. Record 108, 521(1950).

This paper is reproduced here in its entirety.

Irradiation during preimplantation (cleavage) stages causes high prenatal mortality but only a negligible incidence of abnormalities in animals surviving to term, the relative magnitude of these two effects being the reverse of that found following irradiation of postimplantation stages. To determine time of death, inbred females which had received 200 r on day $\frac{1}{2}$, $1\frac{1}{2}$, $2\frac{1}{2}$, $3\frac{1}{2}$, or $4\frac{1}{2}$ after mating were dissected on day $10\frac{1}{2}$ or $13\frac{1}{2}$ of gestation. A control was handled simultaneously with each irradiated female. Altogether 831 embryos and resorbing bodies were observed. In over-all effect, the earliest stages are more sensitive; the average number of living embryos per treated female is approximately 20% of the controls in groups irradiated on days $\frac{1}{2}$, $1\frac{1}{2}$, or $2\frac{1}{2}$, but 31 and 57% following treatment on days $3\frac{1}{2}$ and $4\frac{1}{2}$, respectively. In groups irradiated on days $2\frac{1}{2}$ and $3\frac{1}{2}$, the major part (81 and 53%, respectively) of the reduction in live embryo count is accounted for by death after implantation; whereas in groups irradiated on day $\frac{1}{2}$, $1\frac{1}{2}$, and $4\frac{1}{2}$, the majority of the deaths (71, 71, and 75%, respectively) occurs before implantation. Postimplantation death probably occurs considerably before day $10\frac{1}{2}$. The main or sole expression of preimplantation death is on entire litters in groups other than those irradiated on day $\frac{1}{2}$ or $1\frac{1}{2}$ where 39 and 22%, respectively, of the preimplantation death is due to selective mortality within litters. Total-litter death may be due to radiation effect on the mother rather than direct lethal action on embryos.

1748

Russell, Liane Brauch, W. L. Russell, and Mary H. Major. THE EFFECT OF HYPOXIA ON THE RADIATION INDUCTION OF DEVELOPMENTAL ABNORMALITIES IN THE MOUSE. Anat. Record 111, 455(1951).

This report is an abstract and is reproduced here in its entirety.

Several investigations have shown that hypoxia protects against various types of radiation damage (chromosome breakage, sex-linked lethal mutations, immediate lethality). To determine whether protection can also be achieved against radiation induction of developmental abnormalities (previously studied by us in a survey of the entire gestation period), mouse embryos at equal developmental stages were exposed to various doses of x-rays either in 5% O₂ + 95 % He or 21% O₂ + 79% He (i.e., oxygen per cent equivalent to air), having also been preflushed with the respective gas mixture 10 min. prior to raying. Doses used were 0, 100, 200, 300, or 400 r. Irradiation was administered by whole-body exposure to the pregnant mothers: C57B females fertilized $11\frac{1}{2}$ days before by NB males. Our earlier work on critical periods had shown this stage to be convenient for quick assays of differences. The 460 newborns obtained were examined externally, then processed for detailed skeletal study. Hypoxia in itself has no effect on the embryo under the conditions administered. Combined with irradiation, however, it exerts marked protection against damage in all the characters radiosensitive on day $11\frac{1}{2}$ that have so far been studied. These include birth weight, viability, tail length, tail shape, forefoot and hind foot structure. Detailed skeletal findings will be described in future. The magnitude of protection is similar for all the characters so far tabulated, the median abnormality doses in the 5% O₂ mixture ranging from roughly 100 to 160% above those in the 21% O₂ mixture.

1749

Sadun, Elvio H., Joseph N. Ane, Frances Willard Fuller, and Ruth Lewis. THE EFFECT OF X-RAY UPON THE GROWTH AND INFECTIVITY OF ENDAMOEBIA HISTOLYTICA. Am. J. Trop. Med. 30, 635-40(1950).

A brief study of the effect of x-ray treatment in vitro upon the culturability, reproduction, and infectivity of Endamoeba histolytica was carried out. It was observed that single irradiations up to 120,000 r failed to kill or inactivate the organisms in Shaffer-Frye and Balamuth media. Exposure of the "streptobacillus" up to 120,000 r failed to produce any change in its ability to permit growth of amebae in S-F medium. Exposure of amebae in Balamuth culture up to 30,000 r did not seem to affect visibly the normal cycle of population growth. On the other hand, exposures to 60,000 and 120,000 r seemed to inhibit, somewhat, amebic population growth. Viable amebae were observed for 16 transfers after irradiation with 120,000 r. Injection of the progeny of the x-rayed amebae (120,000 r) into normal guinea pigs produced severe intestinal lesions just as did the unexposed controls. (NSA)

1750

Salzgeber, Berthe. STERILIZATION AND INTERSEXUALITY OBTAINED IN CHICKEN EMBRYOS BY X-IRRADIATION. PRELIMINARY REPORT. Bull. biol. France et Belg. 84, 225-33(1950).

Localized irradiation of the gonads of chick embryos with 900 to 1200 r in the 24 to 37 somite stage, followed 1 to 2 days later by total irradiation with 300 r, caused some sterilizations in male and female chicks, and 13 of 21 males became intersexes. Irradiation-produced disturbances in hormone production probably caused these abnormalities. (NSA)

1751

Singleton, W. Ralph. NO STIMULATION FROM X-RAYS OR GAMMA RAYS. Brookhaven National Lab. [nd] 2p. (AECU-804)

The document is in abstract form; it is reproduced below in its entirety.

Various workers have reported at different times preliminary data showing stimulation of slight amounts of radiation. Most, if not all, of these reports are based on limited data and, so far as we are aware, no extensive experiments have corroborated these preliminary indications of stimulation.

Last summer an experiment was planned to determine any stimulating effects of x-rays and gamma rays. The x-ray used was set at 160 kv and 10 ma. Doses given were 250, 500, 1,000, and 2,000 r. Comparable doses of gamma rays were given by placing the seeds (in Petri dishes) at a distance of approximately $\frac{1}{2}$ meter from a 16-curie source of Co⁶⁰. Four different 4 by 4 latin squares were planted with seed given the four different dosages of x-rays and gamma rays. In two latin squares standard early field corn was grown. In the other two, short hybrids with the reduced gene (rd) were grown. These were used because it was thought that small differences in height might be more readily detected. In all the latin squares, 4-row plots were planted, using a split-plot technique whereby two rows were checks with no treatment and for two rows the seed was radiated.

Height measurements were made at weekly intervals on one of the four replications of each latin square, and total height was obtained on the mature plants on all plots. There was no significant difference in height of any of the 4 x-ray treatments or the 4 gamma-ray treatments in

comparison with the controls. Likewise, the yields showed no significant difference for any treatment. Experiments will be run in 1950, using doses of 2,000, 4,000, 8,000, and 16,000 r of both x- and gamma rays. On the basis of present information it seems unlikely that a stimulating effect will be found. Certainly none was found, using doses of 250, 500, 1,000, and 2,000 r of either x-rays or gamma rays. Neither was a depressing effect formed for any of the dosages used.

1752

Skoog, Folke. **THE EFFECT OF X-IRRADIATION ON AUXIN AND PLANT GROWTH.** *J. Cellular Comp. Physiol.* **7**, 227-70(1935).

By the application of hard x-rays to the plant growth hormone, auxin, in solution and to the plant the hormone is inactivated. The mechanism is through the oxidation by strong oxidizing agents formed by irradiation. Thus in a water solution x-rayed in the absence of O_2 there is no hormone destroyed. A comparable inactivation can be carried out also in white light by the use of small concentrations of eosin as a catalyst. Extracted and synthetic heteroauxin, beta-indolyl acetic acid, as well as auxin A are similarly inactivated in aqueous solution. In green plants such as *Pisum* and *Vicia* the subsequent formation of auxin is also inhibited, but in the *Avena* coleoptile in the dark there is no lasting effect on the formation of auxin. The mechanism of transport of auxin in the plant is not affected by irradiation. The application of auxin to treated plants shows that the capacity for growth is as great in irradiated as in control plants. The development of lateral buds in irradiated plants is correlated directly with the removal of auxin and is not due to any stimulation of growth by the x-rays. It is concluded that the effect of irradiation on auxin and on the process of its formation is the major factor in the immediate x-ray inhibition of growth in plants. (BA)

1753

Smith, G. F. and H. Kersten. **ROOT MODIFICATIONS INDUCED IN ZEA MAYS SEEDLINGS BY IRRADIATING DRY SEEDS WITH SOFT X-RAYS.** *Plant Physiol.* **17**, 455-64(1942).

Unsoaked seeds were treated with radiation from a gas-type Cu target x-ray tube operated at 30 peak k.v., 10 ma. for 100 minutes. External modifications include: decreased root-length; failure of lateral root formation; growth cessation after a short period of germination. Histological modifications include: distortion of the primary root tip meristem; distortion of the pericycle in lateral root initiation and of cells of adventitious root-primordia in the first internode; early and rapid formation of lysigenous cavities in the pith region of modified roots as compared with their formation in normal roots; formation of schizogenous cavities due to cell wall splitting in various portions of the pith. (BA)

1754

Sparrow, A. H. and E. Christensen. **EFFECTS OF X-RAY, NEUTRON, AND CHRONIC GAMMA IRRADIATION ON GROWTH AND YIELD OF POTATOES.** *Am. J. Botany* **37**, 667(1950).

This document is reproduced below in its entirety.

Latin-square plots of Katahdin potatoes were planted following exposure of the tubers to 18.75, 75, 300, 1200, and 4800 r of 200 kvp x-rays. Control pieces were taken from each tuber before irradiation and included in each Latin square. Irradiation was given at a constant rate of about 4800 r per hour. Statistical analysis showed no significant effect on yield following 18.75, 75, and 300 r, but did show a significant adverse effect following 1200 and 4800 r.

These yielded, respectively, 75% and 4% of the controls. The latter dosage is shown to be near the lethal limit for Katahdin tubers. True seed was collected from the 18.75, 75, and 300 r groups. Statistical tests of germination showed a significant trend toward better germination in the seed from the 300 r group over the 18.75 and 75 r groups. Further tests are under way. Latin-square plots of the same variety were planted in a field where a centrally located gamma source of approximately 16 c of Co^{60} provided continuous irradiation of 0.26, 1.15, 4.8, 19.5, and 79.7 r per day to give full-season totals of approximately 28, 123, 516, 2086, and 8529 r, respectively. Chronic gamma irradiation over this range of dosages produced no significant relation between dosage and yield. There was no adverse effects on growth or yield even at the highest dosage. The effects of fast-neutron acute irradiation are also under investigation. Significant data will be reported. (NSA)

1755

Tahmisian, Theodore N. **THE EFFECT OF X-RADIATION ON THE METABOLIC PROCESSES OF THE RESTING CELL.** *J. Exptl. Zool.* **112**, 449-63(1949).

Studies on the effect of high dosages of x-rays on respiration and the relationship of nuclear degeneration to the anabolic processes of the cell were conducted utilizing grasshopper eggs (*Melanoplus differentialis*) of known chronological, morphological, and physiological ages. After reaching the age of 40 days, and when in diaphase, the eggs were divided into six groups, five of which were irradiated at 200 kv with no filtration except the petri dish, at a target distance of 2 cm and at the dosage rate of 1,563 to 1,588 r/min; doses were 25,000 r, 50,000 r, 100,000 r, 150,000 r, and 200,000 r for the different groups. Immediately following the irradiation each group was equally divided and one-half was maintained at 0°C and the other half at 25°C while respiration was measured; physiological, and morphological examinations were carried for a period of 40 days after the irradiation. It was found that dosages of 25,000 to 200,000 r did not completely inhibit respiration. Anabolic enzymes were found to be associated with the nuclear material and were more susceptible to the radiation damage than the catabolic enzymes; in a resting cell a nucleus was found to be necessary for the maintenance of the status quo. Pyknosis of the resting nucleus was found to depend upon the x-ray dosage, the state of metabolism and the time. Repression of irradiation damage to the cell could be obtained by subjecting the cells to submetabolic temperatures. (NSA)

1756

Tahmisian, Theodore N. and Dorothy M. Adamson. **THE EFFECT OF ANOXIA ON X-RAY-INDUCED INJURY IN MELANOPLUS DIFFERENTIALIS EMBRYOS.** *Anat. Record* **108**, 516(1950).

This paper is reproduced here in its entirety.

Melanoplus differentialis grasshopper embryos placed in an atmosphere of N_2/CO_2 (95%/5%) for 24 hr developed normally. If these anoxic embryos are irradiated at 25,000 r after 24 hr of anoxia and placed at 25°C in air, negative growth does not occur as with eggs irradiated in air. Upon interrupting diapause by cold treatment for 3 months, when returned to 25°C these embryos irradiated under N_2/CO_2 unlike those irradiated in air show development. Namely, they undergo blastokinesis, increase in size, resting nuclei appear normal, respiration is normal, mitosis resumes, the embryos grow, and the oxidative enzyme due to x radiation does not appear. These do not hatch, however. Since any oxygen which is dissolved in the egg is theoretically used up in $\frac{1}{2}$ hr the irradiation effect on these embryos under N_2/CO_2 is in complete metabolic standstill. Evi-

dently, in orthoptera no anaerobic glycolysis takes place, so that no form of energy release known to us is possible. Since the oxygen substrate moiety is interrupted, we may regard metabolism stopped, and under such conditions irradiation damage is at a minimum.

1757

Toolan, H. W. **PROLIFERATION AND VASCULARIZATION OF ADULT HUMAN EPITHELIUM IN SUBCUTANEOUS TISSUES OF X-IRRADIATED HETEROLOGOUS HOSTS.** *Proc. Soc. Exptl. Biol. Med.* **78**, 540-3(1951).

In 6 experiments, minced fragments of normal adult human epithelium implanted subcutaneously in previously x-irradiated heterologous hosts (rats and hamsters) became vascularized, proliferated and increased for approximately 15 days. After this period they died suddenly. In unirradiated control animals the epithelial material survived in poor condition for 3-7 days but did not become vascularized. When transferred every 10 days to new groups of x-irradiated animals, however, epithelium remained viable and in active mitosis for the duration of the experiment (3 generations or 31 days). (Author's Summary)

1758

Toole, E. H., Vivian K. Toole, J. M. Power, Victor J. Kilmer, and L. T. Alexander. **EFFECTS OF "ALPHA-TRON" AND OTHER RADIOACTIVE MATERIALS ON GERMINATION AND EARLY GROWTH OF VARIOUS CROPS.** U. S. Department of Agriculture. Apr. 24, 1950. 12p. (AECU-852)

The effect of alphanatron (α -emitting material) on germination and early growth of seedlings of wheat, alta fescue, soybean, cucumber, cabbage, radish, tomato, pepper, and corn was studied. The results indicated no consistent trend of any effect either on amount of germination or on early growth of the young seedlings. (NSA)

1759

Umanskii, E. E., B. M. Varshavskii, and V. P. Kudokotsev. **SENSITIZATION OF TISSUES TO X-RAYS.** *Doklady Akad. Nauk S.S.S.R.* **65**, 581-3(1949).

Injection of fluorescein, Neutral red, or Congo red into specimens of *Triturus cristatus* with amputated legs, followed by x-ray irradiation of various levels, showed that fluorescein is the most active sensitizer, so that even a 1000 r dosage of x-rays almost completely represses regeneration of the limb. The other 2 dyes showed very little effect and only at higher x-ray dosages. (CA)

1760

Villée, Claude A. **SOME EFFECTS OF X-RAYS ON DEVELOPMENT IN DROSOPHILA.** *J. Exptl. Zool.* **101**, 261-80(1946).

Drosophila larvae, prepupae, and pupae of 11 genotypes and a variety of ages were irradiated with dosages ranging from 1,096 to 7,000 r at several different intensities. The phenocopies produced varied with the age of the irradiated fly, the stock used, and the intensity and total dosage of the irradiation. Pupation was retarded by all but the smallest dosages used. An irradiation given at high intensity (5,540 r/min.) caused a much higher lethality, both before and after pupation, than an irradiation of comparable total dosage given at low intensity (78 r/min.). Flies irradiated 28 hours after puparium formation showed only the suppression of some microchaetes. Flies irradiated as late larvae or early prepupae showed the suppression of macrochaetes, small, rough, or Lobe eyes, crippled legs, and abnormalities in the formation of mesonotum, scutellum and abdomen. The main effects of irradiating larvae 70-100 hours old were the overgrowth or duplication of parts and examples of abnormal histogenesis: leg-like antennae, formation of palps in the eye, prothoracic palps or wings,

and others. No evidence was found of an interaction between irradiation and the homeotic genes in causing changes in development. Waddington's hypothesis of the indirect action of x-rays in producing their pervasive effects is discussed. (BA)

1761

Warren, Shields and Frank J. Dixon. **EFFECTS OF CONTINUOUS RADIATION ON CHICK EMBRYOS AND DEVELOPING CHICKS. I. GROWTH RATE, GONADS, AND BONE. II. BONE MARROW, LYMPHOID TISSUE, AND PERIPHERAL BLOOD.** *Radiology* **52**, 714-29(1949).

Three sets of experiments were performed on chick embryos and young chicks utilizing P^{32} combined as KH_2PO_4 in order to study the effects of radiation on these organisms. In the first group, White Leghorn embryos in the fourth to fourteenth day of incubation were given single injections, varying in amounts of P^{32} from 47.5 to 300 μ c. In the second group, chicks 1 to 37 days old were given single subcutaneous injections with isotonic solutions of P^{32} , in concentrations of 115-1,050 μ c. The third group consisted of chicks receiving multiple P^{32} injections, the total dosage being 180-3,696 μ c. Part one deals with the effect of radiation on the bones, growth and sex organs of the chicks and embryos. The results show that the P^{32} was mainly concentrated in the long bones of both the embryos and the chicks, and caused considerable over-all growth retardation, resulting in small but well proportioned birds. Both the testes and the ovaries were found to be among the most radiosensitive of the organs and were the least able to recover from the injury caused by continuous radiations. The primitive sex cells in either gonad were the most sensitive element. The spermatogenic cells of the testes remained extremely radiosensitive throughout their development, while the ova became more radioresistant as they matured. The somatic cells of the gonads were much more radioresistant than the sex cells, but their rate of growth was inhibited following injury to the sex cells. In bone growth retardation, the cartilage cells of the epiphysis were much more radiosensitive than the osteoblasts and osteoclasts. After radiation ceased, the bones regained a normal histologic structure but remained dwarfed. Part two deals with the effects of radiation on the bone marrow, lymphoid tissue and the peripheral blood of the Leghorn chicks and embryos. The radiations had crucial effects on the blood-forming tissues, since the P was concentrated most heavily in the bone marrow; maturation of the hematopoietic cells was inhibited and mitotic activity was reduced. These changes were reversible and after the radiation had diminished, the bone marrow returned to normal. The larger doses of radiation, which eventually caused a fatal anemia, produced an immediate and virtually complete cessation of mitotic activity and maturation. In this group, after the radiation had decreased significantly, the few remaining hematopoietic and reticulo-endothelial cells began to show mitotic activity and maturation, but in an amount insufficient to prevent the development of an anemia which proved fatal several days later. The lymphoid tissue of the thymus was also very sensitive to radiation and showed an almost immediate marked reduction of mitotic activity, which lasted until most of the retained P^{32} had been concentrated in the bones. Recovery was rapid, and all but the most severe of these injuries to the lymphoid tissue were reversible. Peripheral blood counts followed a definite pattern during and following irradiation: the lymphocyte count fell first and recovered before the other cell types; the granulocyte count fell next most rapidly and recovered most slowly; the red cell count dropped most slowly and returned to normal midway between lymphocyte and granulocyte counts. (NSA)

1762

Weber, R. P. and S. A. Gordon. THE RADIOSENSITIVITY OF AUXIN BIOSYNTHESIS, p.79-80 of DIVISION OF BIOLOGICAL AND MEDICAL RESEARCH; QUARTERLY REPORT, MAY, JUNE, JULY, 1951, Austin M. Brues, ed. [nd] 3p. (ANL-4676(p.79-80))

The capacity of the plant tissues to produce the growth hormone auxin is rapidly decreased by low doses of ionizing radiation (25 to 100 r). Our experiments also indicate that the radiosensitivity lies in the lability of the enzymes involved in auxin production rather than a sensitivity either of the intermediates of auxin biogenesis, or of auxin itself. (Authors)

1763

Weber, R. P. and S. A. Gordon. THE RADIOSENSITIVITY OF AUXIN BIOSYNTHESIS, p.91-3 of DIVISION OF BIOLOGICAL AND MEDICAL RESEARCH; QUARTERLY REPORT, AUGUST, SEPTEMBER, OCTOBER, 1951, Austin M. Brues, ed. [nd] 3p. (ANL-4713(p.91-3))

Groups of seven-day mung bean seedlings were x-irradiated with dosages ranging from 50 to 1000 r. Determinations were made of the capacity of these plants for converting infiltrated tryptophane to auxin immediately after and for several days following irradiation. Evidence of enzyme damage is apparent immediately after irradiation with low doses; the extent of inhibition of the tryptophan converting system becoming greater as the X ray dose increases. With dosages of 500 r or less, recovery from the inhibitory effect occurs within two weeks; even with doses of 1000 r, recovery is virtually complete at the end of the same period. These findings strikingly correlate an enzymatic radiosensitivity with the effect of low radiation dosages on native auxin levels in kidney bean and cocklebur plants. (Authors)

1764

Welander, A. D., et al. THE EFFECTS OF ROENTGEN RAYS ON THE EMBRYOS AND LARVAE OF THE CHINOOK SALMON. Growth 12, 203-42(1948).

An evaluation was made of the effects of x-rays of 250, 500, 1,000, 2,500, 5,000, and 10,000 r on the eyed embryos of chinook salmon, *Oncorhynchus tshawytscha*, using criteria such as death rate; change in growth rate, of both body weight and length; development of the fins, eyes, coloration and other structures; edematous or other degenerative effects; and histopathological effects on the hemopoietic tissue of the kidney, spleen, gonads, and interrenal bodies. Cell counts and other quantitative measures revealed that the gonads were the most sensitive to x-rays with the hemopoietic tissue second. Most tissues and organs reacted to x-rays of 1,000 r or more, indicating temporary retardation of development for the most part. Mortalities of 52.5% occurred in the 1,000 r group over the period of 125 days of investigation. Severe damage to the organs and tissues and 100% mortalities resulted from doses of 2,500 r or more. (ADD)

1765

Welander, Arthur D., Lauren R. Donaldson, Richard F. Foster, Kelshaw Bonham, Allyn H. Seymour, and Frank G. Lowman. THE EFFECTS OF ROENTGEN RAYS ON ADULT RAINBOW TROUT. University of Washington Applied Fisheries Lab. [nd] 20p. (AECU-188; UWFL-17)

Nearly mature adult rainbow trout were subjected to 25 ma, 200 kv, copper and aluminum filtered x-rays of 50, 100, 500, 750, 1,000, 1,500, and 2,500 r at 8.25 r/min. A total of 148 fish was used in the experiment which lasted 64 weeks. When compared with an unirradiated control group mortalities were significantly higher in fish exposed to 1,000 r or more. Doses of 2,500 r killed all fish in a

period of 13 weeks with the majority dying during the 8th week. Exposures to 1,500 r killed 56% in 13 weeks and 87% in 64 weeks. Mortality in the controls was 15%. Injuries symptomatic of radiation were seen in autopsied fish treated with 500 r or more. The injuries, such as hemorrhage, necrosis, growth of fungus and intestinal damage were generally proportional to the amount of x-ray given. Growth in length and weight was retarded in all irradiated groups as compared with controls. The growth increment during the fastest growing period of the experiment was significantly less in a fish irradiated with 750 r or more and proved to be a sensitive measurement of radiation damage and directly proportional to the amount of radiation given. (NSA)

1766

Whiting, Anna R. FAILURE OF PUPATION OF EPHESTIA LARVAE FOLLOWING EXPOSURE TO X-RAYS. Anat. Record 108, 609(1950).

This paper is reproduced here in its entirety.

The Mediterranean flour moth *E. künniella*, belongs to the group of insects (homodynamic) in which a continuous succession of generations occurs so long as conditions are favorable. In the course of several experiments full-grown larvae were irradiated with doses ranging from 40,000 to 160,000 r. Following a short period of inactivity they moved about normally and were readily stung and fed upon by the parasitic wasp *Habrobracon*. Those not exposed to the parasite continued to crawl, and none pupated. All lived for at least a few days and some (41/177 or 23.16%) were still alive 30 to 40 days after exposure. Control larvae pupated 3 days after time of exposure of treated larvae. The behavior of the irradiated larvae resembles that of diapause larvae in forms (heterodynamic) which show a prolonged arrest of growth in this stage. Whether the x-ray-induced inhibition is due to an interference with secretory processes controlling pupation or to injury to cells of the larval imaginal disks vital to pupal formation is not known. Two irradiated in prepupal stage pupated but have failed to close.

1767

Wilson, C. W. SOME EFFECTS OF THE GAMMA RAYS OF RADIUM ON THE DEVELOPING CHICK EMBRYO. I. THE DEPENDENCE OF THE DELAYED LETHAL DOSE ON THE AGE OF THE EMBRYO. II. THE RECOVERY AND DEVELOPMENT OF CHICK EMBRYOS AFTER IRRADIATION AT VARIOUS AGES. Acta Radiol. 16, 719-34(1935).

Chick embryos of 1-6 days' incubation were uniformly irradiated with γ -rays at an intensity 5.3 r/min. The dose given by 3 hrs. exposure (approx, 1000 r) is near the borderline which permits the complete recovery of an irradiated embryo, with subsequent hatching and this dose is the same for all ages between 1 and 6 days. The radiosensitivity of the chick decreases regularly for the first 3 days of incubation, decreases more rapidly from 3 to 5 days and then remains fairly stationary. There is a possible differential action of roentgen rays and γ -rays on the developing chick embryo. (BA)

1768

Wilson, James G. EFFECTS OF X-IRRADIATION ON EMBRYONIC DEVELOPMENT IN THE RAT. Anat. Record 103, 520-1(1949).

The following is an abstract and is presented here in its entirety.

On the 10th day of gestation rats were opened surgically and shielded with lead plates in such a manner as to permit irradiation of 2 to 5 implantation sites, without exposure of the mother or remaining implantation sites. After post-irradiation intervals of 24, 48, 72, 96, or 120 hours

both irradiated and nonirradiated embryos were removed, weighed and prepared for histologic study. Exposure to 50 r had no effect on embryonic development. Dosage with 100 r. increased slightly the incidence of intrauterine death, reduced temporarily the rate of growth, and caused retarded or anomalous development of eyes in 60% of embryos. These effects were apparent within 24 hours but did not become appreciably more pronounced after longer intervals. Treatment with 200 r. caused similar but more intense effects; higher death rate, slower growth, more severe developmental defects; after progressively longer intervals, death rate and developmental abnormalities increased. Exposure to 400 r. always caused embryonic death within 24 hours after exposure. The eye was the organ most sensitive to the deleterious effects of x-ray, and was the only structure frequently malformed or completely suppressed by irradiation. The brain was second in order of sensitivity to irradiation but it was more often retarded than aberrant in development. Parts of the urinary system, i.e., mesonephros and urogenital sinus, were affected almost as often but rarely as severely as the brain.

1769

Wilson, James G. and John W. Karr. DIFFERENCE IN THE EFFECTS OF X-IRRADIATION IN RAT EMBRYOS OF DIFFERENT AGES. *Anat. Record* **106**, 259-60(1950).

Pregnant rats were opened surgically on the 9th and 10th days postovulation and shielded with lead plates so as to permit direct irradiation of selected implantation sites without exposure of remaining implantation sites or the mother. Irradiated and nonirradiated embryos were removed 3 or 4 days later and prepared for histologic study.

Subsequent development was altered much more severely by x-irradiation on the 9th than on the 10th day of gestation. Exposure to 200 r on the 9th day usually resulted in the death of all embryos, whereas on the 10th day a dosage of 400 r was required to obtain a similar lethal effect. Sublethal dosages at either age caused specific malformations in the survivors, but to produce defects comparable to those produced by 50 r on the 9th day, it was necessary to use 200 r on the 10th day. In both instances the eye was the most common site of maldevelopment (anophthalmia and microphthalmia), the brain was often hypoplastic, and the heart, urinary tract, and brain were occasionally malformed. Situs inversus and malformation of the spinal cord, however, were noted only after irradiation on the 9th day.

Also more prevalent after the earlier exposure were abnormal growths of compact masses of nervous-like cells in the mesenchyme surrounding the brain. Although apparently of neural origin, these islands of aberrant tissue were growing independently of the neural tube. (NSA)

1770

Wilson, James G. and John W. Karr. EFFECTS OF IRRADIATION ON EMBRYONIC DEVELOPMENT. I. X-RAYS ON THE 10TH DAY OF GESTATION IN THE RAT. *Am. J. Anat.* **88**, 1-33(1951).

Doses of 50, 100, 200, or 400 r were given at a single exposure to intrauterine rat embryos the 10th day of gestation, with shielding of the mother animal as well as of the remaining portions of the uterus. Four types of biological effects resulted: general retardation of growth, localized retardation of growth, aberrant growth or malformation, and embryonic death. Exposure to 400 r always caused embryonic death within 24 hr. Malformations of brain, urinary organs, liver, limbs, and inversion of aortic arches occurred after exposure to 100 or 200 r. Improvement or recovery by later accelerated mitotic rate can occur. Malformation of eyes was prevalent and complete regression may occur. 29 figures. (NSA)

1771

Wort, D. J. X-RAY EFFECTS ON THE GROWTH AND REPRODUCTION OF WHEAT. *Plant Physiol.* **16**, 373-83 (1941).

Twenty-four hour-old seedlings of Marquis spring wheat grown from seeds 57 months old and 9 months old were irradiated by x-rays of 19 to 228 r-units, using a 1 mm Al screen. Controls were plants receiving no treatment. Irrespective of the age of the seed greatest growth rate and height were produced by 114 r-unit treatments. Greatest fresh and dry weights of plants grown from the older seeds resulted from the use of 76 r-units; of fresh seeds, from 57 r-units. X-radiation of from 76 to 114 r-units accelerated heading and flowering of plants grown from old seed by as much as three days, but retardation of heading and flowering occurred when fresh seed was irradiated. Height and weight of Fulvio winter wheat seedlings were increased considerably by all doses of x-rays used, the maxima occurring when the dosage was 114 r-units. (BA)

VII GENETICS

1772

Anderson, E. G. ON THE FREQUENCY AND TRANSMITTED CHROMOSOME ALTERATIONS AND GENE MUTATIONS INDUCED BY ATOMIC BOMB RADIATIONS IN MAIZE. *Proc. Natl. Acad. Sci. U. S.* **34**, 387-90(1948).

Samples of maize seed of the single cross L289 × I205 were exposed to the atom bomb radiations at Bikini. Other samples were exposed to 15,000 r units x-ray. They were then tested for hereditary chromosomal alterations and gene mutations. The seeds exposed at Bikini were found to have received nearly 15,000 r units x-ray. In maize, chromosomal alterations can be readily detected by partial pollen sterility. In this study the frequency of alteration was found to be 4.7-6.4% in progenies not entirely random. Random frequency was estimated to be between 4.5 and 5.0%. Gene mutation frequency was very high with probably more than 50% of the gametes of the exposed generation carrying one or more gene mutations. The frequencies of chromosomal alterations and of gene mutations in the Bikini group were roughly equal to those in the x-rayed group. (NSA)

1773

Anderson, E. G., A. E. Longley, C. H. Li, and K. L. Retherford. HEREDITARY EFFECTS PRODUCED IN MAIZE BY RADIATIONS FROM BIKINI ATOMIC BOMB. I. STUDIES ON SEEDLINGS AND POLLEN OF THE EXPOSED GENERATION. *Genetics* **34**, 639-46(1949).

This report deals with the immediate generation of plants grown from five lots of maize seed exposed to atomic radiation, and includes observations on the effects shown in the seedling stage and observations and analyses of the effects shown in the pollen stage; the lots were compared with lots exposed to 5,000 r, 10,000 r, 15,000 r, and 20,000 r of x-radiations. Bikini Lot A showed effects slightly less than those observed in the 15,000 r lot; the effects on the Bikini Lot were, however, more uniform. The percentages of central spikes of the tassels of the plants showing one or more sectors of partially sterile pollen were 4.0-63.1% for the Bikini series, and 29.5-70.4% for the x-ray series. It is estimated that there were between two and three partially sterile sectors per plant of average size of about two branches in the Bikini Lot A. It is concluded that the data indicate that cell competition in the growth of the apical meristem eliminates the more affected cells, thus modifying the dosage frequency relations in the plants. (NSA)

1774

Anderson, Edward H. THE EFFECT OF OXYGEN ON MUTATION INDUCTION BY X-RAYS. Proc. Natl. Acad. Sci. U. S. 37, 340-9(1951).

The effect of a high oxygen tension on the induction of mutations by x-rays has been examined for a streptomycin dependent strain and for a purineless strain of *E.coli*. Back mutation rates to streptomycin nondependence were studied under comparative exposures to x-rays in the presence of oxygen and nitrogen. The sensitivity of both strains to the lethal effects of x-rays was similarly increased by the presence of oxygen during irradiation. Mutation rates of both strains were increased with length of exposure to x-rays in the presence of either oxygen or nitrogen. Oxygen was found to have but slight additional effect over nitrogen on x-ray induction of back mutations in the streptomycin-dependent strain. On the other hand the back mutation rate of the purine-dependent strain was found to be profoundly increased by the presence of oxygen during irradiation. The dose-reduction value of oxygen for the genetic effect for this strain is the same as that for the lethal effect. This is interpreted as an indication that the same mechanisms are involved in the lethal and this specific genetic effect of x-rays in the purineless strain. Different mechanisms appear to be involved in these two effects of x-rays on the streptomycin-dependent strain. (NSA)

1775

Atwood, K. C. RADIATION INDUCED MUTATIONS IN MICROORGANISMS, p.17-20 of CONFERENCE ON BIOLOGICAL APPLICATION OF NUCLEAR PHYSICS, JULY 12-27, 1948. Brookhaven National Lab. July 1948. 154p. (BNL-C-4(p.17-20))

Data suggesting factors, other than lethal mutations, that contribute to the lethal effects of radiation. It remains to be seen whether many of the findings in microorganisms can be brought into line with the target theory. (S.V.S)

1776

Auerbach, Charlotte. INDUCTION OF GENETICAL CHANGE BY CHEMICAL AGENTS, p.44-5 of INTERNATIONAL CONGRESS OF RADIOLOGY, 6th Congress, London. 1950.

At the beginning of the war, research on the pharmacological properties of mustard gas and related poisons showed that these substances, like X-rays, have a preferential effect on dividing cells. This is being used in cancer therapy. Genetical tests with *Drosophila*, and subsequently with other organisms, showed that the mustards, like X-rays, produce their effects in part through an action on chromosomes and genes. The similarity between the genetical effects of these "radiomimetic" poisons and ionising radiations is indeed striking; but closer analysis has revealed certain differences, study of which may lead to a better understanding of the mutation process. Search is being made in several laboratories for other substances which affect chromosomes, in order (a) to test the validity of certain theories about the production of mutations and chromosome breaks (attack on -SH groups; production of OH radicals; depolymerization of nucleic acid; cross-linkage of protein chains), and (b) to find a chemical property shared by all these substances which might be presumed the essential factor for producing nuclear effects of this type. In recent years, several effective substances have been discovered, but their chemical diversity is so great that their action cannot be covered by any existing theory. A further difficulty in this work on the genetical effects of chemical substances is the selective response of certain organisms, cell types, and developmental stages. Thus, formalin which produces mutations in *Drosophila*,

acts only on male germ cells of a definite developmental stage. Diazomethane is highly effective in producing mutations in *Neurospora*, but not in *Drosophila*. With ethylnimine, the situation is reversed.

1777

Baker, William K. THE PRODUCTION OF CHROMOSOME INTERCHANGES IN *DROSOPHILA VIRILIS*. Genetics 33, 603-4(1948).

Males of *D. virilis* were treated with X-ray dosages of 1000, 2000, 3000, and 4000 r units. Any translocations induced in the sperm of these males between chromosomes 2, 3, 4, 5, and Y were detected by a conventional genetic analysis. In strictly comparable experiments, the temperature at the time of irradiation was maintained at either 3° or 28°C. A significantly greater number of translocations are produced at the lower temperature. The results of the cold series, in regard to both the percent of translocations induced and the minimum number of induced breaks, agree very closely at all dosage levels with the mathematical expectations based on the following main assumptions: (1) the number of breaks per sperm follows the Poisson distribution, (2) each of the major autosomes is equally likely to be broken, (3) the mean number of breaks increases linearly with dosage, and (4) the broken chromosome ends unite independently and at random. The decrease in the number of interchanges produced at the warm temperature cannot be attributed to an alteration in the process of joining of the broken ends since the relative numbers of translocations involving two, three, or four chromosomes in both the warm and the cold temperature experiments agree with the expectation. It appears, therefore, that this differential effect is caused by a direct or indirect action of heat on the breakage of the chromosome thread. (G)

1778

Baker, William K. and Elizabeth Sgourakis. ALTERATION OF THE X-RAY SENSITIVITY OF *DROSOPHILA* BY MEANS OF RESPIRATORY INHIBITORS. Genetics 35, 96(1950).

Males of the Oregon-R strain of *D. melanogaster* were subjected to X radiation (1000, 3000, or 5000 r units, 250 kvp, 15 ma) while in an atmosphere of either O₂ or N₂ at an approximate temperature of either 27° or 2°C. The number of X-chromosomes which bear recessive lethal mutations was determined by mating the treated males to the females of Muller-5 stock using the technique outlined by Spencer and Stern (Genetics 33: 43-74, 1948). Depending upon the dosage, a 40-70 per cent reduction in the number of sex-linked lethal mutations is observed in the sperm from the flies irradiated in N₂ as compared to those treated in O₂. Indirect evidence also indicates that the induced frequency of dominant lethals is greatly reduced when the flies are X-rayed in N₂. A significantly greater number of mutations is induced in the flies treated in O₂ at the cold temperature than in those maintained in O₂ at the warm temperature. This "temperature effect" is not evident when the flies are irradiated in N₂ thus indicating that this effect is related to the O₂ concentration in the sperm. The data are compatible with the differences in solubility of O₂ at the temperatures used. Control experiments were performed in which series of flies were subjected to each gas at the two temperatures without irradiation. These experiments show no alteration of the spontaneous mutation rate. (G)

1779

Baker, William K. and Elizabeth Sgourakis. THE EFFECT OF OXYGEN CONCENTRATION ON THE RATE OF X-RAY INDUCED MUTATIONS IN *DROSOPHILA*. Proc. Natl. Acad. Sci. U. S. 36, 176-84(1950).

A striking reduction has been found in the number of recessive sex-linked lethal mutations induced in *Drosophila*.

ila melanogaster males when they are exposed to x-rays while in an atmosphere of low oxygen concentration. Although an increased number of mutations were induced in flies irradiated in oxygen at 2°C over those treated in oxygen at 27°C, this increase was not due to the temperature *per se* but rather it was apparently caused by a higher oxygen tension within the irradiated sperm at the lower temperature. Additional evidence also indicates that fewer dominant lethal mutations and chromosome aberrations are induced in flies maintained in a near oxygen-free atmosphere during irradiation. (NSA)

1780

Bateman, A. J. and W. K. Sinclair. **MUTATIONS INDUCED IN DROSOPHILA BY INGESTED PHOSPHORUS-32.** *Nature* **165**, 117-18(1950).

Radioactive phosphorus, P^{32} , was administered to the larvae of *Drosophila melanogaster* in order to determine the number of mutations which could be induced by the radioisotope. The highest specific amount introduced into the larvae bottles was 1 mc/bottle; this resulted in the death of all the insects before pupation. A 0.1 mc amount resulted in the death of an appreciable number of the specimens, while the introduction of 0.01 mc of P^{32} resulted in no appreciable number of deaths. Flies emerging from the 0.1 mc bottles were further studied; their activity was measured and, though it was variable, the mean figure was 0.0122 μ c/fly two to three days after emergence. The over-all lethal mutation rate observed (7.3%) is the rate which would be expected for an x-ray dose of 2,500 r. The lethal mutation-rate/g-r was derived for the P^{32} and for a dose of 2,500 r of x-rays and was found to be similar, but the author cautions that much significance should not be attached to this similarity. The high mutation-rate of visible produced by the P^{32} corresponds to the expectation from 12,000 r of x-rays. It is concluded that additional work is necessary to confirm whether P^{32} is really four times as efficient as x-rays in the production of visible mutations. Further work on the general effects of the radioisotopes on mutations is in progress. (NSA)

1781

Beadle, G. W. and E. L. Tatum. **GENETIC CONTROL OF BIOCHEMICAL REACTIONS IN NEUROSPORA.** *Proc. Natl. Acad. Sci. U. S.* **27**, 499-506(1941).

By means of x-rays, mutant strains were induced in *Neurospora* which are characterized by their inability to carry out specific biochemical processes. In one the ability to synthesize vitamin B_6 is largely or wholly lost; in another strain the ability to synthesize the thiazole half of the vitamin B_1 molecule is absent; in the third, para-aminobenzoic acid is not synthesized. Inability to synthesize vitamin B_6 is apparently differentiated by a single gene from the ability of the ability of the organism to elaborate this essential growth substance. It was later established that inability to synthesize both thiazole and p-aminobenzoic acid is also inherited as though differentiated from normal by single genes. (BA)

1782

Beal, J. M. **NEGATIVE RESULTS FOLLOWING EXPOSURE OF SEVERAL KINDS OF SEEDS TO COSMIC RAYS AND OTHER RADIATIONS AT HIGH ALTITUDES.** *Botan. Gaz.* **112**, 533-4(1951).

Seed from several species of angiosperms were exposed to cosmic radiations at high altitudes. No mutagenic effects were observed in seedlings grown from these seeds.

1783

Blano, Richard and Werner Braun. **PHENOCOPIES AND X-RADIATION IN DROSOPHILA MELANOGASTER.** *Univ. Calif. (Berkeley) Pubs. Zoöl.* **49**, 31-50(1942).

Pupae of inbred Oregon-R stock were treated when 0-12 hours of age, from $\frac{1}{4}$ to $4\frac{1}{2}$ minutes at about 940 r-units per minute. Percentage of flies showing phenocopies increased with increasing exposures to 100% at 3,290 r-units, with the S-curve showing a linear relation from 235 to 2,115 r-units. The increase in phenocopies per fly is in linear proportion to radiation increase from 1,410 to 3,290 r-units. Frequencies of individual phenocopies were studied, especially reduction of macrochaetes. Anterior and post dorsocentral bristles showed different rates of increase in numbers affected, but anterior and posterior scutellars were similarly affected as dosage increased. Specific x-ray sensitive periods were suggested, but were different from the temperature-effective periods for the same phenocopies. The action of x-rays in producing phenocopies is discussed. A statistical appendix is given. (BA)

1784

Blano, Richard and Claude A. Villee, Jr. **THE EFFECT OF X-RADIATION UPON BRISTLE PATTERN IN DROSOPHILA MELANOGASTER.** *Univ. Calif. (Berkeley) Pubs. Zoöl.* **49**, 51-60(1942).

The effects of x-radiation on bristle reduction are compared for wild Canton-S controls, and several scute and heterozygous scute stocks and compounds with genetic suppression of various bristles. The number and percentages of bristle suppression effects and the differences between treated and control for males and females are shown in tables. Most cases of extreme increase following treatment occur for suppression of these bristles which are genetically affected in a proportion of the controls. The influence of factors other than the scute alleles is suggested in different lines of males with the same scute x-chromosome. (BA)

1785

Blumel, Johanna. **THE ACTION OF RADIOACTIVE PHOSPHORUS IN DROSOPHILA.** *Science* **111**, 205 6(1950).

In the present investigation, radioactive P^{32} was used to study the action of β rays on *Drosophila melanogaster* and *Drosophila virilis*. Pairs of mature flies were placed in shell vials containing a culture medium, consisting of a standard *Drosophila* culture medium and added radioactive H_3PO_4 ; the original volume (about 300 ml) of medium, with a count of 265,000 cpm/ml, was distributed among 50 vials in 6 ml amounts. Twelve days after exposure, the distribution of radioactivity in the various tissues of the insects was determined; few of the *D. virilis* generation hatched in the radioactive solution survived, and none of the adults were tested, but in the case of *D. melanogaster*, the hatch was normal and all present, adults and larvae, were examined. All hatched individuals of *D. virilis* strain were morphologically abnormal, the abnormalities pertaining mostly to the eyes, legs, abdomen, wings, and genitalia. Other data indicate that radioactive P^{32} not only produces mutations in *D. virilis* but also chromosomal rearrangements. The tolerance to such irradiation is considered to be high. (NSA)

1786

Bonner, David. **RADIATION, GENES, AND ENZYMES,** p.51-4 of **BIOLOGICAL APPLICATIONS OF NUCLEAR PHYSICS,** JULY 12-27, 1948. Brookhaven National Lab. July 1948. 3p. (BNL-C-4(p.51-4))

Since the famous experiments of H. J. Muller, it has been known that organisms subjected to irradiation with x-rays or ultraviolet light frequently show heritable morphological changes. In the course of the past decade a great deal of work has been carried out in an effort to obtain a clearer understanding of this phenomenon, since the prob-

lem of the effects of irradiation are intimately associated with the general problem of the nature of gene action. While we are, as yet far indeed from a complete understanding of the mechanism of gene action, the progress of the past decade is most encouraging. This paper is a brief review of the work carried out on this general problem with the fungus *Neurospora crassa*, and includes a discussion of the question of how irradiation with x-rays and ultraviolet light affects this action. (Author's Summary)

1787

Bonnier, Gertrude. **THE INDIRECT ACTION OF X-RAYS ON CHROMOSOMES**, p.45 of **INTERNATIONAL CONGRESS OF RADIOLOGY**, 6th Congress, London. 1950.

In accord with the theory of direct mutagenic action of X-rays (target theory), Bonnier and Lüning found that when males of *Drosophila melanogaster* were irradiated, the rate of mutations, in specified loci, was linearly dependent upon dose. However, when extrapolating to the dose $r = 0$ the "expected" rate thus calculated was distinctly higher than the rate actually found in controls. This indicates that besides the direct action there is some action of an indirect kind. Patterson (1931) showed that after the irradiation of *Drosophila* females gynandromorphs occur due to elimination of the untreated paternal as well as of the treated maternal X-chromosome. The elimination of the untreated chromosome must thus be due to indirect action of X-rays. He found about equal numbers of maternal and paternal eliminations. We have mated irradiated females to untreated males using two different sets of marker genes. One of these gave a great excess of eliminations of the untreated chromosome, the other about equal numbers of treated and untreated. The indirect action in the elimination process may be due to disturbances in the spindle forming substances and/or breaks in the untreated chromosome. After irradiating white-eyed females and mating to non-white males we found 5 mutations from red to white in a progeny of 267,115 females as compared with 1 mutation in 123,263 controls. This finding taken with the other results indicates an indirect mutagenic effect of X-rays. Tentatively we suggest that the ionising action of X-rays produces chemical mutagens which are capable of inducing gene mutations and chromosome breaks.

1788

Bonnier, Gertrude and K. G. Lüning. **STUDIES ON X-RAY MUTATIONS IN THE WHITE AND FORKED LOCI OF DROSOPHILA MELANOGASTER, I. A STATISTICAL ANALYSIS OF MUTATION FREQUENCIES**. *Hereditas* **35**, 163-89(1949).

X-ray experiments on a wild variety of *Drosophila melanogaster*, involving reasonably low doses and observations on a few of the most easily discernible loci, are described. The method used permitted estimates of variations in group doses and statistical analysis of the experimental results. Doses of 727 r, 1,454 r, 2,181 r, and 2,908 r were administered to different groups by means of Sievert's ionization chamber. The 1,216,698 female progeny of the irradiated males formed the basis of the statistical investigation. Results of control experiments indicated a non-linear relationship between mutations and dose. No final conclusions are drawn in this paper. (NSA)

1789

Bonnier, Gertrude, K. G. Lüning, and Ann Margaret Perje. **STUDIES ON X-RAY MUTATIONS IN THE WHITE AND FORKED LOCI OF DROSOPHILA MELANOGASTER, II. A STUDY OF THE FORMATION OF GYNANDROMORPHS AND OTHER KINDS OF MOSAICS**. *Hereditas* **35**, 301-35 (1949).

This paper discusses certain aspects of the formation of mosaics of different kinds after x-irradiation of wild males of *Drosophila melanogaster*. A study was made of the 140 gynandromorphs occurring after crossing yellow white singed females to wild males irradiated with 2,908 r; cases with small female (wild type) areas isolated within male areas were especially investigated. Cases of gynandromorphs with sexcombs on wild-type forelegs are described; other results are summarized, and the results of a previous investigation are reviewed. (NSA)

1790

Born, H. J. and K. G. Zimmer. **INCREASE OF X-RAY INDUCED MUTATION RATE, AS AFFECTED BY HEAVY ATOM SALTS INTRODUCED INTO THE BODY**. *Z. indukt. Abstamm. Vererbungsl.* **78**, 246-50(1940).

Chemical analysis for Fe (colorimetric method with "Rhodankalium") and for U (through reaction with K ferrocyanide) shows that flies fed with salts of these metals show a slight increase in their content over controls. Analysis for Fe of ash from gonads alone shows an insignificant increase of fed over control flies. Similar results were obtained from analysis for Pb. The increase in x-ray absorbing ability caused by the increased metal absorption is about 1%. Since mutation rates in fed flies were increased by 30-50%, this mutational increase cannot be explained by the greater ability of the treated flies to absorb x-rays. (BA)

1791

Brown, Meta S. **ABERRATIONS FOUND IN THE PROGENIES OF PLANTS GROWN FROM IRRADIATED COTTON SEED**. Naval Medical Research Section, Joint Task Force One. [nd] 10p. (NP-1903)

A report has been presented previously (NSA 4-5568) giving a cytological description of 14 cotton, *Gossypium hirsutum*, plants grown from seeds exposed to γ radiation at Bikini. Plants grown from seeds harvested from these 14 cotton plants have now been studied for possible mutations and other transmitted changes. It is concluded that, although chromosome breaks are readily induced, gene mutations are infrequent. (NSA)

1792

Buchmann, W. and G. Sydow. **THE EFFECT OF HEAVY METAL SALTS ON X-RAY INDUCED MUTATIONS IN DROSOPHILA MELANOGASTER. EXPERIMENTS USING URANYL ACETATE**. *Biol. Zentr.* **60**, 137-42(1940).

About 40%-50% of 1- to 2-day-old wild-type $\sigma\sigma$ died after 3-4 days on food containing 1% uranylacetate. For the survivors the sex-linked mutation rate (CIB method) increased significantly from 8.6% to 14-9%, after an X-ray treatment of 3000 r. The few visible mutations affected mostly the wings. (BA)

1793

Buchmann, Walter and Karl G. Zimmer. **INCREASE OF X-RAY INDUCED MUTATION RATE AS AFFECTED BY HEAVY ATOM SALTS INTRODUCED INTO THE ORGANISM**. *Z. indukt. Abstamm. Vererbungsl.* **79**, 192-8(1941).

Feeding of Pb acetate to *Drosophila* in larval and imaginal stages increases the rate of lethal mutations induced by subsequent X-ray treatment, the increase varying with wave length in accordance with the mass absorption coeff. of Pb. This is in contrast with the absence of wave length dependence of increased mutational susceptibility due to iron-feeding and hence supports the contention that the results with Fe cannot be explained by a mere increase in physical absorption. (BA)

1794

Burkholder, P. R. and Norman H. Giles, Jr. **INDUCED BIOCHEMICAL MUTATIONS IN *BACILLUS SUBTILIS***. *Am. J. Botany* **34**, 345-8(1947).

Irradiation of spores or vegetative cells of *B. subtilis* with either ultraviolet or x-ray has resulted in the production of numerous biochemical mutant strains differing from the parent strain in their inability to synthesize specific growth factors. From 4,260 isolates, 143 singly deficient mutants have been identified. The number of mutants occurring in each of the three general classification categories is as follows: 33 strains requiring specific B vitamins; four requiring nucleic acid components; and 106 requiring amino acids. The growth of the singly deficient mutants which have been tested is proportional to the amount of the growth substance supplied. A few isolates having multiple requirements have been obtained. Nine independent mutant strains requiring riboflavin at 30°C were found to be temperature insensitive types, since these strains also require the vitamin at lower temperatures. The relatively high yield of mutants which was obtained with irradiation and with immediate plating of spores supports the view that the spores of *B. subtilis* are uninucleate and haploid. (Author's Summary)

1795

Caldecott, Richard S. and Luther Smith. **THE INFLUENCE OF HEAT TREATMENTS ON THE INJURY AND CYTOGENETIC EFFECTS OF X-RAYS ON BARLEY**. *Genetics* **36**, 546(1951).

Dormant seeds of Himalaya barley were subjected to the following treatments: 1) Control; 2) X-radiation only (15,000r); 3) Heat only (ranging from 75°C to 85°C for 30 minutes in different tests); 4) X-radiation followed immediately by heat; 5) Heat followed immediately by X-radiation. — The effects of these treatments were measured by: 1) Injury (height of seedlings at 14 days); 2) Survival to maturity; 3) Frequencies of chromosomal aberrations in root-tip cells and in pollen mother cells of X_1 plants (those grown from the treated seeds); 4) Frequencies of seedling mutation in X_2 head progenies. — The heat treatments alone had no perceptible influence on the injury, chromosomal aberrations, or mutations. However, such heat treatments applied before the X-radiation significantly reduced the injury resulting from the irradiation. The effect on injury was more variable if the treatments were applied in the reverse order, that is, X-radiation followed by heat. In some of these comparisons the injury was more and in others less than that resulting from X-radiations alone. Chromosomal aberrations (as measured by chromatid bridges at anaphase in root-tip cells and by interchanges at the first meiotic division in pollen mother cells) were reduced by 30-50 per cent, regardless of whether the heat treatment was applied before or after the irradiation. On the other hand, the mutation frequency was increased from 30-50 per cent in the seeds given these combination heat and X-ray treatments. Thus, the same combination treatments resulted in: 1) A decrease in chromosomal aberrations, and 2) an increase in mutations—a clear lack of parallelism between these two effects of ionizing radiations. (G)

1796

Carter, T. C. **RADIATION-INDUCED MUTATIONS IN MAMMATION TISSUE: THE EFFECT OF CHRONIC LOW-DOSE-RATE GAMMA-IRRADIATION ON THE MUTATION RATE OF VISIBLE MUTANTS IN MALE MICE**, p.46 of *INTERNATIONAL CONGRESS OF RADIOLOGY*, 6th Congress, London. 1950.

A pilot investigation into the effect of chronic low-dosage-rate whole-body gamma-irradiation (radium) on the mutation rate of visible mutants in male CBA-strain mice is being made. Dosage rates of 6r, 1.2r, 0.24r, and 0.0r. per 16-hour day are used and irradiation is continued for 25 five-day weeks. Spermatozoa from irradiated males are analysed for recessive visible mutants by one of two methods, namely (i) treated males are mated to females homozygous for several recessive visibles and the F_1 mice are examined for recessive phenotypes, (ii) treated males are mated to CBA females and the F_1 mice (each representing one irradiated spermatozoon) are analysed for recessive visibles by the backcross technique used by Paula Hertwig. Four visible mutants have been found, including two recurrences of known mutants and at least one new recessive visible ("ataxia"); but in each case it has been possible to show that the mutation was spontaneous and not radiation-induced. Much valuable information has been gained about the problems of planning and executing work of this type, but the conclusions to be drawn about induced mutation rates are purely negative. The results suggest an unexpectedly high spontaneous mutation rate.

1797

Caspari, Ernst and Curt Stern. **THE INFLUENCE OF CHRONIC IRRADIATION WITH GAMMA RAYS AT LOW DOSAGES ON THE MUTATION RATE IN *DROSOPHILA MELANOGASTER***. *Genetics* **33**, 75-94(1948).

The rate of lethal sex-linked mutations in *Drosophila* exposed to gamma-rays of 2.5 r units per day through 21 days (total 52.5 r) was determined. In a total of 108,215 chromosomes tested, no significant difference between experimental and controls was found. The difference between experimental and controls found in the present investigation is significantly different ($P = 0.012$) from that found by Spencer and Stern with the same amount of x-radiation given as one dose. By comparing the present results with those obtained by Spencer and Stern and by Raychoudhuri, it is concluded that it is unlikely that the relative inactivity of the irradiation is due to wave length and temperature of glass containers. As possible causes for the inactivity of irradiation, different sensitivity of sperm at different stages of aging, and dependence of induced mutation rate of low dosages on a time factor are considered. (NSA)

1798

Caspari, Ernst. **PRODUCTION OF MUTATIONS BY IONIZING RADIATIONS**, p.21-6 of *CONFERENCE ON BIOLOGICAL APPLICATIONS OF NUCLEAR PHYSICS*, JULY 12-27, 1948. Brookhaven National Lab. July 1948. 154p. (BNL-C-4)

Author concludes: main reason for assuming the theory of direct action of radiation has been the linear proportionality between dosage and mutation rate. But this result only indicates a characteristic statistical connection between the primary effect which must follow the hit theory and the observable biological end effect. It would, therefore, only be necessary to assume that any intermediate effect would not be sensitive to changes in environmental and intracellular factors. It must be concluded that, as far as gene mutations go, the difference between direct and indirect action is not as large as would appear at first glance. (S.V.S.)

1799

Catcheside, D. G. **GENETIC EFFECTS OF RADIATION**. *Brit. Med. Bull.* **4**, 18-23(1946).

The following topics are discussed: 1) Stability in chromosomes and genes; 2) radiation-induced mutation in *Drosophila melanogaster*; 3) induced chromosome aberrations. A diagram shows the mode of production of some chromosome structural changes, namely chromosome break, symmetrical interchange and asymmetrical interchange. For each of these three types the chromosomes are shown as unbroken, broken, in reunion, metaphase configuration and anaphase configuration. (BA)

1800

Catcheside, D. G. GENETIC EFFECTS OF RADIATIONS, p.271-358 of ADVANCES IN GENETICS, Volume II, M. Demerec, ed. Academic Press, Inc., New York. 1948.

In this review the author is concerned only with the genetic effects of radiation in so far as these throw light on the mechanisms involved or upon the nature of the genetic changes and of the gene itself. No detailed consideration is afforded genetic effects of radiation such as the induction of non-disjunction, of attached-X detachment, of oogonial and spermatogonial crossing-over in *Drosophila*, of phenocopies, or of position effects. Author discusses general cytological effects of radiations; types of structural change; sequence of induced structural change in the mitotic cycle; quantitative relations: relative frequency of inter- and intrachanges, distribution amongst nuclei, location of breaks in chromosomes, restitution, modifying factors, dependence of yield on radiation intensity, dependence of yield on dose, relative efficiencies of different wavelengths and types of ionizing radiations, structural changes induced by ultraviolet light; time of split of chromosomes; mechanism of induction of chromosome structural changes: direct action breakage, initial separation of exchange breaks, proportion of breaks that reconstitute; relative efficiencies of different radiations; structural change in *Drosophila*; production of mutations by radiations; recessive lethal mutations in *Drosophila*; other mutagenic agents; cosmic rays and mutations; radiations and gene size; the nature of sex-linked recessive lethals in *Drosophila*; the nature of visible mutations; and genetical effects of ultraviolet light. (S.V.S.)

1801

Catcheside, D. G. and D. E. Lea. THE RATE OF INDUCTION OF DOMINANT LETHALS IN *DROSOPHILA MELANOGASTER* SPERM BY X-RAYS. *J. Genet.* 47, 1-9(1945).

Dominant lethals were induced by 5 x-ray doses over the range from 1,124-11,420 r units in Oregon-R wild type and in *w* mutant flies. The results checked well with those obtained by other workers, and amount, at low doses, to 12% per 1,000 r for death in the embryo stage and 20% per 1,000 r for death at any stage between zygote and adult. At higher doses of x-rays both rates increase, so that over the whole dose range the dose-action curve does not fit a single-hit type of action, although this is approximated at low doses. Ratio of females to males declines about 2.5% per 1,000 r. (BA)

1802

Catsch, A., A. Kanellis, G. H. Radu, and P. Welt. INDUCTION OF CHROMOSOME MUTATIONS OF *D. MELANOGASTER* BY ROENTGEN RAYS OF VARIOUS WAVELENGTHS. *Naturwissenschaften* 32, 228(1944).

The literature to 1942 contains no definite proof that chromosome mutation induced by x-rays is a function of wavelength. The author proposes to study the problem more statistically. He chose the rate of the II/III-translocation as a test, with developed sperm of *D. melanogaster*. Doses of 1,000 r, 2,000 r, and 4,000 r were given at each

of the effective wavelengths 0.5 A, 0.4 A, and 0.15 A. Excitation potential of x-ray tube 35 KV (0.5 mm, Al filter, H.V.L. = 0.5 mm Al) 70 KV (ditto, H.V.L. = 0.9 mm Al) and 180 KV (0.5 mm Cu = 0.5 mm Al filter, H.V.L. = 1.1 mm Cu). An analysis of the results from the 913 to 2,342 samples at a given wavelength showed that the effectiveness of soft and hard x-rays was not statistically differentiable. Neither the mutation constant nor the form $T = CD^{1.5}$ of his lethal-dosage-curve (Catsch, Radu, and Kanellis, *Naturwiss.* 31/32, 1943) was changed. In the above reference T is the translocation rate, D the dose in r units, and C a proportionality constant. (BA)

1803

Catsch, A., O. Peter, and P. Welt. A COMPARISON OF THE EFFECTS OF ROENTGEN RAYS AND HIGH SPEED NEUTRONS ON THE CHROMOSOME MUTATION RATE OF *D. MELANOGASTER*. *Naturwissenschaften* 32, 230-1 (1944).

Do x-rays and neutrons differ in their ability to change the rate of chromosome mutations? The II/III translocation, expressed in per cent, was established as a function of the dose in r units to which the chromosomes of nature sperm of *D. melanogaster* were exposed. The radiation-dose of high speed Li + D-neutrons was evaluated in r-equivalent units after the method of K. G. Zimmer (*Strahlenther.*, 63, 1938); (*Physik. Zeitschr.*, 42, 1941). Neutron doses (r-units) were 1,050, 2,160, 4,480. Numbers examined at each dose were 3,287, 3,159, 2,665. Percentages of observed II/III-translocations were 1.07 ± 0.18 , 1.87 ± 0.24 , 4.09 ± 0.38 . X-ray doses (r-units) were 1,006, 2,000, 4,000. Numbers examined were 6,016, 5,775, and 10,223. Per cent observed II-III-translocations, 1.33 ± 0.15 , 3.79 ± 0.25 , 11.09 ± 0.30 . Conclusions: The efficiency of neutrons is less than the x-ray radiations. The dosage proportionality curve (the lethal effectiveness) for x-rays is best represented by $T = cD^{1.5}$ where T = translocation rate, D = dose and c an experimental constant. The shape of the curve allows the author to deduce that a multiple hit (target theory) process is involved. The data from neutrons (where $T = cD$) imply a single hit process involved. (BA)

1804

Cavalli, L. L. and N. Visconti di Modrone. BACTERIAL MUTATIONS FOR RESISTANCE TO RADIATIONS AND TO NITROGEN MUSTARD. *Proc. Intern. Congr. Genetics* 8th Congress, Stockholm 1948 (Suppl. to *Hereditas*) 550-1(1949).

E. coli B, producing mutants resistant to radiation (B/r) were investigated. Regarding resistance to radiations, the resistant cells appearing in cultures of the B strain are very similar to B/r cells. They are not mutants but phenocopies. When single resistant B cells are subcultured, they show a gradual loss of resistance, even before division, and when kept in saline after irradiation. Thus resistance occurring in the largest proportion of cells is not inherited, but is simply of a physiological nature; only a very small fraction of these resistant cells seem to be the true, stable, resistant mutant B/r, which is spontaneously produced at a rate between 10^{-8} and 10^{-7} per cell per generation. Tests with B and B/r strains for resistance to nitrogen mustard (Ny) showed the latter strains to be considerably more resistant than the original B strain. Similarly, the B strain cultured in the presence of Ny showed an increase of resistance due to the selection of resistant mutants (B/Ny) which proved to be resistant to radiation as well. No further increase in resistance was obtained with B/r. It appears that B/r and B/Ny are the same

mutation, isolated through the different selective agents. (CA)

1805

Charles, Donald R. SUMMARY OF MOUSE GENETICS WORK. Univ. of Rochester. [nd] 2p. (AECU-378)

The objectives of the work of this laboratory have been: (1) to determine how often dominant mutations occur in the sperm of mice exposed daily to x-radiation as a function of the daily dosage and number of exposures; (2) to find a way of judging whether certain of these mutations (semi-sterilities) would, if they occurred in humans, have serious consequences for individuals inheriting them; (3) to investigate the extent and duration of chromosome damage, produced by single x-ray doses ranging from 58-229 r, in certain "poietic" tissues whose main activity is constant and rapid production of new cells, as a possible cause of the reduction, after x-ray exposure, in the cell populations normally replenished by the poietic tissues. Results have been obtained as follows: (1) At least twenty mutations are found to have occurred in the sperm of exposed and control males. Of the twenty mutations, nine are semi-sterilities, three are sex-linked lethals, and eight are dominant gene mutations. (2) Uterine deaths of offspring from semi-sterile humans should occur before the end of the seventh week and thus should not be a serious medical problem. (3) Broken chromosomes are increasingly frequent in cells dividing within the first hour after exposure. Two days after exposure few or no broken chromosomes are to be found. (NSA)

1806

Charles, Donald R. RADIATION-INDUCED MUTATIONS IN MAMMALS. Radiology 55, 579-81(1950).

The seriousness of the effects of radiation-induced mutations is considered. Data on the mutation rates and types of genetic changes induced in mice by repeated small exposures of x-rays and neutrons is presented. New mutations occur in about 1% of mouse sperm for each 100 r of exposure at low-dosage rate. Of these mutations, about 40% would perhaps not be a real health hazard to individuals inheriting them. Another 40%, the recessives, would not be apparent for probably many generations. Only 20%, the dominants, would have immediate effects on offspring receiving them. The death rate caused by semi-sterility mutations in humans has been estimated by studying the time equivalence between mouse and human development. The tentative conclusion is reached that women with inherited semi-sterility would lose half their offspring in the embryonic period, before the 7th week, and so presumably without really serious effects. (NSA)

1807

Chatters, R. M. INDUCTION BY FAST NEUTRONS OF MUTATIONS IN ANTIRRHINUM. II. GENETICS. Am. Naturalist 74, 283-5(1940).

Mutations were produced (or hastened) by irradiating dry seeds with fast neutrons. The mutants, after self pollination, produced like progeny in a significantly large number of cases. (BA)

1808

Cole, Leon J. and Harold E. Finley. THE PRODUCTION OF SOMATIC MUTATIONS IN THE PIGEON WITH X-RAYS. Genetics 27, 138(1942).

The exhibit shows flight feathers from ash-red pigeons of genotype B^AB. Feathers on the right panel are from the right wing; on the left are the corresponding feathers from the left wing. In the top row are feathers plucked before any treatment; they show relatively little flecking. Immediately after plucking the empty follicles in the right wing were exposed to 750 r and 1000 r of X-rays; those in the

left wing received no treatment. In the second row are the feathers regenerated from these follicles. It is evident that the amount of flecking has been greatly increased in the treated feathers. That a permanent change has been produced is indicated by the tendency to reproduce the flecking pattern in three subsequent feather-generations from these same follicles (rows 3,4 and 5) without further treatment. This increase in flecking may be attributed to mutations produced in the feather germ by the X-rays, either by change of the B^A gene to B or b, or by the production of a deficiency in that region; the present experiment is not decisive as to which. (G)

1809

Corberi, E. PRODUCTION OF NEW FORMS OF EUTORULOPSIS DUBIA BY ACTION OF X-RAYS. Boll. Soc. ital. biol. sper. 25, 526-8(1949).

A type of *Torula rosea*, renamed *Eutorulopsis* by Ciferri and Redaelli, was submitted to x-rays, and certain new forms were produced, with somewhat different pigmentation. These proved to have the same properties as far as gelatin-hydrolytic and sugar-fermentative powers were concerned, but differed in the production of smaller amounts of catalase and in O metabolism. (CA)

1810

Crouse, Helen V. THE RESISTANCE OF SCIARA (DIPTERA) TO THE MUTAGENIC EFFECTS OF IRRADIATION. Biol. Bull. 97, 311-14(1949).

A review is presented on data from previous workers in which it was noted that gross and minute chromosome rearrangements could be induced by irradiation of the germ cells of the *Sciara* (Diptera) but visible mutations appeared at a negligible frequency. The experiments reported in this paper were originally performed in connection with cytogenetic studies on the unusual behavior of the sex chromosome of the *Sciara*; in one experiment, nine females of the *Sciara coprophila* strain were bred singly to adult males which had been irradiated with 4,000 r of x-rays, and it was found that the dominant lethal value for the number of offspring compared almost identically with that found in *Drosophila* irradiated at the same intensity. Several factors are offered as possible reasons for the great difference between *Sciara* and *Drosophila* in the visible mutation rates: the external appearance of this fly (bristle pattern, pigmentation, etc.) is such that only the most conspicuous visible changes are likely to be noticed; and, there is a distinct difference between the autosomal and sex-linked mutations, suggesting that the induced mutation rate in this genus is considerably greater than the detected mutation rate. (NSA)

1811

Davis, B. D. PHENOMIC DELAY IN RADIATION-INDUCED REVERSION OF *E. COLI* AUXOTROPHS TO NUTRITIONAL INDEPENDENCE. Genetics 35, 661-2(1950).

We have reported, in connection with the penicillin method, that phenotypic expression of UV-induced auxotrophic mutations requires growth. UV-induced reversions (without reference to genetic location) have given similar results. *Tryp*⁻ strain 19-2, irradiated in washed suspension (survival 50% to 1%) and plated on minimal medium, shows little induced reversion. A trace of tryptophan (0.002-0.1 γ/ml.), however, produces up to 300-fold increases in reversion rate with irradiated inocula, but none with unirradiated controls. Similar effects of trace enrichment have been obtained with other amino acid, purine, and vitamin auxotrophs. The phenomenon could be due to requirement of growth for the action of a mutagen produced by UV irradiation. Similar delay, however, is encountered with X-irradiation, which, in contrast to UV, does not pro-

duce a photochemically reversible mutagen. True phenomic delay therefore appears more likely, according to which the gene has mutated but cannot start to form the previously deficient enzyme until the cell is supplied with the product of that enzyme. This "pump-priming" effect implies that the metabolic turnover of the non-growing cell fails to provide a substrate, or exhaust an inhibitor, of some reaction essential for the synthesis of the previously deficient enzyme. With most strains reversions are heterogeneous with respect to growth rate, as are prototrophs obtained by genetic recombination. Reversions were induced by irradiation in all auxotrophs studied, but not in a *lac*⁻ strain (Lederberg's Y-87) with a spontaneous reversion frequency of 2×10^{-6} , despite the opportunity for phenomic development. No explanation is available. (RG)

1812

Dean, A. C. R. and Cyril Hinshelwood. INDUCED AND OTHER VARIATIONS IN BACTERIAL CULTURES. PART II. GENERAL SURVEY OF CHANGES PRODUCED IN *BACT. LACTIS AEROGENES* (*AEROBACTER AEROGENES*) BY ULTRA-VIOLET LIGHT AND SOME OTHER MUTAGENIC AGENTS. J. Chem. Soc. 1159-68(1951)

A general survey is made of the changes induced in *Bact. lactis aerogenes* by exposure to ultraviolet light, to β and γ radiation from S^{35} , and to certain chemical agents (proflavine and Fenton's reagent). A significant proportion of mutants appears only when the fraction of survivors is very small. The chief effects are reduction in growth rate in a minimal medium, and modification of sugar-fermentation tests. An almost continuous spectrum of behavior is manifested. Specific amino acid requirements seldom appeared and were never absolute with this organism (which is normally very nonselective as regards nitrogen source). (NSA)

1813

Demerec, M. INDUCED MUTATIONS AND POSSIBLE MECHANISMS OF THE TRANSMISSION OF HEREDITY IN *ESCHERICHIA COLI*. Proc. Natl. Acad. Sci. U. S. 32, 36-46(1946).

The rate of mutation from sensitivity to resistance to bacteriophage T₁ in the B strain (resistant to radiations) of *E. coli* was measured after treatment with ultraviolet radiation (wave length 2537 Å, 4.2 ergs per sec. per sq. mm. for 1-4 min.) and with x-rays (10,000 - 50,000 r). Both radiations produced a substantial increase in the mutation rate, especially with the higher doses of radiation. The induced mutations were indistinguishable from spontaneous B/1 mutations. Some of the induced mutants showed up immediately after treatment, while the appearance of a large proportion of them was delayed until after several bacterial generations. After approximately 13 generations the mutation rate had decreased to normal. Several possible interpretations are discussed. Difficulties are found with the simple hypothesis that these bacteria were diploid and with the hypothesis that there is a certain proportion of haploid, diploid, and polyploid individuals. Alternatively, it is suggested that there may be delay in the utilization of some substrate, or there may be two effects of irradiation, one producing gene changes and the other increasing mutability. (BA)

1814

Demerec, M. and U. Fano. FREQUENCY OF DOMINANT LETHALS INDUCED BY RADIATION IN SPERMS OF *DROSOPHILA MELANOGASTER*. Genetics 29, 348-60 (1944).

The dependence of the frequency of dominant lethals on the radiation dosage agrees with Pontecorvo's interpretation of the origin of dominant lethals. Dependence of the sex ratio on the dosage, however, requires some modifica-

tion of this interpretation. The proportion of organisms that die during the larval stage is approximately the same for different radiation treatments of the parent males. Equal treatments induce approximately the same frequency of dominant lethals in different stocks of flies. The results obtained with the same inbred stock at different times are qualitatively reproducible, but quantitative differences are noticeable. The uncertainty involved in the determinations of the frequency of dominant lethals may be considerably greater than expected on the basis of the sampling error alone. (BA)

1815

Demerec, M., B. P. Kaufmann, and E. Sutton. GENETIC EFFECTS PRODUCED BY NEUTRONS IN *DROSOPHILA MELANOGASTER*. Genetics 27, 140(1942).

Oregon-R, wild-type males were treated with neutrons using the Institution's electrostatic generator, with a lithium target. During the treatment, which lasted several hours, flies were kept at constant temperature and humidity, and shielded from beta rays by one-fourth inch of lead. Dosage measurements were made with a 25 r Victoreen chamber and are expressed in arbitrary n-units. — Two groups of males were treated with about 1500 n-units, and two with about 2000 n-units. Part of the males from each group were mated with CIB females in order to determine the frequency of induced X-chromosome lethals. The remaining males were mated with wild-type females, and the salivary gland chromosomes of the F₁ female larvae were analyzed for breaks. — The lower dosage produced 23/1221 = 1.88 percent lethals, and the higher dosage gave 30/1068 = 2.81 percent. From X-ray studies of the Ore-R line by Demerec, and from Timoféeff-Ressovsky's and Zimmer's studies on the production of lethals by neutrons it is inferred that in this experiment n-units can be transferred into r-unit equivalents by multiplying values by a factor of about two. Cytological analysis showed for the lower dosage 18.43 ± 2.43 percent altered sperms and 46.66 percent breaks per total sperms, and for the higher dose 20.2 ± 2.33 percent altered sperms, and 53.5 percent breaks. Comparable values for equivalent treatment with X-rays are: 18.82 ± 1.60, 49.23; 29.8 ± 3.12, and 85.58 percent respectively. These results indicate that the frequency of breaks induced by neutrons does not differ appreciably from the frequency induced by an equivalent dose of X-rays. Breaks are also distributed at random throughout the chromosomes. (G)

1816

Demerec, M. and R. Latarjet. MUTATIONS IN BACTERIA INDUCED BY RADIATION. Cold Spring Harbor Symposia Quant. Biol. 11, 38(1946).

Using bacterial mutation resulting in resistance to a bacteriophage as a criterion, the authors tested the genetic effect of radiations immediately following treatment and also after the treated cells had been allowed to divide. Two lines of the B strain of *E. coli* were used in these experiments. Bacteriophage T₁, known also as "alpha" and "P28", was used to isolate mutants resistant to this phage. With this technique, two types of effect were observed: one immediate, producing phenotypic changes in the treated cells, and the other delayed, responsible for phenotypic changes appearing in the offspring of these cells. All detectable induced mutations were expressed after about 13 bacterial generations (end-point mutations). The results shown indicate a complex situation for ultraviolet radiation and a simpler one for x-radiation. Similar results were obtained with resting and with growing bacteria, and with the two different strains, which differ in their resistance to radiations. The results show no evidence of any relation between the ability of a radiation to produce sterilization

and its ability to produce mutations. The highest rate of mutation, 2.8 per 100 survivors, was obtained after ultraviolet treatment with $6,500 \text{ ergs} \times \text{mm}^{-2}$. When similar amounts of energy are absorbed by the cell, either from ultraviolet or from x-radiation, similar rates of mutation are observed; while the sterilization rate is considerably higher with x-rays than with ultraviolet. (S.V.S.)

1817

Dempster, Everett R. DOMINANT VS. RECESSIVE MUTATION. *Proc. Natl. Acad. Sci. U. S.* **27**, 249-50(1941).

After x-ray, the Oregon-R strain of *D. melanogaster* exhibits both a lower recessive lethal mutation rate and a higher dominant lethal mutation rate than the Swedish-b strain. Sensitivity of the sperm chromosomes to induction of dominant lethal mutations increased with the age of the males, being about 1% when males were one day old, and 60% when 16 days old. Neutron-produced ions used in the induction of recessive sex-linked mutations were only 0.75 as efficient as x-ray produced ions. (BA)

1818

Dempster, Everett R. ABSENCE OF A TIME FACTOR IN THE PRODUCTION OF TRANSLOCATIONS IN *DROSOPHILA* SPERM BY X-IRRADIATION. *Am. Naturalist* **75**, 184-7(1941).

Genetical tests of translocations produced in *Drosophila* sperm by 5,000 r units of x-rays at 220 kvp filtered with $\frac{1}{2}$ mm Cu and 1 mm Al showed 117 translocations ($17.2 \pm 1.46\%$) when the irradiation was applied at 167 r/min and 136 translocations ($17.0 \pm 1.33\%$) when applied at 12.5 r/min. (BA)

1819

Deringer, M. K., W. B. Heston, and E. Lorenz. BIOLOGICAL EFFECTS OF LONG CONTINUED WHOLE BODY IRRADIATION WITH GAMMA RAYS ON MICE, GUINEA PIGS, RABBITS. IV. BIOLOGIC ACTION OF GAMMA RADIATION ON THE BREEDING BEHAVIOR OF MICE. Oct. 25, 1946. Decl. Aug. 4, 1947. 30p. (MDDC-1247; CH-3729)

Female mice exposed to total doses of 770 r and 880 r on the 8.8 r and on the 4.4 r per 24 hours per day, and on the 8.8 r per 8 hours per day levels showed sterility effects, some producing litters of reduced size and others being sterile. Females exposed to a total dose of 550 r on the 4.4 r per 8 hours per day level bred but with reduced litter size. Male mice receiving a total dose of 1,760 r at the rate of 8.8 r per 8 hours per day were sterile on removal from the field but regained fertility in two months. Males receiving total dose of 880 r and 1,100 r on the 8.8 r per 8 hours per day level bred normal size. Males receiving total doses up to 1,100 r on the 4.4 r per 8 hours per day and on the 4.4 r per 24 hours per day levels bred comparably to the controls. Breeding results obtained for female mice on 1 hr., 8 hr., and 24 hr. exposures do not differ significantly and failed to demonstrate any effect on the rate of administration of the dose. Female mice exposed to a single dose of 800 r whole body x-radiation at the rate of 41 r per minute produced one litter of reduced size and were sterile thereafter. The sterilized females did not recover their fertility but the males did. Breeding results for female mice exposed to a total dose of 440 r at the rate of 4.4 r per 24 hours per day entering the field at 3, 4, and 5 months of age failed to show any age effects. No evidence for the production of genetic changes was obtained in mice receiving chronic exposures, or for the production of translocations in the offspring of male mice receiving a total dose of 1,100 r at the rate of 8.8 r per 8 hours per day or of female mice receiving a total dose of 770 r at the rate of 8.8 r per 24 hrs. per day. (ADD)

1820

Devi, P., G. Pontecorvo, and C. Higginbottom. X-RAY INDUCED MUTATIONS IN DRIED BACTERIA. *Nature* **160**, 503-4(1947).

X-ray irradiation of a strain of *Bacterium aerogenes* produced mutants at rates of up to 1%. Irradiation of bacteria preserved in the dry state was effective, showing that it is not necessary for organisms to be in active division for mutants to be induced. Mutants differed in having some additional nutritional requirement, presumably owing to the mutant having lost the ability to perform one step in the synthesis of an essential metabolite. A high proportion of the mutants were of the "adaptable" type. Whereas a non-adaptable mutant would never grow in a medium of glucose and inorganic salts without the addition of a particular nutrient, an "adaptable" mutant would grow after a lag of some 24 hours. In the mutant an enzyme system may be changed or suppressed, allowing an alternative enzyme system to function; alternatively, a gene may be inactivated which normally controlled the rate of growth of a plasmogene identical with, or a precursor of, the enzyme. It may be possible to discover whether adaptability is a property of the enzyme or of the cell producing the enzyme. (AWM)

1821

Ellis, Frank. THE GENETIC EFFECTS OF NON-STERILIZING DOSES OF PENETRATING RADIATION. *Brit. J. Radiol.* **21**, 1-4(1948).

Non-sterilizing doses of radiation which cause no demonstrable deleterious effect on the health of the individual may cause serious changes in the chromosomes of the spermatozoa or ova, resulting in manifest disability of various types in subsequent generations. Irradiation changes the hereditary materials, no matter how small the dose. The effects produced are all cumulative with increasing dose, being simply additive for some type of change, but increasing geometrically for others. These changes are almost entirely harmful and therefore undesirable. This information has been gained from the study of organisms other than man. A discussion is given of its application to man and permissible dosage. (NSA)

1822

Evans, Robley D. QUANTITATIVE INFERENCES CONCERNING THE GENETIC EFFECTS OF RADIATION ON HUMAN BEINGS. *Brit. J. Radiol.* **23**, 175-83(1950).

By extrapolation from known facts of human genetics the author finds it unlikely that any increase in hereditary anomalies will occur, even after many generations, from daily doses of radiation up to 0.1 r given to a small fraction of the population. (R)

1823

Evans, Robley D. QUANTITATIVE INFERENCES CONCERNING THE GENETIC EFFECTS OF RADIATION ON HUMAN BEINGS. *Science* **109**, 299-304(1949).

Genetic concepts and experiments pertinent to the question of mutations induced by irradiation are reviewed and calculations are made. It is noted that the induced mutations, which are similar in type to those appearing spontaneously in nature, have an average probability of about 3×10^{-8} per gene per roentgen for an irradiation of 0.6 roentgens per hour, higher. Experimental results suggest that the effective average radiation sensitivity of immature sperm and eggs may be less than the sensitivity of mature sperm and eggs. Dominant mutations may become visible in the first generation offspring. Recessive mutations may appear only in homozygous individuals of a later generation, and therefore recessive mutations accumulate in the population as a result of both spontaneous and induced mutations. From the appropriate mathematical theory, and

the experimental data now available, it seems safe enough to conclude that no detectable increase in hereditary abnormalities is likely to result, even after many generations, if a small fraction of the population receives daily radiation doses up to 0.1 roentgen per day. It is also noted that it is only rarely that any individual receives the maximum permitted dose of 0.1 r per day and that the average daily dose at installations like the Hanford Engineer Works and the Oak Ridge National Laboratory is about 0.005 r per day. 29 references. (NSA)

1824

Fano, U. ON THE INTERPRETATION OF RADIATION EXPERIMENTS IN GENETICS. *Quart. Rev. Biol.* **17**, 244-52(1942).

Lack of influence of the wave-length of x-rays on their genetic effects can be understood independently of the hit theory. A generalized treatment of the dependence of the effectiveness of radiation on the ion-density enables us to consider the influence of several hitherto neglected factors. A modified pattern of biophysical analysis of the x-ray action is suggested. (BA)

1825

Fano, U. NEUTRON-INDUCED LETHALS IN *DROSOPHILA*. *Genetics* **28**, 74-5(1943).

Wild type males of *Drosophila melanogaster* were treated with approximately 600 and 1200 neutron units from the COLUMBIA UNIVERSITY cyclotron, and their offspring were tested for dominant and recessive lethals. One neutron unit is energetically equivalent to about 2.5 r X-rays. The frequency of dominant lethals was found to be approximately 73 percent and 96 percent for the two treatments; the same effect is produced by about 3000 and 6000 r X-rays, respectively. Thus the ratio between the energies delivered to tissue by X-ray and neutron doses having equal dominant lethal effect approaches 2; the value 1.5 was reported previously for this ratio by DEMPSTER. Among the offspring of 170 males treated with 1200 units, 998 CIB tests were performed, yielding 60 recessive lethals; no "grouping" of lethals was observed in the offspring of individual males. All but one of the lethal-bearing chromosomes were further tested genetically and cytologically. Only two chromosomes were clearly shown to carry two separate lethals, a coincidence that may be attributed to chance. Genetic analysis indicates that more than 30 percent of the recessive lethals are associated with gross chromosomal rearrangements. According to partially completed cytological analysis, this estimate may be slightly increased; no association of lethals with minute deficiencies has thus far been revealed. (G)

1826

Fano, U. EXPERIMENTS ON MUTATIONS INDUCED BY NEUTRONS IN *DROSOPHILA MELANOGASTER* SPERMS. *Genetics* **29**, 361-9(1944).

New experiments on the phenomena of "grouping" of sex-linked lethals reported by Nagai and Locher (1938) and Nishina and Moriwaki (1941) seem to disprove their existence. The theoretical difficulties raised by the interpretation of those phenomena are thus removed. A large percentage of neutron-induced lethals is associated with chromosomal rearrangements; certain difficulties that had previously been met in discussing this association are thus considerably increased. A new measurement of the frequency of neutron-induced dominant lethals is reported, but the comparative efficiency of neutrons and x-rays in producing various types of chromosomal change in *Drosophila* sperms is not satisfactorily elucidated thereby. (Author's Summary)

1827

Fano, U. NOTE ON THE THEORY OF RADIATION-INDUCED LETHALS IN *DROSOPHILA*. *Science* **106**, 87-8(1947).

A rather complete theory of induced lethals in *Drosophila* which was proposed by Lea and Catcheside (1945) has met with objections. In radiation-induced lethals there is difficulty in the interpretation of the dependence of frequency on dose. There is a nonlinear effect, leading to a very significant discrepancy between this theory and the experimental data. An estimate of the great importance of this discrepancy is discussed. (BA)

1828

Fano, U. and M. Demerec. MEASUREMENTS OF THE FREQUENCY OF DOMINANT LETHALS INDUCED IN SPERM OF *DROSOPHILA MELANOGASTER* BY X-RAYS. *Genetics* **26**, 151(1941).

A large amount of data on the frequency of production of dominant lethals has been collected. The fraction of eggs which after fertilization by X-rayed sperms fail to give rise to adult flies has been taken as an indicator of dominant lethals. The results of 50 independent measurements will be demonstrated, corresponding to 18 different X-ray doses varying between 0 and 11,000 roentgens and including counts of about 60,000 eggs. A large amount of work has been devoted to experiments at very low dosage. The production of dominant lethals is apparently proportional to the X-ray dose for small dose and the survival ratio decreases exponentially for high dose. On the whole, however, the "dose-action" curve does not seem to fit the "single hit" type very well. This would indicate that the phenomenon is not simple, which is very plausible. About 1 percent of the eggs still gave rise to adult flies in the case of 11,000 roentgens. The percentage of dominant lethals produced by 1000 roentgens (about 15 percent) is so large that it cannot be accounted for by the production of inviable chromosome aberrations, which should appear at a rate corresponding to that of viable inversions or translocations. (G)

1829

Fries, N. X-RAY INDUCED MUTATIONS IN THE PHYSIOLOGY OF *OPHIOSTOMA*. *Nature* **155**, 757-8(1945).

Twelve physiological mutations (strains) were induced in the fungus *O. multiannulatum*, by x-rays. The manner in which they differed is shown in a table. The physiological properties were heritable. Some of the properties of the different strains are discussed. (BA)

1830

Frolik, E. F. and Rosalind Morris. XENIA EFFECTS OF IRRADIATING CORN POLLEN IN A NUCLEAR REACTOR. *Agronomy J.* **42**, 293-7(1950).

Xenia effects in corn crosses involving tassels irradiated in a nuclear reactor were determined in comparison with crosses involving x-rayed and nonirradiated tassels. Irradiations were made in the thermal neutron column of the heavy water pile at the Argonne National Laboratory for periods of 0.5, 1, 2, 4, 8, and 16 min, respectively. The x-ray dosage consisted of 1200 r units. In general, the percentage of entire mutations increased with increase in length of time of exposure in the nuclear reactor. The effectiveness of pile radiation varied markedly with date of treatments. There was considerable uniformity in the response of individual plants to comparable irradiation treatments. The effectiveness of x-ray treatment varied somewhere between 0.5 min and 4 min of pile irradiation, depending on date of treatment and on the character involved. The percentage of mutations for both sources of radiation

varied for the characters under study in the following decreasing order of frequency: (a) defective kernels, (b) colorless aleurone, (c) sugary endosperm, and (d) red aleurone. The frequency of chimeras was affected far less than that of entire mutations by the pile radiations. No association was apparent between frequency of recoveries and either pile radiation or x-radiation. No qualitative differences between the two types of radiation were noted in these tests. 13 references. (NSA)

1831

Frolík, E. F. and Rosalind Morris. EFFECTS OF IRRADIATING MAIZE POLLEN IN A NUCLEAR REACTOR ON THE F_1 PLANTS. *Science* **111**, 153-4(1950).

This paper constitutes a preliminary report on the inherited changes induced by irradiating maize pollen in a nuclear reactor. Mature maize tassels were placed in the thermal neutron column of the Argonne pile, which was operated at a power in the neighborhood of 300 kev. The average flux of neutrons at the position of the tassels was 7×10^{10} neutrons/cm²/sec, and the exposure times varied from 0-16 minutes. Crosses were made by collecting pollen from the tassels and placing it on the untreated female plants. The seeds were then planted and the percentage stands of the different seed groups is tabulated. Other effects of the irradiation, such as the types of abnormalities produced, are described in the article. (NSA)

1832

Fryer, H. C. and John W. Gowen. AN ANALYSIS OF DATA ON X-RAY INDUCED VISIBLE GENE MUTATIONS IN *DROSOPHILA MELANOGASTER*. *Genetics* **27**, 212-27 (1942).

This paper presents some new data on x-ray induced, visible gene mutations and shows how a satisfactory analysis of such data can be made by means of the χ^2 distribution. (S.V.S.)

1833

Genter, Clarence F. and Hubert M. Brown. X-RAY STUDIES ON THE FIELD BEAN. *J. Heredity* **32**, 39-44 (1941).

Lots of dormant and germinated (18 and 36 hours) seeds of Michelite white pea beans, *Phaseolus vulgaris* were x-rayed with four dosages, 2,160, 6,500, 13,000, and 26,000 r-units. Of the 1,434 2nd generation progenies grown from treated seed, 150 showed mutations which were classified in 32 types. Ninety per cent of the mutants were distinguished within five weeks after emergence and of these 67% were chlorophyll abnormalities. Other characters affected were plant size; branching; leaf size, shape and texture; fertility; and earliness of maturity. The rate of mutation varied roughly with the dosage and length of germination period prior to treatment and tended to increase with the later harvest dates and with size of progeny. The great variability of the mutant ratios indicated that the x-rays affected only limited sectors of the treated embryos rather than the entire embryos. (BA)

1834

Giles, Norman H., Jr., Anne E. Flynn, and Dorothy L. Giles. INDUCED REVERSIONS OF INOSITOL-REQUIRING MUTANTS IN *NEUROSPORA CRASSA*. *Records Genet. Soc. Am.* **17**, 38-9(1948).

Treatments of microconidial suspensions from inositol-less mutants of *Neurospora crassa* with ultra-violet (2537 Å) or X-rays produce a greatly increased frequency of adaptation (inositol-independent cultures) in certain strains. Genetic studies of several independently produced adaptations indicate that these are the result of reverse mutation at the inositolless locus to the original wild-type allele controlling inositol synthesis. There is no evidence that gross chromosomal rearrangements are present in

the induced inositol-independent stocks. The relation between frequency of reversions and radiation dosage is being investigated. Present results indicate that the percentage of reverse mutations with ultra-violet continues to increase, even at dosages well beyond the point of one percent microconidial survival. Previous studies of the frequencies of induced reversions in several independently produced, apparently allelic, inositolless mutants, have indicated that some of these strains differ markedly in their mutability. An extensive comparison has been made of two strains: S-37401, which regularly reverts with radiation treatment, and S-46802, which has failed to revert with any treatment so far attempted. Crosses of these two mutants, followed by serial ascospore isolations, yield cultures which are phenotypically indistinguishable. Such progeny can however be separated by reversion studies since, of the 8 cultures from a single ascus, four regularly adapt when conidial suspensions are treated with ultra-violet or X-rays while the remaining four do not. (R.G.)

1835

Glass, H. Bentley. DIFFERENTIAL SUSCEPTIBILITY OF THE SEXES OF *DROSOPHILA* TO THE EFFECT OF X-RAYS IN PRODUCING CHROMOSOME ABERRATIONS. *Genetics* **25**, 117(1940).

Treatment of mated females of *D. melanogaster* by X-rays provides simultaneous exposure of sperms and premeiotic eggs to identical doses. Offspring from eggs laid in the first five days following treatment yield approximately equal frequencies of lethal mutations in σ and ϕ germ-cells. 55 translocations were all produced in σ germ-cells. This disproportion is significantly greater than would be expected from the elimination of translocations in eggs undergoing meiosis. Inversions have been obtained from both σ and ϕ germ-cells. They are more frequent in the former, but the significance of the difference is not yet established. (G)

1836

Glass, H. Bentley. THE EFFECT OF X-RAYS UPON THE ACTION OF A SPECIFIC GENE IN *DROSOPHILA MELANOGASTER*. *Genetics* **29**, 436-46(1944).

Embryos, 10 hours old at 26 C, of a brown scarlet (*bw; st*) stock were given 1,000 r units. Of 221 flies emerging as adults, 94.1% had a growth from the center of one or both eyes, varying from a mere protrusion of the eye in the central area to an eruption of a palp-like structure bearing bristles and sometimes segmented. The effect of the x-rays on this stock was confirmed in a second experiment. No such effect was found when other stocks were given similar treatments. This effect has been shown, by means of appropriate crosses, to be due to a semi-dominant gene *erupt* (*er*) in chromosome 3 of the *bw; st* stock, near *e*³; and to a semi-dominant gene, *Suppressor-erupt* (*Su-er*), in chromosome 2 of the same stock, the effect of which upon *er* is inactivated by the x-ray treatment. *Erupt* is not an allele of the nearby, similar homoeotic mutant, *kidney*. The significance of the specific inactivation of a gene affecting the eye by a treatment given before even the cephalic rudiment is invaginated is discussed. Various stocks tested, including those lacking the mutant *er*, carry the same or a similar suppressor of *erupt*. Such inhibitory modifier systems are to be regarded as widespread and of considerable evolutionary significance. (BA)

1837

Glass, H. Bentley. THE EFFECTS OF SUPPLEMENTARY TREATMENT WITH INFRARED RADIATION ON X-RAY INDUCED LETHALS AND CHROMOSOME ABERRATIONS IN FEMALES OF *DROSOPHILA MELANOGASTER*. *Genetics* **35**, 109-10(1950)

Infra-red pretreatments and posttreatments of 4 hours have been applied to ♂♂ and ♀♀ of *D. melanogaster* given a dose of X-rays amounting to ca. 2000 r units, the dose varying slightly for different series, but being always identical for ♂♂ and ♀♀ of the same series. Translocations induced in ♂♂ were 6 in 85 tested gametes (7.1%) when pretreated with infra-red, and 7 in 113 (6.2%) when post-treated. The differences are not significant, a fact at variance with the results of Kaufmann, who found no effect of posttreatment with infra-red. The rate in controls is about two-thirds as great. In ♀♀, 0 translocations were found in 218 gametes tested when pretreated with infra-red, 1 in 169 (0.6%) when posttreated. The translocation is the first one ever found by the author in treated *D. melanogaster* ♀♀, in series amounting to a total of 1832 tested gametes. The salivary gland chromosomes show that this translocation involved a high number of breaks. — Sex-linked lethal mutations have been scored in both ♂♂ and ♀♀, with and without infra-red posttreatment: 15/569 (2.64%) in ♂♂ with X-rays only; 10/569 (1.76%) in ♀♀ with X-rays only; 14/281 (5.0%) in ♂♂ with X-rays plus infra-red; 2/222 (0.9%) in ♀♀ with X-rays plus infra-red. The difference between the two groups of ♂♂ and the similar difference between ♀♀ are not significant; but the difference between ♂♂ (combined) and ♀♀ (combined) is significant (2% level). The frequency of induced lethals in ♀♀ is about half that in ♂♂. (G)

1838

Gowen, John W. **MUTATION IN DROSOPHILA, BACTERIA, AND VIRUSES.** Cold Spring Harbor Symposia Quant. Biol. 9, 187-93(1941).

This paper presents evidence on the spontaneous frequency of variants in viruses, bacteria, and *Drosophila*. The rate of spontaneous variation is shown to be small. The frequency of variants in the three forms is increased when they are exposed to comparable x-ray dosages. The rates at which variants appear are of the same order of magnitude. This evidence is interpreted as indicating a common basic structure for inheritance in each group, the changes of which are in the nature of mutation. (S.V.S.)

1839

Gowen, John W. and Marie S. Gowen. **CONSTITUTION OF THE SECOND CHROMOSOME OF DROSOPHILA MELANOGASTER AS INDICATED BY X-RAY ANALYSIS.** Genetics 32, 89(1947).

Newly produced lethal mutations in the second chromosome were examined for possible allelism, position within the chromosome, and association with translocations or inversions. The data obtained were analyzed in terms of the chromosomal size of X-ray effects and the relation these effects have to gene number in the second chromosome. Males were subjected to 2000 and 6000 r. Of 153 lethal bearing chromosomes obtained, 8 had incompleting tests, 16 carried two lethals. The 161 lethals treated had 128 occur once, 10 twice, 3 thrice and 1 four times. The lethals were distributed in all chromosome regions. Close agreement between loci occupied by visible genes and the lethals was found for dumpy black, curved plexus, and plexus speck regions. Lethals were in excess in aristaleless dumpy, and black purple regions. About one-third the expected lethals were found in the purple curved region. Estimates of total number of regions capable of showing lethal effects may be had from the relation

$$\left(\frac{n}{142}\right) \frac{161!}{(4!)^3 (2!)^{10}} \frac{1}{n^{161}} \text{ representing the probability of}$$

our sample. The number of these regions is 623. The variance of this estimate is 131. The fiducial limits are 426 as the lower limit and 970 as the upper limit. These results

are not to be considered as estimates of gene loci but rather as average regional effects of the X-rays. The bearing of these results on gene loci in the second chromosome will be discussed. (G)

1840

Gowen, John W. and M. R. Zelle. **IRRADIATION EFFECTS ON GENETIC RESISTANCE OF MICE TO MOUSE TYPHOID.** J. Infect. Diseases 77, 85-91(1945).

This paper reports data on the effects of irradiating mice with x-rays and then determining the survival value of these mice to inoculations of mouse typhoid, *Salmonella typhimurium*, dose 200,000 organisms. The mice belong to six strains, each characterized by a specific genetic resistance to mouse typhoid. The results of these observations may be explained by the hypothesis that the resistance of these mice decreases exponentially with the increased dosage of x-rays to which they are exposed. The rate of this decrease per roentgen of x-rays is small and is statistically similar for the six different strains of mice although these strains are genetically very different in their natural resistance to mouse typhoid. These facts may be rationalized if the leucocytes in the mouse blood also decrease exponentially with increased dosages of x-rays. The fact that even strains of mice which we now consider very susceptible to mouse typhoid may be greatly increased in susceptibility though x-rays shows that mice, in general, are probably much more resistant to this disease than when the disease first contacted the species. (BA)

1841

Granhall, I., A. Gustafsson, F. Nilsson, and E. J. Oldén. **X-RAY EFFECTS IN FRUIT TREES.** Hereditas 35, 269-79(1949).

Radiation dosages of 500-25,000 r were administered to the scions of several varieties of apples, pears, and sweet cherries in order to study the lethality of x-rays and to determine the possibility of inducing favorable mutations by means of the radiations. The scions were grafted on parent plants and observed for growth and other characteristics. At 10,000 r none of the pears and apples survived; the cherries suffered a similar fate at 5,000 r. The ideal dose for the pears and apples appeared to be 5,000 r at which abnormalities appeared without excessive mortality; 2,500 r was the optimum dosage for the cherries. The most typical primary effects were bifurcations of shoots and leaf midribs; other effects, such as change in color and shape of the fruit also occurred. It is concluded that since the apparent effect of the x-radiations is to increase the probability of occurrence of abnormalities ordinarily seen in the fruit (changes in size, shape, and color), that this is a method for the possible production of better fruit of increased size, flavor, resistance to disease and other desirable qualities. (NSA)

1842

Gray, C. H. and E. L. Tatum. **X-RAY INDUCED GROWTH FACTOR REQUIREMENTS IN BACTERIA.** Proc. Natl. Acad. Sci. U. S. 30, 404-10(1944).

Escherichia coli and *Acetobacter melanogenum* were treated with x-ray until 99.99% of the cells were killed. From 800 isolations of survivors of *E. coli*, two strains differ from the parent, one by requiring the addition of biotin to the basic medium, the other by requiring theonine. From 575 isolations, four strains of *A. melanogenum* have been obtained which fail to grow in the basic medium. The first requires a supplement of serine or glycine, the second requires adenine or adenosine, the third glycine and the fourth shows some response to addition of leucine. As contrasted to the excellent growth of the parent strain in the appropriate minimal medium, the x-ray treatment

modified the capacity of bacteria for carrying out specific biochemical reactions, the growth of each mutant strain being a function of the concentration of the required supplement. Ultraviolet light produced no similar effects. The production by x-ray of new strains of 2 spp. of bacteria offers indirect support for the existence of specific genes controlling biosynthesis in bacteria. (BA)

1843

Griffen, A. B. THE B^S TRANSLOCATION IN D. MELANOGASTER AND MODIFICATIONS OF THE BAR EFFECT THROUGH IRRADIATION. Genetics 26, 154-5(1941).

T(1;4)A-B^S is a translocation involving the X and IV chromosomes with breaks at 102F₂/102F₃ and between the repeat sections of the B duplication which was present in the original stock. The B^S effect is confined to the XR fragment, while the XL has no B effect although it bears one of the original members of the duplication. Irradiation of B^S males has produced further facet reduction and complete returns to normal eye shape; some of these changes are associated with visible changes in the IV-XR fragment and some appear to be simple mutations without visible rearrangement. In one case a B effect has been induced in the XL fragment through deletion of the facet-forked interval, thus causing an association of white (w³C₂) and the first band (16A₁) of the left B section; this new XL effect is independent from that of XR. The mutant cases are instances of duplication of chromosome material with loss of visible effects and are examples of one method for increasing the amount of genic material in the species. (G)

1844

Griffen, A. B., Mary Warters, and James D. Mohler. THE POSITION EFFECTS BAR, WHITE-MOTTLED, AND CUBITUS INTERRUPTUS IN DROSOPHILA MELANOGASTER. Genetics 35, 112(1950).

Comparisons of X-ray induced reversals of position effects at the Bar, white, and ci loci indicate that each locus may revert to wild type action either by mutation or by virtue of new chromomere associations resulting from new chromosome rearrangements. In the case of B^S, mutation accounts for approximately one-third of the phenotypic changes from B^S to wild type. (G)

1845

Gustafsson, Ake. MUTATION EXPERIMENTS IN BARLEY. Hereditas 27, 225-42(1941).

Seed samples of the pure line "Golden" barley were x-rayed with 5,000 and 10,000 r. Three degrees of seed hydration were used: 10 and 15% moisture and seed soaked for 24 hours in water or in auxin solution. The author believes that the direct proportionality in barley between dosage and mutation rate is only apparent. Those associated with profound chromosomal disturbances (highly sterile) and those arising in entirely fertile plant progenies do not show direct proportionality when considered alone. Mutations associated with small but evident changes do show a direct proportionality. The intentional direction of the process of mutation may take place to a certain extent in the following ways: (1) Albina mutations arise more frequently than other chlorophyll types at low dosages and to a greater extent in fertile progenies. They occur about three times as often in water-soaked seed as in those of lower moisture. (2) Xantha mutations are produced most often at the higher dosage in slightly sterile X₁ plants. (3) Alboviridis mutations occur as frequently in dry as in soaked series, but chiefly in progeny of sterile plants. (4) Alboxantha mutations occur only in soaked seed. (5) Viridis mutations occur in highly sterile plants which result from high dosage, and soaked seed. (6) Finally, Ti-grina arose exclusively from dry seed. In addition to the

chlorophyll mutations a number of morphological forms have arisen which fall within the range of known variations in cultivated barley. Some of these mutations, such as straw-stiffness, size of kernel, and earliness, are thought to constitute practical improvements as compared with the original variations, although their comparative yielding capacity has not been determined. (BA)

1846

Gustafsson, Ake. PRELIMINARY YIELD EXPERIMENTS WITH TEN INDUCED MUTATIONS IN BARLEY. Hereditas 27, 337-59(1941).

Ten fertile mutations obtained from x-raying Golden barley were compared with the Golden and Maja variations for yield and other characteristics. Seven mutant forms yielded less, but three equalled or surpassed the mother strain. Other characteristics which were changed in both directions from Golden were grain size and weight, number of ripe kernels, germination ripeness and protein and starch content. A general discussion concerning the significance of mutations to evolution as well as induced mutations to plant breeding, followed. (BA)

1847

Gustafsson, Ake and Ewert Aberg. TWO EXTREME X-RAY MUTATIONS OF MORPHOLOGICAL INTEREST. Hereditas 26, 257-61(1940).

In irradiated barley of the Golden variation (Hordeum distichum var. mutans) the authors found (1) a 2-flowered mutant (i.e., 2 flowers were formed within each lemma) yielding a segregation of 3 normal to 1 mutant, the latter being sterile; and (2) a mutant in which the glumes were lemma-like with a long awn, whereas the normal glume in Golden barley is linear with short awns. (BA)

1848

Gustafsson, Ake and Nils Nybom. COLCHICINE, X-RAYS AND THE MUTATION PROCESS. Hereditas 35, 280-4 (1949).

A special strain of Ymer barley seed was tested for the effects of irradiation and colchicine. Twenty-four hours before irradiation, seeds were set to germinate in five different colchicine solutions of 0.1, 0.05, 0.005, 0.01, and 0.001% strength; the x-ray dosages were 5,000, 10,000 and 15,000 r. It was found that the four highest concentrations of colchicine caused a complete c-mitosis, while the lowest concentration was ineffective. From the results it is concluded that: the course of the mutation process is considerably altered by the application of colchicine previous to the irradiation; the xantha and alboviridis types, as well as very rare mutants, increase in number as a result of such a pretreatment; the viridis mutants become rarer; and, the different groups of mutation, at least with regard to albina, xantha, and viridis types, show a conspicuous connection with the sterility conditions of the ancestor plants. (NSA)

1849

Haldane, J. B. S. THE FORMAL GENETICS OF MAN. Proc. Roy. Soc. (London) B, 135, 147-70(1948).

With sublethal genes such as hemophilia, achondroplastic dwarfism, epiloia, retinoblastoma, Pelger anomaly and aniridia, mutation rate lie between 8×10^{-5} and 4×10^{-6} per locus per generation. Less common anomalies have mutation rates much lower: lobster claw 10^{-7} , and porcupine men, 10^{-10} . These rates suggest that much human mutation may be due to natural radiations. (BA partial summary)

1850

Hanson, H. J., W. C. Myers, G. L. Stahly, and J. M. Birkeland. VARIATIONS IN PENICILLIUM NOTATATUM

INDUCED BY BOMBARDMENT OF SPORES WITH NEUTRONS. J. Bacteriol. **51**, 9-18(1946).

Marked variations appeared in cultures from spore suspensions of *P. notatum* which were exposed to a bombardment with slow neutrons for periods ranging from one hour to 134 days. The number of variants increased as time of exposure lengthened. Actively growing cultures which were treated with slow neutrons for three hours showed no definite evidence of induced variation. Variations similar to those induced by slow neutrons occurred when moist or dry spores were bombarded with fast neutrons for 15 and 30 minutes. However, an exposure of 180 minutes was lethal to all spores. Isolation and study was made of 150 varieties which were characterized by differences in color, texture, rate and quantity of vegetative growth and sporulation, color and colonies. The variant strains differ greatly in their ability to produce penicillin. Some lost this property and some had it markedly increased over the parent strain. None of the variants showed great differences when their effect was tested against 10 different bacteria. (CA)

1851

Hayden, Barbara and Luther Smith. THE RELATION OF ATMOSPHERE TO BIOLOGICAL EFFECTS OF X-RAYS. Genetics **34**, 26-43(1949).

Barley seeds x-rayed while in a vacuum consistently showed better germination and growth and a lower frequency of chromosomal aberrations than seeds x-rayed in air. In one test the seedling mutation rate from test of plants grown from germinating seeds x-rayed in a vacuum was $2.1 \pm 0.32\%$ as compared with $3.4 \pm 0.35\%$ for seeds x-rayed in air. This difference was slightly more than three times the standard error. Root-tip cells from seeds irradiated in air averaged 4.7 times as many chromatinic bridges as root-tip cells from seeds irradiated in a vacuum. (NSA)

1852

Heidenthal, Gertrude. THE OCCURRENCE OF X-RAY INDUCED DOMINANT LETHAL MUTATIONS IN HABROBRACON. Genetics **30**, 197-205(1945).

Haploid males of the parasitic wasp *Habrobracon* were x-rayed with dosages ranging from 500 r to 10,000 r units. Dominant lethals induced in the sperm were detected by counting the F_1 female and male progeny and calculating the sex ratios. In the 3-allele cross involved, all F_1 male progeny were haploid and all female progeny diploid. Under the conditions of the experiment the number of F_1 males remained constant, as expected, but the number of F_1 females decreased with increasing x-ray dosage. The curve of mortality due to dominant lethals was found to be similar to comparable curves for *Drosophila*. Tests at very high dosages (approx. 152,000 and 168,000 r units) indicated not only that every sperm had at least one dominant lethal (no female progeny occurred), but that a fairly high per cent (roughly 40%) were not able to take part in the fertilization process. (BA)

1853

Herskowitz, Irwin H. THE RELATIONSHIP OF X-RAY INDUCED RECESSIVE LETHALS TO CHROMOSOME BREAKAGE. Am. Naturalist **80**, 588-92(1946).

Employing the CIB technique, recessive lethal changes were obtained in the Canton S stock of *Drosophila melanogaster* after x-ray dosage at 1000 r and 5000 r. Lethal cultures were then tested in a crossover generation for their association with chromosomal rearrangements. These were detailed by a reduction in crossing over of 50% or more in either or both regions of the X chromosome tested. Of the F-2 cultures $0.3 \pm 0.21\%$ at 1000 r and

$3.57 \pm 1.3\%$ at 5000 r showed lethals associated with the regions of chromosomal rearrangement. Of 43 recessive lethals tested, none showed chromosomal rearrangements unassociated with a lethal. Analysis of the available data suggests x-ray induced lethals are produced primarily at breakage points and relegate to position effect and non-breakage mutation a relatively small part as sources of recessive lethals. (BA)

1854

Herskowitz, Irwin H. THE GENETIC BASIS OF X-RAY INDUCED RECESSIVE LETHAL MUTATIONS. Genetics **36**, 357-63(1951).

Several hypotheses concerning the origin of x-ray induced recessive lethals are discussed. It is found that those postulating a single, or even a double, origin for recessive lethals are not consistent with the available data and theory. An hypothesis is suggested that recognizes lethals arising from three origins: point mutation, independent of breakage; breakage alone; and position effect following rearrangement of breaks. When the number of X chromosome break-free point mutation lethals in 100 viable sperm per 1000 r is assumed to be 0.6, the chance for a break not involved in gross rearrangement to bear a lethal 23 per cent, and the chance for lethality for a break included in a viable gross rearrangement 31.6 per cent, the number of breaks involved corresponds to the number postulated by Haldane and Lea (J. Genetics **48**, 1-10(1947)) for different doses, and a linear increase in recessive lethals with dose is obtained for viable sperm. (NSA)

1855

Hertwig, Paula. HEREDITARY SEMISTERILITY IN MICE CAUSED BY RECIBROCAL CHROMOSOME TRANSLOCATIONS AFTER X IRRADIATION. Z. indukt. Abstamm. Vererbungsl. **79**, 1-27(1940).

Studies of progeny from male mice of which the sperm were irradiated showed reduction of fertility due to lethality both of gametes and zygotes. Litter size was reduced to one half or more in all of the F_1 , and in one half of the offspring of the survivors. Transmission ratios of the semisterility indicate the presence of a translocation, and that some individuals homozygous for the translocation survive. There is no evidence for the survival of hyper- and hypoploid zygotes. No cytological studies were made. (BA)

1856

Hollaender, Alexander, W. K. Baker, and E. H. Anderson. EFFECT OF OXYGEN TENSION AND CERTAIN CHEMICALS ON THE X-RAY SENSITIVITY OF MUTATION PRODUCTION AND SURVIVAL. Cold Spring Harbor Symposia Quant. Biol. **16**, 315-26(1951).

This paper deals with some of the work which has been published during the last two or three years together with some work which has not been published. The major part of the discussion involves the effect of oxygen tension on x-ray sensitivity as measured by the lethal effects, chromosome changes, and bacterial mutations. The better part of the paper is concerned with the effects of chemicals on x-ray sensitivity. (S.V.S.)

1857

Hollaender, Alexander and C. W. Emmons. INDUCED MUTATIONS AND SPECIATION IN FUNGI. Cold Spring Harbor Symposia Quant. Biol. **11**, 78-84(1946).

Studies on the effects of ultraviolet radiation and x-rays on fungi revealed lethal effects, temporary physiological changes, and up to 40-80% mutants in the surviving spores. Representative mutants, selected from several hundred mutants of *Trichophyton mentagrophytes* induced by ultraviolet radiation and carried in culture for six years, still

exhibit the characteristic features that led to their selection. When the conidia of the fungus (strain of the variable species *Trichophyton mentagrophytes*) were exposed to sufficient ultraviolet radiation (2537 or 2650 Å) so that 90–99% of them were killed, a high percentage (up to 40%) of the surviving conidia gave rise to colonies strikingly different from the parent. These mutations were permanent. Some of the mutants produced by radiation resemble closely certain naturally occurring fungi which have been generally accepted as sep. "species". Other mutants are of a type that could be classified as new "species" if one did not know that they had originated from certain fungus cultures. Since it has been possible to produce mutants in certain fungi by irradiation with wave lengths in the ultraviolet spectrum that are present in sufficient intensity in sunlight coming to the earth's surface, the question is raised whether they may be a factor in the production of mutations in nature. Besides *Trichophyton*, a number of other fungi have been studied, particularly *Aspergillus terreus* and *Penicillium notatum*, and the same results were observed. A detailed investigation of the effects of monochromatic radiation of 2967 and 3130 Å was made. These wave lengths were especially interesting because they are present in the biologically effective part of sunlight reaching the surface of the earth, that is 2900 to 3150 Å. The two wave lengths that were tested were found to be effective in the production of mutations in *A. terreus*. The biologically effective radiation on an average bright and sunny day in June amounts to about 2,000 milliw. sec./sq. cm. It requires approximately 230 milliw. sec./sq. cm. to produce a 6% mutation rate in the 10% of spores of *A. terreus* surviving 2967 Å radiation. It should thus be possible in about one hour's exposure to bright sunlight around noon in June to produce in this fungus a significant increase in mutation rate. (CA)

1858

Hollaender, Alexander and C. P. Swanson. MODIFICATION OF THE X-RAY INDUCED MUTATION RATE IN FUNGI BY PRETREATMENT WITH NEAR INFRARED. *Genetics* 32, 90(1947).

In general the mutation rate in fungi increases linearly with increased exposure to X-rays. A significant increase of the X-ray produced mutations is found if the spores are irradiated with near infrared radiation before X-ray exposure. The infrared used covered the region from 7000 to 18000 Å with a maximum at 10000 Å. The experimental arrangement for infrared irradiation is such that the temperature rise in the culture is not more than 2 to 5° above room temperature. Infrared alone does not induce mutation. This increase of mutation rate has been observed with *Aspergillus terreus* and *Trichophyton mentagrophytes*. The significance of these findings will be discussed in relation to the increased percentage of deletions found in *Tradescantia* if infrared is given before or after X-ray treatment (SWANSON and HOLLAENDER, in press) and the increased percentage of chromosome rearrange-in *Drosophila* if infrared is given before X-ray exposure. (KAUFMANN, HOLLAENDER and GAY; *Genetics* 31: 1946). (G)

1859

Hollaender, Alexander and E. M. Zimmer. THE EFFECT OF ULTRAVIOLET RADIATION AND X-RAYS ON MUTATION PRODUCTION IN *PENICILLIUM NOTATUM*. *Genetics* 30, 8(1945).

Spore suspensions of *Penicillium notatum* were irradiated with monochromatic ultraviolet radiation between 2280 and 2967 Å and medium hard x-rays. The mutation rate increased with increasing ultraviolet energy up to a maximum, and dropped with further irradiation. The most

efficient wave length in the production of stable alterations was 2650 Å. Such results have been previously observed in *Trichophyton mentagrophytes*, *Aspergillus toneus* and *Neurospora crassa*. In the x-ray series the pattern of mutation production followed a linear relation with increasing energy. The highest (morphological) mutation rate obtained was about 40% of the surviving spores. More often a rate of 20% occurred at the peak of the curve in the ultraviolet. Different strains showed a varied response to ultraviolet. The morphological types of mutants will be demonstrated.

1860

Hungate, F. P. and T. Mannell. SULFUR-35 AS A MUTAGENIC AGENT. *Genetics* 36, 555-6(1951).

Radioactive sulfur was chosen as a desirable isotope to test for mutagenic properties. Sulfur is a part of the sulfhydryl group which is known to be essential to some enzymes. The possibility that genes and enzymes are similar suggests that sulfur may be necessary in the functioning of some genes. Sulfur-35 is easy to use in the laboratory due to its weak beta particle and its convenient half-life of 87 days. — *Neurospora crassa* was grown on Fries Medium in which sulfur-35 as sulfate had been substituted for the normal sulfur. After growing the mold for varying periods of time, the conidiospores were suspended and plated according to the method of Tatum, Barratt, and Cutter (*Science* 1949). — When the radioactive sulfur was undiluted with non-radioactive sulfur, a recovery of more than 10% biochemical mutants was obtained even when the radiation absorbed by the mold was well below 10,000 reps. When non-radioactive sources of sulfur were also present, this rate was reduced. The fact that the presence of carrier sulfur reduces the mutation rate suggests that the mutations may be induced not only by the ionizing beta particle but also by the transmutation itself. — The mutants identified have in most part shown an inability to synthesize some amino acid. Those whose requirements have been identified include arginineless, methionineless, and leucineless, as well as some having more complex requirements. (G)

1861

Hunter, Matthew C., Grant L. Stahly, and Wm. G. Myers. VARIATIONS OF *LISTERIA MONOCYTOGENES* PRODUCED BY BETA PARTICLES FROM RADIOPHOSPHORUS. *Ohio J. Sci.* 50, 253-9(1950).

Cells of *Listeria monocytogenes* bacteria were suspended in a medium containing radioactive phosphorus at a total radiation level of approximately 45,000 equiv. r over an 11-day period. At 24-hr intervals samples were removed and streaked on suitable media. Nineteen strains were isolated which showed variations from the parent in their colonial characteristics. Some of these also showed variations in physiological characteristics, in their antigenicity, and in their capacity to produce disease. (NSA)

1862

Kerschner, Jean. THE INFLUENCE OF THE Y-CHROMOSOME ON X-RAY INDUCED MUTATION RATE IN *DROSOPHILA MELANOGASTER*. *Proc. Natl. Acad. Sci. U. S.* 35, 647-51(1949).

The experiments described were performed in order to determine the effect of an extra Y-chromosome on x-ray induced visible and sex-linked recessive lethal mutation frequency in *Drosophila melanogaster*. A medium-voltage (135 kv) therapy machine was used with no filter at a target distance of 17 cm and at an average output of 450 r/min; the total dosage was 2,000-4,000 r. The extra Y-chromosome, when present was shown to decrease x-ray induced visible and sex-linked lethal mutation frequency in the male fly; in the female, it appeared to be without effect. The possible mode of action of the Y-chromosome was discussed and future lines of investigation were proposed. (NSA)

1863

Kimball, R. F. INHERITANCE OF MUTATIONAL CHANGES INDUCED BY RADIATION IN *PARAMECIUM AURELIA*. Oct. 1, 1948. 27p. (ORNL-175).

A study has been carried out in *Paramecium aurelia* of the inheritance of effects of beta and x-radiation which first expressed themselves as reductions in vigor of some of the exautogamous progeny of irradiated animals. The technique used in investigating the inheritance was to cross the irradiated animals to unirradiated ones by conjugation. In some cases, the products of the cross were crossed to unirradiated animals. The genotypes of the products of the crosses were tested by sending their descendants through autogamy to bring about complete homozygosis. The clones from both members of the conjugant pairs were in the majority of the cases of normal vigor. The exautogamous progeny from both members of the pairs often included a high proportion of clones of reduced vigor indicating that the effect was transmitted to both members as would be expected if nuclear mutations were involved. There was clear evidence that the two members of a pair produced exautogamous generations which were more alike, on the average, than were those from different pairs from the same irradiated animal. This finding is in agreement with the fact that the two members of a conjugant pair should be of identical genotype as a result of conjugation.

It was possible to calculate the average number of mutations per micronucleus in the irradiated animals and in the animals resulting from the cross of irradiated to unirradiated. The average number in the former was approximately twice that in the latter as would be expected if gene mutations were involved. In one experiment an anomalous type of inheritance was found for which no adequate explanation can be offered. Viable homozygous clones of lowered fission rate have been obtained by autogamy in the descendants of irradiated animals. The lowered fission rate can be shown to be transmitted through both members of conjugant pairs between the low fission rate clones and normal animals. A noticeable feature of such viable but low fission rate clones is the great intracolon variability in respect to fission rate and even viability itself. The conclusion was drawn that non-genic changes were not a major contributing factor to be reduced vigor resulting from radiation. It was also concluded that the results of the crosses have confirmed the assumption that reduced vigor in the exautogamous progeny of irradiated animals is an expression of micronuclear mutations induced by the radiation. (NSA)

1864

Kimball, R. F. THE INDUCTION AND INHERITANCE OF MUTATIONS IN *PARAMECIUM AURELIA*. Genetics 33, 616(1948).

Beta radiation up to 13,000 r.e.p. has no immediate effects on stock 90 of variety 1 of *Paramecium aurelia*. When the descendants of rayed animals are sent through autogamy to make them homozygous, many are of reduced vigor. Evidence from inheritance studies indicates that the reduced vigor results from segregation into homozygous form of mutational changes induced in the micronuclei. Doses given in small daily fractions were just as effective as those given as a single exposure. Thus two-hit chromosomal aberrations could not have made a major contribution to the effect. However, the relation of the average fraction of exautogamous clones of reduced vigor to dose showed that a multiple hit phenomenon was involved. This is interpreted to mean that the majority of the effect is due to the combined action of mutant genes which are individually undetectable. A formula was developed relating the average fraction of reduced vigor to the mean

number of mutations per micronucleus. The formula gives results consistent with the expectation that animals resulting from a cross of rayed to non-rayed should have on the average half as many mutants per micronucleus as the original rayed animals. From the formula, it was calculated that approximately two mutations per micronucleus were induced per 1,000 r.e.p. This rate is quite high and suggests that the method can detect mutations in the great majority of all loci in *Paramecium*. (G)

1865

Kimball, R. F. THE INDUCTION OF MUTATIONS IN *PARAMECIUM AURELIA* BY BETA RADIATION. Genetics 34, 210-22(1949).

Beta radiation from an external P-32 source in doses up to 13,000 rep has no immediate marked effect upon vegetatively multiplying *Paramecium aurelia*. When the progeny of rayed animals are sent through autogamy, many of the exautogamous clones are of reduced vigor as judged by total growth in 4 days. This reduced vigor is interpreted as the expression of mutational changes in the micronuclei partly because it first appears when the animals are made homozygous by autogamy, partly because data on inheritance to be published in a separate paper support this view. Radiation given in a period of about an hour before cytoplasmic division is less effective than radiation given at other stages of the fission cycle. No adequate explanation is available for this phenomenon. The relation of the percentage of exautogamous clones of reduced vigor to dose shows that most of the mutational changes cannot be gene mutations with individually detectable effects. His belief that most of the detectable reduction in vigor is due to the combined effect of mutant genes with individual effects too small to be detected. The mathematical relation between the average fraction of exautogamous clones of reduced vigor and the mean number of mutations per micronucleus has been worked out for this hypothesis. By approximation calculations, a value of about two mutations per micronucleus per 1000 rep has been obtained. (Authors Summary)

1866

Kimball, R. F. THE EFFECT OF RADIATIONS ON GENETIC MECHANISMS OF *PARAMECIUM AURELIA*. J. Cellular Comp. Physiol. Suppl. 1, 35, 157-69(1950).

Paramecium presents several advantages for analyzing the effect of radiation on genetic mechanisms. One of these advantages is the possibility of studying the effects of radiation on both the nuclear and the cytoplasmic mechanisms of inheritance. Cytoplasmic inheritance has been studied fairly extensively in this organism previously. The purpose of this paper is to present some results of studies on the effects of radiation on both types of inheritance, and in so doing, give some idea of the possibilities of the material. Inactivation studies have been carried out, in a preliminary way, using ultraviolet from a germicidal lamp having its major output around 2537 Å. Inactivation occurs but the data are still not sufficient to define with any exactness the form of the curve. There is a possibility that it will turn out to be of the exponential type expected for single event occurrence. The rest of the work is concerned with mutations induced in the micronucleus by β radiation. An external source of β radiation was used by means of the phosporus plaque technique developed in this laboratory. (NSA)

1867

Kimball, R. F. and Nenita T. Gaither. PHOTORECOVERY OF THE EFFECTS OF ULTRAVIOLET RADIATION ON *PARAMECIUM AURELIA*. Genetics 35, 118(1950).

Four different effects of ultraviolet radiation and one of X-rays upon *Paramecium aurelia* have been examined for

the action upon them of intense illumination with a lamp (GE H-5) having its major output in the long ultraviolet and short visible. The animals were exposed to ultraviolet of wave length 2650 Å or 2804 Å or to X-rays and immediately afterwards exposed to the H-5 lamp. Except during this exposure, dark conditions were maintained as far as possible. The effects studied were as follows: (1) mutation as measured by death and reduced division rate after autogamy; (2) temporary reduction in division rate in the first few days after irradiation and in the absence of autogamy; (3) death, presumably nongenic, in the first few days after irradiation and in the absence of autogamy; (4) a microscopically visible change in the structure of the macronucleus requiring a few hours to reach complete expression. In all four cases, light from the H-5 lamp greatly reduced the effects produced by the shorter ultraviolet. The induction of mutations by X-rays was not affected. The fact that light from the H-5 lamp affects several kinds of changes produced by short ultraviolet suggests that it may act upon some process basic to all the changes. The failure to detect an effect upon X-ray induced mutations suggests that they may be different in some way from those induced by ultraviolet. (G)

1968

Kimball, R. F. and Nenita Gaither. **MODIFICATION OF THE ACTION OF X-RAYS UPON *PARAMECIUM AURELIA*.** *Genetics* **36**, 558(1951).

A number of agents which previously have been shown to modify one or more effects of X irradiation have been tested on *Paramecium aurelia*. The mutagenic action of X rays in doses of one to six kiloroentgens was found to be reduced when the irradiation was performed in an atmosphere of nitrogen or in the presence of 0.7 M ethyl alcohol. On the other hand, 0.001 M sodium hydrosulfite, a reducing agent, had no influence on mutagenesis. No effect of the metabolic state was found since irradiation of either fed or starved paramecia, with or without incubation with 0.01 M sodium formate, produced identical amounts of mutation. Likewise the rapidity of multiplication of the cells after irradiation, as influenced by temperature, was without influence. Two nongenetic actions, division retardation and death within twenty-four hours, were studied using doses of 100 to 300 kiloroentgens. Both the amount of division retardation and of death were decreased by 0.7 M ethyl alcohol present during irradiation. Sodium hydrosulfite (0.001 M) clearly protected against the lethal action but had no influence upon division delay or, perhaps, enhanced it. Neither starvation nor incubation with formate was found to have any effect. Thus there is at least one agent which affects a variety of different kinds of radiation damage in *Paramecium*. It may be suggested that some step which is common to the various effects is involved. However, it is possible that some agents influence the steps leading to certain kinds of damage only or else act more effectively upon one kind than the other. (G)

1869

King, Edward D. **EFFECTS OF TEMPERATURE DURING X-RADIATION ON *DROSOPHILA*.** *Genetics* **32**, 93-4(1947).

Males of *D. melanogaster* were X-rayed at dosages multiples of 600 r-units from 600 to 3600 r-units at 0°C and room temperature respectively. At low temperatures for all dosages the frequencies of induced mutations were approximately twice as great as those for the same dosages at room temperature. The viability in the cold series dropped sharply at increasing dosages. (G)

1870

King, Edward D. **THE EFFECT OF LOW TEMPERATURE UPON THE FREQUENCY OF X-RAY INDUCED MUTATIONS.** *Genetics* **32**, 161-4(1947).

Special stocks of *Drosophila* were irradiated at various dosages from 600 to 3,600 r at room temperature and at 0.5°C. For all dosages the frequency of induced lethal mutations was greater at the low temperature, with an average increment of x2.3. The relation between dosage and frequency of lethal mutations was linear at both temperatures. (BA)

1871

King, R. C. **GENETIC CHANGES ACCOMPANYING THE UPTAKE OF P^{32} BY *DROSOPHILA MELANOGASTER*.** *Genetics* **35**, 118-19(1950).

Adults or larvae of *Drosophila melanogaster* are found to incorporate large amounts of P^{32} into their tissue after feeding on yeasted cornmeal-molasses-agar media to which various amounts of $H_2P^{32}O_4$ had been added previously. P^{32} is distributed among the head, thorax, gut, gonad and abdominal shell in the ratio of 20:50:10:10:10 for males fed as adults on the P^{32} -containing medium regardless of the total activity of the fly. Radioautographs made of the spermathecae and associated organs of untreated females fertilized by treated males gave direct evidence that the sperm were radioactive. Some treatments have produced sex-linked lethal mutation rates as high as 26% as measured in adult males of an inbred Canton-S stock by the M5 technique. Among a combined total of some 1,951 treated X's so far tested from all experiments 90 sex-linked recessive lethals and 11 viable mutants have been recovered. (G)

1872

Knudson, Lewis. **PERMANENT CHANGES OF CHLOROPLASTS INDUCED BY X-RAYS IN THE GAMETOPHYTE OF *POLYPODIUM AUREUM*.** *Botan. Gaz.* **101**, 721-58 (1940).

The spores of *P. aureum* may be treated with Ca hypochlorite up to 50 minutes at least, with no deleterious effect on germination and growth. Irradiation of spores with dosages as high as 30,000 r units is without effect on the per cent of germination. With higher dosages the per cent of spores germinating decreases. The growth rate is decreased with dosages as low as 10,000 r-units, and progressively decreases with increased dosage. From 72 cultures in which were sown nearly 300,000 spores, 51 prothallia having abnormal chloroplasts were isolated. Twenty-seven prothallia survived. These have been classified according to the characteristics of the chloroplasts. Including the normal, 11 types were noted. These prothallia have been propagated vegetatively during a period of seven years. The plastid types persist. Certain types are transmitted to the sporophyte as a result of sexual reproduction and retransmitted to the new generation of the gametophyte. The grouping of the plastids (type B) disappears in the adult leaves of the sporophyte and does not reappear in the new gametophyte generation. On theoretical grounds it is suggested that the plastid changes may be independent of any genic changes, and that certain plant mutations may be due solely to plastid changes. (BA)

1873

Koller, P. C. **SEGMENTAL INTERCHANGE IN MICE.** *Genetics* **29**, 247-63(1944).

By exposing male mice to 750-900 r, three different 'semi-sterile' lines with varying sterility were obtained. The chromosome mechanism responsible for semi-sterility is analysed and described in detail. The degree of semi-sterility depend on the size and position of the translocated chromosome segments. (BA)

1874

Lea, D. E. **EFFECTS OF RADIATION ON GERM CELLS, DOMINANT LETHALS AND HEREDITARY PARTIAL STERILITY.** *Brit. J. Radiol. Suppl.* **1**, 120-41(1947).

Chromosome structural changes induced by the irradiation of sperm or eggs may be viable or non-viable. Non-viable structural changes account for dominant lethals, e.i., for failures of zygotes to develop to maturity when the sperm or the egg has been irradiated before fertilization. Viable structural changes give rise (in the mouse) to hereditary partial sterility. Experimental data on the induction of dominant lethals by x-rays and neutrons in *Drosophila*, *Habrobracon*, the mouse, rat, guinea pig, rabbit, and frog, and on the induction of viable chromosome structural changes in *Drosophila* and the mouse, are reviewed. The relation to be expected between the dose of radiation and the yield of viable and non-viable types of chromosome structural change is discussed on the assumptions that: the mean number of chromosome breaks primarily produced in a germ cell is proportional to the dose; a proportion, p , of the breaks primarily produced neither reconstitute nor exchange with other breaks, but behave as dominant lethals, probably as a result of sister-union of chromatids occurring; and union is random among the remaining breakage ends. (NSA)

1875

Lefevre, George, Jr. THE RELATIVE EFFECTIVENESS OF FAST NEUTRONS AND GAMMA RAYS IN PRODUCING SOMATIC MUTATION IN *DROSOPHILA*. *Genetics* 33, 112(1948).

Following exposure to gamma rays and fast neutrons 26 hours after egg laying, the incidence of white and light eye color mosaics was four times as high in eosin males as in wild-type males, and twice as high as in eosin with mutations at various other loci, rather than from a high mutability of the eosin gene. Using the data from wild-type males, a mutation constant for somatic mutation at the white locus was calculated, showing the same order of magnitude as that for germinal mutation. Mosaic incidence following neutron exposures was higher than expected compared to gamma ray exposures, indicating that neutrons are not less effective per ionization, in producing mosaics. (NSA)

1876

Lefevre, George, Jr. THE RELATIVE EFFECTIVENESS OF FAST NEUTRONS AND GAMMA RAYS IN PRODUCING SOMATIC CROSSING OVER IN *DROSOPHILA*. *Genetics* 33, 113(1948).

Heterozygous white and eosin-white female larvae were exposed 24 to 30 hours after egg laying to gamma rays and fast neutrons. The incidence of resulting eye color mosaics was much higher than in males, and was dependent upon the rate at which the total dose was administered. Heterozygous females with a double inversion in one x-chromosome showed no increase in mosaic incidence. Neutrons were relatively much more effective, per ionization, than gamma rays. Evidence was found that mosaic size and age at exposure are not simply related. Twin mosaics in eosin-white females showed great inequality in size. Possible mechanisms for radiation induced somatic crossing over that require two hits within a limited length of time are considered. (NSA)

1877

Lefevre, George, Jr. X-RAY-INDUCED GENETIC EFFECTS IN GERMINAL AND SOMATIC TISSUE OF *DROSOPHILA MELANOGASTER*. *Am. Naturalist* 84, 341-65(1950).

Attempts were made to induce reverse mutations in both germinal and somatic tissue of *Drosophila melanogaster*. No evidence of reverse germinal mutation was found following irradiation with 5,000 r of some 166,000 recessive X-chromosome loci. In the somatic studies no reverse mutations of white were found in tests equivalent to the

exposure of 600,000 white loci to 5,000 r. White alleles of three diverse origins were used: (a) spontaneous, (b) x-ray induced, and (c) mustard-gas-induced. Serious question is thus thrown on the reliability of the early reports of x-ray-induced reverse mutation in *Drosophila*. The conclusion was also reached that x-ray-induced mutability of the w^+ locus is not significantly affected by the kind of cell in which it is located. A comparison of the influence of various intrinsic and extrinsic factors on x-ray-induced and spontaneous mutation indicates that the two mutation processes are qualitatively different. In all likelihood mutations induced by ionizing radiation in *Drosophila*, as in maize, are losses or destructions of genetic material; and unlike spontaneous mutations, induced mutations are incapable of further change. (NSA)

1878

Lefevre, George, Jr. X-RAY INDUCED SOMATIC CROSSING OVER IN *DROSOPHILA MELANOGASTER*. *Anat. Record* 108, 623-4(1950).

This paper is reproduced here in its entirety.

Eye color mosaics were produced by irradiating larval stages of *Drosophila* with 1300 r at the rate of 59 r/min 48 hr after egg laying. The mosaic incidence in heterozygous white females was 0.65 per eye. In similar females, but also bearing a double inversion in one X-chromosome, the mosaic incidence was 0.06 per eye. In males an incidence of less than 0.02 white mosaics per eye was found. In males, mosaics result mainly from somatic mutation; in females, deletion, chromosome loss, translocation, abnormal disjunction, and somatic crossing over also may produce mosaics. The presence of inversions should not alter the effectiveness of any of the mosaic-producing mechanisms, except the last. Thus, in normal heterozygous females the great majority of mosaics result from somatic crossing over, or possibly from nonhomologous segmental interchange. The distribution of induced somatic cross-overs was studied by comparing the mosaic incidence in heterozygous white (locus 1.5), heterozygous garnet (44), and heterozygous carnation (62.5) females. The results indicate that an appreciable amount of somatic crossing over must take place in the heterochromatic portion of the X chromosome; but it is not equally distributed throughout the X chromosome, being greater in the right than in the left end. A similar distortion of the normal pattern of crossing over is found when various agents are used in order to induce excessive germinal crossing over. (AR)

1879

Lefevre, George, Jr. X-RAY INDUCED GENETIC EFFECTS IN GERMINAL AND SOMATIC TISSUE OF *DROSOPHILA MELANOGASTER*. *Genetics* 35, 120(1950).

The rate of X-ray induced direct mutation was compared following irradiation of germinal and somatic tissue. Various data regarding the frequency of mutation to white after exposure of adult w^+ males indicate that the average germinal mutation constant for the mutation of w^+ to w is about 12.5×10^{-8} . Possible errors inherent in the estimation of a somatic mutation constant can be evaluated, and by employing proper techniques reliable data on the somatic mutation rate of w^+ to w can be obtained. From the incidence and average size of white eye-color mosaics produced by irradiation of + male larvae, a somatic mutation constant of 14.2×10^{-8} was calculated. Thus, X-ray induced mutability of the w^+ locus is not significantly affected by the kind of cell in which it is located. Attempts were made to induce reverse mutations in both germinal and somatic tissue. No evidence of reverse germinal mutation was found following irradiation with 5000 r to 166,000 recessive X-chromosome loci, including y , w , sn^2 , and f . In somatic studies no reverse mutations of white were found in tests

equivalent to the exposure to 5000 r of 600,000 *w* alleles of three diverse origins: (a) spontaneous, (b) X-ray induced, and (c) mustard gas induced. Serious question is thrown on the reliability of early reports of X-ray induced reverse mutation in *Drosophila*. A comparison of the published data regarding the influence of various intrinsic and extrinsic factors on X-ray induced and spontaneous mutation suggests that the two mutation processes are qualitatively different. (G)

1880

Lefevre, George, Jr. and F. J. Ratty, Jr. X-RAY INDUCED EFFECTS IN THE WHITE-NOTCH REGION OF WILD-TYPE AND WHITE-MOTTLED-4 CHROMOSOMES OF *DROSOPHILA MELANOGASTER*. *Genetics* 36, 560-1(1951).

Canton-S + and *w*^{m4} males were exposed to similar X-ray doses of approximately 5000 r. The relative frequencies of viable white mutations, inviable white changes, notches, and simultaneous losses of both the white and Notch loci were determined. Examination of nearly 35,000 offspring disclosed that the incidence of white lethals was sensibly the same in the two series, likewise the Notches. However, viable whites were twice as numerous in *w*^{m4} as in Canton-S +, and white-Notch deletions about 16x more frequent in *w*^{m4}. In each series the number of Notches was almost exactly equal to the sum of the number of viable white plus the white lethals. — The failure to find more white lethals in *w*^{m4} than in Canton-S +, even though the *w*-N deficiencies were enormously more frequent, implies that many of the viable whites induced in *w*^{m4} were actually deficiencies that would have been inviable if a loss of similar extent had been produced in a normal chromosome where the *w*⁺ locus is surrounded by euchromatin. A consistent interpretation of the results can be made on the assumption that all X-ray induced effects, viable and inviable, actually are the result of destruction of genetic material. When viable, the loss may consist of only one gene or less, and be cytologically undetectable. Longer euchromatic deficiencies will be almost invariably lethal. The Notch locus may well be more "important" than the *w*⁺ locus. Any loss in the former, however small, is homozygous inviable. (G)

1881

Lincoln, Ralph E. PRODUCTION AND RATE OF MUTATION IN *PHYTOMONAS STEWARTII* BY X-RADIATION. *Genetics* 25, 125-6(1940).

Broth cultures of *Phytomonas stewartii* were treated with X-radiation of 0.7A and 1.5A at intensities which reduced a culture of 100,000,000 viable cells to less than 1,000 viable cells within a period of 25 minutes. Inactivation curves for this organism are of the single absorption type—that is semilogarithmically linear. Variation was observed in colony type, colony color, virulence and mucoid characters. Mutation increases in proportion to exposure time. Under conditions where only one out of every 100,000 cells treated remains viable, the mutation rate is about 200 times higher than the natural mutation rate after growth in broth, or about 10,000 mutations per million treated cells as compared to 55 per million cells after growth in broth. In general the same pattern and type of variation was found after X-radiation as after growth in broth. Most mutations observed are stable, heritable and transmissible from parent to daughter cell, although certain stocks have been isolated in which it is impossible to stabilize the variant type. (G)

1882

Lincoln, Ralph E. and John W. Gowen. MUTATION OF *PHYTOMONAS STEWARTII* BY X-RAY IRRADIATION. *Genetics* 27, 441-62(1942).

This paper presents a comparative study of mutations in *Phytomonas stewartii* under natural conditions and under the stimulus of X-irradiation of low quantum energy. Irradiation was at an intensity such that 100,000,000 viable cells suspended in broth were reduced to about 1,000 in 25 min. of treatment. Survival during irradiation follows the simple exponential function—survival ratio = e^{-ar} . Mutations were observed in colony color, surface appearance and size. The rate of mutation following x-irradiation is greater than the observed spontaneous rate. X-ray-induced mutation differs from spontaneous mutation only in frequency of occurrence, no differences in the kind of mutation produced being observed. The pattern of mutation observed in two widely different stocks of *Ph. stewartii* was similar. Mutations of colony characters may be accompanied by either increased or decreased virulence for maize. Except for mutations to an unstable form, mutants appear to be as stable as the parent strain from which they were derived. From evidence secured in this study it would appear that the terms "mutant", "variant", "saltant", and "dissociant", as applied to bacteria are synonymous and are applied to phenomena resulting from gene mutation. From this point of view the physical basis of inheritance of *Ph. stewartii* is similar to that of higher organisms. (Authors' Summary)

1883

Lindegren, Carl C. and Gertrude Lindegren. X-RAY AND ULTRA-VIOLET INDUCED MUTATIONS IN *NEUROSPORA*. *J. Heredity* 32, 404-12(1941).

X-ray treatment of the uninucleate spermatia of *N. crassa* induced both gene mutations and chromosomal aberrations, one of which was specifically identified as an inversion; ultra-violet treatment induced gene mutations and many of the ultra-violet treated variants were degenerate phenotypes which did not yield to genetical analysis. No chromosomal aberrations were found among the ultra-violet treated variants. These experiments followed by breeding tests are the first which specifically test induced fungal variants as to their genic and chromosomal nature. In most of the previous abundant work on the induction of mutation in fungi, the source material has not been properly purified, and it has not been possible to distinguish between induced mutations and mutations already present in the stock, or selected by the treatment, as compared to mutations actually induced by the treatment. (BA)

1884

Lindegren, Carl C. and Gertrude Lindegren. X-RAY AND ULTRA-VIOLET INDUCED MUTATIONS IN *NEUROSPORA*. II. ULTRA-VIOLET MUTATIONS. *J. Heredity* 32, 435-40(1941).

Ultra-violet treatment of the uninucleate spermatia of *N. crassa* induced many stable simple gene mutations. None of the ultra-violet mutants showed the diminished fertility characteristic of chromosome inversion. Nearly half of the mutants were degenerate phenotypes which did not yield to genetical analysis. (BA)

1885

Lindegren, Carl C. and Gertrude Lindegren. X-RAY AND ULTRAVIOLET INDUCED MUTATIONS IN *NEUROSPORA*. *Genetics* 27, 154(1942).

The uninucleate thin-walled spores (spermatia) of *Neurospora crassa* were treated by ultraviolet and X-rays cultured individually in separate test tubes and compared with an adequate number of controls. The variants induced were true gene mutations, for when mated with mycelia of opposite sex, factors differentiating the variations segregated at meiosis. A considerable number of the mutations, from both sources, reverted. Reverse mutations are much more easily brought into expression and have an opportunity to obtain supremacy in the fungi because the nuclei

are haploid and the thallus is structureless and coenocytic. A reverse mutation in any one of the nuclei in the thallus may change the phenotype. It is possible that the so-called "temporary changes" found by Emmons and Hollaender are likewise mutations which reverted. Fifty percent of the spermatia treated with X-rays were killed and over 99 percent of those treated with ultraviolet were killed at the dosages used. A considerable number of the X-ray variants gave evidence of the presence of chromosomal aberrations, while this was not true of any of the ultraviolet variants. (G)

1886

Luce, Wilbur M., H. B. Chase, and Henry Quastler. EFFECTS OF GRADED DOSAGE OF X-RAYS ON THE PRODUCTION OF EYE FACETS IN THE BAR-EYED RACE OF *DROSOPHILA MELANOGASTER*. *Genetics* **33**, 115(1948).

The eggs and larvae of an inbred strain of the Bar-eyed mutant of *Drosophila* were treated with x-rays of dosages of 115, 460, 920, 1380 r delivered from 5, 20, 40, 60 seconds respectively. The flies were kept at 28°C. The eggs and larvae were irradiated at different ages ranging from 5 to 86 hours after deposition. The irradiation caused a reduction in facet number provided the time of treatment occurred during an effective period with limits between 48 and 72 hours of egg-larval life. The extent of the reduction increases with the x-ray dosage ranging from 6.75 per cent with 115 r to 41.20% with 1,380 r in males, and from 2.83% with 115 r to 34.76% with 138 r in females. Irradiation outside the effective period had no significant effect on facet number except with the lowest dosage, 155 r. In this case treatment before the beginning of the effective period increased the facet number 7.30% in males and 5.92% in females. A comparison of the location of the effective period for x-rays with that for temperature indicates that the former begins earlier. Near the time of the beginning of the x-ray effective period the frontal sacs of the larvae are separating into the optic and antennal lobes. This suggests that the x-rays can act only after these areas are determined. After their separation the optic and antennal lobes begin to grow rapidly. The x-rays produce their effects during this period. (NSA)

1887

Luce, Wilbur M., Henry Quastler, and Herman B. Chase. REDUCTION IN FACET NUMBER IN BAR-EYED *DROSOPHILA* BY X-RAYS. *Genetics* **36**, 488-98(1951).

Larvae of Bar-eyed *Drosophila*, kept at a temperature of 28°C., which were irradiated with X-rays of dosages varying from 115 to 1840 r, developed into adult flies whose compound eyes had a smaller number of facets than untreated controls. With a dosage of 920 r the effect of x-rays was largely confined to a radiosensitive period extending from about 55 to 70 hours of egg-larval life with a maximum reduction occurring between 57 and 67 hours. The radiosensitive period closely corresponds to similar sensitive periods for other environmental agents affecting facet number in Bar-eyed *Drosophila*. The reduction in facet number following application of x-rays during the sensitive stage was nearly proportional to the dosage applied. In males the reduction in facets per unit dose was always greater than in females. The biological effects of x-rays and the nature of the mode of action of the Bar mutants are discussed. (Authors' Summary)

1888

Luce, Wilbur M., Henry Quastler, and Lester S. Skaggs. BIOLOGICAL EVALUATION OF 20 MILLION VOLT ROENTGEN RAYS. III. RECESSIVE SEX-LINKED LETHALS IN *DROSOPHILA MELANOGASTER*. *Am. J. Roentgenol. Radium Therapy* **62**, 555-8(1949).

The mutagenic effect of roentgen rays has been investigated by means of the C1B test in *Drosophila melanogaster*. Three types of apparatus were used: the betatron, and conventional machines for deep and superficial therapy. The results obtained are consistent with an effectiveness of 70% of the high energy rays, as compared to low energy rays, both referred to the 25 r condenser thimble as the common standard. (Authors' Summary)

1889

MacKey, James. NEUTRON AND X-RAY EXPERIMENTS IN BARLEY. *Hereditas* **37**, 421-64(1951).

Dry and presoaked seed of barley were treated with x rays and fast neutrons, and the biological effect of the irradiation was followed through the first and second generation. For dry, dormant seed the germinability was normal even after the heaviest dose applied. The retardation of the initial seedling growth was, however, pronounced, giving a sigmoid relation to x-ray dose and an exponential one to neutron dose. The frequency of mature plants, i.e., the survival fraction, seems to be nearly equal in X_1 and N_1 at comparable tissue doses. The cytological response in the first mitotic cycle to irradiation showed an N/X efficiency quotient of 10, if the frequency of fragments and bridges were registered, whereas the fraction of affected seeds, the plant fertility, and the rate of induced chlorophyll mutations gave N/X ratios of $66/18$. For the two last-mentioned biological events a pronounced saturation effect was, however, intervening in X_1 , indicating that a contra-selection had set in. Presoaking of the seed did not change this difference in the biological action of x rays and neutrons. In X_1 the increased sensibility of the chromosomes was paralleled by an increased physiological killing. A more pronounced energy absorption due to the high moderating effect of water in the case of neutrons explains why the lethality after presoaking in N_1 falls considerably below that of X_1 . The types of induced chlorophyll mutations and their relative proportions were the same in X_2 and N_2 . At the high doses used in the present study no correlation between degrees of sterility in the first generation and different categories of chlorophyll mutation in the second has been found. After both types of radiation the mutations were to a great extent associated with chromosome disturbances. 108 references. (NSA)

1890

Markert, C. L. COMPARATIVE GENE STABILITY IN *GLOMERELLA* AND *NEUROSPORA*. *Genetics* **36**, 564(1951).

More than 100 auxotrophic mutants of *Glomerella* have been induced by the mutagenic radiations—ultraviolet light, X-rays, and fast neutrons. The specific nutritional requirements of 74 of these mutants have been determined by methods comparable to those commonly used with *Neurospora*. These data make possible (1) a comparison of the qualitative mutagenic effects of the three types of radiation, and (2) a comparison of the relative frequencies of the various kinds of radiation-induced auxotrophic mutants in *Neurospora* and *Glomerella*.—The data do not reveal any qualitative differences in the types of mutants induced by the three radiations used. However, ultraviolet irradiation appears to induce the most easily repaired type of genetic damage, since ultraviolet-induced mutants revert to wild type much more frequently than X-ray or neutron-induced mutants.—Since *Glomerella* and *Neurospora* are related fungi, it is not surprising that the commonly occurring mutants of *Neurospora* are also found in *Glomerella* and in similar relative proportions. Thus the genes which control homologous reactions in these two organisms appear to possess, in general, comparable stabilities. In contrast to *Neurospora* all auxotrophic mutants of *Glomerella* are

visibly different from wild type on a complete medium. Two unusual types of *Glomerella* mutants are those requiring biotin and one which requires glutathione. (G)

1891

Martin, Albert, Jr. THE SIGNIFICANCE OF THE ACTION OF RADIOACTIVE PHOSPHORUS ON *HABROBRACON JUGLANDIS* ASHMEAD. *Proc. Penn. Acad. Sci.* 24, 60-4(1950).

A summary of the results of the effects of radioactive phosphorus on *Habrobracon juglandis* wasps is presented. Wild-type stock 33 were used throughout the experiment and were subjected to β rays of radioactive $\text{Na}_2\text{H}^{32}\text{O}_4$. Females were placed in exposure vials in contact with non-radioactive P salts while depositing eggs which became the control. They were then placed in exposure vials with the P^{32} salt on the basis that the β radiation penetrates up to 1 cm of matter and would completely penetrate the body of the wasp. Among the progeny of each exposed female, virgin or nonvirgin, there were on the average 28% abnormal individuals as against 1 or 2% in control cultures. Abnormalities such as misshapen wings, different numbers of antennae, short legs, and small over-all body size are described and discussed. (NSA)

1892

Martin, Albert, Jr., J. N. Dent, and L. Joseph. EFFECTS OF BETA-RAYS ON *HABROBRACON JUGLANDIS*. *Genetics* 33, 619-20(1948).

A technique for exposing *Habrobracon juglandis* females to β -rays has been developed and utilized. Wild-type females exposed to dried radioactive phosphorus produce abnormal progeny with a frequency of approximately 25 percent, while untreated females produce abnormalities at the rate of about 5 percent. Some of the abnormalities in the test material have proved to be mutations, while none of the abnormalities in the controls have been transmitted to their offspring. Frequency of abnormalities does not vary appreciably between progeny of treated virgins and non-virgins. Abnormalities occurring most frequently are those of the wings, antennae, and feet in that order. Mutations of wings and antennae have been checked through three generations. Reduplication of the right primary wing breeds true but with varying degrees of penetrance, even to the point of overlapping with wild-type. Wrinkled wings (primary and secondary) and drooping antennae appear in combination, indicating either a one-gene hit or a two-gene hit with genes so closely linked that they have so far shown no crossing-over. A clear-cut reduplication of the tarsal segments of the left mesothoracic leg has not bred true, but the abnormality indicates the severity of possible effects of β -radiation. Current investigation indicates the need for extreme caution in the utilization of radioactive isotopes, particularly when used internally. (G)

1893

McElroy, W. D. and C. P. Swanson. THE THEORY OF RATE PROCESSES AND GENE MUTATION. *Johns Hopkins Univ. [nd]* 42p. (AECU-1713)

Genetic changes are pictured as being initiated by a chemical mutagen, which may be naturally occurring, radiation-induced, or artificially applied, and which in combination with a particular group in the genic structure initiates a series of reactions which give rise to an intermediate semi-activated state. This state may lead to a permanent change in the genic structure or it may, after a period of time, revert to a normal state. Environmental circumstances affecting the probability of the change's going one way or the other are discussed. The theory of absolute reaction rates as applied to gene mutation is reviewed and reevaluated. Energy levels necessary for a molecule to reach the activated state are considered. Re-

action rate and factors affecting frequency of mutations are illustrated with reports of experimental work by the authors using plants. The potentiating effect of infrared radiation on changes induced by x rays, and changes produced by pressure and temperature on the mutagenic effects of nitrogen mustard are reviewed. (NSA)

1894

Mittwoch, Ursula. STUDIES IN THE GENETICS OF SOME X-RAY-INDUCED MORPHOLOGICAL MUTANTS IN *COPRINUS LAGOPUS*. *J. Genetics* 50, 202-5(1951).

The method used for the culture of the hymenomycetes fungus *Coprinus lagopus* and for the production of x-ray mutants is described. The mating type exhibited is outlined, and the independent inheritance of the mating-type genes is shown. Four morphological mutants were found, one of which is linked with one of the mating-type genes. The action of natural selection with regard to the binucleate condition of the secondary mycelium is discussed. (NSA)

1895

Moh, C. C. and Luther Smith. AN ANALYSIS OF SEEDLING MUTANTS (SPONTANEOUS, ATOMIC BOMB-RADIATION-, AND X RAY-INDUCED) IN BARLEY AND DURUM WHEAT. *Genetics* 36, 629-40(1951).

The study involved atomic bomb- and X ray-induced, and spontaneous seedling mutants in barley and durum wheat. Progeny tests were made of 650 X_2 plants, representing 397 independent mutants; and of 5,653 X_3 plants, representing 581 mutants. It was concluded that chromosomal aberrations (possibly deficiencies) associated with a considerable portion of the mutations, or pleiotropic effects of the mutant genes, best accounted for the fact that over 20 percent of the mutants tested segregated in ratios that deviated significantly from the theoretical 3:1. The results could readily be accounted for if it were assumed that a considerable portion of the mutations were in fact deficiencies rather than gene or "point" mutations—an hypothesis which is being checked by further tests. (NSA)

1896

Muller, H. J. AN ANALYSIS OF THE PROCESS OF STRUCTURAL CHANGE IN CHROMOSOMES OF *DROSOPHILA*. *J. Genetics* 40, 1-66(1940).

The frequency of gross structural changes induced by the irradiation of chromosomes in spermatozoa is proportional to the ionization produced, regardless of λ of the radiation, from 50 kv x-rays to γ -rays; concentration of the dose in time, whether continuous treatment or fractionation over three weeks; fertilization immediately or after one month's delay; radiation intensity from 0.05–250 r/min.; temperature from 5° to 37°C. These data constitute evidence that the "primary effects" of individual ionizations accumulate independently until fertilization, the number of structural changes produced depending on the final total. Since the frequency of rearrangements varies as the $\frac{3}{2}$ power of the total dosage from 1,000–4,000 r, the primary effects are breakages, followed secondarily by rearrangements only some of which survive. At lower doses, the exponent appears to approach 2, as expected if all rearrangements represent combinations of independent primary changes. Evidence that the latter are actually breakages comes from data showing that whole chromosome losses of the X_1 presumably resulting from simple breakage followed by attachment of sister fragments, follow a linear proportionality. It is suggested that gynandromorphs and mosaics arise not from treatment of occasional spermatozoa in which chromosomes are already split, but from a delay in the union of broken ends until after chromosome division, followed by differential behavior of the broken sister—chromatids. Multiple exchange translocations (involving a ring chromosome) increase in frequency with dosage more

rapidly than ordinary translocations (not involving a ring chromosome), and are more frequent at all dosages than expected on a basis of random attachment of broken ends. These data support the hypothesis of initial breakages followed by unions favored by the original proximity of broken ends. Minute rearrangements have a linear dosage-frequency relation. Their breaks are interdependent, demonstrating the spread of the effect of a single ionization to nearby points on the chromonema spiral. This renders insecure the assumption that the genetic effects of radiation result solely from the ionization of atoms in the genetic material itself. The "sensitive volume" is not to be identified with the gene. The mortality of cells from treated sperm can be accounted for as due to the sum of induced gross and minute structural changes plus dominant lethal gene mutations. Part of the necrosis in irradiated proliferating cells must arise from these genetic causes, but not all, for the relative mortalities of irradiated triploid equal those of diploid *D. embryos*. The demonstration of the "breakage first" character of induced structural rearrangements is considered as throwing light, by analogy, on the mechanism of crossing over. The interpretation of all gene mutations as minute or ultra-minute structural rearrangements of the chromosomes is also considered. It is shown that ultra-violet produces gene mutations without first breaking the chromosomes, since ultra-violet produces mutations but not translocations. (BA)

1897

Muller, H. J. INDUCED MUTATIONS IN *DROSOPHILA*. Cold Spring Harbor Symposia Quant. Biol. 9, 151-65(1941).

There is evidence that gene mutations start as changes in individual atoms, in consequence of which by transfer of energy or chain of reactions gene mutation results. Radiation acts through single atom changes and a resulting chain of reactions to break the chromosema. If fusion of broken chromosome ends has not occurred before chromatid formation, two sister fragments can unite with subsequent loss of dicentric and acentric chromosomes. This is usually lethal. There is a tendency to restitution as opposed to rearrangement and chromosome loss. Evidence shows that broken *Drosophila* chromonemata seldom "heal" except by the union of broken ends with one another. It is shown that in minute rearrangements one individual atom-change must initiate a chain of reactions in two or more directions so that two or more different but nearby breaks of the chromonema are induced with subsequent fusion of ends from different breaks. The atom whose change initiates a mutation dose not necessarily lie within the gene. Some evidence appears to favor the idea of a certain similarity between minute rearrangements and gene mutations. Other evidence gives reasons for inferring that breaks occurring in both gross and minute rearrangements do not separate individual amino acid units but take place between much larger structures. (MF)

1898

Muller, H. J. THE ROLE PLAYED BY RADIATION MUTATIONS IN MANKIND. *Science* 93, 438(1941).

This paper is an abstract and is reproduced here in its entirety.

Calculations are presented of the average number of generations to be expected between the production of a recessive gene mutation in man and its manifestation in a homozygous individual. The chance of the mutated gene meeting another like it that originated by an independent mutation depends on the frequency of such mutations, on the survival value of the abnormal type and on the randomness of breeding. Taking the maximal values for these factors (the values favoring the highest frequencies of recessive abnormalities) it turns out that at least 30 or,

more likely, over 100 generations would on the average occur—i.e., 750 to 3000 years or more—before a seriously harmful recessive abnormality (one having less than 90% of normal survival) would manifest itself by this process. Another mechanism of manifestation involves the meeting of two genes, each descended from the same original mutated gene. The frequency of this depends upon the total degree of inbreeding. A new method for gauging this is presented, involving the principle that the frequency of homozygosis from this cause is one fourth of the frequency of marriages between two related individuals having the same name. From statistics on this point and on cousin marriages it is found that, even in the most closely inbred groups in modern civilized society, the chance of a mutated gene manifesting itself by this process is not over 0.5%. This represents a "latent period" of some 5000 years. Both processes together would give over 600 and probably thousands of years of latency. The large number of mutated genes accidentally dying out while thus "under cover" are compensated for by those accidentally multiplying. Thus the inherited damage from irradiation, though so long postponed, is in no wise prevented. Judging by results in mice (P. Hertwig) we may provisionally take the order of frequency of seriously harmful recessive mutations induced by 300 r as one to several per cent (perhaps doubling the natural frequency). This chance of damage would seldom outweigh the direct benefits of diagnostic or therapeutic irradiations, excepting those designed to stimulate or temporarily inhibit reproduction. However, in irradiation intended for other parts, the gonads should be shielded. Natural radioactivity, while of no consequence in flies, may appreciably influence human mutation frequency. For the long duration of the human generation sometimes allows the reception of ten or more r. Thus under special conditions, the amount might conceivably be enough to be significant in evolution.

1899

Muller, H. J. THE PRODUCTION OF MUTATIONS. *J. Heredity* 38, 259-70(1947).

This is the text of the Nobel prize lecture delivered by the author before the Caroline Inst., Stockholm, Sweden, December 12, 1946. He reviews modern techniques for the marking, identification, and manipulation of mutations in breeding experiments. Comparing mutations to chemical reactions, he points out that single mutations correspond with individual molecular changes. An extended series of mutations in a great number of identical genes in a population, spread out over thousands of years corresponds with the course of an ordinary chemical reaction that takes place in a fraction of a second or a few seconds. Chromosome analysis, radiation effects, somatic radiation effects, and frequency of mutations are other topics discussed. Induced and natural mutations are compared, and the importance of selection is emphasized, since we are unable to control and direct mutations at will, even though the frequency of their occurrence can be stimulated. The address is concluded with a warning to radiologists of their obligation to protect human germplasm against the danger of injury during medical treatment, industrial use of radiation and peace-time uses of atomic energy. (BA)

1900

Muller, H. J. THE PRODUCTION, ACCUMULATION, AND AVOIDANCE OF MUTATION. Argonne National Laboratory. Aug. 14, 1947. 27p. (ANL-4023)

A comprehensive discussion of mutations is presented. Though the mutant may be called "abnormal" in the given respect, if we carefully define our term abnormal, nevertheless the phenomenon of mutation itself, i.e., the occurrence of changes which become reproduced in subsequent

generations, is in a sense the most normal thing about all living matter, being the property that most basically distinguishes living matter from non-living and that has allowed living matter to develop, in its evolution, all the further peculiarities of its marvelous organization. For, on the modern genetic view of evolution, our entire bodily structure, with all its complicated physiology and biochemistry, has been built up through hundreds of millions of years by means of a long succession of mutations, probably millions of them in all. The thousands of different kinds of genes which we now contain, and which we call normal genes, cooperate in most complicated ways in the formation of every bodily organ and characteristic. Our whole complicated bodily organization is thus built up of a fabric of genes all of which were mutant in their day, but which happened to succeed and so are called "normal" by this time. Techniques using the *Drosophila* fruit fly are used as examples together with warnings against incidental exposure to x-rays handled by unformed individuals and possible effects of atomic bomb warfare. (TIS)

1901

Muller, H. J. RADIATION DAMAGE TO THE GENETIC MATERIAL. *Am. Scientist* 38, 33-59(1950).

Germinal genetic changes rather than the somatic effects of radiation are described and suggested in this paper. The origin of mutations is reviewed along with their general effect on the population. Approx. 99% of the mutations are harmful in some way, and as to be expected, eventually die out because of the lower viability of the individuals containing these mutated genes. Radiation is the only type of agent yet known to which human beings are likely to be exposed in quantity sufficient to cause any considerable production of mutations in them. Expts. on animals indicate that mutations resulting from radiation are similar to those arising naturally but the speed of their production is greatly increased, being as much as 100 times as many per generation in fruit flies. Danger to future human generations is implied when the amount of radiation is considered that received by women for such things as inducing ovulation; and the use of fluoroscopy and X-ray for diagnosis of disease in both men and women, even when the sex organs are not located immediately in front of the plate. The accumulated effects of these radiations may be observed in later generations by mutated genes. Few physicians or technicians keep a record of the total amount of radiation received by a patient and when the patient moves about the country and receives similar treatments in a number of places the danger is enhanced. We are much more concerned with the daily and present-generation somatic conditions than with the future development of detrimental genes. In this method of treatment the type of selection is lacking which would be needed to counteract the harmful effects of an increase of the mutation frequency, and that increase, if it occurred, would spell retrogression rather than progress. (BA)

1902

Muller, H. J. RADIATION DAMAGE TO THE GENETIC MATERIAL. II. EFFECTS MANIFESTED MAINLY IN THE EXPOSED INDIVIDUALS. *Am. Scientist* 38, 399-425(1950).

This article reviews some of the more recent work in the field. Some of the topics discussed are the induction of gene mutations in somatic cells, chromosome breakage by radiation, and its effects, the validity of the distinction between gene and chromosome changes, factors predisposing to the production of chromosome changes, the accumulation of radiation damage to the individual emphasizing the risk of repeated, low dosage exposures, and the danger of using what are normally considered reliable criteria, such as

change in blood count, loss of sperm mobility, reddening of the skin, and loss of hair in estimating radiation damage to an individual, and other biological effects of radiation, such as the inhibition and regression of mitosis caused by low doses and the influence of certain chemicals on the damage of biological material by radiation. (NSA)

1903

Muller, H. J. SOME PRESENT PROBLEMS IN THE GENETIC EFFECTS OF RADIATION. *J. Cellular Comp. Physiol. Suppl.* 1, 35, 9-70(1950).

The frequency of the primary genetic effects of ionizing radiation, gene mutations and chromosome breaks, is proportional to that of the ionizations produced, and, within wide limits, it is independent of wavelength, and of the time-intensity distribution of treatment. It is not, however, independent of the genetic and environmental conditions accompanying treatment. Since gross arrangements of chromosome parts require two or more chromosome breaks, which in the case of x and γ rays are usually independent, their frequency follows a higher power of the dose than one. In *Drosophila*, but probably relatively little in most organisms other than *Diptera*, these rearrangements are accompanied by changes in the functioning of genes, often including lethal effects, near the sites of breakage. The question is considered why the frequency of lethals appears to remain proportional to dose even at high doses, despite the existence at such doses of a considerable class of lethals caused by the position effect of rearrangements whose increase in frequency follows a higher power of the dose than one. It is pointed out that this is probably because the rise in lethal frequency which would be caused in this way is at least partly compensated for by the presence of another kind of lethals, due to small rearrangements, especially deficiencies, which as the dose rose would increasingly come into combination with gross rearrangements and so become in part irrecoverable and in part lost to view as separate lethals. Not enough is yet known about the preferences of broken chromosome ends for one rather than another type of union to permit reliable calculations to be made of the expectations for different types of lethals at high doses, where there is much competition for union. Examples of some of the as yet unsolved problems concerning the manner of origination of chromosome changes are given together with some new evidence concerning them. It is shown that a high proportion of induced small deficiencies must result from two breaks in the same chromosome or chromatid, followed by deletion of the interstitial piece rather than by exchange of unequal segments between sister chromatids. Evidence of the high frequency of cases of restitution is presented, based on data from ring chromosomes, but the total frequency of restitutions is still unknown. Grounds are given for concluding that the distinction between chromosome structural changes, even small ones and gene mutations, is valid, despite the fact that these processes are in some ways related. Some problems are considered concerning the amount and the mode of manifestation of radiation damage to the genetic material of the somatic cells of an exposed individual. (NSA)

1904

Muller, H. J. PARTIAL DOMINANCE IN RELATION TO THE NEED FOR STUDYING INDUCED MUTATIONS INDIVIDUALLY. *J. Cellular Comp. Physiol. Suppl.* 1, 35, 205-10(1950).

There is evidence for the existence of a significant amount of dominance on the part of apparently recessive mutant genes. At first sight this dominance seems to make it possible to estimate the total genetic effects by studying the first few generations following exposure to radiation

but the more analytical method of detecting individual mutant genes and comparing their effects in homozygous and heterozygous condition is indispensable. The most direct evidence for the existence of a small but significant degree of dominance of most "recessive" mutant genes is derived from cases like that of miniature wing in which measurement of a group of heterozygotes has demonstrated a significant statistical difference from normal in the direction of the homozygous mutants. Further evidence has been derived from consideration of the limitation in size of deficiencies that are recoverable heterozygously. Evidence for the incomplete dominance of normal genes ("haplo-insufficiency") lies also in the phenomenon of dosage compensation. There must be an important difference between one dose and two doses of the normal gene in the same sex or there would be no selective pressure to readjust the effects in the two sexes in the manner observed. "Recessives" that are not fully lethal but only detrimental are harder to detect than lethals. But unless a sample of the "recessives" can be detected as individual mutants no idea of their numbers, amount of dominance or consequent rate of extinction in the population can be obtained. The only fair criterion of the amount of genetic damage done to a population by a given treatment is the sum total of that damage throughout all succeeding generations. (MF)

1905

Muller, H. J. and G. Pontecorvo. THE SURPRISINGLY HIGH FREQUENCY OF SPONTANEOUS AND INDUCED CHROMOSOME BREAKAGE IN DROSOPHILA, AND ITS EXPRESSION THROUGH DOMINANT LETHALS. *Genetics* **27**, 157-8(1942).

The unusually low ratio of daughters to sons of irradiated males having ring X-chromosomes is shown to be mainly due to death of zygotes with affected X's. For, at 4000 r, only about 3% of females are found to be converted into males by induced loss of an X, whereas the relative number of females is reduced by about 35%. Allowing for deaths from X-translocations (some 10%) most of this dominant lethal effect on the females must be due to "simple breakage," which in rings must often be followed, in cases which would otherwise be restitutional, by formation of dicentrics, occasioned by twisting of the chromonema or chromonema-pair before re-union. The results show over 75% of these sister-dicentrics to be lethal (translocational dicentrics being still oftener lethal). Breaks in non-rings are presumably induced by irradiation as often in rings, but here the great majority are followed by perfect restitution. Thus at 4000 r nearly all offspring contain one or more restituted chromosomes nevertheless the lethal losses of non-ring X's are frequent enough (ca. 5% at 4000 r) to show that a considerable part of the dominant lethal effect of sperm irradiation results from "simple breakage" with sister-dicentric formation. The frequency of spontaneous lethal and viable losses of rings (ca. 13% and 2.5%) is likewise surprisingly high, and may be due to spontaneous breakage. This probably occurs similarly in non-rings but is followed by perfect restitution. Since so few spontaneous structural changes arise, this breakage would usually occur in pre-spermatogonium stages, allowing prompt restitution. (G)

1906

Muller, H. J. and J. I. Valencia. THE LOCALIZATION OF THE MUTAGENIC ACTION OF NEUTRON-INDUCED IONIZATIONS IN DROSOPHILA. *Genetics* **36**, 567-8 (1951).

The frequency of translocations induced by fast neutron irradiation of *Drosophila* spermatozoa was found to vary linearly with dose even at doses sufficient to produce multiple proton tracks per sperm. This shows that broken

chromosome ends derived from different breaks caused by the same track undergo recombination with one another much oftener than with those of different tracks. Our interpretation is that breaks caused by the same track tend to occur near together, this proximity favoring union between the broken ends. Thus the pieces would usually unite before greatly changing their relative positions. It must further be inferred that in this material a break usually occurs close to the point of origin of the ionization that induces it, i.e., that remote breakage effects, resulting from migration of ionization-induced, relatively stable mutagens over microscopically appreciable distances, are uncommon.— Further evidence for this conclusion is provided by the finding that loci, like that for white eyes, which with X-rays give "visible mutations" seldom accompanied by a lethal effect unless there is a microscopically visible deficiency or other rearrangement, give with neutrons "visible mutations" that are usually accompanied by a lethal effect, even when there is no cytologically demonstrable alteration. This concatenation of two mutagenic effects in close proximity (whether in these cases usually breaks or gene mutations or both is not yet decided) would result from the crowding of ionizations in proton tracks, provided the mutagenic action of the ionizations remained narrowly localized. —Work supported by grant from American Cancer Society. (G)

1907

Muller, H. J., R. M. Valencia, and J. I. Valencia. THE PRODUCTION OF MUTATIONS AT INDIVIDUAL LOCI IN DROSOPHILA BY IRRADIATION OF OOCYTES AND OOGONIA. *Genetics* **35**, 126(1950).

To study mutagenesis in interphase nuclei females undergoing semi-starvation were X-rayed with 4600 r and then passed through a series of cultures, usually at 4-day intervals. Offspring from first cultures represented irradiated later oocytes, with chromosomes relatively condensed, and those from later cultures "resting" oogonia or, more rarely, early oocytes, with chromosomes attenuated. The genetic technique described in our parallel paper on spontaneous mutation was used, mutations at the 11 specified loci being looked for in non-disjunctionally produced daughters. 8,865 such daughters from the first cultures were observed, 94,380 from later cultures. Over 200 mutants were obtained, and about 100 bred and analyzed cytogenetically. In the attenuated chromosomes, gene-mutations were induced with a frequency apparently somewhat below but at least half as high as that previously obtained from spermatogonium irradiation. Presumptive deficiencies were however far less abundant than from treated spermatozoa. Their frequency, in relation to gene-mutations, seemed like that in the untreated material. Only 2 of 9 presumptive deficiencies examined proved cytologically visible. None of the mutations analyzed involved gross rearrangements. The more condensed chromosomes (later oocytes) gave frequencies of both gene-mutations and presumptive deficiencies sensibly similar to results from treated spermatozoa. For deficiencies, the difference from oogonia was highly significant. But again, gross rearrangements were absent. Chromosome breakage evidently occurs as frequently here as in spermatozoa, but union of fragments must occur fairly promptly, i.e., prior to the movements of the meiotic divisions. Mosaic mutants appeared with only the spontaneous frequency, there being no evidence of delayed mutation. (Work aided by grant from American Cancer Society, recommended by Committee on Growth of National Research Council). (G)

1908

Murray, M. J. AN ATTEMPT TO OBTAIN SEX-LINKED MUTATIONS IN A DIOECIOUS PLANT. *Genetics* **25**, 128(1940).

A normal female plant of *Acnida tamariscina* (Nutt.) Wood was pollinated with x-rayed pollen. Seed from 474 different F_1 open-pollinated females were grown. No visible sex-linked mutations were found in over 250,000 F_2 seedlings and approximately 10,000 mature F_2 plants. This suggests that the Y chromosome has a full complement of allelomorphs. However, ten chimeras were obtained. These were chlorophyll changes associated with fifty per cent bad pollen in the affected areas. (G)

1909

Myers, W. G. and Hazel Jean Hanson. NEW STRAINS OF *PENICILLIUM NOTATUM* INDUCED BY BOMBARDMENT WITH NEUTRONS. *Science* 101, 357-8(1945).

Spore suspensions of a stable variant of *P. notatum* in normal saline in test-tubes were bombarded with neutrons from a cyclotron. About 100 new strains or mutations were produced. The antibiotic activity of many of the new strains were qualitatively similar to the parent strain. The number of new strains was fairly proportional to the amount of bombardment. (BA)

1910

Newcombe, H. B. SECTORING IN COLONIES FROM IRRADIATED CELLS OF *ESCHERICHIA COLI*. *Genetics* 36, 570(1951).

Colonies from ultraviolet- or gamma-irradiated cells of *E. coli*, grown on mannitol-tetrazolium agar, are frequently sectorized for colour response. With ultraviolet doses of 500 to 1000 ergs per sq. mm. 15 to 20 per cent of the colonies were sectorized, and with gamma doses of 40,000 to 80,000 r 6 to 7 per cent. This was at first thought to be due to the presence of more than one nucleus in the treated cells. However, if this were the correct interpretation one would expect to eliminate the sectoring by selecting the descendants from a single nucleus. To do this, selection for induced mutations to phage resistance was carried out on the mannitol-tetrazolium agar, the treated cells being allowed a short period of growth and then sprayed with a mixture of phages T1 and T5. Contrary to expectation, a proportion of the colonies arising after further incubation were still sectorized for colour. This proportion, however, was roughly half that observed in the non-selection experiments. Essentially similar, although less extensive, results were obtained using streptomycin as the selective agent. — The sectoring which survives selection could be due to: (1) delayed mutation, (2) genetic interchange between two nuclei in the treated cell, (3) mutation in incompletely split chromosomes, or (4) mutation in hereditary particles other than the chromosomal genes. (G)

1911

Novitski, E. and C. Stern. THE VIABILITY OF INDIVIDUALS HETEROZYGOUS FOR RECESSIVE LETHALS. *Science* 108, 538-9(1948).

Tests of daughters of females known to be heterozygous for a sex-linked lethal show that the viability of individuals heterozygous for a lethal is not equivalent to that of individuals free from a lethal. The percent of lethal-bearing daughters should, within statistical limits, fall equally about 50 percent. Thirty three lethals showed a marked inequality of distribution with 5 lethals above and 23 below the expected midclass. The range of values is also unequal, the lowest being 42.1 percent of lethal-bearing daughters and the highest 53.7 percent. It is pointed out that decreased viability of lethal heterozygotes in populations where the frequency of the lethal gene is very low, might be more important than the loss of rarely occurring homozygotes. (NSA)

1912

Okami, Yoshiro and Hamao Umezawa. STUDIES ON THE MUTATION OF *STREPTOMYCES GRISEUS* NO. 200 BY X-RAY IRRADIATION. *J. Antibiotics (Japan) Suppl. B*, 3, 7-9(1950).

S. griseus No. 200 which produced streptomycin abundantly in Waksman's medium was x irradiated at the rate of 300,000 r/hr (length of time not given). Five black-pigment-producing mutants and one albino-type mutant were obtained. These morphological mutants did not produce streptomycin. After x-ray treatment strains which produced more than 1000 μ g/ml of streptomycin were found, but they were not physiological mutants because they were not stable in their streptomycin-producing ability. Both English and Japanese versions of this article are presented. (NSA)

1913

Opatowski, I. ON THE MUTATION OF THE TOBACCO MOSAIC VIRUS. *J. Gen. Physiol.* 33, 171-6(1949).

Experiments on x-ray-induced mutations of tobacco mosaic virus with radiation doses of 0 to 49,000 r and mutation rates of 0.079 to 5.275% are analyzed on the basis of ionization theory. Three alternate assumptions are used in calculating the size of the volume in which the primary mutation process develops: this volume is a protein, from which it is found that the volume is identical with the hexagonal cell unit described by x-ray diffraction studies on virus protein; this volume is nucleic acid, from which it is found that one-fourth of the total nucleic acid content is involved in the mutation process; this volume is phosphorus, from which it is found that half of the total P content is involved in the mutation process. The relation between induced and spontaneous mutation is examined, and the author concludes that natural ionizing radiations are insignificant for the spontaneous mutation of the virus. (NSA)

1914

Opatowski, I. ON THE INTERPRETATION OF THE DOSE-FREQUENCY CURVE IN RADIOGENETICS. *Genetics* 35, 56-9(1950).

It is shown that assumptions opposite to those which are made in the single event theory of induction of mutations by radiation, lead to a relation between radiation dosage and frequency of induced mutation which is practically linear within its experimentally pertinent range. It is concluded from this that the apparent linearity of the experimental data on the dependence of the mutation frequency upon the administered dose cannot be considered as a proof that the mutation is caused by a single primary event. (NSA)

1915

Opatowski, I. and Alice M. Christiansen. ON THE SINGLE EVENT HYPOTHESIS IN RADIOGENETICS. *Bull. Math. Biophys.* 12, 19(1950).

It is shown that the assumption of a cumulative action of many independent random events as the primary cause of induction of a mutation fits the experimental data at least as well as the single event hypothesis. The theory is illustrated on the existing data of x-ray induced lethals in the X-chromosome of *Drosophila*. Possible shortcomings of the single event theory in connection with these experimental data and alternative ways of its modification are indicated. (Author)

1916

Otani, Shohei and Hyuga Okada. ON THE VARIATION OF *PENICILLIUM CHRYSOGENUM* Q 176 INDUCED BY RADIUM IRRADIATION. *J. Antibiotics (Japan)* 3, 819-32 (1950).

To induce saltation or mutation of microbes by radioactivity, the spores of *P. chrysogenum* Q 176 were irradiated with radium. Germination was prevented to the extent of about 2% by 5-day irradiation. Various variants appeared by the end of this irradiation. The variation rate was 15%. From the variants the authors isolated one strain without specific yellow pigment. This strain was called "RaO." No particular variants which would yield higher potency could be obtained. The isolated variants were investigated by monospore culture and other methods as to whether they are induced by saltation or by fluctuation and also were examined for penicillin yield. It was found that variations of the color of spores and of the form of colonies were induced by saltation; variation of spore numbers was induced by fluctuation; the strains which have few spores produce little penicillin, and there were intermediate forms between saltation and fluctuation. By shake culture and tank fermentation the pigmentless strain "RaO" was found to be a saltant. It produced 470 μ cc, the same potency as the parent strain, by shake culture. The potency in the test tank was 267 μ /cc. This strain may be a promising one. Filtered broth was always pigmentless, and the resulting amorphous penicillin was white. (NSA)

1917

Plough, Harold H. **PENICILLIN ISOLATED BIOCHEMICAL MUTATIONS IN *SALMONELLA TYPHIMURIUM*: THEIR PROPORTIONALITY TO X-RAY DOSAGE, AND THEIR FAILURE TO SHOW RECOMBINATION.** *Genetics* 35, 130(1950).

Biochemically deficient strains of *Salmonella typhimurium* were isolated from suspensions subjected to X-radiation and then screened with penicillin according to the method of Davis. The original strain was used by Gowen in his studies of the genetic basis of virulence, and was derived from a single cell isolation by Zelle. Successive suspensions are X-rayed at dosages from 11,000R to 57,000R units, incubated 24 hours in complete medium, centrifuged, washed, resuspended in minimal medium (salts plus glucose) containing 200 units of penicillin per ml. and again incubated for 48 hours. This treatment kills most of the parent type organisms and from dilution plates made on complete medium 100 colonies at random are isolated. Preliminary platings showed that the X-radiation killed from 60% at 11,000R to more than 99% at 57,000R. Tests by the paper disc method of assay of the clones isolated as noted gave 9% biochemical mutants from the unirradiated controls increasing up to 80% of mutations from the suspensions receiving the maximum X-radiation dosage. Over 250 mutant strains resulted each of which requires one or more specific nutrients for growth which the parent strain does not need. Specific amino acid requirements are most numerous with purine requirements second. The most frequent amino acid requirements are cysteine, histidine, methionine, proline, tyrosine, levsine, threonine, and valine. Several tests for possible sexual fusion and recombination by the method of Tederberg have proved entirely negative perhaps indicating that *Salmonella* is a haploid uninucleate cell. Many interesting biochemical interactions are being further investigated. (Author)

1918

Plough, Harold H. **RADIATION INDUCED MUTATIONS IN CHEMICAL REQUIREMENTS IN *SALMONELLA TYPHIMURIUM*.** *J. Cellular Comp. Physiol. Suppl.* 1, 35, 141-55(1950).

Attention is directed to the desirability of pathogenic bacteria of the genus *Salmonella* as objects of genetic study using radiation as a mutagenic agent. Isolation methods are described and four different classes of mutations, iso-

lated and investigated in *Salmonella*, are depicted. At least one other class, i.e., antigenic variants, is also indicated. Differences in the spontaneous frequency of these classes of mutations are suggested by the relative numbers isolated from irradiated lines. (NSA)

1919

Plough, Harold H., Helen N. Young, and Madelon R. Grimm. **PENICILLIN-SCREENED AUXOTROPHIC MUTATIONS IN *SALMONELLA TYPHIMURIUM* AND THEIR RELATION TO X-RAY DOSAGE.** *J. Bacteriol.* 60, 145-57(1950).

Suspensions of *S. typhimurium* have been exposed to x-radiation up to 57,000 r units and then screened with penicillin on minimal medium containing essential salts and glucose. Of the 457 strains isolated and tested, 234 proved to be auxotrophic mutant strains having a constant requirement for one or more food substances that the parent strain can synthesize for itself. The frequencies of these mutations are directly related to the x-ray dosage, suggesting that they are gene mutations similar to those found in higher organisms. Most of the mutant strains required one of the amino acids or one of the purines, but alternative and multiple requirements were found. The data indicate that at radiation dosages up to 35,000 r a cysteine-requiring mutant is the most numerous, whereas above that level the mutant most frequently isolated requires histidine. A test of the efficacy of the penicillin screening of mixtures of wild-type and x-ray-induced mutations is given. The value of auxotrophic mutations for studies of the steps in bacterial synthetic processes is suggested. (NSA)

1920

Pomper, Seymour. **RECENT DEVELOPMENTS IN YEAST GENETICS.** *Wallerstein Labs. Commun.* 14, (44) 31-41 (1951) (ORNL-696)

This review paper is limited, in the main, to work that has been performed in the past decade. Among the topics discussed are the early genetic studies with *Saccharomyces*; mating types, crossing procedures, and sporulation; genetic markers (unique characteristics which can be demonstrated to be heritable); and biochemical mutants involving such agents as x-radiation and compounds such as potassium cyanide, lithium chloride, and camphor. (NSA)

1921

Pontecorvo, G. **THE INDUCTION OF CHROMOSOME LOSSES IN *DROSOPHILA* SPERM AND THEIR LINEAR DEPENDENCE ON DOSAGES OF IRRADIATION.** *J. Genet.* 41, 195-215(1941).

Non-lethal losses of the X and Y chromosomes, produced by x-ray treatment of mature sperms, were detected by testing exceptional *y w f* females obtained from crosses of *y w f* attached-X/sc. *Y^L* females by *f X.Y^S/sc. Y^L* irradiated males. The tests indicated that 64-71% $\pm$ 7-9% of the exceptional yellow (*w f*) females had arisen from a complete loss of either the *X.Y^S* or the *so. Y^L* chromosome. These losses are not lethal to the zygote, but a comparison with data showing the amount of change in the sex ratio caused by equivalent dosages indicates that lethal losses are probably three times as numerous as non-lethal. At dosages of 0, 1,000 r, and 4,000 r the frequencies of the non-lethal losses vary approximately as a linear function of the dosage and certainly less than the 1.5 power of the latter, like gross rearrangements. The mechanism whereby these losses originate is therefore held to be through single breakage, followed by a lateral fusion of sister chromatids at the breakage point. This results in the formation of dicentric chromosomes that immediately or subsequently become lost. (BA)

1922

Pontecorvo, G. and H. J. Muller. THE LETHALITY OF DICENTRIC CHROMOSOMES IN *DROSOPHILA*. *Genetics* 26, 165(1941).

The fact that viable translocations formed after x-raying spermatozoa are proportional in frequency only to the $\frac{3}{2}$ power of the dose has been shown to signify that union of broken ends of chromosomes occurs without reference to presence or absence of centromere on fragment, the zygote with aneucentric rearrangements, i.e., with chromosomes other than monocentric, dying. If death is due solely to the genic unbalance resulting directly from the loss of the non-monocentric chromosomes, then, if extra chromosomes homologous to those lost were introduced, in compensation for the losses, the resulting zygote would survive. This can be tested, in *Drosophila melanogaster*, by crossing irradiated males to triploid females; homozygous recessive markers in the triploids allow recognition of the exceptional offspring. Thus, losses of a single paternal autosome, as by simple breakage, will allow one autosomal recessive to show in the F_1 , while losses of two autosomes, as by aneucentric translocation, will "uncover" two recessives simultaneously. Among 8,880 F_1 , from crosses of brown ebony triploids by non-brown non-ebony males given 4,000 r, 133 showed just one autosomal recessive, and only 3 (one being the approximate expectation for the coincidence of two independent losses) showed both recessives. But the frequency of aneucentric translocations produced must have been such as to have resulted in over 800 zygotes showing both recessives, had these zygotes lived. Hence over 99 percent of these aneucentric rearrangements are lethal *per se* even though many aneucentrics formed from union of sister chromatid fragments after simple chromosome breakage are not lethal. Investigation of the mechanism involved is proceeding. (G)

1923

Powers, E. L. Jr. DEATH AFTER AUTOGAMY IN *PARAMECIUM AURELIA* FOLLOWING EXPOSURE IN SOLUTION TO THE RADIOACTIVE ISOTOPES P^{32} AND Sr^{90} , Y^{90} . *Genetics* 33, 120(1948).

Sister animals derived from a single exautogamous organism were grown in graded specific activities of P^{32} and of Sr^{90} , Y^{90} , all beta-emitters. After 48 hours' exposure, 7 to 8 cell divisions had occurred, sufficient to incorporate the radioactive substances into the protoplasm to the extent of more than 99% of the theoretical maximum. At this time a series of isolations from each of the solutions was made, and the lines so obtained were allowed to go into autogamy. Survival after autogamy was measured by isolating 108 autogamous animals and noting the proportion that survived six divisions after isolation. The physical parameter was determined by measuring the current output from a vibrating reed-air ionization chamber system for equal volumes of each of the P and of the Sr solutions. Each activity is expressed in terms of a constant uranium source measured by the same system. In the low dose range, the effect of radioactive P on post-autogamy death is much more marked than that of equivalent levels of radioactive Sr, Y. In terms of ionizations in air, levels of Sr^{90} , Y^{90} necessary to produce a degree of death after autogamy exceed by a factor of 4 to 6 the level of P^{32} necessary to produce the same amount of death after autogamy. (NSA)

1924

Powers, E. L. Jr. and Deborah Shefner. LETHAL CHANGES INDUCED BY X-RAYS IN *PARAMECIUM AURELIA*. *Genetics* 33, 624-5(1948).

Cultures of *P. aurelia*, stock 51, "killer" animals of variety 4, mating type VIII were irradiated with 250KV X-rays at about 450 r/minute at 17 dose levels from 500 to 25,000 r. Lines derived from isolates from each of the irradiated cultures were allowed to go into autogamy and the fractions of the surviving exautogamous organism were noted. Death following autogamy increases with increasing dose. Above 12,000 r the curve approaches 100 percent death very slowly, total death not being achieved in these experiments. Organisms which survived autogamy showed only control death following the next autogamy regardless of the degree of effect. Conjugation of irradiated with non-irradiated organisms resulted generally in increased survival following the next autogamy. These two results are expected if the effect of X-rays at these dose levels are genetic ones in the micronucleus. No significant difference can be seen between the genetic damage induced by X-rays as demonstrated here and that caused by β particles of radioactive Strontium and Yttrium in solution as reported previously. (G)

1925

Randolph, L. F. CYTOLOGICAL AND PHENOTYPICAL EFFECTS INDUCED IN MAIZE BY X-RAYS AND THE BIKINI TEST ABLE ATOMIC BOMB. *J. Cellular Comp. Physiol. Suppl.* 1, 35, 103-17(1950).

The cytological and phenotypical effects of the Bikini atomic bomb were qualitatively similar to those induced by x-rays. With respect to retardation of plant growth, seedling mottling, partial sterility, and the production of leaf sectors involving morphological abnormalities and chlorophyll deficiencies, most heavily irradiated Bikini sample was comparable to an x-rayed sample that had received 15,000 r units, except that a significantly higher frequency of chlorophyll sectors and dead tissue occurred in the bombed sample. Chromosomal mutations including reciprocal translocations, deletions, and inversions were observed with approximately the same frequency in the plants grown from the bombed and x-rayed seed, and in both lots there were many more translocations than there were other types of chromosomal alterations. (NSA)

1926

Randolph, L. F., A. Longley, and C. Li. CYTOGENETIC EFFECTS IN CORN EXPOSED TO ATOMIC BOMB IONIZING RADIATION AT BIKINI. *Science* 108, 13-15 (1948).

The experiments included a comparison of the effects of the radiation of the bomb with measured doses of x-ray. Seed germinability was not affected by the radiations from the bomb or by the x-ray treatments. A comparison of other effects of radiation from the bomb and x-ray treatment is given. (N)

1927

Ray-Chaudhuri, S. P. THE VALIDITY OF THE BUNSEN-ROSCOE LAW IN THE PRODUCTION OF MUTATIONS BY RADIATION OF EXTREMELY LOW INTENSITY. *Proc. Roy. Soc. Edinburgh B* 62, 66-72(1944).

Sperm of *Drosophila* were irradiated in the body of impregnated females with 70 mg of radium for 720 hours at two dosages of 2,000 r and 400 r with an intensity of 0.556 r and 2.78 r per hour respectively. The frequency of sex-linked lethals produced was found to be directly proportional to the dosage independent of the intensity of irradiation. The mutation rate was independent also of the duration of the treatment when flies were radiated with an intensity of 29 r per hour, giving a total dose of 1,300 r. (BA)

1928

Regehr, Hulda, T. J. Arnason, and H. E. Johns. INDUCED MUTATION BY HIGH-ENERGY X-RADIATION PRODUCED BY A 23-MEV BETATRON. *Nature* **166**, 228-9(1950).

Male *Drosophila melanogaster* received a single dose of 2000, 5000, or 7000 r of x-radiation at 100 r/min. All the irradiated X-chromosomes which were tested for mutations were obtained from sperms which functioned in fertilization within 20 days of the treatment. The average percentage mutation per 1000 r high-energy x-rays is 1.70%. The corresponding figure for ordinary x-rays as given in the literature is 2.89%. This would indicate that the high-energy radiations are only 0.59 as efficient as ordinary x-rays for the production of lethal mutations. The reason for the difference in effectiveness is discussed. (NSA)

1929

Rick, Charles M. THE GENETIC NATURE OF X-RAY INDUCED CHANGES IN POLLEN. *Proc. Nat. Acad. Sci. U. S.* **28**, 518-25(1942).

X-radiation of microspores of diploid spp. of *Tradescantia* shortly after meiosis increases variability in pollen grain length and per cent of aborted grains, indicating that size and viability are due in part to the genotype of the pollen itself. The effect is greater after treatment at 3° than at 33°. Similar radiation of autotetraploid spp. confirms this conclusion by failing to give similar results, since unaffected dominant alleles mask the recessive mutations. Statistical analysis in the pea, *Pisum sativum*, where four kinds of hybrid pollen are intermediate in size and more variable than either parent further confirms the theory of self determination of pollen size by a large number of genes. (BA)

1930

Rick, Charles M. THE X-RAY INDUCED MUTATION RATE IN POLLEN IN RELATION TO DOSAGE AND THE NUCLEAR CYCLE. *Genetics* **28**, 237-52(1943).

Mean length and variation of length of pollen grains and per cent of aborted grains were studied for a period of two months following application of 62.5, 125, 250, and 500 r to inflorescences of diploid *Tradescantia*. The inter- and intra-treatment variation was studied statistically. The mutational response of pollen abortion after treatment during the post-meiotic period varied approximately linearly with dose; the response of variance of length was intermediate between a linear and squared relationship. Length changes were all or nearly all toward smaller grains. Number of changes involved greatly exceeded total number of gross chromosomal aberrations induced by the same doses. Resemblance between these changes and mutational effects in other organisms is considered further evidence that the changes in pollen are the phenotypic expression of mutation induced by the x-ray treatment. High pollen sterility was induced by treatment during meiosis and the first gametophytic mitosis. According to evidence presented these sterility responses correspond more closely to chromosomal aberration than to intragenic change. Pollen changes of smaller degree result from treatment before meiosis, although measurements are complicated by a very irregular return to normal sterility. (BA)

1931

Rowell, J. B., E. C. Stakman, and E. E. Butler. THE MUTAGENIC ACTION OF DILUTE COLLOIDAL POLONIUM ON FUNGI. *Minnesota Univ.* [nd] 6p. (AECU-1823)

Extremely dilute quantities of polonium 210 (0.5 to 1.0 µc/ml) readily induced mutation in vegetative cells or

spores of various fungi in aqueous suspensions held at 8°C for appropriate periods of time. Spores germinated directly in water containing 1 µc of polonium per ml will grow and produce normal colonies. Lethal and mutagenic effects do not appear until the cells are held in this mixture at low temperatures over a long period of time. The effective length of time of exposure varied with the species of organism tested. In simultaneous trials with *Ustilago zeae*, *Saccharomyces cerevisiae*, *Chaetomium globosum*, and *Penicillium roquefortii* the respective exposures in days for LD99 were 21, 4, 9, and 2; and the percentages of visible mutation were 1.0, 6.1, 10.1 and 3.5. The most numerous mutants obtained have been those having reduced growth or reproductive rates. The amount of radiation associated with the cells in this method approximates dosages of x rays similarly affecting fungi as one µc of polonium produces 326 rep per day. (NSA)

1932

Rubin, B. A. THE MECHANISM OF GENETIC EFFECT OF P³² IN BACTERIA. Brookhaven National Lab. [nd] 13p. (BNL-1069)

The biological effect of absorbed unstable isotopes is related, in some cases, to the chemical changes resulting from radioactive decay rather than to the accompanying radiations. The special geometric and metabolic characteristics of bacterial cultures are employed to show that genetic effects of P³² may be attributable to the rupture of the phosphate bond in desoxyribose nucleic acid. Other examples illustrate the use of the nuclear disintegration technique as an indicator of the specific chemical changes which can produce biological and genetic effects. Possible evolutionary significances are discussed. (NSA)

1933

Rubin, B. A. THE RELATION OF NUCLEIC ACID METABOLISM TO THE GENETIC EFFECT OF RADIATION IN BACTERIA. *Genetics* **36**, 573-4(1951).

Levels of continuous radiation (x-rays or β-rays) which rapidly kill resting bacteria (*E. coli* B/r) permit the growth of metabolizing organisms. When resting cells are inoculated into a fresh medium the inception of growth (lag) is delayed as a direct function of the radiation dose rate; but when multiplication begins, the rate of increase of cell mass during continuous radiation is equal to that in unirradiated controls and the same final culture densities are reached. Average cell size increases with the number of generations that have occurred during irradiation, but this accounts for only a fraction of the cell mass, the logarithmic increase in viable count makes up the rest. — An examination of the mutant population (resistant to streptomycin) in cultures which have grown from 0 (resting) to 14 generations during irradiation indicates that the mutation rate is affected by the radiation dose, but not by the number of genetic reduplications during irradiation. Under the same conditions, changes in nucleic acid metabolism appear which are related to the extent of synthesis that has occurred during irradiation. (G)

1934

Rubin, B. A. and P. Steinglass. THE GENETICS OF STREPTOMYCIN RESISTANCE INDUCED BY ABSORBED RADIOACTIVE PHOSPHORUS (P³²). [Brookhaven National Lab.] [nd] 2p. (AECU-765)

The document is in abstract form; it is reproduced below in its entirety.

In the study of the mechanism of genetic effect induced by P³² in *E. coli* B/r, the use of the phenomenon of streptomycin resistance has proved to be both a good quantitative tool and an interesting subject in itself.

As a genetic tool, it has been possible to develop techniques similar to those used in the phage studies. Rapid and accurate estimates of the background mutation rates are now possible, which also provide simple methods for the isolation of the various types of resistant mutants. In this manner it has been possible to readily demonstrate the additional biochemical dependence of the mutants, their streptomycin requirements, and relative growth rates. Many of the objections to similar phage studies are eliminated by the stability of the drug and its lack of response to mutagenic agents—in this case, specifically β radiation and the products thereof.

In the radiation experiments the variations in delay of phenotypic expression have necessitated kinetic studies which could interrelate the pattern of genetic events. The kinetics were useful in their ability to demonstrate qualitative as well as quantitative genetic changes, produced by variations in the proportion of mutant types.

In these experiments the mutants varied with regard to their acquired need for the drug, but all organisms selected in 200 units/ml were resistant to 100,000 units/ml. Such characteristics are of significance in understanding the problems of chemotherapy. The responses of bacterial populations to streptomycin have helped elucidate quantitative aspects of drug resistance. Good predictions can now be made of the likelihood of producing resistant organisms and of methods for preventing this difficulty under conditions of practical therapy. (NSA)

1935

Russell, W. L. THE INCIDENCE OF STERILITY AND PARTIAL STERILITY IN THE DESCENDANTS OF X-IRRADIATED MICE. *Genetics* **35**, 689-90(1950).

This paper is reproduced here in its entirety.

The data reported here were obtained incidentally in the course of another investigation. Adult male mice were given a single, whole-body, 80 r/min dose of 500, 750, or 1000r, and then were mated. 22 male and 15 female offspring, all conceived within 2 to 30 days after irradiation of the sire, were tested for fertility. Averaging the results over wide dose ranges is not justifiable, because of non-linearity of effect with dose, but is perhaps permissible, over the range used here, for a rough comparison with the results of other workers. Of the 37 animals tested, and whose sires received a mean dose of 669 r, 8.1% were found to be completely sterile and 27.0% partially sterile. These percentages are in remarkably close agreement with the results of Snell and Hertwig for similar dose ranges. All of the 10 partially sterile animals obtained in this experiment, and one other from another test, were found to transmit partial sterility to some of their descendants. Two of the 11 lines, however, do not fit the simple interpretation of reciprocal translocation which Snell and others have established as the cause of the partial sterility in at least some cases. Both of these lines are producing some completely sterile descendants, one also yielding some almost sterile descendants. The data obtained so far are not adequate to determine whether a different type of change is involved or whether an additional translocation or other chromosomal or gene change has occurred.

1936

Russell, W. L. X-RAY-INDUCED MUTATIONS IN MICE. Cold Spring Harbor Symposia Quant. Biol. **16**, 327-6 (1951).

In an attempt to obtain information that would be useful in the estimation of the genetic hazards of ionizing radiation in man, wild-type male mice were exposed to a single dose of x rays and mated to a stock homozygous for seven autosomal recessive visible genes. Control, unexposed

animals were also mated to the test stock. The offspring were observed carefully for mutations at the seven specific loci and cursorily for dominant visible mutations at any locus. Dominant mutations with obvious visible effects proved to be rare. Six have so far been found in the irradiated group and none in the controls. However, a dominant effect on size was found in about one half of the mutations at one of the specific loci. Approximately 61 mutations at the specific loci have been observed in the irradiated group, while only two were found in the control group. The frequencies of mutation at the seven loci in the irradiated group ranged from none at the A locus to 28 or more at the S locus. Each of nine mutations in the irradiated group has now been tested for its phenotypic effect when homozygous. Two were found to be lethal, two sublethal and five viable. Three mutations to intermediate alleles were found in the irradiated group. Out of a total of eight mutations at either the D locus or the closely linked Se locus in the irradiated group, none showed a change at the associated locus. The mean observed mutation rate, for irradiated spermatogonia, at the seven loci is $25.0 \pm 3.7 \times 10^{-8}$ per roentgen, per locus. The rate is not appreciably dependent on the length of the interval between irradiation and fertilization. Comparison with similar data from *Drosophila* shows a higher induced mutation rate in the mouse. This indicates that estimates of human hazards based on *Drosophila* mutation rates may be too low.

1937

Russell, W. L., J. C. Kile, Jr. and Liane B. Russell. FAILURE OF HYPOXIA TO PROTECT AGAINST THE RADIATION INDUCTION OF DOMINANT LETHALS IN MICE. *Genetics* **36**, 574(1951).

To test whether hypoxia would protect against radiation induction of dominant lethals in mice, groups of males were: (a) X-irradiated with 800r in air, (b) non-irradiated in air, (c) X-irradiated with 800r in a 5% oxygen, 95% helium mixture, or (d) nonirradiated in the same mixture. The gas was passed through the exposure chamber for five minutes prior to irradiation and during irradiation in exposed groups and for the equivalent time in non-irradiated groups. Females fertilized by these males shortly after treatment were opened just before term and their uterine contents examined. Classifying embryos as alive or dead (including resorption sites) gave the following mean numbers of the two respective types per litter, with from 47 to 50 litters in each group: (a) 3.9 and 3.6, (b) 8.2 and 0.98, (c) 3.6 and 3.5, (d) 8.3 and 0.96. Repetitions of the experiment with 30 minutes pretreatment in the same gas mixture and irradiation in this or in 2% oxygen 98% helium gave similar results. These data give no evidence for protection by hypoxia against the induction of dominant lethals to which the excess death of embryos from irradiated sires is attributable. This is in contrast to the protection against genetic damage found by others in various organisms. It is also in contrast to protection by hypoxia, in this experiment, against direct radiation effects on the exposed males: acute radiation death reduced from 92% to 0%, length of sterile period and graying of hair decreased. (G)

1938

Sansome, Eva R., M. Demerec, and Alexander Hollaender. QUANTITATIVE IRRADIATION EXPERIMENTS WITH *NEUROSPORA CRASSA*. I. EXPERIMENTS WITH X-RAYS. *Am. J. Botany*. **32**, 218-26(1945).

Microconidia were irradiated with x-rays. The increase in mutation rate with increase in energy followed a straight-line relationship at low dosages and reached 78.5% at 126,000 roentgens. Increase in intensity led to an increase in the mutation rate. Phenotypic normal and mu-

tant cultures obtained from irradiated spores often showed partial sterility when crossed with a standard wild type, but this was more frequent in phenotypic mutants than in phenotypic normals. Partial sterility is believed to result from chromosomal aberration. An analysis of the sterility and mutation rates at different dosages and intensities indicates that there are two types of mutants, one caused by chromosomal aberration and the other not. However, the latter class may consist partly or entirely of changes that are potentially capable of being associated with aberrations. (BA)

1939

Sansome, Eva R., Alexander Hollaender, E. Zimmer, and M. Demerec. QUANTITATIVE EFFECTS OF RADIATION ON MUTATION PRODUCTION IN NEUROSPORA CRASSA. Genetics 30, 19-20(1945).

(This report is an abstract and is reproduced here in its entirety).

The heritable nature of alterations produced in fungi by monochromatic ultraviolet irradiation was verified by genetic analysis of a fungus having a sexual stage. Microspores of the "fluffy" type of Neurospora crassa were used in this study. The effects of wave length and dosage on the mutation rate resembled those reported for some Fungi Imperfecti. To eliminate contaminants, the mutants were routinely crossed with the conidial "wild" type. Certain of the ascospore progeny were germinated and studied in more detail. Of the 40 crosses, where the ascospores were sown at random, more than one type of "fluffy-mutant" was recovered from about half. This suggests a high incidence of mutations. Unstable mutants were subjected to microspore analysis and classified. — Experiments with X-rays, indicate that visible mutants were produced with a frequency which increased linearly with dosage. For dosages given at an intensity of 270 r/min., the frequency of mutants increased from 2.8% at 2,250 r to 24.6% at 31,500 r. About half the spores survived the treatment of 31,500 r. When dosages up to 126,000 r were given at 5,400 r/min., the mutation rate increased to 78.5% with a survival of 0.01%. The observation of the Lindegrens that X-ray induced mutants, when crossed with the wild type, often gave more aborted ascospores than the control crosses was confirmed. It was found that treated cultures which were phenotypically normal were also sometimes sterile, but that the proportion of steriles among the mutants was higher than among the normals.

1940

Drew Schwartz. 1. GAMETE FACTOR ON CHROMOSOME 9. 2. THE EFFECT OF OXYGEN TENSION ON THE RADIOSENSITIVITY OF CHROMOSOMES. Oak Ridge National Lab. [nd] 1p. (AECU-1876)

Gamete factor on chromosome 9. A gamete factor was found which shows close linkage with the waxy gene. In back crosses of heterozygous Ga wx/ga Wx as the male to homozygous waxy plants, only 10% starchy kernels are obtained. Further testing of these B₁ starchy kernels revealed that 30% of them are due to functioning of ga Wx pollen and 70% are crossovers. These data indicate that there is 3% functioning of ga pollen in competition with Ga and 7% crossing over between the Ga and Wx loci. The effect of oxygen tension on the radiosensitivity of chromosomes. Experiments conducted on the irradiations of pollen in different atmospheres revealed that there is a 3.2-fold decrease in chromosome aberrations when the exposures are made in 100% N as compared with exposure in air. The A₁-Sh₂ region was used in this study. A₁ Sh₂ pollen was irradiated and used to pollinate a₁ a₁ sh₂ sh₂ tester plants. Aberrations were detected in the endosperm

as entire losses of the dominant characters and as mosaics. Irradiation in nitrogen decreased the frequency of entire losses by a factor of 2.7 while the mosaics were decreased by a factor of 9.9. This difference is statistically significant and strongly suggests that the effect of oxygen tension during irradiation is on the recovery process of broken ends rather than on the initial breakage mechanism as had previously been postulated. (Entire report.)

1941

Singleton, W. R. EFFECT OF CONTINUOUS GAMMA RADIATION ON MUTATION RATE IN MAIZE. Genetics 36, 575-6(1951) (AECU-1461)

The report is reproduced here in its entirety.

Continuous gamma radiation from Co⁶⁰ was used in studying the mutations induced in maize pollen. The intensity varied from 125 to 0.09 r/day. Four endosperm characters were studied: R, Pr, Su, and Sh. Pollen from the dominant stock A, B Pl C R Pr Su Sh growing in the radiation field was placed on silks of a multiple recessive A b pl C r pr su sh growing in a field with only background radiation. The following results were obtained: (1) There was no increase in mutation rate over the control when the radiation was less than 5 r/day. (2) Above 5 r/day there was a gradual increase up to 31 r/day with a more marked increase from 31 to 55 r/day. From 55 to 125 r/day the increase in mutations was even more marked. The increase in mutation rate at the higher intensities of radiation was greater than expected if the increase is linearly proportional to dose. (3) The logarithm of the mutation rate seemed to show a linear relationship with dose received. (4) The gene with the greatest spontaneous mutation frequency (R) showed a smaller increase in induced changes than the other three genes Su, Sh, and Pr. (5) In control plots the mutations detected in the microspore were appreciably higher than those found in the megaspore. This is expected since only those mutations that occur at or before the first mitotic division of the megaspore mother cell will be detected because of the triple fusion forming the endosperm. (G)

1942

Smith, Luther. A COMPARISON OF THE EFFECTS OF TESTABLE ATOMIC BOMB IONIZING RADIATION AND X-RAYS ON SEEDS OF BARLEY, WHEAT, AND OATS; APPENDIX NO. 25 TO THE FINAL REPORT. Naval Medical Research Station, Joint Task Force One. [nd] 17p. (NP-1900)

Comparisons were made of the biological effects on dormant seeds of barley, rye, and durum and common wheats of radiations from an atomic bomb and from known dosages of x rays. Effects studied included germination, flecking or mottling on the first leaves, chimeras, interchanges in X₁ plants grown from the irradiated seeds, mutation frequencies in X₂ seedlings, and types of mutants obtained in X₂. Seeds most heavily irradiated from the bomb burst were estimated to have received irradiation equivalent to 16,000 r of x ray. Plants from seeds which were subjected to 16,000 r x irradiation were used for comparison. There were no clear-cut differences in the types of seedling mutants obtained from the 2 sources of radiation nor in the relative proportions of these types. (NSA)

1943

Smith, Luther. HEREDITARY SUSCEPTIBILITY TO X-RAY INJURY IN TRITICUM MONOCOCCUM. Am. J. Botany 29, 189-91(1942).

A mutant in einkorn wheat was found which is more severely injured by X-ray treatment of the dormant seeds (4,000—20,000 r units) than other mutants or normal vars.

tested. In one trial the germination of a normal line was reduced 12% by 20,000 r while the susceptible was reduced 84%. The injury exhibits itself in greater flecking on the leaves, slower growth, and death from smaller doses than are required to produce similar effects in non-susceptible seeds. Preliminary tests indicate that the susceptibility is inherited as a simple recessive character, the factor has no effect on mutation rate and does not reduce the ability of seeds to withstand heat injury, and the moisture content of the seeds and the size of the chromosomes in the susceptible line are normal. (BA)

1944

Smith, Luther. EFFECTS OF ATOMIC BOMB RADIATIONS AND X-RAYS ON SEEDS OF CEREALS. *J. Heredity* **41**, 125-30(1950).

The biological effects of radiations from an atomic bomb and from known dosages of x-rays on dormant seeds of barley, durum, and common wheats have been determined. The relation of age of barley seeds to susceptibility to radiation effects also has been studied and limited macroscopic observations have been made on plants grown from seeds of oats that had been exposed to atomic-bomb ionizing radiation. (NSA)

1945

Smith, Luther and R. S. Caldecott. MODIFICATION OF X-RAY EFFECTS ON BARLEY BY PRE- AND POST-TREATMENT WITH HEAT. *J. Heredity* **39**, 173-6(1948).

By applying a heat treatment immediately before or after x-radiation, it was possible to modify the biological effects of a given dose of irradiation on dormant seeds on barley. A heat treatment that was just short of killing the seeds, reduced by half the frequency of chromatic bridges in meristematic cells of roots grown from treated seeds. This was true whether the heat treatment was applied before or after the irradiation. Such a heat treatment after x-radiation resulted in an increase in the seedling mutation rate from 5.8 ± 0.6 to $9.1 \pm 0.6\%$; whereas the equivalent heat treatment applied just before the irradiation resulted in a lesser (not statistically significant) increase to $6.9 \pm 0.6\%$. There was not a close correlation between injury symptoms and the frequencies of chromatinic bridges or mutation rates resulting from the various treatments. (BA)

1946

Snell, George D. INDUCTION BY ROENTGEN RAYS OF HEREDITARY CHANGES IN MICE. *Radiology* **36**, 189-96(1941).

A review of previously reported experiments on the induction of hereditary changes (especially translocations) by irradiation of males with either x-rays or neutrons and of females with x-rays. (BA)

1947

Sommermeier, K. RADIATION BIOLOGICAL DETERMINATION OF GENE NUMBERS IN THE X CHROMOSOME OF DROSOPHILA. *Z. indukt. Abstamm. Vererbungsl.* **79**, 240-4(1941).

The "saturation effect" of Timofeeff-Ressovsky and Zimmer's neutron-induced lethal mutations is probably related to a greater size of those radiation-sensitive volumes pertaining to chromosome injury than of those pertaining to recessive lethal mutation; D. E. Lea's calculations of gene number are based on the untenable assumption that an ionization within a gene's radiation-sensitive volume would practically always induce a recessive lethal mutation. (BA)

1948

Sparrow, Arnold H. TOLERANCE OF TRADESCANTIA TO CONTINUOUS EXPOSURES TO GAMMA RADIATION FROM COBALT⁶⁰. *Genetics* **35**, 135(1950).

Plants of a clonal line of *Tradescantia paludosa* were exposed under field conditions to continuous gamma radiation (1.1 and 1.3 Mev) of approximately 122, 30.4, 7.5, 1.8, 0.41 and 0.084 r per day, for 8, 16, 32 and 64 days. Dosage rates of 122 and 30.4 r per day permitted little or no growth, while fairly normal growth occurred at 7.5 r per day or less. Complete pollen abortion was produced after 16 days at 122 r per day. Chromosome breaks as such were not scored, but micronuclei at the microspore resting stage were counted. These are assumed to represent acentric fragments which lagged and remained in the cytoplasm at second telophase. A significant increase in the frequency of micronuclei was obtained with as low as 84 mr per day after 32 days exposure (total dose 2.69 r). Dosage curves for various exposure times will be presented. An attempt will be made to relate growth-inhibiting and lethal doses to the percentage of microspores containing micro-nuclei. (G)

1949

Spencer, W. P. and Curt Stern. EXPERIMENTS TO TEST THE VALIDITY OF THE LINEAR r DOSE. MUTATION FREQUENCY RELATION IN DROSOPHILA AT LOW DOSAGE. *Genetics* **33**, 43-74(1948).

200,801 x-chromosomes of mature sperm of a Canton Special stock of *D. melanogaster* were tested for the origin of new lethal mutations. Of these chromosomes, 73,901 were controls, 51,907 were subjected to x-rays at a dosage of 25 r units, 31,560 at 50 r, 23,195 at 150 r, 6,634 at 500 r, 6977 at 1000 r, and smaller numbers at 2000 r, 3000 r, and 4000 r. There were 72 control lethals found, 88 at 25 r, 77 at 50 r, 74 at 150 r, 87 at 500 r, and 147 at 1000 r. It is concluded that even for x-ray dosages as low as 25 r and 50 r, the linear r-dose/mutation frequency relation holds. The data showed a doubling of the control mutation frequency at an exposure of about 50 r. Several cases of control "lethal clusters" were found and interpreted as mutation in early stages in the germ tract. The possible implications of the findings in connection with the exposure of large numbers of the human race to low dosages of x-rays are considered briefly. A parallel, but less extensive, study of visible mutation rates gave an over-all lethal-visible mutation ratio of 5.2:1. Linkage studies on 229 lethals and visibles showed these to be distributed over the length of the genetic map of the x-chromosome, with high frequencies near the scute and forked loci, and a low frequency near region 10. (Authors' Summary)

1950

Stadler, L. J. THE EFFECT OF X-RAYS UPON DOMINANT MUTATION IN MAIZE. *Proc. Nat. Acad. Sci. U. S.* **30**, 123-8(1944).

In order to estimate the frequency of a dominant mutation in maize, a gene (a, colorless aleurone) was studied which rarely if ever shows spontaneous mutation but which mutates frequently in the presence of another (Dt). The frequency of losses of color and the number of cells involved were counted on other seeds of the same ears and provide a basis for estimation of the number of opportunities for occurrence of detectable mutation. X-rays failed to induce mutation of a to A (or to any other aleurone allele) in populations large enough to yield approximately 400,000 mutations to A under the influence of homozygous Dt or 900,000 losses of A by deficiency or by mutation to a colorless allele. (BA)

1951

Stadler, L. J. and Herschel Roman. THE GENETIC NATURE OF X-RAY AND ULTRAVIOLET INDUCED MUTATIONS AFFECTING THE GENE A IN MAIZE. *Genetics* **28**, 92(1943).

The genetic nature of X-ray and ultraviolet induced mutations affecting the gene A in maize. — Among a large number of alterations affecting A induced by X-ray treatment, and a smaller number induced by ultraviolet treatment, those most nearly approaching the typical genetic behavior of gene mutations were selected for detailed study and comparison. With X-rays, only a very small proportion of A-alterations are haplo-viable, and only two cases were found with normally developed pollen. The X-ray mutants studied included these two ($a-X_1$ and $a-X_2$) and a defective pollen type, $a-X_3$, which is haplo-viable in the female gametophyte. The ultraviolet mutants studied, all of which produce normal pollen, include $a-U_1$, $a-U_2$ and $a-U_3$, with phenotypic effects similar to a , and A^t , with phenotypic effects intermediate between A and a . — All three X-ray mutants show lowered haplo-viability, as indicated by transmission of the mutant a (general designation a^*) through σ and φ germ cells of $A a^*$ individuals. Transmission of $a-X_1$ is lowered thru σ , gametophytes and normal thru φ ; $a-X_2$ much lowered thru σ , somewhat lowered thru φ ; and $a-X_3$ lacking thru σ , much lowered thru φ . Both $a-X_1$ and $a-X_2$ are lethal when homozygous, and compounds of the X-ray mutants in all three possible combinations are lethal. Crossing over in $A a^*$ plants is approximately normal with $a-X_1$, lowered with $a-X_2$, and much lowered with $a-X_3$. In all four ultraviolet mutants, σ and φ transmission is normal, homozygotes and compounds are viable and are normal in development, and crossing over is normal. — By the use of an unstable duplication covering the A region, homozygotes and compounds of the various mutants were produced and sectors resulting from loss and alteration of the duplication segment studied. These studies show that all three X-ray mutants involve loss of the effects not only of A but of additional genes affecting chlorophyll development and cell viability. All four ultraviolet mutants are free from these associated effects. (G)

1952

Stadler, L. J. and Herschel Roman. THE EFFECT OF X-RAYS UPON MUTATION OF THE GENE A IN MAIZE. *Genetics* **33**, 273-303(1948).

In order to study the nature of the mutations at the A locus induced by x-rays, selected F_1 progenies produced by an $aa \times AA$ cross after irradiation of the male parent just before pollination with a 1,000 r dose were extensively studied for mutations, gametophyte viability, homozygote and compound viability, crossing-over effects, pachytene cytological changes, and effects noted from unstable duplications. From 415 A losses, two normals which were free of segregating pollen defects and one which showed segregation of subnormal, but not aborted pollen, were selected for thorough studies on lethality, transmission, and crossing-over. The results are extensively reported and discussed. 18 references. (NSA)

1953

Stroman, Govan N. and Thomas H. Lewis. A STUDY OF GENETIC EFFECTS OF COSMIC RADIATION ON COTTON SEED. *J. Heredity* **42**, 210-13(1951).

Samples of seed from individual cotton plants known to be heterozygous for certain seedling defects were exposed to high-altitude radiation in an experimental type V-2 rocket. An altitude of 90.5 miles was reached during 595.5-sec flight. The exposed seed were grown through the second generation against controls from the same parent plants. Changes noted in the radiated material remain to be finally evaluated, and cannot as yet be designated as cosmic radiation effects. (NSA)

1954

Strömnaes, Øistein. THE PRODUCTION OF DOMINANT LETHALS WITH X-RAYS IN AGED *DROSOPHILA MELANOGASTER* SPERM. *Genetics* **34**, 462-74(1949).

Experiments to determine the effect of the age of the gametes at the time of x-ray treatment on the percentage of dominant lethals induced in *Drosophila melanogaster* sperm are presented. The dosages were delivered at 200 kv through 1 mm Al and 0.25 Cu filters at a distance of 31-41 cm and consisted of doses of 2,219-2,308 r; the sperm was aged 1-23 days. It was found that the sensitivity to x-rays increases with an increase in age; the age effect was also found when eggs were aged. No age effect was noted when the males were stored with the females; the age effect, moreover, was noted only in the sperms from early developing males. 15 references. (NSA)

1955

Strömnaes, Øistein. X-RAY INDUCED LETHAL MUTATIONS IN SEVERAL STRAINS OF *DROSOPHILA MELANOGASTER*. *Hereditas* **37**, 532-59(1951).

Males from 31 strains of *Drosophila melanogaster* were tested in regard to their sensitivity to the induction of dominant lethal mutations by 2300-r x rays. Genetic differences in the sensitivity to induction of dominant lethal mutations by x rays were found to exist between unrelated strains. (NSA)

1956

Swanson, C. P. THE DIFFERENTIAL EFFECTS OF COMBINED RADIATIONS ON CHROMOSOME BREAKAGE AND MUTATION RATE. *Science* **107**, 458(1948).

One of the important problems of cytogenetics is the relationship between chromosome change and gene mutations. The solution of the problem is difficult, particularly since the usual mutagenic agents, such as x-rays and short ultraviolet light, also alter chromosome structure. A possible avenue of approach is through the use of additional agents which, while ineffective of themselves, can, when combined with x-rays, or ultraviolet, increase or decrease the rate of chromosome change without effecting mutation production, or vice versa. Infrared, when combined with X-rays, increases the rate of chromosome change (in *Tradescantia*) and the rate of morphological mutations (in *Aspergillus*). The chromosome effect is probably due to the infrared affecting the rate of recombination of broken ends of chromosomes but not the initial rate of chromosome breakage. It is likely that the increased rate of mutations is the result of additional chromosome changes having phenotypic effects, since infrared, when combined with ultraviolet (2,537 Å) is ineffective in altering the mutation rate. Infrared, therefore, does not affect the stability of the gene. Ultraviolet, when combined with x-rays, does not alter the x-ray-induced chromosome changes. This selectivity of radiations permits the separation of gene mutations from chromosome changes. The former result from initial absorptions of energy which are not affected by combined treatments, while the chromosome changes which depend upon initial breakage of chromosomes followed by recombination of broken ends, are influenced by addition agents which effect the recombination rather than the initial breakage phase of chromosome alteration. (NSA)

1957

Swanson, C. P., Ale ander Hollaender, and B. N. Kaufmann. MODIFICATION OF THE X-RAY AND ULTRAVIOLET-INDUCED MUTATION RATE IN *ASPERGILLUS TERREUS* BY PRETREATMENT WITH NEAR INFRARED RADIATION. *Genetics* **33**, 429-37(1948).

To determine the effect on mutation rates of near-infrared irradiation from 250 w, 115 v sources, filtered by 1.5 cm of iodine saturated CCl_4 and heat resistant glass filters, spore suspensions of *Aspergillus terreus* were continuously irradiated for three days after which they were x-irradiated by two Coolidge-type tubes operating at 170 kv, with 0.25 Cu and 1.06 mm Al filters delivering 8,500 r/min for 1 to 20 minutes, or were irradiated by ultraviolet light delivered at 15 w, 115 v with a 90% radiation below 3,000 Å. The per cent mutation rates for ultraviolet or x-irradiation alone are compared with rates for these combined with infrared pretreatment. The data and results are given and extensively discussed. The authors conclude that with x-ray induced mutations infrared pretreatment causes a significantly increased mutation rate throughout the range tested, but that this does not effect the mutation induced by low ultraviolet doses although it does increase the mutation rate of high doses; an unknown mechanism is postulated whereby the mutated spores can utilize the infrared energy to recover and grow. (NSA)

1958

Tatum, E. L. EFFECTS OF RADIATION ON FUNGI. J. Cellular Comp. Physiol. Suppl. 1, 35, 119-31(1950).

The evidence so far suggests that in *Neurospora*, sensitivity to mutation is dependent on the inherent properties of the gene rather than on the nature of the mutagen, although specific action of particular mutagens will remain as a possible cause of certain infrequent mutant types until more adequate data are obtained. The results of mutational treatment of microconidia indicate that in *Neurospora*, the extranuclear determination of biochemical characters is rare, if not absent. This supports the current views on the over-all rarity of cytoplasmically inherited characters. At present hopes for specific mutagenic activity seem poor, and what evidence there is seems to point only to the possibility of quantitative, rather than qualitative specificity in mutagenic activity of different agents in different organisms. It would seem theoretically possible that genes may similarly differ in susceptibility to particular agents, and the discovery of mutagens with a high degree of genic specificity seems hopeful. (NSA)

1959

Tatum, E. L., R. W. Barratt, Nils Fries, and David Bonner. BIOCHEMICAL MUTANT STRAINS OF NEUROSPORA PRODUCED BY PHYSICAL AND CHEMICAL TREATMENT. Am. J. Botany 37, 38-46(1950).

Plating techniques and cultures have been developed which permit the efficient isolation of homocaryotic strains of *Neurospora crassa* from uninucleate microconidia. With these techniques, x-radiation, ultraviolet radiation, bis- and tris-nitrogen mustards, and methylcholanthrene have been examined for their effects in producing biochemical mutants in *Neurospora*. Treatment with x-rays was carried out by placing a drop of a dense suspension of microconidia on the surface of solidified 4% agar in a petri plate and allowing the water to be imbibed by the medium. The layer of microconidia remaining was treated directly with x-rays; following an exposure to about 20,000 r, about 0.01% of the organisms survived. Treatment of either microconidia or macroconidia with nitrogen mustards induces mutations which appear quantitatively and qualitatively similar to those induced by irradiation; the types of biochemically deficient mutants obtained are described. No indication has yet been found for extranuclear control of biochemical deficiencies in *Neurospora*. (NSA)

1960

Thomas, Lyell J. and Henry Quastler. PRELIMINARY REPORT OF X-RAY EFFECTS ON THE NEMATODE RHABDITIS STRONGYLOIDES. Science 112, 356-7(1950).

The nonlethal effects of x-irradiation on the characters of adult individuals of a bisexual nematode, *Rhabditis strongyloides*, have been investigated. This worm appears to be different, in respect to observable changes and genetic response, from animals, plants, and bacteria used in conventional genetic studies. Exposures of 100 to 10,000 r produced no visible physical changes in the worms, 20,000 r applied to wet cultures caused the appearance of larvae with marked changes in the refractive index of the rhabditin granules of the intestine, and 40,000 r produced vacuolate, probably sterile reproductive systems, looped or spiral-like intestines, variations in egg size and shell structure, and the appearance of "dauer"-like worms. The same effects were obtained with dry cultures exposed to 40,000 r as were obtained with 20,000-r-irradiated wet cultures. These changes are shown to be genetic and to be perpetuated for generations in crowded mass cultures. (NSA)

1961

Thompson, K. F., J. MacKey, A. Gustafsson, and L. Ehrenberg. THE MUTAGENIC EFFECT OF RADIO-PHOSPHORUS IN BARLEY. Hereditas 36, 220-3(1950).

The mutagenic effect of P^{32} on barley was studied by soaking seeds in water containing various quantities of radioactive phosphate ions and by subsequent measuring of the chlorophyll-mutation rates per spike progeny in the second generation. Radiophosphorus was found to be highly mutagenic, its mode of action lying between those of x-rays and neutrons and its mutation range being wider than that of x-rays. Since P^{32} is easy to handle, it is expected to become very useful in mutation work and plant breeding. (NSA)

1962

Timoféev-Ressovskii, N. W. SPONTANEOUS AND RADIATION INDUCED MUTABILITY IN GEOGRAPHICALLY DIFFERENT RACES OF DROSOPHILA MELANOGASTER.

None of eight stocks from widely scattered geographic regions deviated significantly from the average of the spontaneous mutation rate (0.143%) nor from the average of the x-ray (3,000 r) induced rate (8.35%) for sex-linked mutations, as determined by the CIB-method. No correlation was found between the spontaneous and the x-ray induced rates. The normal allele at the white locus for a Russian and an American stock showed a difference on the border of statistical significance. If the difference is real it lies in the structural difference at the white locus and not in an influence of the rest of the genome. The extensive data show that stock conditioned differences in the total mutation rate can be neither large nor frequent. (BA)

1963

Uphoff, Delta E. and Curt Stern. THE GENETIC EFFECTS OF LOW INTENSITY IRRADIATION. Science 109, 609-10 (1949).

In contrast to previous findings no significant difference in mutation rates in the sperm of *Drosophila melanogaster* was obtained between controls and experimentals which had been subjected to a dose of 52.5 r in gamma rays administered continuously for 21 days at a rate of 2.5 r per day. This unexpected result required further tests. After consideration of various factors, the following were regarded as possible causes for the apparent inactivity of irradiation in the experiment: low sensitivity to irradiation of aged sperm, dependence of induced mutation frequency at low dosages on a time factor, and errors of sampling which might have obscured a true difference between control and experimental rates. Three new tests which are described gave an increased frequency of mutations in the treated sperm as opposed to the controls. Viewing all experiments together, it appeared that irradiation at low dosages, administered at low intensity induces mutations in *Drosophila* sperm. (NSA)

1964

Wagner, Carroll E. and G. W. Beadle. MUTATIONS PRODUCED BY ATOMIC BOMB IRRADIATION OF NEUROSPORA CRASSA; APPENDIX NO. 16. Naval Medical Research Institute, Bethesda and California Institute of Technology. Mar. 7, 1949. 8p. (NP-1904)

Eighty biochemical mutants observed in red bread mold, *Neurospora crassa*, exposed to Tests Able and Baker have been classified. Of these, 32 are classified as unknowns, meaning that these mutants require for growth, compound not yet identified. No attempt was made to classify the various morphological mutants found. The numbers of recovered mutants are so small that no attempt has been made to correlate them with dosages measured by physical means at the various stations. (NSA)

1965

Wallace, Bruce. AUTOSOMAL LETHALS IN EXPERIMENTAL POPULATIONS OF DROSOPHILA MELANOGASTER. *Evolution* 4, 172-4(1950) (AECU-1716)

Preliminary work indicating that a large proportion of induced lethals in the second chromosome of *D. melanogaster* are incompletely recessive is reported. Three experimental populations of *D. melanogaster* were analyzed for lethal second chromosomes. The original flies of two of these populations were treated with x rays. Frequencies of lethals in experimental populations is presented in tabular form. Data indicate that less than one-half of the original induced lethals persist through six generations. (NSA)

1966

Wallace, Bruce. MUTATIONS INDUCED BY CHRONIC RADIATION. *Genetics* 35, 698(1950).

Males and females of the ore-R strain of *D. melanogaster* have been subjected to chronic irradiation in a number of experiments. (1) Chronic x-ray treatment of approximately 108 r per day (7 min per treatment) for 5, 10, 15, 20, and 25 days after deposition of eggs gave, in males, $1.21 \pm 0.22\%$, $3.99 \pm 0.59\%$, $4.60 \pm 0.42\%$, $6.14 \pm 0.66\%$, and $5.20 \pm 1.23\%$ sex-linked lethals. The control rate was $0.19 \pm 0.10\%$. The proportion of recoverable lethals increased linearly with dose for 20 days; there was no increase after that time. (2) Males and females carrying lethal-free second chromosomes were exposed continuously to γ rays for 18 days (~2200 r) at 25°C while they developed from eggs to adults. In all, 3772 second chromosomes from these treated males were tested for lethals; 456 ($12.1 \pm 0.5\%$) were recovered. No attempt was made to test for clusters. Likewise, 1187 second chromosomes from treated females were also treated; 69 ($5.8 \pm 0.7\%$) lethals were obtained. The difference between the frequencies of recoverable lethals in the two sexes is significant. Preliminary tests for translocations coincident with these lethals indicate that they occur with a low frequency; no translocations were coincident with the 69 lethals derived from females, 3 were present among 99 independent, "randomly" chosen lethals from treated males. A test for allelism made with 100 lethals of independent origin (obtained from different males) gave 14 cases of allelism in 4950 tests. A minimum of 400 (234-718) loci on the second chromosome are capable of mutating to lethality under these conditions. (G)

1967

Wallace, Bruce. GENETIC CHANGES WITHIN POPULATIONS AFTER X IRRADIATION. *Genetics* 36, 612-28 (1951) (AECU-1107)

Genetic analyses have been made of populations of *Drosophila melanogaster* exposed to single x-ray treatments. The parental males of population 1 received 7125 r; females of population 1 and males and females of population 2 received 1012.5 r; the flies of population 3 were untreated.

Before treatment, all flies carried second chromosomes that were free of lethals and drastic subvitals. The recessive lethals of population 1 decreased from an original 18.3 to 10.1% in approximately four generations and then increased at a rate comparable to that of the control. The early elimination of lethals from population 1 indicated a selective disadvantage of heterozygotes of 0.5, and was adequately explained by lethal-translocation association. Analyses of lethals, semilethals, average viabilities of flies homozygous for "normal" chromosomes, and variances of the array of "normal" viabilities indicate that changes occurred at a more rapid rate in population 1 than in the control. The discussion touches briefly on general problems of irradiated populations. (NSA)

1968

Wallace, Bruce and J. C. King. GENETIC CHANGES IN POPULATION UNDER IRRADIATION. *Am. Naturalist* 85, 209-22(1951) (AECU-1442)

A general account is given of studies made on experimental populations of *Drosophila melanogaster* which are exposed to radiations. A consideration of the frequencies of lethals, semilethals, and subvitals within the populations and of the estimates of the adaptive values of the populations suggests that heterotic gene combinations have been developed within some of these populations. The bearing these results have on estimation of radiation damage resulting from gene mutation is briefly mentioned. (NSA)

1969

Whiting, Anna R. IMMATERNATE MALES AND HIGH VISIBLE MUTATION RATE FROM EGGS IRRADIATED IN PROPHASE I. *Genetics* 31, 235-6(1946).

Unmated wild type females of *Habrobracon* were heavily X-rayed and mated to recessive untreated males. Surviving progeny (about 10 percent for 28,000 r) were from eggs irradiated in prophase I. They consisted of the expected wild type, haploid impaternate males and diploid biparental heterozygous females and, in addition, recessive haploid immaterbate (androgenetic) males. The last resembled their fathers in every respect, were fully fertile and non-mosaic. Percentages of androgenesis (immaterbate $\sigma\sigma \times 100/\text{immaterbate } \sigma\sigma + \text{♀♀}$) were 4.21 (15/356) for 28,000 r, 23.06 (3/13) (corrected 13.36) for 29,300 r and 12.50 (1/8) for 42,000 r. Correction is applied to second group because crosses made were two-allele and therefore 50 percent of zygotes should be diploid males and inviable. Production of normal individuals from untreated sperm in heavily irradiated cytoplasm strengthens views that X-ray injury is directly chromosomal. The heterozygous females were bred unmated. 252 tested from 28,000 r treatment produced seven or more sons. Among these, heterozygosis for visible mutations was 12.69 percent. Tests of four from 29,300 r yielded no mutations and four from 42,000 r yielded one. These results suggest possibility of obtaining readily dose-action curves for visibles for comparison with those already available for lethals in this material. (G)

1970

Whiting, Anna R. MOTHERLESS MALES FROM IRRADIATED EGGS. *Science* 103, 219-20(1946).

Unmated females of an inbred wild type stock of *Habrobracon* were heavily x-rayed, then mated to untreated males with recessive mutant traits. The progeny included among the expected wild type males and females, a few males normal in structure and behavior and with recessive mutant traits. Breeding tests showed that their gonads were also paternal in origin. Their normal fertility was proof of their haploidy. (BA)

1971

Whiting, Anna R. ANDROGENESIS, A DIFFERENTIATOR

OF CYTOPLASMIC INJURY INDUCED BY X-RAYS IN HABROBRACON EGGS. Biol. Bull. 97, 210-20(1949).

Wild type parasitic wasp females, *Habrobracon juglandis*, were x-rayed and mated to untreated males with one or more types recessive to the wild type. Two kinds of haploid males were produced, the gynogenetic with x-rayed chromosomes in x-rayed cytoplasm, and the androgenetic with untreated chromosomes in x-rayed cytoplasm. A simultaneous cross-firing technique was used to deliver the radiations at a kv of 182 with a filtering value of 0.2 Cu at an intensity of 7,210 r/min and a target distance of 9.5 cm. Doses were 50-144,200 r and were fractionated in some cases. It was found that at doses of 50-15,000 r death of the eggs was due to chromosomal injury, and was not reduced by fractionation or changes in intensity. Above 15,000 r, x-rays induced chromosomal injury which may have exerted a lethal effect on developing embryos; the lethal effect was reduced by fractionation of the dose. Gynogenetic males developed from the unfertilized eggs, androgenetic males from the fertilized eggs; the lethal dose for the gynogenetic males was about 2,400 r and about 54,000 r for the androgenetic males. It was determined that injured cytoplasm acts in a direct manner in killing the embryo and not indirectly through injury to the untreated chromosomes. The author concludes that the evidence supports the target theory of chromosomal injury. (NSA)

1972

Whiting, Anna R. THE NON-INDUCTION OF MUTATIONS BY X-RAYED CYTOPLASM. Genetics 35, 139-40(1950).

Unfertilized *Habrobracon* eggs develop into haploid gynogenetic males. Of several thousand irradiated in first meiotic metaphase, none have hatched after any dose higher than 2,500 r. Cytological observations demonstrate a consistent pattern of chromosome injury. When severe, this injury retards movement of egg pronucleus after which the egg, fertilized by an untreated sperm, may develop into a haploid androgenetic male. Eggs are fertilized between one and seven hours after exposure. From 6,714 x-rayed unmated wild type females crossed to untreated recessive males, 170 recessive androgenetic males have been obtained. These developed in egg cytoplasm exposed to doses ranging from 1,350 to 65,000 r, the latter dose about twenty-five times as great as that fatal to egg chromosomes in this stage. No mutations appeared in any of these males and of thirty-two tested, all were fully fertile and transmitted only paternal traits. Of 2,389 half-sisters of androgenetic males developed from eggs x-rayed in first meiotic prophase and fertilized by untreated sperm, 129 or 5.39% produced mutant sons. This differs significantly from the results obtained on androgenetic males. Evidence supports the theory that x-rays induce visible mutations directly in the chromosomes. (G)

1973

Whiting, Anna R. and Bernice Goldis. DOSE-ACTION CURVES FOR X-RAY-INDUCED DOMINANT LETHAL AND VISIBLE MUTATIONS IN HABROBRACON EGGS. Genetics 32, 112(1947).

Data are being collected for visible mutation rate of eggs X-rayed in prophase I with doses ranging from 6,400 r to 37,200 r. The dose-action curve suggests a direct relation to dose, thereby agreeing with work of previous investigators on this subject. Percentages of surviving eggs producing visibles range from 3.7 for 6,400 r to 15.6 for 37,200 r. This curve is compared with that of dominant lethality previously published by senior author for prophase I. The latter is complex and tends to become exponential with fractionation of dose which increases resistance to treatment. (G)

1974

Whittinghill, Maurice. SOME EFFECTS OF GAMMA RAYS UPON RECOMBINATION FREQUENCIES AND ON CROSSING OVER IN *DROSOPHILA MELANOGASTER*. Genetics 35, 140-1(1950).

In testcrosses of heterozygous *cu/ru h th st + sr e^h ca* females irradiation by 4,000 r of gamma rays increased recombinations in the spindle attachment region to 2½ times the control value. Other increases of successively smaller magnitudes relative to control values were found in the flanking regions grading down to terminal decreases. The coincidence curve for all treated testcrosses showed a similar regular shape when the absolute changes were divided by the possible increases. Coincidences were higher in all regions in treated material. These increases also graded up to a peak at the spindle region. Both these curves are qualitatively predictable from the hypothesis that irradiation induced a rather small amount of genetic crossing over in oogonial cells. There was a considerable variation between females in the amount of response and also in the place of response to irradiation, resembling previous results from treated males. 4,120-r gamma-ray treatment of *SL⁴/Cy Pfd* females produced "clusters" of crossovers, of appreciable size in some families. A similar treatment of males produced crossovers also in a nonrandom manner appropriate to spermatogonial crossing over. The implications to the collection of data for standard maps are considered. (G)

1975

Whittinghill, Maurice. SOME EFFECTS OF GAMMA RAYS ON RECOMBINATION AND ON CROSSING OVER IN *DROSOPHILA MELANOGASTER*. Genetics 36, 352-5(1951).

γ-ray treatment of 4000 r given to adult *Drosophila melanogaster* females altered crossover values in a regular pattern in rucuca heterozygotes. Increases were greatest, relative to controls, in the spindle-attachment region in the middle of the third chromosome, progressively less in each successive region farther out, and negative in the two most distal regions. Coincidence of double crossover combinations was increased relative to control coincidence values in a similar curve but without distal decreases. Great individual variation in crossover production after γ-ray treatment was shown by regular females, by inversion females, and by regular males. The changes might have originated in meiotic or in gonial cells. The distribution of crossovers among families from γ-ray-treated Curly Lobe⁴ inversion heterozygotes had a probability of 0.001 of resulting from meiotic crossing over. It has been attributed to oogonial crossing over in these females. The 4000-r treatment induced crossovers in 14 of 59 treated males in an even greater nonrandom distribution which was due to spermatogonial crossing over. A new crossover-selector system of testing was employed here. Expression in ratio form of the regionally different effects of starvation of larvae upon crossover production shows a maximum increase in the spindle region and other graded increases as found here using γ rays. During three different 8-hr periods of the day irradiation of adult rucuca heterozygotes seemed to be equally effective in producing changed recombination values. (NSA)

1976

Wijsman, R. A. ON THE INTERPRETATION OF THE DOSE FREQUENCY CURVE IN RADIOGENETICS. Genetics 36, 478-87(1951).

The question whether a linear relationship between mutation frequency and radiation dose is a strong indication that a mutation is caused by a single event has been investigated in several cases, and answered in the affirmative.

The results of the calculations, supporting this conclusion, are shown in graphs, in which the curves for multiple-event models are compared with the curve for a single-event model. An exception has to be made for the possibility that some events may occur with much higher probability than any of the others in which case a multiple-event model could give rise to a single-event type curve. However, this case is physically unlikely. Finally it is shown that Opatawski's curve, which is supposed to represent a many-event mechanism, actually represents a lone-event mechanism, so that his conclusion that a many-event theory can give rise to a linear curve is unjustified. (auth)

1977

Witkin, Evelyn M. A CASE OF INHERITED RESISTANCE TO RADIATION IN BACTERIA. *Genetics* 31, 236(1946).

When a sample of Strain B of *Escherichia coli* is exposed to ultra-violet radiation, the last survivors prove to be relatively resistant to both ultra-violet and X-rays. The resistance is stable and heritable. —Survival curves for the radiation-resistant strain at various doses of ultra-violet differ markedly in shape from similar curves with X-rays. Survival curves for the normal strain with X-rays and ultra-violet are identical in shape. —The lag phase of the resistant strain in broth is only one-half the length of the normal lag phase. This apparent selective advantage disappears, however, when the two strains are mixed and incubated together for some time—the lag phase of the resistant strain becomes the same as that of the normal strain. —Microscopic examination of ultra-violet irradiated cells of the normal and resistant strains reveals striking differences. At low doses, normal cells elongate for many hours without dividing while resistant cells begin to divide soon after treatment. This difference is the basis of a technique for the accurate determination of the number of resistant cells in a sample, without which genetic analysis would be very difficult. —Resistance to radiation is in this case a mutation arising spontaneously in the bacterial culture, independently of treatment with radiation. This was demonstrated by following directly the increase with time of the proportion of resistants in a normal culture. (RG)

1978

Witkin, E. M. GENETICS OF RESISTANCE TO RADIATION IN *ESCHERICHIA COLI*. *Genetics* 32, 221-47(1947).

Strain B of *E. coli* gives rise to a variant which is characterized by relative resistance to the lethal effects of both ultraviolet radiation and x-rays. This character is stable and heritable. Some additional properties of radiation-resistant, strain, B/r, derived from the parent strain by culturing a last survivor of an irradiation with ultraviolet, are described. This strain exhibits relative resistance to the division-inhibiting effect of radiation, as well as to its lethal effect, and is also relatively resistant to the lethal and division-inhibiting action of penicillin and sodium sulfathiazole. Strain B/r exhibits a shorter lag phase in broth at 37°C than the parent strain, and a somewhat lower final titre. Survival curves of strains B and B/r with ultraviolet radiation and x-rays are compared. A technique is described whereby radiation resistant mutants can be detected quantitatively in samples from the parent strain. This technique designated as the double-irradiation treatment, provides an absolute selective procedure for the detection of the variant. Resistance to radiation is shown to be due to a spontaneous mutation, occurring in cultures of strain B at a rate of about 10^{-6} mutations per bacterium per generation. The rate of occurrence of the mutation to radiation-resistance can be increased considerably by treatment of the parent strain with high doses of ultraviolet radiation. At least 4 independent mutations are demonstrated, each of

which results in resistance to radiation, but distinguishable by the presence or absence of associated resistance to penicillin, or sodium sulfathiazole or both. The mutation to radiation-resistance, when it is accompanied by resistance to penicillin, act as a modifier of an independent mutation to penicillin-resistance, adding quantitatively to its effect. Some preliminary experiments in population dynamics are described. When strains B and B/r are artificially mixed and carried by daily subculture neither strain is at a selective disadvantage. When the mixtures are aged without subculture, however, the mutant strain is at a distinct selective disadvantage approaching complete lethality. Interpretations are offered for certain features of the results. (Author's Summary)

1979

Wright, Sewall. DISCUSSION ON POPULATION GENETICS AND RADIATION. *J. Cellular Comp. Physiol. Suppl.* 1, 35, 187-205(1950).

A strong possibility exists that cumulative doses of the order of 300 r may have important effects on the offspring and descendants of those affected and that doses as small as 30 r may not be negligible. There is little or no threat to the persistence of a population as a whole from the cause. However, there are such enormous gaps in the knowledge of the subject that no judgements of the genetic consequences of radiation in man can be taken very seriously. (NSA)

1980

Zimmer, K. G. and N. W. Timoféev-Ressovskii. DOSIMETRIC AND RADIATION BIOLOGICAL EXPERIMENTS WITH FAST NEUTRONS. *Strahlentherapie* 63, 528-36 (1938).

The authors studied the effect of fast neutrons on mutations produced in the fruitfly. There was a definite increase in the rate following exposure to fast neutrons which was directly proportional to the dose. The effect per dose unit or per pair of ions produced in tissues was less than that of roentgen or γ rays. The experimental results were in good agreement with those calculated according to the target theory. (BA)

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1981

Arnason, T. J., Elaine Cumming, and J. W. T. Spinks. CHROMOSOME BREAKAGE INDUCED BY ABSORBED RADIOACTIVE PHOSPHORUS, P^{32} . *Can. J. Research* 26, 109-14(1948)

Radioactive phosphorus (P^{32}) was made available to individual germinating seeds and seedlings of *Triticum vulgare*, *T. durum*, *T. monococcum*, and *Hordeum distichon*. Each treated plant was provided with either 0.18 or 0.018 of P^{32} . Both concentrations were effective in causing chromosome breakage and rearrangements. Many aberrant chromosome configurations occurred in microsporocytes of treated tetraploid and hexaploid plants. Only one chromosome aberration was found in *T. monococcum* and none in barley. Structural changes occurred also in chromosomes of vulgar wheat grown in soil to which fertilizer containing P^{32} was added. It is possible that the effectiveness of small amounts of P^{32} in inducing mutations is increased by its inclusion in chromosome molecules. Emitted β particles would then be shot off very close to the sensitive target. Further, the recoiling atomic nucleus is almost certain to have enough energy to break any chemical bond. In any case since there is a change in atomic number (from 15 to 16) and in valence (P valence 5, S valence 2), molecular bonds must be released in the process. (NSA)

1982

Beal, J. M. SOME HISTOLOGICAL EFFECTS OF CARBON 14 ON THE LEAVES OF CERTAIN MEDICINAL PLANTS. *Botan. Gaz.* **110**, 600-3(1949).

A cytological description is given of the leaves of *Digitalis purpurea*, *Digitalis lanata*, *Papaver somniferum*, *Nicotiana rustica*, and *Atropa belladonna* which had been grown in a $C^{14}O_2$ atmosphere for various periods of time. The atmospheres contained 400, 900, and 1,400 μc of the $C^{14}O_2$ in the various experiments; the authors conclude on the basis of these observations that the C^{14} does not effect the protoplasm with which it comes in contact, but that the differences noted are all alterations in the pattern of tissue differentiation. (NSA)

1983

Beal, J. M. and N. J. Scully. CHROMOSOMAL ABERRATIONS IN ONION ROOTS FROM PLANTS GROWN IN AN ATMOSPHERE CONTAINING $C^{14}O_2$. *Botan. Gaz.* **112**, 232-5(1950).

The roots showed both chromosome and chromatid breaks and fragments in dividing cells, bridging, and micronuclei. (CA)

1984

Bishop, Charles J. DIFFERENTIAL X-RAY SENSITIVITY OF TRADESCANTIA CHROMOSOMES DURING THE MITOTIC CYCLE. *Genetics* **35**, 175-87(1950).

The results of an investigation to determine the stage and range of sensitivity in the mitotic divisions of pollen grains of *Tradescantia* are described. A direct analysis of chromosome alterations was performed. X-radiations were delivered at 160 kv through inherent filtration at a target distance of about 65 cm; the dosage used was 250 r. Both before and after x-ray treatment the plants were kept in the greenhouse, remaining there until the buds to be analyzed were opened. The x-ray effects were analyzed at the metaphase stage of the pollen division from slides prepared over a period extending from the second to the seventh day after treatment. The data obtained indicate there was a period of low sensitivity during the postmitotic resting stage, and two points of high sensitivity, one at the time of chromosome doubling during the prophase of the pollen tube division and the other at metaphase-anaphase of the pollen grain division, the latter being the greater of the two. It is suggested that the prophase peak of chromosome sensitivity to x-ray breakage occurred about 3 days after actual chromosome doubling. It is also suggested that the metaphase-anaphase peak of sensitivity was due to the prevention of restitution by (a) factors of longitudinal tension induced with the chromonema by changes during the spiralization cycle and later by the spindle mechanism, and (b) the chromosome matrix which reduced fragment movement after breakage and separation. X-ray breaks induced during the stages before the prophase of the generative nucleus division were shown to remain open and to be capable of sister chromatid reunion when the chromosome became double, which was as long as 2 days after the x-ray treatment. 24 references. (NSA)

1985

Bishop, Charles J. THE INFLUENCE OF POLYPLOIDY ON THE X-RAY SENSITIVITY OF CELLS. *Genetics* **35**, 654(1950).

The report is in abstract form; it is reproduced here in its entirety.

A study of comparative sensitivity to x radiation has been made by treating developing microspores and pollen grains of diploid and tetraploid species of *Tradescantia* with equal doses of x rays. Treatments were given at a time just previous to the prophase of the pollen grain divi-

sion and at a stage before chromosome doubling in the generative nucleus division. The aberrations produced were analyzed at the pollen grain division and the pollen tube division, respectively. Results indicate that the sensitivity of the two types of cells is the same if the comparison is based on the number of x-ray-induced breaks per chromosome. A comparison of the number of breaks per cell shows that the cells from the tetraploid plants have approximately double the number of breaks found in those from the diploid plants. (NSA)

1986

Bishop, Charles J., Victor D. McLaughlin, and Donald F. Tapley. X-RAY TOLERANCE OF LIVING CELLS AS MEASURED BY CYTOPLASMIC STREAMING. *Can. J. Research* **27**, 262-8(1949).

An investigation was undertaken to determine the immediate effects of x-radiations on living, non-dividing cells, using the rate of cytoplasmic streaming as an indication of cell vitality. The observations were carried out on the stamen hairs and pollen tubes of *Tradescantia paludosa*, a diploid species, and on *Tradescantia virginiana*, a tetraploid species. In each experiment cultures were checked for rates of streaming and then were subjected to large, uninterrupted dosages of 250,000-450,000 r for the stamen hairs and 100,000-125,000 r for the pollen tubes; subsequent dosages of 25,000 were given until cytoplasmic streaming ceased. The radiations were administered by a standard Coolidge x-ray tube having a filtration of 1 mm Al and operated at 140 kv with a beam intensity of 1200 r/min. In both diploid and tetraploid stamen hairs, 700,000 r was required to stop all streaming, while in the pollen tubes of diploid and tetraploid plants, streaming was stopped by 250,000 r and 200,000 r, respectively; greater sensitivity was found with an increased initial dosage of continuous irradiation. 12 references. (NSA)

1987

Bishop, D. W. CYTOLOGICAL DEMONSTRATIONS OF CHROMOSOME BREAKDOWN SOON AFTER X-RADIATION. *Genetics* **27**, 132(1942).

This paper is reproduced here in its entirety.

First spermatocyte prophase stages of Orthoptera are used to demonstrate x-ray induced chromosome breaks. Three minutes after irradiation breaks in one of the four diakinetid chromatids can be demonstrated (*Chortophaga viridifasciata* treated with 540 r). In *Melanoplus bivittatus*, fixed six minutes after irradiation (270 r) many cases of breaks are found in one of the two visible threads of pachytene chromosomes and in one of the chromatids of diakinetid chromosomes. Within this time interval no cases of simultaneous breakage of two visible threads occurs. However, within 30 minutes (270 r) two-thread as well as one-thread breaks occur in diakinetid chromosomes. A few double breaks were found within 8 minutes at 540 r. These results are evidence for an almost immediate effect of the irradiation in contrast to a delayed effect. However, the breakage reaction seems to be a gradual rather than an instantaneous event, judging from the longer time required for two-thread breaks at the same dosage. Chromosome fragments are found in spermatogonial and spermatocyte anaphases within 30 minutes after irradiation. The point of breakage in prophase chromosomes is at random. In normal and in treated cells neither the pachytene nor the diakinetid chromosomes are in contact with one another; if the breakage mechanism is the same as that leading to inversions and translocations, the evidence supports the breakage-first as opposed to the contact hypothesis.

1988

Bishop, D. W. SENSITIVITY OF SPERMATOCYTE CHROMOSOMES TO ABERRATIONS INDUCED IN THE EMBRYOS BY X-RADIATION. *Genetics* 27, 132-3(1942).

Gonads were removed from adult and late nymphal grasshoppers (*Circotettix verruculatus*) which had been irradiated (150 to 750 r) as embryos still within the chorion. In the first meiotic anaphase there are chromosome alterations, not found in any other mitotic stage, and not included among the usual cytogenetic changes. These aberrations affect one or both of the diad components of the tetrad, and include constrictions, attenuations, and breaks. They are invariably located between the point of spindle attachment and the nearest region of association of the arms of the homologs ("chiasm"). The second spermatocytes thereby produced frequently contain large duplications and deficiencies and are inviable. All of the cells within an affected cyst have been derived from a single treated cell by at least seven divisions. Yet no abnormalities in the previous spermatogonial, diakineti, or first spermatocyte metaphase chromosomes predict the aberrations that will occur at meiotic anaphase. Comparisons with chromosome rearrangements involving reciprocal translocations (multiples), inversion-crossovers (dicentric and acentric), and small deletions, demonstrate that some other mechanism of chromosome alteration pertains. The distribution of aberrations is non-random, concerning the regions affected within particular chromosomes as well as different chromosomes within a cell. A large proportion of aberrant chromosomes show homologous breaks, symmetrically placed, in the two members of a tetrad. The conclusion is drawn that the X-ray effect is general and the chromosomes become fragmented at points of natural weakness. (G)

1989

Bozemann, Martha L. and Charles W. Metz. FURTHER STUDIES ON SENSITIVITY OF CHROMOSOMES TO IRRADIATION AT DIFFERENT MEIOTIC STAGES IN OOCYTES OF *SCIARA*. *Genetics* 34, 285-314(1949).

X-ray doses of 1,100 r were used to determine the chromosome sensitivity of maturing oocytes of *Sciara ocellaris* to radiations. The results indicate that the chromosome sensitivity is almost zero for a long period of time preceding the breakdown of the nuclear membrane at the beginning of the first meiotic division. Then it rises rapidly to a peak, in anaphase, apparently dropping off somewhat in the late anaphase, at which time the mitotic activity is arrested, pending fertilization. Different types of chromosome rearrangements differ greatly in actual frequency. Only one translocation was secured. The author points out that the data suggest the intervention of a cytoplasmic agent which reaches the chromosomes after breakdown of the nuclear membrane and which either induces rearrangements directly, by transmitting an influence already produced by the irradiation, or sensitizes the chromosomes to irradiation so that treatment is effective after, but not before, the entrance of the agent. A third possibility is also considered. (NSA)

1990

Brown, Meta S. CHROMOSOME IRREGULARITIES PRODUCED BY ATOMIC IRRADIATION. *Genetics* 33, 98(1948).

Acetocarmine smears were made of the P.M.C. of eleven cotton plants grown from seed exposed to atomic bomb radiation at Bikini during "Operation Crossroads". In four plants quadrivalents were found at metaphase, one plant having two such multivalent associations per nucleus. Three plants were mosaic for normal and altered chromo-

some constitution. In two of these a chromosome had been lost, producing monosomic tissue, and in the other a quadrivalent was present. In one plant two chromosomes were frequently found as univalents, or paired with a chiasma only. No chromosome abnormalities were detected in four plants, which had 26 pairs of chromosomes, as was true for plants grown from unexposed seed of the same lot. The types of meiotic irregularities found indicate that gamma ray irradiation had produced translocations, loss of chromosomes, and possibly an inversion in the embryonic tissue of the cotton seed. Morphologically no plants showed any deviation from normal, except one plant which was slightly fasciated at an early seedling stage. (NSA)

1991

Brown, Meta S. COTTON FROM BIKINI. CHROMOSOME IRREGULARITIES FOUND IN PLANTS GROWN FROM SEED EXPOSED TO GAMMA RADIATION. *J. Heredity* 41, 115-21(1950).

Cytological analyses of cotton plants grown from seed exposed to an atomic bomb explosion have been made. Irregularities in chromosome pairing have been found and attributed to changes in chromosome structure. (NSA)

1992

Brues, Austin M. and Leola Rietz. EFFECTS OF EXTERNAL AND INTERNAL RADIATION ON CELL DIVISION. *Ann. N. Y. Acad. Sci.* 51, 1497-1507(1951).

The effects of radiation upon cell division were studied, using regenerating rat liver. After partial hepatectomy, the liver was exposed to x radiation given in a single dose (10 to 3000 r), injected Pu^{239} and P^{32} , and continuous exposure to a point source of β rays, using small glass beads containing carrier-free Y^{90} . The Y^{90} bead experiment was of most quantitative value in determining the degree of suppression of mitosis. Effects of ionizing radiations on mitosis were shown to include reversible delay in cell division, followed by visible chromosome damage and changes in the mitotic figure. The amount of β radiation required to reduce liver mitosis by one-half was shown to be of the order of 1 rep/hr over a 48-hr period. (NSA)

1993

Brumfield, Robert T. EFFECT OF COLCHICINE PRE-TREATMENT ON THE FREQUENCY OF CHROMOSOMAL ABERRATIONS INDUCED BY X-RADIATION. *Proc. Natl. Acad. Sci. U. S.* 29, 190-3(1943).

Treatment of onion roots for 45 minutes with 0.05% colchicine solution prior to roentgen irradiation, resulted in less than $1/3$ as many chromatid aberrations as found in non-colchicine-treated controls. (CA)

1994

Buchsbaum, Ralph and Raymond E. Zirkle. SHRINKING AND SWELLING AFTER ALPHA IRRADIATION OF VARIOUS PARTS OF LARGE ERYTHROCYTES. *Proc. Soc. Exptl. Biol. Med.* 72, 27-9(1949).

Erythrocytes from *Amphiuma* and from human blood were irradiated in vitro with $Po \alpha$ -particles from an extended source (4 mm diameter) and also with a small beam 20 μ in diameter. The cells first shrank, then swelled and hemolyzed. Local irradiation of part of a single cell resulted in shrinkage only in the irradiated portion. This was followed by swelling of the whole cell and hemolysis. (CA)

1995

Carlson, J. G. IMMEDIATE EFFECTS OF 250 R OF X-RAYS ON THE DIFFERENT STAGES OF MITOSIS IN NEUROBLASTS OF THE GRASSHOPPER, *CHORTOPHA*-

GA VIRIDIFASCIATA. J. Morphol. **66**, 11-23(1940).

Two hours after x-radiation of neuroblasts with 250 r all middle prophase through early telophase stages have disappeared. Statistical and observational evidence indicates that middle prophase is the stage most susceptible to the x-ray effect that causes cessation of mitosis; for after treatment some of the cells in this stage, instead of entering late prophase, revert to earlier stages or at least undergo changes in their chromatin that stimulate reversion. Late prophases and metaphases decrease steadily in numbers by passing into successively later stages until they have disappeared at the end of 75 minutes. Both anaphases and early telophases decrease in numbers by passing into successively later stages during the first 30 minutes, increase at 45 minutes, and then fall steadily, the former reaching zero at 90 minutes, the latter at 120 minutes. The simultaneous fall in the numbers of late prophase and metaphase stages and the increase simultaneously in the numbers of anaphases and early telophases at 45 minutes indicate that x-rays alter the rate of change from stage to stage in cells undergoing mitosis at the time of treatment and that this change in rate differs with the stage of mitosis and with the time elapsing after irradiation. (EA)

1996

Carlson, J. G. AN ANALYSIS OF X-RAY INDUCED SINGLE BREAKS IN NEUROBLAST CHROMOSOMES OF THE GRASSHOPPER, *CHORTOPHAGA VIRIDIFASCIATA*. Proc. Natl. Acad. Sci. U. S. **27**, 42-7(1941).

The single chromosomal break is considered the result of a single event—a single ionization or excitation—which occurs at random. This hypothesis is supported by (1) the linear proportionality existing between dosage measured in r-units and number of chromosomal breaks, (2) the apparent absence of any threshold below which breaks do not occur, (3) the close correspondence between the observed and expected distribution of the breaks among different cells after each of the doses. The analysis of single breaks in terms of ion pairs per chromosome indicates that only a small proportion of the ionizations produced by x-rays is effective in the production of breaks. (BA)

1997

Carlson, J. G. IMMEDIATE EFFECTS OF 31 R OF X-RAYS ON THE DIFFERENT STAGES OF MITOSIS IN MICROBLASTS OF *CHORTOPHAGA*. J. Morphol. **71**, 449-62(1942).

Treatment of neuroblasts of the grasshopper, *C. viridifasciata* with 31 r of x-rays at the rate of 200 r/min. leads to alterations in the average number of middle prophase, late prophase, metaphases, anaphases, and early telophases per embryo. After a brief latent period mitotic cessation of cells in advanced middle prophase and initial late prophase with less or no effect on those in early prophase, metaphase, anaphase, and early telophase leads to the accumulation of large numbers of middle prophases and the disappearance of advanced late prophases, metaphases, anaphases, and early telophases. The simultaneous recovery of a large proportion of the middle prophase cells and their mitotic progress into successively later stages result subsequently in abnormally large numbers of late prophases, metaphases, anaphases, and early telophases. Certain evidence suggests that the mitotic progress of cells phases. Certain evidence suggests that the mitotic progress of cells may be altered mainly through effects of the x-rays on the prophase chromosomes. (BA)

1998

Carlson, J. Gordon. EFFECTS OF RADIATION ON MITOSIS. J. Cellular Comp. Physiol. **35**, Suppl. 1, 89-101(1950) (ORNL-570)

The effects of x- and ultraviolet radiations upon the mitosis of grasshopper embryo neuroblasts is discussed. The approach is primarily cytological and is concerned with how the individual cell is affected by radiation. The inhibition of mitosis by x-irradiation is noted, and the effects of total dosage, dosage rates, and the mitotic stage at which the x-radiation is administered is pointed out. A certain "critical period" for inhibiting mitosis—late prophase—has been noted. The effects of ultraviolet radiation are compared with x-radiation. Instead of a clear-cut mitotic stoppage at a "critical period", cells throughout most of interphase and prophase may be retarded mitotically by relatively low dosages of ultraviolet radiation. The author concludes that although there is much information available on the manner in which various radiations affect mitosis, the mechanism by which excitation and ionization of atoms within the cell are transformed into large scale mitotic effects is not understood. He states that the effectiveness of very low ionizing radiation dosages in interfering with enzyme systems is highly suggestive. (NSA)

1999

Carlson, J. Gordon, Mary Louise Snyder, and Alexander Hollaender. RELATION OF GAMMA-RAY DOSAGE RATE TO MITOTIC EFFECT IN THE GRASSHOPPER NEUROBLAST. J. Cellular Comp. Physiol. **33**, 365-72 (1949). (AECU-243; ORNL-348)

Eggs of the grasshopper, *Chortophaga viridifasciata* (De Geer), containing 14-day embryos (at 26°C) were exposed to known doses of γ rays given at certain selected dosage rates and then made into hanging-drop culture preparations. Treatment was at room temperature, (about 22°C). Treated and control embryos were prepared from the same pod of eggs. They were studied at 38 ± 0.3°C in an incubator enclosing the lower portion of a microscope. A gamma-ray dose of 8, 32, or 64 r produced the same degree of mitotic inhibition, whether administered at a rate of 2 r per minute or 32 r per minute. A γ -ray dose of 128 or 256 r was more effective in depressing mitosis if given at 32 r per minute than at 2 r per minute. This document is a revision and amplification of MDDC-1576. (NSA)

2000

Carothers, E. E. A CYTOLOGICAL STUDY OF X-RAYED GRASSHOPPER EMBRYOS. J. Morphol. **66**, 529-59 (1940).

Melanoplus differentialis embryos after receiving 250 or 300 r in a single dose in early predispausa, developed. The immediate effect of radiation is direct injury to the chromatin of cells actually undergoing mitosis at the time of treatment. This injury is of such a nature that these cells die in amphase with pycnotic nuclei. Twenty-four hours later these nuclei are found scattered throughout the germ-band. Later such cells are either engulfed by other embryonic cells, absorbed in situ or extruded from the embryo. Within 48 hours certain cells show liquefaction of the cytoplasm and within five days lesions due to cytolysis appear. This cytolysis may be due to direct injury to the cytoplasm by the x-rays or to a toxic effect from the phagocytized necrotic cells. Mitotic activity is increased perhaps due to liberation of intercellular hormones. Yolk cells phagocytize injured cells and remove them from the vicinity of the embryo. They are also capable of assuming the function of serosa cells and secreting impervious yellow cuticle thus walling off necrotic areas. There is some evidence that the chromosomes respond differentially to general injury of the organism. About the onset of diapause the nuclei of groups of cells become pycnotic due probably to lack of necessary cellular associations. The terata

seem to be due to the isolation of groups of healthy cells from their normal associations in the embryo. Many of the chromosomal complexes in such misplaced parts are normal. Finally the embryos die due to lack of organization rather than to absence of differentiation since all types of tissue may be present. (Author's Summary)

2001

Catcheside, D. G. EFFECTS OF IONIZING RADIATIONS ON CHROMOSOMES. *Biol. Revs. Cambridge Phil. Soc.* 20, 14-28(1945).

The information about the process of chromosome breakage and structural change in somatic chromosomes, especially of *Tradescantia*, is reviewed. The number of primary breaks induced at resting stage of prophase greatly exceeds the total number of breaks observed at the subsequent metaphase. The majority of the breaks reconstitute after being open for a few minutes, during which time the formation of exchanges is possible. The yield of x-ray induced exchanges is proportional to the square of the dose if the radiation is given at a high intensity. The yield is proportional to a lower power of the dose if the dose is given at a lower intensity. Only breaks with an initial separation of $1\ \mu$ or less have an appreciable chance of taking part in an exchange. In neutron and α -ray experiments, the yield of exchanges is linearly proportional to dose and independent of intensity; thus the majority of exchanges are between pairs of breaks produced simultaneously by the same ionizing particle. An ionizing particle may break both chromatids of a split chromosome at the same locus and an isochromatid break usually results. A proportion of the primary breaks are unjoinable; hence a proportion of interchanges are incomplete, a proportion of isochromatid breaks show non-union, and a proportion of breaks not taking part in exchanges persist as visible chromatid breaks instead of reconstituting. The number of primary chromatid breaks differs for equal doses of different radiations. A proton of α -ray traversing a chromatid has almost unit probability of causing a break. An electron is likely to cause a break only if the last $0.3\ \mu$ of its ionized track traverses the chromatid; hence a minimum of 15-20 ionizations must be produced in a chromatid of diameter $0.1\ \mu$ for the breakage probability to approach unity. The relative efficiencies of different wavelengths and types of radiation can be explained on this basis. (BA)

2002

Catcheside, D. G. and D. E. Lea. THE EFFECT OF IONIZATION DISTRIBUTION ON CHROMOSOME BREAKAGE BY X-RAYS. *Genetics* 45, 186-96(1943).

Chromatid breakage is not equal in frequency for equal doses of x-rays of different wave-lengths, dosage being calculated as ionization in the tissue. The effect is a maximum at $\lambda = 4.1\ \text{\AA}$, falls off slowly with decreasing wave-length ($\lambda = 1.5\ \text{\AA} - \lambda = 0.15\ \text{\AA}$) and rapidly with increasing wave-length ($\lambda = 8.3\ \text{\AA}$). This is interpreted as meaning that only the densely ionizing tails of the electron tracks are effective in breaking chromosomes and only then if they completely traverse the chromosome, since the Al-K radiation ($\lambda = 8.3\ \text{\AA}$), for which the electron track is shorter than a chromatid diameter, is relatively ineffective. The probability of survival of chromatid breaks is equal for pollen grain and pollen tube nuclei. Since isochromatid breaks are far less frequent (27%) in the latter, sister-chromatids must be in contact 24 hours before metaphase of the pollen tube division. The probability of interchange in the elongated cylindrical pollen tube nucleus is greatly reduced (ca. 75%) by the different packing of the chromosomes. (BA)

2003

Catcheside, D. G. and D. E. Lea. DOMINANT LETHALS AND CHROMOSOME BREAKS IN RING X-CHROMOSOMES OF *DROSOPHILA MELANOGASTER*. *J. Genetics* 47, 25-40(1945).

Ring x-chromosomes treated with 4,000 r units of x-rays were examined cytologically. Among 749 chromosomes, 23 inversions, 9 intercalations, 4 complex interchanges, and 3 deficiencies were found, but no case of a simple rod-shaped chromosome resulting from a break. There is therefore no positive evidence from this experiment that broken chromosome ends can heal. The significance of the absence of healed breaks was estimated by deriving the number of non-restituted breaks in the x-chromosome from the observed frequencies of induced structural changes in rod and ring x's and the different x-ray-induced depressions of the sex ratio in rod and ring x-chromosome stocks. It was first concluded that the chance of restitution of a break in the X was 0.74, the chance of remaining open 0.26; then, that there would be 16 primary breaks per 100 rod X's per 1,000 r, or 78 per 100 sperms per 1,000 r. This estimate agreed well with those based on other considerations. It was finally concluded that 3.8 non-restituted breaks were produced per 100 ring X's per 1,000 r, and therefore 105 in the 749 analyzed chromosomes. Since recovery of a rod chromosome from a broken ring chromosome would require simultaneous healing greater than 0.17 per chromosome end is excluded by these data. A terminal inversion in chromosome 2 was found, and also a complicated interchange between ring X and chromosome 3 in which a new end was provided by the ring X and the right end of 3 became intercalary. This is held to provide no support for Muller's conception of the special character of the chromosome end, or telomere. (BA)

2004

Catcheside, D. G., D. E. Lea, and J. M. Thoday. TYPES OF CHROMOSOME STRUCTURAL CHANGE INDUCED BY THE IRRADIATION OF *TRADESCANTIA* MICRO-SPORES. *J. Genetics* 47, 113-36(1946).

Tradescantia microspores were irradiated with x- and with gamma-rays, using different doses, exposure times and temperatures, and fixed after 18-23 hours. Chromatid breaks, isochromatid breaks, intrachanges and interchanges were observed. Symmetrical and asymmetrical types of exchange occur with about equal frequency, suggesting that there is no sort of polarization favoring the union of proximal with distal fragments against the union of proximal with proximal or distal with distal. There is a correlation between the facts that a proportion of chromatid breaks remain visible and do not reconstitute, that a proportion of interchanges are incomplete, and that sister-union does not occur at some isochromatid breaks. The determination of the proportions of interchanges which are incomplete and of isochromatid breaks which show non-union enables an estimate to be made of the proportion (f) of breaks which are unjoinable, and which therefore remain visible as chromatid breaks. As well as exchanges between chromatid breaks (c/c), exchanges occur between chromatid and isochromatid breaks (i/c), and the relative proportions of these two types of exchange must be related to the numbers of chromatid and isochromatid breaks primarily produced. From this observation a second estimate is obtained of the proportion of chromatid breaks primarily produced which remain visible at the time of fixation. The two estimates of f agree in giving values about 0.09 for x-rays. The number of chromatid breaks primarily produced is calculated to be 0.09 per roentgen of x-rays. (From Authors' Summary)

2005

Catcheside, D. G., D. E. Lea, and J. M. Thoday. **THE PRODUCTION OF CHROMOSOME STRUCTURAL CHANGES IN TRADESCANTIA MICROSPORES IN RELATION TO DOSAGE, INTENSITY AND TEMPERATURE.** *J. Genetics* **47**, 137-49(1946).

The yield of chromatid breaks is proportional to dose, independent of exposure time at a given dose, and only slightly dependent (between 1 and 30°) upon the temperature at which the irradiation is made. The yield of isochromatid breaks increases slightly more rapidly than the first power of the dose, possibly decreases slightly with increase of exposure time at a given dose, and diminishes markedly with increase of irradiation temperature (especially between 20 and 30°). Most of the isochromatid breaks are 1-hit, e.e. produced by a single ionizing particle which traverses both sister chromatids, but a small proportion are 2-hit, e.e. produced by separate ionizing particles. The yield of interchanges produced by x-rays increases slightly less rapidly than the square of the dose when the doses are given in a constant time. The yield produced by a given dose diminishes with increase of exposure time at 1 and 20°. The yield diminishes with rise of temperature as with isochromatid breaks. Interchanges produced by x-rays are mainly 2-hit, but a small proportion are 1-hit, and this proportion is relatively more important when long exposure times are used. The separation at the moment of formation of breaks which exchange is of the order of 1 μ . Most of the exchanges occur within a few minutes of irradiation, but a few take much longer. For the same dose in roentgens, α -rays produce slightly fewer interchanges than do x-rays. (Authors' Summary)

2006

Conger, A. D. **X-RAY SENSITIVITY OF THE STAGES OF MITOSIS.** *Am. J. Botany* **34**, 582(1947).

The x-ray sensitivity of the stages of mitosis was studied in onion root tip cells. The production of polyploid cells by colchicine treatment was used to distinguish cells which were in meta-anaphase stage from the cells in the other stages when x-rayed; cells in meta-anaphase when x-rayed were the first to progress to the 4N Metaphase, when chromosomal aberrations were analyzed. The relative sensitivity was determined by comparing the chromosomal aberration frequencies resulting from x-raying at the different stages of mitosis. Aberration frequency of cells rayed in resting stage was assigned a sensitivity value of 1. Other stages compared with resting stage showed relative sensitivities of approximately 1.7 to 3.4 from early to late prophase, 11.8 in anaphase, and 37 times as great in metaphase. The high sensitivity of metaphase chromosomes is believed to be due to an increase in the factors which have been found to operate in the other stages to increase aberration frequency, as stresses of movement and coiling and spatial relationships, and possibly the additional sensitivity of the process of duplication of the gene string which may be operative at this stage only. The occurrence of single chromatid deletions in 4N cells which were x-rayed at diploid metaphase is evidence that the chromosome can be effectively four strand to x-rays at metaphase, or two strand at anaphase. (GPR)

2007

Conger, Alan D. **THE CYTOGENETIC EFFECT OF SONIC ENERGY APPLIED SIMULTANEOUSLY WITH X-RAYS.** *Genetics* **33**, 607(1948) (ORNL-101)

An experiment has been performed to test the influence of sonic energy on the yield of x-ray induced chromosomal aberrations in a clone of *Tradescantia paludosa*. Chromosomal aberration frequency was determined at the micro-

spore mitosis from aceto-carmine amears made four days after treatment. Inflorescences were immersed in water contained in a steel cup used for the sonic treatment. The bottom of the cup was a vibrating diaphragm which transmitted the sonic energy to the plant buds via the water. The instrument used was Raytheon Mfg. Co. magnetostriction oscillator, run at 9,100 cycles/sec., and at a power of 30 watts. Two treatments were given to inflorescences inside the sonic cup: (a) 250 r x-rays (78 r/min.) as measured in air outside the cup, and (b) 250 r x-rays (as above) plus sonic treatment begun with and continued for five minutes after the x-radiation ceased. The frequency of all types of chromosome aberrations was higher when the sonic treatment was given in addition to the x-rays. The ratio of x-ray plus sonic energy/x-ray aberrations was 1.3/1 for both exchanges and simple deletions. The sonic treatment alone, as given here, did not cause aberrations. This increased yield of aberrations is probably due to an increased amount of chromosome movement caused by the transmission of sonic energy through the cells during and after the x-radiation; movement would separate the broken ends from a single chromosome break (reducing restitution) and bring together broken ends from different breaks (increasing new reunions)—both would increase aberration frequency. (ACD)

2008

Conger, Alan D. **THE CYTOGENETIC EFFECT OF SONIC ENERGY APPLIED SIMULTANEOUSLY WITH X-RAYS.** *Proc. Natl. Acad. Sci.* **34**, 470-4(1948).

The cytogenetic effects of simultaneous treatment of *Tradescantia* inflorescences with x-rays (250 r) and sonic energy (9100 cycles/second) are described. Simultaneous treatment with sonic energy and x-rays increases the yield of x-ray induced chromosomal aberration about 1.3 times the yield obtained with the same amount of x-rays alone. The sonic treatment alone did not cause aberrations. The increased yield is probably due to an increased movement of chromosomes and chromosome fragments caused by the sonic treatment resulting in a decrease in the amount of restitution and an increase in the amount of detectable new reunions between the broken ends of chromosomes. (NSA)

2009

Conger, Alan D. **THE EFFECT OF BORON ENRICHMENT ON SLOW NEUTRON IRRADIATED TISSUES.** *Genetics* **35**, 102(1950).

The effect of slow neutrons on tissue is an indirect one, and results from the ionizing radiations emitted by atoms which have captured a slow neutron. A previous investigation of the effect of slow neutrons on *Tradescantia* chromosomes had indicated that 99 per cent of the ionization dose absorbed in tissue was due to only three elements, hydrogen (emitting a γ ray), nitrogen (proton) and boron (alpha particle). Boron alone was responsible for 32 per cent of the ionization dose absorbed. The considerable importance of boron in these slow neutron exposures was surprising in view of its minute amounts in tissue, only 2.9 p.p.m. of the wet weight in this case, but was due to two factors: (1) the very high probability that a boron atom will capture a neutron, and (2) the fact that the α particle emitted loses all its energy within the tissue. The reaction is: $B^{10} + \text{neutron} \rightarrow [B^{11}] \rightarrow Li^7 + \alpha \text{ particle}$. To test and confirm the importance of boron in tissues, inflorescences from *Tradescantia* plants grown in boric acid solution for about two months were exposed to slow neutrons, and the frequency of chromatid aberrations induced was compared with the frequency from normal non-enriched inflorescences. It was found that, for the same

dose of slow neutrons, the boron enriched plants showed from four to five times as many chromatid aberrations as the nonenriched plants, confirming the expectation that boron, in spite of its micro amounts, is one of the most damaging elements when small volumes of tissue are exposed to slow neutrons. (G)

2010

Conger, A. D. and L. M. Fairchild. THE INDUCTION OF CHROMOSOMAL ABERRATIONS BY OXYGEN. *Genetics* **36**, 547-8(1951).

Treatment of dry pollen grains of the plant *Tradescantia* with oxygen (greater than 99.5% pure) produces chromosomal aberrations which can be observed at the pollen tube division on pollen culture slides. The aberrations produced are identical with those found after irradiation with X or γ rays. Pollen treated with oxygen from two different cylinders (evacuated 5 times, gas flushed 5 times) and pollen merely flushed with oxygen, all had aberration frequencies equivalent to that produced by about 600r of X rays in air. Control pollen (not evacuated) and air pollen (evacuated 5 times, air flushed 5 times) had almost no aberrations. - Exposure of oxygen-treated pollen to but 2 r of γ rays caused so many chromosomal breaks that an analysis could be made of fragment frequency only. The fragment frequency was higher than oxygen alone, and roughly about what would be expected from 1000 r of γ rays in air. (G)

2011

Conger, Alan D. and Norman H. Giles, Jr. THE CYTOGENIC EFFECT OF SLOW NEUTRONS. *Genetics* **35**, 397-419(1950). (ORNL-409)

The cytogenetic effect of thermal neutrons from a special facility in the thermal column of the Oak Ridge nuclear reactor has been investigated. The production of chromosomal aberrations, both chromatid and chromosome types, in *Tradescantia* microspores has been compared with the production of the same aberrations by x-rays. Calculations of the number of rep absorbed from thermal neutron capture in tissue indicate that three elements, hydrogen, nitrogen, and boron are responsible for about 99% of the ionization dose produced by neutron capture, and that about 77% of this dose is due to the protons and α rays from nitrogen and boron capture reactions. These conclusions are substantiated biologically by the observed linear increase of exchange aberrations with dose, which is characteristic of particulate radiation (with electromagnetic radiation, exchange aberrations increase as a power of the dose). An equivalence of thermal neutrons/x-rays has been derived by comparing the production of chromosomal aberrations by the two radiations. The best value seems to be $\sim 5 \times 10^8$ thermal neutrons per $\text{cm}^2 = 1$ r of x-rays in biological effect; this would make the 8-hour tolerance dose (the same amount of effect as 0.1 r of x-rays) as based on this effect $\sim 5 \times 10^8$ thermal neutrons per cm^2 . A comparison of the x-ray equivalent effect produced by unit dose of thermal neutrons with the calculated number of rep generated by the same dose shows that thermal neutrons are about 11 times as efficient as x-rays per unit dose in producing this biological effect. If only the nitrogen protons and boron α rays from thermal neutron capture are considered, their efficiency compared with x-rays seems to be about 15/1. These biological efficiencies are about 3 to 4 times as great as have been observed when the same types of radiations were delivered from external sources. It is believed that this difference in the effectiveness of protons and α rays when they are administered to a tissue from an external source and these same radiations when they originate from the atoms of the tissue itself is

not due to any difference in the effect of the protons and α rays themselves, but is due to a difference in their place and manner of origin. (NSA)

2012

Costello, Donald P. and Catherine Henley. EFFECTS OF RADIO-PHOSPHORUS (P^{32}) ON MITOSIS IN LARVAL TAIL-TIPS OF *AMBLYSTOMA PUNCTATUM*. *Anat. Record* **108**, 578-9(1950).

Young larvae (of appropriate age) of *Amblystoma punctatum*, from which tail-tips had been clipped, were permitted to degenerate in media containing various concentrations of radiophosphorus. The exact dosage of β radiation within the epithelial cells of the regenerating tail-tip cannot be calculated, but a sufficient range of dosage was used to give variations in effects on mitosis from zero to complete inhibition. Submaximal dosages produced a wide variety of mitotic abnormalities, some types of which have never before been observed by the authors with other types of treatment. Many deletions (production of chromosome fragments) resulted similar to those induced in classical plant material, such as *Tradescantia*, by irradiation. Several extreme multiple deletions were obtained, showing 30 or 40 or more chromosome fragments within a single cell. There was a paucity of multipolar mitoses among the abnormalities produced by the irradiation. Multipolar mitoses are among the most common of the mitotic anomalies produced by temperature effects. The demonstration that *Amblystoma punctatum* larval tail-tips are a favorable material (comparable, in some respects, to *Tradescantia*) for the study of the effects of radioisotopes on cells and mitosis is of considerable importance. Investigations of the effects of radiations on animal cells have lagged considerably behind similar work on plants, due largely to a lack of suitable material. Tail-tips of 580 treated larvae have been studied to date, with adequate numbers of controls. (NSA)

2013

Creighton, M. THE EFFECTS OF X-RAYS ON MITOTIC AND MEIOTIC CHROMOSOMES AND CELL DIVISION IN *CHORTHIPPUS LONGICORNIS* (ORTHOPTERA). *J. Exptl. Zool.* **87**, 347-69(1941).

Spermatogonia, embryo cells, and primary spermatocytes were treated with graded doses of x-rays and the chromosomes were examined at varying intervals thereafter. The kinds of breaks were noted and the frequency of chromosome abnormalities in terms of per cent normal anaphases was recorded. It was not possible to determine the time of chromosome doubling by the order of appearance of chromatid and chromosome breaks after irradiation. The most sensitive stage for the mitotic chromosomes is three hours before anaphase which corresponds to a period just prior to prophase or in early prophase. The most sensitive stage for the meiotic chromosomes is 9 hours before anaphase. The slopes of the dose effect curves for the spermatogonia and embryo cells were identical and more than six times as great as the slope for the primary spermatocytes. The spermatogonia and embryo cells are very sensitive to inhibition of mitosis by x-rays, the primary spermatocytes much less so. In the embryo cells those cells which have the most sensitive chromosomes, i.e. those in stages just prior to prophase or in early prophase, are also the most sensitive to inhibition of mitosis. They are delayed longer than other cells and on reaching anaphase produce a characteristic dip in the curves for per cent normal anaphases at different times after irradiation. (BA)

2014

Creighton, M. and B. H. Evans. SOME EFFECTS OF

X-RAYS ON THE GERM CELLS OF *CHORTHIPPUS LONGICORNIS* (ORTHOPTERA). J. Morphol. **69**, 187-202(1941).

Male grasshoppers of the sp. *C. longicornis* were given a dose of 3,000 r of x-rays and their testes examined at intervals thereafter. Spermatogonia and secondary spermatocytes show many abnormalities of the chromosomes during division within 90 minutes after irradiation and by 12 hours they are no longer dividing. Dividing primary spermatocytes show many abnormalities soon after irradiation. X-rays inhibit the division of primary spermatocytes but in this dose do not cause a complete cessation of division. The number of dividing primary spermatocytes decreases rapidly up to six hours after irradiation and increases thereafter to normality at 48 hours. The inhibition is effective in preventing cells from entering prophase. As a result of the inhibition of division, primary and secondary spermatocytes begin to differentiate directly into spermatozoa, forming giant spermatids. The capacity to differentiate into spermatozoa is evidently independent of the maturation divisions. (BA)

2015

Crouse, Helen V. **THE DIFFERENTIAL RESPONSE OF MALE AND FEMALE GERM CELLS OF *SCIARA COPROPHILA* (DIPTERA) TO IRRADIATION.** Am. Naturalist **84**, 195-202(1950).

Comparative studies have been made on the response of male and female germ cells of *S. coprophila* to irradiation. The following results were obtained: (1) When adult females are exposed to x-rays 43 to 45.5 hr after eclosion, no gross rearrangements of any type are recovered; but oocytes irradiated between 46 and 72 hr of adult life yield inversions. (2) Approximately the same number of breaks leading to gross rearrangements are induced by 2,000 r in oocytes and 4,000 r in sperm. (3) Irradiation of sperm results in both reciprocal translocations and inversions. (4) Tests for reciprocal translocations involving the x chromosome yielded 9 such translocations among 108 sperm tested but none among the 42 oocytes examined. The failure to recover interchromosomal exchanges following irradiation of oocytes is discussed. (NSA)

2016

Da Câmara, A., M. Wagner, and A. Gardé. **LOCATION OF BREAKS INDUCED BY X-RAYS IN CHROMOSOME OF TRITICUM.** Proc. Intern. Congr. Genetics 8th Congr. Stockholm 1948 (Suppl. to Hereditas) 555(1949).

Investigations made on chromosomes of 3 groups of the genus *Triticum* indicate that ruptures induced by x-rays are more frequent near the centromere or near the free ends. It is suggested that the points particularly vulnerable to x-radiation show this condition as a consequence of the chemical activities near the centromere and not because of a special susceptibility of the chromonemata in those regions. (CA)

2017

Daniels, E. W. **STUDIES ON THE EFFECT OF X-IRRADIATION UPON *PELOMYXA CAROLINENSIS* WITH SPECIAL REFERENCE TO NUCLEAR DIVISION AND PLASMOTOMY.** J. Exptl. Zool. **117**, 189-209(1951).

The effect of x irradiation upon reproduction of *Pelomyxa carolinensis* (an amoeboid Protozoa) was studied. The median lethal dose was determined to be 96,000 r, and the shape of the survival curve to be sigmoid. With dosages between 15,000 and 140,000 r, a pronounced delay was shown in the first plasmotomy (division) following x irradiation during interphase. Greater delay was produced as the dosage was increased. X irradiation did not change the frequency of simple plasmotomies. Plas-

mogamy (fusion) of x-irradiated halves to their nonirradiated sisters tended to prevent the delay otherwise observed between exposure and the first mitosis. In cellular systems containing both x-irradiated and nonirradiated nuclei (and cytoplasm), the nuclei still, as in a normal individual, were observed to undergo mitosis at precisely the same time. (NSA)

2018

Demerec, M. **A COMPARISON BETWEEN THE X-RAY INDUCED AND THE SPONTANEOUS NOTCHES.** Genetics **25**, 115-16(1940).

Salivary gland chromosome study of an unselected series of 27 X-ray induced Notches shows that 3 had the full complement of bands, in 7 cases one band was missing, in 4 cases 2 to 5 bands were missing and in 13 cases more than 6 bands were missing. Similar study of a series of 10 spontaneous Notches shows 1 case in the first group, and 3 cases in each of the other three groups. The spontaneous series consisted of Notches kept in stock at various laboratories and obtained from them for this study. Since long Notch deficiencies have poor viability it is probable that in this series natural selection may have eliminated some of the long deficiencies. Such a possibility finds support in the genetic analysis by Li and Bridges of spontaneous Notches collected at random; it was found that 4 out of 25 involved the white locus as well and were thus long deficiencies extending to the left of Notch. In my X-ray series 7 out of 27 involve white, while in the spontaneous series only one out of ten is white, suggesting the working of natural selection in the case of the spontaneous series. When this is taken into consideration the two series show a striking similarity in the frequency distribution between the four groups differing in the length of the deficient segment. (G)

2019

Diderer, P. H. **THE PRODUCTION OF GIANT SPERMATOCYTES IN *PHILOSAMIS CYNTHIA* BY MEANS OF X-RAYS.** J. Morphol. **67**, 159-73(1940).

Irradiation of testes of *Philosamis cynthia* was undertaken to determine if there might be some visible effect of x-rays on the chromosomes of the spermatocytes, such as the clumping of two together, or an increase in their number. Pupae were irradiated under the following conditions: distance from target, 35 cm, filter of 2.5 celluloid, 0.5 Al, and 0.16 Cu; 200 kv, 32 ma, for periods of 11, 27-1/2, and 44 minutes at the rate of 180 r/min, calculated as amounting to a total of 2,000, 5,000, and 8,000 r, respectively. This irradiation caused the formation of giant cells within the cysts of growing spermatocytes. The number of affected cysts increased with the dosage, being relatively few after a dosage of 2,000 r units, and increasing considerably after a dosage of 5,000 and 8,000 r units. Correlated with this, the number of empty cysts and the amount of cellular debris also increased. Some giant cells were mononucleate; others, binucleate or multinucleate, were probably produced by the fusion of cells. The spermatogonia remained apparently unaffected by low and medium doses. After high dosage usually only a very few cells remained, but among them some divisions occurred. No distinctive giant spermatogonia were observed. There was no visible effect of irradiation upon the chromosomes of the spermatocytes. In all favorable metaphase plates, the chromosomes were normal in number and in appearance. Irradiation affected similar cells in a testis very unequally, allowing some to complete the formation of spermatozoa, causing others to degenerate as spermatids, while those which became giant cells did not survive beyond the growth period. (SVS)

2020

Duryee, William R. THE NATURE OF RADIATION INJURY TO AMPHIBIAN CELL NUCLEI. J. Natl. Cancer Inst. **10**, 735-96(1949).

In order to determine the physiological mechanisms by which cell nuclei are damaged by ionizing radiations, the ovarian eggs of salamanders and frogs and whole animals were irradiated with various doses of x-rays. Two Coolidge tubes were mounted above each other and operated from the same transformer at 182 to 194 kv; no filters were employed, and the target distance from the center of the irradiated area was 35 cm for whole animals and 9.5 cm and 12.7 cm in the case of eggs and nuclei; the irradiation rate was 6,100 to 7,600 r/min. for the isolated cells and 450 to 500 r/min. and 2,800 to 6,100 r/min for the whole animals. The total doses were 300 to 100,000 r with the great majority of the experiments being performed at the 30,000 to 60,000 r level for the eggs and at the 300 r level for the whole animals. The details of the experimental procedure are presented. At 3,000 r, 98% of the small eggs showed intranuclear damage within 10 days. Nuclear components irradiated in situ showed differential susceptibility; exposures to low temperature (5°C) delayed the nuclear injury up to 18 days but were unable to prevent pyknosis upon rewarning of the animals. Nuclear and chromosomal injuries in ovarian eggs were roughly paralleled by those in the theca cell nuclei; typical radiation damage in nonirradiated cells could be produced by micro-injections of cytoplasmic material withdrawn from irradiated eggs. The conclusion drawn from these and other results is that cellular radiation damage is a triple phenomenon, consisting of: primary physical or radiochemical changes in the cytoplasm; chemical metabolic processes which allow protoplasmic nuclear toxins to form or accumulate in the cytoplasm; and, transmission of toxic substances into the nucleus in 10 to 30 minutes at 23°C. (NSA)

2021

Ehrenberg, I., A. Gustaffson, A. Levan, and U. von Wettstein. RADIOPHOSPHORUS, SEEDLING LETHALITY, AND CHROMOSOME DISTURBANCES. Hereditas **35**, 469-89(1949).

The cytogenetical effects of radiophosphorus, P^{32} , on the cereal seed of two-rowed barley, hexaploid spring wheat (*triticum vulgare*), and tetraploid wheat (*triticum dicoccum*) were investigated. In the different experiments the concentrations of the isotopic were 0.02-25.0 $\mu\text{c}/\text{seed}$, usually in 5 ml of solution for 72 hours. It was found that doses of 5 $\mu\text{c}/\text{seed}$ or more were lethal to the tetraploid wheat and nearly so to the hexaploid wheat; the cytogenetical disturbances compared with those produced by x-irradiation with 25,000 r. Barley was found to be less susceptible but with a dose of 5 μc , more than half of the cell divisions analyzed contained chromosome disturbances. Even with 2.5 μc in 100 ml of solution it was found that a treatment lasting three days produced chromosome fragmentation, and higher dosages demonstrated an increasing amount of such disturbances as pseudochiasmata, fragments, bridges due to stickiness (in the first three hours) or reunions and finally, pronounced chromosome erosions leading to full lethality. The greater susceptibility of the wheat seeds compared to the barley seeds is explained and discussed. (NSA)

2022

Fabergé, A. C. AN EXPERIMENT ON CHROMOSOME FRAGMENTATION IN TRADESCANTIA BY X-RAYS. J. Genetics **39**, 229-48(1940).

Twelve treatments were used on *T. bracteata* buds: Three dosages (1320, 2640, 3960 r units) X continuous (18 min.) vs. fractionated (3 hr) exposure X 15° C vs. 30°C. The number of chromosomal objects (whole chromosomes and fragments) per cell was adapted as an objective basis for scoring. To get a valid estimate of error, replication was used. This proves necessary in such expts. since variance between slides made from different buds treated alike was 10-12 times greater than variance within slides. The analysis of variance within the data shows that the effect of increasing dosage is linear; fractionating the dose decreases the number of chr. objects, more so at higher dosage; higher temp. reduces the number of chr. objects, more so at higher dosage; the effect of fractionation is alike at both temps.; and there is no significant effect at higher order interactions. The simplest interpretation is that irradiation causes breaks and rejoining takes place afterwards. Unlike *Drosophila*, the amount of rejoining is an inverse function of the initial number of breaks, and also depends on the total dose. Higher temps. allow more breaks to rejoin, again unlike *Drosophila*. Many repairs probably restore the original sequence. (BA)

2023

Fabergé, A. C. ACTION OF TEMPERATURE DURING X-RAY TREATMENT OF TRADESCANTIA CHROMOSOMES. Genetics **33**, 104(1948).

There is agreement among a number of workers that in *Tradescantia*, the number of chromosome aberrations is smaller if irradiation is conducted at higher temperature. It is plausible to think that it is an effect on rejoining, but attempts to demonstrate this directly by changing the temperature after treatment have not been successful. An experiment is reported in which the time of treatment and the time of temperature change were reduced to a minimum (500 r units in 80 seconds; half period of temperature change 15 seconds), and were short relative to the time that a break remains free, about four minutes. The results show that within these time limits, temperature is effective during treatment only, and not if applied before or after treatment. It was also found that change of temperature in either direction immediately preceding treatment increases considerably the number of aberrations. A temperature gradient may subsist in the material as a result of such a temperature change, and this gradient can cause thermal diffusion leading to movement of the chromosome threads. The effect may thus be parallel to that observed when cells are centrifuged during irradiation. (NSA)

2024

Fabergé, A. C. CHROMOSOME ABERRATIONS IN TRADESCANTIA PRODUCED BY X-RAY TREATMENT AT LIQUID AIR TEMPERATURE. Genetics **33**, 609 (1948).

A technique has been devised for freezing ripe *Tradescantia* pollen down to liquid air temperature, about -192°C. This pollen can be subsequently germinated on standard medium, and metaphase chromosomes observed at the division of the generative nucleus in the tube. Liquid air treatment by itself has no observable effect on subsequent division, which appears quite normal in every way. If X-ray treatment is applied to pollen while it is in liquid air, chromosome breaks and aberrations are produced which, qualitatively, do not seem to differ from those obtained by X-raying at room temperature. The number of breaks and aberrations is, however, several times less than would be the case at ordinary temperature, and to get a comparable frequency, a very much heavier X-ray dose

has to be used. This decreased sensitivity is quite different from the effects within the physiological range of temperature observed in *Tradescantia* microspore divisions. In this range (about +2°C to +35°C) more aberrations are produced at lower temperatures, as has been shown by several workers. It is hoped that this method, by eliminating chromosome movement and presumably also restitution, may simplify some of the problems of radiation cytology. (G)

2025

Fabergé, A. C. CHROMOSOME BREAKAGE BY X-RAYS AT LOW TEMPERATURE AND THE RADIODECOMPOSITION OF WATER. *Genetics* 35, 104-5(1950).

A year ago data were presented at the meeting of this Society, showing that when *Tradescantia* pollen is X-rayed at liquid air temperature, the sensitivity of the chromosomes (as measured by the number of breaks observed in pollen tube divisions) is about one fifth of that at +25°C. Several intermediate temperatures have not been explored. The sensitivity curve has a dip in the region of 0°C., and thereafter falls gradually. Its general character resembles the curve of H₂O₂ production plotted against temperature, when water containing oxygen is X-rayed (Bonet-Maury and LeFort, 1948, *Nature* 162: 381-382) but differs in that H₂O₂ production stops completely below -116°C., whereas chromosome breaks are still produced at -192°C. All previously reported effects of temperature on the X-ray sensitivity of *Tradescantia* chromosome could be explained in terms of restitution and rejoining. The author believes that the effect now described is not of the kind, and occurs largely or entirely at the level of the chemical steps which intervene between ionization and chromosome breakage. X-ray action can still usefully be regarded as particulate, and a target theory is still possible, but a factor must be added to take into account the spread of effect around ionization columns. (G)

2026

Fabergé, A. C. RELATION BETWEEN THE ACTION OF COLD AND OF NITROGEN IN DECREASING THE FREQUENCY OF CHROMOSOME ABERRATIONS. *Genetics* 35, 663(1950).

Two methods drastically reduce chromosome breaks produced by X-rays in *Tradescantia*. One can irradiate at a very low temperature (Fabergé, 1948, *Genetics* 33:609) or in the absence of oxygen (Thoday and Read, 1947, *Nature* 160:608; Giles and Riley, 1949, *P.N.A.S.* 35:640-646). The order of magnitude is the same. There is a parallelism between the amount of H₂O₂ produced by X-rays at various low temperatures and chromosome sensitivity (Fabergé 1950, *Genetics* 35:104-105); H₂O₂ production also depends on oxygen. Experiments are now reported in which both agencies are applied, the material being *Tradescantia* pollen, later germinated to observe tube mitoses. Pollen was placed in a stream of either dry air or nitrogen, at room temperature, for 10 minutes before irradiation. During irradiation the gas streams continued. Nitrogen reduces sensitivity if irradiation is conducted at +20°C, but has no detectable action if irradiation is done at -191°C. It is the writer's view that information accumulated from the irradiation of *Tradescantia* shows the traditional antithesis between direct and indirect action to lack realism. Experiments with oxygen and with extreme cold strongly suggest an indirect chemical step. This might represent spread of effect around an ionisation cluster. In terms of formal Target theory, a factor of 5× in sensitivity represents a change of only 1.7× in linear dimensions so that there is no occasion to abandon geometrical theories, at least in principle. (G)

2027

Fabergé, A. C. ULTRAVIOLET INDUCED CHROMOSOME ABERRATIONS IN MAIZE. *Genetics* 36, 548-9 (1951).

A comparison has been made between the effects of 2537A. Ultraviolet radiation and of medium hard X-rays on the chromosomes of *Zea mays* endosperm. Pollen carrying four linked dominant markers, I, Sh, Bz, Wx, all affecting endosperm characters, was treated and used for pollinating plants recessive at these loci. By the detailed analysis of the mosaic patterns obtained, a method due to McClintock, several kinds of chromosome aberrations can be identified. Information obtained by this method is different from that given by standard cytological examination. All four markers are located in the short arm of the 9th chromosome, which represents only 2.7% of the pachytene length of the entire complement. Only aberrations involving this marked arm are identified. No aberrations are missed because of selection since even the complete absence of this entire arm is viable under these circumstances. Simple deficiencies can be recognized, and breakage-fusion-bridge cycles initiated at any point distal to Wx. With certain limitations, rings, dicentric translocations and inversions if accompanied by a breakage-fusion-bridge cycle can be identified. Ultraviolet radiation produces all of these aberrations in large numbers. One of the most common effects is the production of breakage-fusion-bridge cycles. The same is true of X-rays. At the time of writing this summary, no consistent differences between X-rays and ultraviolet have appeared, though the analysis of further data may reveal such differences. It is particularly desired to emphasize that these conclusions apply only to maize endosperm. (G)

2028

Ford, C. E. CHARACTERISTIC DIFFERENCES IN THE PRODUCTION OF CHROMOSOME STRUCTURAL CHANGES BY NITROGEN MUSTARD TREATMENT AND BY IONISING RADIATIONS, p.46-7 of INTERNATIONAL CONGRESS OF RADIOLOGY, 6th Congress, London. 1950.

A detailed comparison of the chromosome breaks and rearrangements (structural changes) produced in *Vicia faba* root tips by nitrogen mustard and by gamma rays has revealed a number of characteristic differences which are considered to be incompatible with a common mode of action of the two agents. These differences are as follows:— Although the two agents cannot be distinguished by the types of structural changes produced, there are marked differences in the ratios of the frequencies of the different type. For instance, nitrogen mustard treatment yields a much lower proportion of simple chromatid breaks and a much higher proportion of minute fragments as compared with gamma radiation. Structural changes occur as early as 1½ hours after irradiation, whereas they are not found until 4 hours after nitrogen mustard treatment. At temperatures of 1°-5°C. the usual types of structural change are found after irradiation; after nitrogen mustard treatment none have been found so long as the low temperature is maintained. But if seedlings treated with nitrogen mustard at 1°-5°C. are subsequently warmed to 20°C. structural changes soon appear in the metaphase chromosomes. These facts are accounted for if: (i) after the onset of prophase the nitrogen mustard (unlike X-rays) is unable to bring about structural changes identifiable at the immediately following metaphase; (ii) at low temperature only those nuclei which have already entered prophase complete mitosis; (iii) at low temperature mitosis is greatly protracted. By far the great majority of the chromosome

breaks induced by nitrogen mustard treatment occur in one or other of a number of short regions which appear to coincide with the median heterochromatin of the short chromosomes. Gamma ray breaks, to a first approximation, are distributed uniformly over the whole chromosome complement.

2029

Garde, Alberto. **SOME CYTOLOGICAL OBSERVATIONS OF X-RAY ACTION ON *TRITICUM MONOCOCCUM*.**

Agronomia Lusitana 10, 25-73(1948).

The author makes a survey of the literature dealing both with natural and artificial radiations and their genetic and cytological effects. The importance of the use of x-rays together with other agencies is discussed, putting special emphasis on chemical substances. The writer in his experiments used lead acetate before x-irradiation. He concluded that: (1) Lead acetate per se, leads only to agglutination and total or partial dissolution of the matrix substance. (2) The supplementary treatment of *Triticum monococcum* root-tips with 1% aqueous solutions of lead acetate decreases the total percentage of chromosome aberrations due to x-rays. Fragment percentage decreases, whereas translocations percentage is not affected or very slightly increased. (3) The main effect of the secondary radiation of lead submitted to x-rays seems to be mutagenic. Different cases of chromosome aberrations are described (delay of division after treatment, cells with an abnormal number of chromosomes, tri- and tetrapolar spindles, fragments, dicentric chromosomes, anaphase bridges, etc.). From these observations the writer concludes that: (1) The type of dicentrics with the two centromeres very near one another seem to be more persistent than any other throughout cell division. The writer thinks that perhaps the closeness of the two centromeres may produce an effect leading to their behavior as a single element. (2) Resistance of the chromosomes of *Triticum monococcum* L. to x-rays seems to be different for different pairs. SAT chromosomes are the most resistant. (3) The centromere plays a very important part in chromosome reaction to x-rays. 113 references. (NSA)

2030

Gaulden, Mary Esther and Marjorie Nix. **EFFECTS OF OXYGEN TENSION ON X-RAY INDUCED MITOTIC INHIBITION.** Genetics 35, 665(1950).

This paper is reproduced here in its entirety.

The large neuroblast cells of the embryo of the grasshopper *Chortophaga viridifasciata* were given 64 r of x rays while exposed to different tensions of oxygen, namely 100%, 21% (air), 2% and 0% (nitrogen, carbon dioxide, or vacuum). The embryos were made into culture preparations. The number of cells in midmitosis (prometaphase, metaphase, and anaphase) was recorded every 22 minutes for 6 hr after treatment. Thus the number of cells completing mitosis was determined, since 22 min is the average duration of mid-mitosis (at 38°C) and since the treatments used do not affect this duration. The results indicate that the sensitivity of mitosis to radiation is reduced when cells are irradiated at the lower oxygen tensions. In other words, the duration of the period of complete mitotic inhibition (period after irradiation during which there are no cells in the mid mitotic stages) is shorter when cells are irradiated in 0 or 2% oxygen than when they are irradiated in 21 or 100% oxygen. Experiments are now in progress to determine the sensitivity of cells to radiation in 5 and 10% oxygen. (NSA)

2031

Gelin, O. E. V. **THE CYTOLOGICAL EFFECT OF DIFFERENT SEED TREATMENTS IN X-RAYED BARLEY.**

The author uses exclusively Golden Barley series 1939: I: 21-24, irradiated with 10,000 r (voltage 160 kv, 7.5 ma, 4 Al, 72 r/min). The pretreatments were as follows: I:21, the seeds contained 10% water; I:24, 15% water; I:22, the seeds were treated with distilled water for 23 hours previous to the x-raying in order to induce germination; I:23 the seeds were treated with 0.01% of a heteroauxin solution for 23 hours for the purpose of still further enhancing gemination. The reaction of the chromosomes is directly influenced by the physiological condition of the seeds. Seeds containing 10% water show 12.66% disturbed divisions, seeds with 15% water 27.99%, and seeds soaked 23 hours in water or in 0.01% hetero-auxin solution 53.80 and 50.99% disturbances, respectively. The disturbed cells show probably a random distribution in different parts of the roots. The cells that first enter into division show the highest frequency of disturbances. If the percentage of cells with fragments and the percentage of cells with bridges are computed in proportion to the total number of analyzed cases, two numerical series are obtained showing good proportionality, approximately the ratio is 1: 2: 4: 4. The frequency of bridges seems to be $\frac{1}{3}$ of the disturbed cells. The proportion of bridges and fragments is, generally speaking, the same in all division classes. There is a marked parallelism between the percentages of disturbed cells, sterility and mutation rate. The most evident feature is that the same proportionality existing between the percentages of disturbed cells in the different series is also found in the percentage of mutations, viz. approximately 1: 2: 4: 4. (S.V.S.)

2032

Giese, A. C. **RADIATIONS AND CELL DIVISION.** Quart. Rev. Biol. 32, 253-82(1947).

A review with about 300 references, including chemical mechanism of cell division. (NSA)

2033

Giles, Norman H., Jr. **THE EFFECTS OF FAST NEUTRONS ON THE CHROMOSOMES OF TRADESCANTIA.** Proc. Natl. Acad. Sci. U. S. 26, 567-75(1940).

Qualitatively there is no difference in neutron and x-ray treatment. Quantitatively, for equal total doses in terms of ionization as measured with a bakelite Victoreen "r" meter, neutrons are from 16-17 times as effective as x-rays in producing chromatid dicentric aberrations. Also, exchange break aberrations, producing chromatid and chromosome rings and dicentrics, show an approx. linear relationship to dosage instead of the exponential relation found with x-rays. This difference may result from the great difference in the types of ionization paths produced by neutrons and x-rays. (BA)

2034

Giles, Norman H., Jr. **COMPARATIVE STUDIES OF THE CYTOGENETICAL EFFECTS OF NEUTRONS AND X-RAYS.** Genetics 28, 398-418(1943).

Comparative effects of neutrons and x-rays were investigated in *Tradescantia paludosa* by a cytological analysis of chromosomal rearrangements induced in the developing microspores. Neutrons and x-rays produced the same qualitative types of rearrangements, but differed in their quantitative effects. For equal total tissue doses of ionization, neutrons were more efficient than x-rays in breaking chromosomes. Furthermore, under the conditions of dosimetry used, neutrons of lower average energy (7.5 Mev) were more efficient than those of higher average energy (15 Mev). Apparently, several ionizations are necessary to break a *Tradescantia* chromosome. For all types of rearrangements induced by neutrons, the relation between dosage and effect was approximately linear, and

there was no time-intensity factor. These results differ from those obtained with x-rays and indicate that most neutron-induced exchanges are produced by single proton ionization paths. Comparative ratios of certain aberration types induced during resting stage and prophase provided evidence that space factors limit the reunion of both neutron and x-ray induced broken chromosome ends. In *Drosophila melanogaster*, neutrons were less efficient than x-rays in inducing sex-linked lethal mutations. This effect is discussed and interpreted in comparison with the results in *Tradescantia* and with those obtained by previous investigators in *Drosophila*. (BA)

2035

Giles, Norman H. CHROMOSOME STRUCTURAL CHANGES IN TRADESCANTIA MICROSPORES PRODUCED BY ABSORBED RADIOPHOSPHORUS. Proc. Natl. Acad. Sci. U. S. 33, 283-7(1947).

Cut *T. paludosa* inflorescences were inserted in various concentrations of radiophosphorus (from 100 $\mu\text{C}/\text{ml}$ to 0.1 $\mu\text{C}/\text{ml}$) for periods of 1 to 9 days. A count was made of cytological changes at the first post-meiotic (microspore) mitosis. The types of aberrations resulting from beta-radiations inside the plant were similar to those caused by neutrons and x-rays. Their frequency shows an increase with time and correlates with the increase in radioactivity measured with an electroscope. Within 24 hours chromatid aberrations were observed and remained the principle type. Chromatid exchanges occurred with a relatively high frequency. It was not until the fourth day that chromosome breaks were observed. At the highest concentration (100 $\mu\text{C}/\text{ml}$) the frequency of one-hit chromatid aberration types after 24 hours was equivalent to that produced by about 40 r of x-rays; the very high breakage rate prevented aberration frequency counts after about 48 hours. (NSA)

2036

Giles, Norman H., Jr. RECENT EVIDENCE ON THE MECHANISM OF CHROMOSOME ABERRATION PRODUCTION BY IONIZING RADIATIONS. Oak Ridge National Lab. Aug. 29, 1950. (ORNL-811)

Recent experiments have demonstrated that oxygen has a marked effect in increasing the sensitivity of chromosomes in *Tradescantia* and other plants to x-rays, as measured by the frequency of cytologically detected aberrations. It has been shown that this is not an effect of oxygen itself on the behavior of broken ends of chromosomes. The effect apparently arises from the production by x-rays, as a result of the radiodecomposition of water in cells containing oxygen, of some substance which causes an increase in aberration frequency. Several independent lines of evidence indicate that this substance may be H_2O_2 . It appears likely that the increased frequency of aberrations arises from an increased production of chromosome breaks when oxygen is present during irradiation, rather than from a modification of the recovery process. Thus a major fraction of the radiation effect on *Tradescantia* chromosomes is to be considered indirect rather than direct. (NSA)

2037

Giles, Norman H. and A. V. Beatty. THE EFFECT OF X-IRRADIATION IN OXYGEN UNDER PRESSURE ON CHROMOSOME ABERRATION FREQUENCY IN TRADESCANTIA MICROSPORES. Genetics 35, 666-7(1950).

Inflorescences of *Tradescantia paludosa*, clone 5, were exposed to 400 r of x-ray at 50 r per minute in atmospheres of 5% and 10% O at normal atmospheric pressure (740 mm.) and at positive pressures of 1, 2, and 3 atmospheres above normal. Similar exposures were made in He and in air (21% O) at normal pressure and at 3 atmospheres above normal. The frequency of both chromosome

interchanges (dicentric and centric rings) and interstitial deletions were determined from slides of the 1st post-meiotic mitosis prepared on the 4th and 5th days following irradiation. The exposures in He indicated that these pressures alone did not alter aberration frequencies. Exposures in 5%, 10%, and 21% O at the different pressures produced aberration frequencies similar to those obtained in comparable partial pressures of O. For example, the effect of 5% O at 1 atmosphere above normal is comparable to that in 10% O at normal pressure. From these and previous results it is evident that O increases x-ray induced chromosome aberrations and that the x amount of O present at the time of exposure determines the extent of the effect. Since no pressure effect was obtained in these experiments in the absence of O, the effect of pressure in the presence of O apparently is, in reality, an O effect.

2038

Giles, Norman H., Jr. and A. V. Beatty. EFFECT OF X-IRRADIATION IN OXYGEN AND IN HYDROGEN AT NORMAL AND POSITIVE PRESSURES ON CHROMOSOME ABERRATION FREQUENCY IN TRADESCANTIA MICROSPORES. Science 112, 643-5(1950).

Aberrations are produced by irradiation in a system containing microspores of *Tradescantia paludosa* in the complete absence of O_2 . A linear increase in the frequency of aberration occurrence results with O_2 between 0% and 10%, leveling off at 20% concentration. At pressures of 1, 2, and 3 atmospheres no further change in aberration frequency occurred following irradiation at all O_2 concentrations employed. Results of H_2 gas in place of the He under the same conditions were similar. The failure to find a significant decrease in aberration frequency when x-irradiation is performed in H_2 may mean that all the residual aberrations induced by x-rays in the absence of O_2 arise as a result of a direct effect of the radiations on the chromosomes. (CA)

2039

Giles, Norman H., Jr., Alvin V. Beatty, and Herbert Parkes Riley. THE RELATION BETWEEN THE EFFECTS OF TEMPERATURE AND OF OXYGEN ON THE FREQUENCY OF X-RAY-INDUCED CHROMOSOME ABERRATIONS IN TRADESCANTIA MICROSPORES. Genetics 36, 552-3(1951).

Inflorescences were irradiated in experiments in which the amount of dissolved oxygen was varied over a similar range in terms of volumes per cent in two different ways: (1) by using a constant percentage of O_2 (5% O_2 plus 95% helium) and making a series of exposures at several different temperatures, between 0.6° and 40°C., and (2) by using a constant temperature (27°C.) and varying the percentage of O_2 in the exposure chamber. Cytological analyses were made of chromosomal aberration types at the four- to five-day interval following irradiation. Exposures were also performed in the absence of oxygen (in pure nitrogen) at various temperatures. The experiments in O_2 demonstrate that the increased yield of aberrations at low temperatures cannot be attributed entirely to increased oxygen solubility. There is a considerable additional effect of temperature itself. In the absence of oxygen, the unexpected result was obtained that the effect of temperature is exactly opposite to that noted in the presence of oxygen—the yield of aberrations is considerably higher than at low temperatures. This situation is true not only for chromosome aberrations but also for all types of chromatid effects. It seems probable that temperature exerts its effect, at least in the presence of oxygen, on either the formation or effectiveness of some substance (or substances) produced in the cell by the radiation and responsible for chromosome breakage. (G)

2040

Giles, Norman H., Jr. and Rene A. Bolomey. CYTO-GENETICAL EFFECTS OF INTERNAL RADIATIONS FROM RADIOISOTOPES. Cold Spring Harbor Symposia Quant. Biol. 13, 104-12(1948).

The results of a cytological analysis to determine the amount of change caused by radiations from isotopes in *Tradescantia* buds and microspore nuclei grown on radiophosphorus, P^{32} , media and in some cases C^{14} media are presented. The rates of uptake of P^{32} and C^{14} , the chromosomal rearrangements produced by the β radiation from these isotopes, and reliability of the available techniques are discussed. (NSA)

2041

Giles, Norman H., Jr. and Alan D. Conger. CHROMOSOMAL INTERCHANGES INDUCED IN TRADESCANTIA MICROSPORES BY FAST NEUTRONS FROM URANIUM FISSION. J. Cellular Comp. Physiol. 35, (Suppl. 1) 83-8 (1950).

Inflorescences of *Tradescantia paludosa* (Sax, clone No. 5) were exposed to fast neutrons from uranium fission, utilizing a special exposure device in the Oak Ridge pile, and the yield of chromosomal interchanges (dicentric and centric rings) was determined in microspore nuclei on the 4th and 5th day following irradiation. A linear relationship was found between neutron dose and interchange frequency, confirming previous evidence that fast neutron induced interchanges are one-hit phenomena. Further evidence has been obtained that the interchange yield for a given ionization dose is inversely related to the energy of the fast neutrons utilized. This relationship can be interpreted in terms of differences in ionization distribution within nuclei. The greater efficiency of less energetic fast neutrons is in accord with the view that several ionizations are required to produce a chromosome break in *Tradescantia*. (NSA)

2042

Giles, Norman H. and Nebel, B. R. AN ANALYSIS OF THE INTENSITY FACTOR IN X-RAY INDUCED CHROMOSOMAL ABERRATIONS IN TRADESCANTIA. Genetics 27, 142-3(1942).

In a series of experiments developing microspores of *Tradescantia* were given equal total doses (308 roentgens) of X-rays at widely different intensities, from 1.3 to 1200 r/min. At the 4-5 day period following irradiation smears were made for an analysis of the percentages of translocations (dicentric and ring types) and of interstitial deletions—small acentric rings according to Rick and Sax (isodiametric fragments in the terminology of Nebel, Wilson and Marinelli) induced during the resting stage at the various intensities. At 50 r/min. and above (150, 600, and 1200 r/min.) the percentage of aberrations in both classes remains approximately constant—there is little or no intensity effect. At lower intensities (20, 10.3, 5.2, 2.5, and 1.3 r/min.) the percentage of aberrations in both classes decreases progressively, but not linearly with decreasing intensity, until at 1.3 r/min. the number of aberrations per cell is somewhat less than half that found at intensities of 50 r/min. and higher. These results are in accord with the hypothesis that the chromosomal aberrations types studied result from two independent potential breaks, and that the reunion of broken ends, occurs during the resting stage. Within a certain time following the initial breakage. When this time is exceeded restitution occurs. (G)

2043

Giles, Norman H., Jr. and Herbert Parkes Riley. THE EFFECT OF OXYGEN ON THE FREQUENCY OF X-RAY

INDUCED CHROMOSOMAL REARRANGEMENTS IN TRADESCANTIA MICROSPORES. Proc. Natl. Acad. Sci. U. S. 35, 640-6(1949).

Comparative exposures of *Tradescantia paludosa* to x-rays were made in air, helium, argon, nitrogen and oxygen, and observations were made on chromosomal changes (interchanges and interstitial deletions) at the first post-meiotic mitosis in the microspores by means of acetocarmine smear preparations at the 4th or 5th day after irradiation. The x-ray source was a Coolidge self-rectifying tube with a tungsten target and operated at 250 kv; the filtration was 3 mm Al plus added filtration through a 0.25 in. lucite exposure chamber, and the dosage rate was usually 45 r/min. Total doses of 90, 180, 270, or 360 r were given. It was found that the frequency of aberrations was strikingly reduced when nitrogen replaced air and increased when oxygen replaced air as the medium; the number of aberrations in the oxygen medium was five times that in the nitrogen medium; aberration frequencies were also reduced in additional exposures in other gases such as helium and argon. The availability of oxygen is considered an important factor in the production of chromosomal changes by irradiation. (NSA)

2044

Giles, Norman H., Jr. and Herbert Parkes Riley. STUDIES ON THE MECHANISM OF THE OXYGEN EFFECT ON THE RADIOSENSITIVITY OF TRADESCANTIA CHROMOSOMES. Proc. Natl. Acad. Sci. U. S. 36, 337-44 (1950) (ORNL-688)

Previous experiments by the authors have demonstrated that the radiosensitivity of *Tradescantia* chromosomes, as measured by the occurrence of x-ray induced aberrations in microspores, is markedly influenced by the amount of oxygen present. Further experiments are reported here. Exposures of inflorescences to a single constant x-ray dose, but in atmospheres containing seven different percentages of oxygen, indicate that there is a rapid rise in aberration frequency between 2 and 21% oxygen, with a gradual increase thereafter. Further studies are being made to clarify the effect of oxygen at levels between 0 and 2%. Other experiments have been performed to determine whether the oxygen effect is exerted by way of the initial breakage mechanism or on the reunion process. These consisted of comparative exposures to a single dose of 300 r in one minute of inflorescences in a vacuum or in oxygen with the addition or removal of oxygen either immediately after or during part of the irradiation period. The experiments show that the presence or absence of oxygen during the actual exposure to x-rays rather than during the post-irradiation period is the important factor, thus demonstrating that the effect of oxygen in increasing the radiosensitivity of *Tradescantia* chromosomes results from an increased production of initial breaks rather than from an influence on the reunion of broken ends. (NSA)

2045

Glucksmann, A. and F. G. Spear. THE EFFECT OF GAMMA RADIATION ON CELLS IN VIVO. II. (1) SINGLE EXPOSURES OF THE FASTING TADPOLE AT ROOM TEMPERATURE. (2) SINGLE EXPOSURES OF THE NORMAL ANIMAL AT LOW TEMPERATURE. Brit. J. Radiol. 12, 486-98(1939).

In the tadpole, mitotic activity can be varied by fasting and by low temps. Tadpoles were used 3 to 6 weeks after hatching, when they were 1.5 to 2.0 cm long, and all at about the same stage of development. They were irradiated with 268 r of γ rays throughout their vol., and then complete serial sections were made of the fixed specimen. Mitotic counts

were made and also counts of the number of degenerate cells (assumed to be the result of radiation). After 1 week's fasting, when there is still some mitosis present, irradiation is followed by the appearance of degeneration in the germinative zone. After 2 weeks fasting, when mitosis is further reduced, radiation is followed by very much less degeneration. Feeding is followed by the appearance of degeneration with the first 15 hrs. of giving food and by the appearance of mitosis after an interval of 5 days. In the absence of radiation, mitosis reaches a higher level on this 5th day. In the chillings expts. alteration in the mitotic count is proportional to the reduction in temp. With a dose of radiation sufficient to produce a marked degeneration in animals at room temp., no degenerate cells are seen as long as the animal is kept chilled. If the animal is brought to room temperature, degenerate cells appear after about 6 hours. Results are similar whether animals are irradiated at low or at room temp. (BA)

2046

Graul, E. H. EXPERIMENTS ON THE IRRADIATION OF LIVING PROTOPLASM OF THE CELL: X-RAY EFFECTS ON EXTRANUCLEAR CELL CONSTITUENTS, p.172 of INTERNATIONAL CONGRESS OF RADIOLOGY, 6th Congress, London. 1950.

The primary biological processes caused by irradiation (ultraviolet and X-rays) are discussed in terms of nuclear and extranuclear processes. A series of experimental results shows that with UV radiation extranuclear effects predominate. The cell membrane, the microsomes, mitochondria and chondrosomes are the structures chiefly involved and our results are discussed in relation to the target theory of Timofeeff-Ressovsky. Changes in the electric properties of the cell membrane are also described. The significance of the amount of current flowing at audiofrequencies in relation to the primary biological response is considered. By UV irradiation of the sharply defined germ layers of *Triton alpestris* (using our modification of the fine beam method) further evidence is given of the importance of the reaction of extranuclear cell structures to radiation. This evidence is supported by a discussion of results of experiments on haemolysis.

2047

Gray, L. H. and John Read. THE EFFECT OF IONIZING RADIATIONS ON THE BROAD BEAN ROOT. VII. THE INHIBITION OF MITOSIS BY ALPHA RADIATION. Brit. J. Radiol. 23, 300-3(1950).

Broad bean roots were irradiated with α particles by immersion in radon solutions; the dose was 12 to 237 energy units (1 energy unit = 1.1 roentgen equivalent physical = 93 ergs/g tissue) delivered over a period of 20 to 90 minutes. Tips were fixed 3 hr afterward and the number of cells seen in mitosis compared with control roots. When the logarithm of the percentage residual mitosis was plotted against the dose, the points defined a straight line. These results are compared with similar results obtained previously with neutron and γ rays. The ratio of the slopes of the neutron and α ray lines is the inverse of the ratio of the linear ion densities, suggestive of an effect brought about by a single recoil proton or an α particle. The relative efficiencies of γ rays, neutrons, and α rays in reducing the number of cells seen in mitosis in the bean root 3 hr after irradiation are 1:2.1:0.6, whereas the corresponding figures for the lethal effect are 1:9:9. (NSA)

2048

Heinrich, H. L., W. Paul, and G. Schubert. THE EFFECT OF X RADIATION AND RAPID ELECTRONS (4-MEV) ON MITOSIS IN ROOT ENDS OF *VICIA FABA*. Naturwissenschaften 37, 544-5(1950).

Roots of *Vicia faba* were x-radiated with 150, 300, 450, and 600 r, 250 r/min or exposed to rapid electrons of Göttingen's atom reactor, and investigated after 72 hr. Chromosomes suffered increasing shortening, mitoses decreased in number, and number of damages of cells in telo- and anaphases increased with increasingly stronger doses. Rapid electrons were less effective than x rays. (NSA)

2049

Helfer, R. G. A COMPARISON OF X-RAY INDUCED AND NATURALLY OCCURRING CHROMOSOMAL VARIATIONS IN *DROSOPHILA PSEUDOOBSCURA*. Genetics 26, 1-22(1941).

The distribution of 347 breaks induced by x-ray treatment in the chromosomes of *Drosophila pseudoobscura* was studied. The frequencies of the breaks in the different chromosomes are in proportion to their relative lengths. The induced breaks in the third chromosome are not distributed entirely at random. The frequency of the breaks in the heterochromatin as compared with those in the euchromatin is much greater than would be expected on the basis of the lengths of the heterochromatic portions in the salivary gland cells but probably smaller than would be expected on the basis of its length in the mitotic chromosomes. Within the euchromatic portions the frequency of breaks increases slightly from the proximal to the distal end. Aside from the regularity mentioned above, the breaks in the third chromosome show no tendency to be concentrated around and "weak points." In any case, a comparison of the induced breaks with those observed in the naturally occurring chromosomal aberrations shows very few coincidences. None of the inversions induced by x-ray treatment proved similar to any of the naturally occurring inversions. The reunion of the chromosome fragments produced by x-ray treatment is not at random, inversions being more and translocations less frequent than expected. Several mosaic chromosomal aberrations are described. An analysis of these aberrations seems to argue in favor of the breakage first, rather than the "contact" hypothesis of the origin of chromosomal aberrations. (auth)

2050

Henshaw, Paul S. THE ACTION OF X-RAYS ON NUCLEATED AND NONNUCLEATED EGG FRAGMENTS. Am. J. Cancer 33, 258-64(1938).

Eggs of *Arbacia punctulata* were irradiated with the following conditions: 195 kv, 150 pv, 30 ma, 4 mm Bakelite filter, 9.5 cm from target to material, making the intensity of irradiation at the point of exposure approximately 7,600 r/min. Usually 45 sec or a dose of 5,700 r was selected as the duration of exposure. Three types of material were used: normal whole eggs, nucleated light parts, and non-nucleated heavy parts. These were irradiated and inseminated and the moment when 50% had divided was determined. It was found that for a given dose of radiation an appreciable delay in cell division of about the same extent was produced in whole eggs and nucleated fragments, whereas no delay was produced in the non-nucleated fragments. It appears that the slowing in cell division brought about in *Arbacia* eggs by x-rays is due to changes produced directly in the nucleus by radiation. (S.V.S.)

2051

Henshaw, Paul S. FURTHER STUDIES ON THE ACTION OF ROENTGEN RAYS ON GAMETES OF *ARBACIA PUNCTULATA*. I. DELAY IN CELL DIVISION CAUSED BY EXPOSURE OF SPERM TO ROENTGEN RAYS. II. MODIFICATION OF THE MITOTIC TIME SCHEDULE IN THE EGGS BY EXPOSURE OF THE GAMETES TO

ROENTGEN RAYS. III. FIXATION OF IRRADIATION EFFECT BY FERTILIZATION IN THE EGGS. IV. CHANGES IN RADIOSENSITIVITY DURING THE FIRST CLEAVAGE CYCLE (with cooperation of I. Cohen). V. THE INFLUENCE OF LOW TEMPERATURE ON RECOVERY FROM ROENTGEN RAY EFFECTS IN THE EGGS. VI. PRODUCTION OF MULTIPOLAR CLEAVAGE IN THE EGGS BY EXPOSURE OF THE GAMETES TO ROENTGEN RAYS. *Am. J. Roentgenol. Radium Therapy* 43, 899-933(1940).

Normal eggs of *Arbacia punctulata* were fertilized with sperm exposed to doses of hard x-rays up to 500,000 r, and the time between insemination and first cleavage noted. The interval was increased by irradiation, the amount of the delay varying exponentially with the exposure. Fertilization was prevented only by doses in excess of 300,000 r. The exposure of either the sperm or the eggs of *Arbacia punctulata* to 62,400 r of hard x-rays did not retard the entrance of the sperm into the egg or its movement through the egg cytoplasm and fusion with the egg nucleus. All phases of the mitotic part of the 1st cleavage cycle were delayed, the prophase to the greatest extent. The eggs were irradiated with 28,800 or 14,400 r of soft x-rays, and fertilized at varying intervals up to 3 hours after irradiation; the delay was somewhat less when the fertilization did not take place until some time after the irradiation, indicating a recovery from the radiation effect. All possible combinations of normal and x-irradiated eggs and sperm of *Arbacia punctulata*, and the zygote irradiated at various minutes up to 45 min. after insemination, were studied for delay in cleavage time. The eggs were more susceptible than the sperm, for doses of 7800-31,200 r. For equal doses of radiation the effect on the zygote was greater than on either gamete and about equal to that on both of them. The zygote increased in radiosensitivity until the pronuclei fused, then decreased during the prophase stage. There was no apparent correlation between change of radiosensitivity and rate of O_2 uptake. Irradiated eggs kept at $0^\circ C$ showed longer delay in cleavage time after insemination than those kept at $24^\circ C$. In addition to the delay in cleavage time, described in preceding studies, abnormal cleavage was often produced by x-irradiation; multipolar cleavage being produced in a high % of individuals if the dose was large enough. Since chromatin deficiency usually results in cell death, it is possible that one of the mechanisms by which radiation causes cell death is the production of accessory asters, resulting in abnormal chromatin distribution at mitosis. Chromatin modification may be a plausible explanation of cancer; this may be an indication of the mechanism by which radiation may produce cell death on the one hand, and cancer on the other. (BA)

2052

Hoffman, R. S. and S. H. Wollman. EFFECT OF X-RAYS ON THE MIGRATION OF CELLS FROM ADULT TISSUE EXPLANTS. *Proc. Soc. Exptl. Biol. Med.* 70, 38-40(1949).

To test the effect of radiation dosages on the latent period before the appearance of cell migration, tissue preparations from adult chicken cardiac muscle were irradiated at a rate of 25 r/min. by a 180-kv machine, filtration of 0.5 mm Cu and 1.65 mm Al, at a distance of 50 cm giving a total dose of 0 to 500 r. Results are presented graphically showing the per cent of explants showing a single migratory cell between 15 and 45 hours after irradiation and the variation of time before appearance of a migratory cell with the dosage. The authors conclude that irradiation with less than 30 r stimulates migration of cells from fresh explants and, irradiation of more than 30 r shows a gradually more extended latent period; this suggests a superimposed inhibition, which does not exceed the excitation effect until dosages go over a 1,000 r level. (NSA)

2053

Hohl, K. COMPARATIVE INVESTIGATIONS OF THE EFFECTS OF X RAYS AND CHEMICAL SUBSTANCES ON MITOSIS. *Radiol. Clin.* 17, 302(1948).

Experiment established the possibility of disturbing the process of mitosis without damaging resting cells. The effects of radiation and several antimitotic chemicals are described in detail. The antimitotic chemicals attack either specific chemical reactions in the mitotic sequence (colchicine) or the albumin metabolism in an unknown way. The target effect is common to both x-rays and chemical substances (nitrogen mustard). (M.F.)

2054

Kaufmann, Berwind P. INDUCED CHROMOSOMAL BREAKS IN *DROSOPHILA*. *Cold Spring Harbor Symposium Quant. Biol.* 2, 82-92(1941).

Salivary gland chromosomes of the *Diptera* provide unique and unparalleled material for quantitative studies of the effects of irradiation. In *Drosophila* such analyses have shown that breaks are distributed at random along the chromosomes except for the proximal heterochromatic region and for similar intercalary regions. The data are in harmony with the theory that breaks in a given region occur in proportion to the length represented by that region during late prophase or metaphase of mitosis. Changes induced in the chromosomes of the sperm are not effective at once in producing rearrangements and probably not until the male pronucleus is formed within the egg. Several lines of evidence indicate that these changes represent potential breaks. The suggestion is offered that they may only be effective if combination with other similar regional alterations is realized. Recombination is not entirely at random but is apparently favored by propinquity of the potential breaks so that when only a few breaks are involved it appears that a restricted recombination zone exists. Evidence from distribution of chromosome and chromatid breaks indicates that the chromosomes of the mature sperm consist of two separate chromatids, both of which can be severed at the same level by the effects of a single "ionization". The number of altered sperms does not increase linearly with the dosage. The frequency of breaks and the frequency of independent rearrangements produced at different dosage levels indicate that the increase follows more nearly the square of the dosage in the range between 1,000 and 5,000 roentgens. All of these findings support the concept that breakage precedes recombination rather than the concept that breakage and recombination are part of a single process and occur simultaneously. Neutrons give a similar or somewhat lower, but not a higher break frequency than x-rays of comparable dosage. These results may be due to a saturation effect being reached at lower doses with neutrons than with x-rays. (SVS)

2055

Kaufmann, Berwind P. EVIDENCE OF DELAY IN RE-ATTACHMENT OF CHROMOSOME FRAGMENTS FOLLOWING X-RADIATION OF SPERM OF *DROSOPHILA MELANOGASTER*. *Genetics* 26, 157(1941).

In order to determine the duration of any interval occurring between the time when chromosome breaks are induced and the time of recombination of the fragments, comparison has been made between the effects of a given dosage when administered continuously and in a series of fractions. Salivary chromosome analysis was used to measure frequency of breakage and types of rearrangements produced. The number of breaks detectable in the fraction-treated material should be lower than in control material if in the interval between successive doses some of the breaks "heal" to restore the original sequences and are therefore unable to participate with subsequently pro-

duced broken ends in the formation of chromosome rearrangements. Moreover, if recombination should occur between successive treatments, the fraction-treated material should show relatively fewer of the complex rearrangements involving a large number of broken ends than the controls. Results of the experiments (in which effects of a series of 1000 roentgen fractions at 24 hour intervals, and 2000 roentgen fractions at 16 day intervals were compared with the controls) indicate that such differences do not exist. The close correspondence between fraction and continuous treatment with respect to numbers of breaks suggests that no appreciable "healing" occurs even when the interval between successive treatments is 16 days. The presence of multiple-break, complex rearrangements following the fractionated dosage strengthens the evidence for the theory that breakage precedes recombination. (G)

2056

Kaufmann, Berwind P. THE TIME INTERVAL BETWEEN X-RADIATIONS OF SPERM OF DROSOPHILA AND CHROMOSOME RECOMBINATION. *Proc. Natl. Acad. Sci. U. S.* **27**, 18-24(1941).

Sperm of *D. melanogaster* were x-radiated with two equivalent doses, one applied continuously, the other fractionally. Comparable frequencies obtained with both types of treatment indicate that no appreciable "healing" occurs, even when the interval between successive fractions is 16 days. The presence of multiple-break, complex rearrangements following the fractionated treatment strengthens the evidence for the theory that breakage precedes reunion. (BA)

2057

Kaufmann, Berwind P. INFLUENCE OF TEMPERATURE ON CHROMOSOME RECOMBINATION FOLLOWING X-RAY-INDUCED BREAKAGE. *Records Genetics Soc. Am.* **12**, 50(1943).

Previous studies have indicated that the potential breaks induced in the chromosomes of the sperm of *Drosophila* by X-ray treatment are not utilized in producing new rearrangements until after the sperm has entered the egg. This separation in time between the periods of irradiation and recombination affords an opportunity to test experimentally the effects of various types of supplementary treatment on the chromosomal changes induced by the X-rays. In this short note are presented some of the results obtained by exposing females, after insemination by sperm from males treated with 4000 roentgens of X-radiation, to controlled temperatures of either 18°C or 28°C, or to the heating effects of near infrared irradiation. (The latter type of treatment was designed by Dr. A. Hollaender, and will be described in detail in a longer paper.) The effect produced by the combination treatment was measured by analysis of the salivary-gland chromosomes of the F_1 larval progeny of the treated parents. — The percentages of altered sperms and of chromosome breaks were found to be lowest (29.5 and 72.4 per cent respectively) following the 18° treatment, somewhat higher (31 and 80.8 per cent) after exposure to 28°, and highest (37.5 and 100.8 per cent) following the near infrared treatment. These results suggest, therefore, that increased temperature, within the range tested, is effective during the time that chromosome recombination is occurring in facilitating those movements that lead to the reunion of broken ends, or to the utilization of potential breaks induced by the X-ray treatment. (RG)

2058

Kaufmann, Berwind P. MODIFICATION OF THE FREQUENCY OF CHROMOSOMAL REARRANGEMENTS INDUCED BY X-RAYS IN DROSOPHILA. III. EFFECT

OF SUPPLEMENTARY TREATMENT AT THE TIME OF CHROMOSOME RECOMBINATION. *Genetics* **31**, 449-53(1946).

Eggs deposited by females of *D. melanogaster* that has been inseminated by males previously treated with 4,000 r of x-rays were exposed to near infrared radiation (λ ca. 10,000 Å) during the period of syngamy and early cleavage. A statistically significant increase, as compared with the effect of temperatures in the range from 18 to 28°C, was obtained in the frequency of chromosomal rearrangements detected by analysis of salivary-gland nuclei. The action of the near infrared in facilitating recombination among the breaks induced by the x-rays is attributed to selective action on certain cellular components rather than to an extension of the range of temperature within which fertility and viability may be maintained. (BA)

2059

Kaufmann, Berwind P. RADIATION INDUCED CHROMOSOME ABERRATIONS p.27-36 of CONFERENCE ON BIOLOGICAL APPLICATIONS OF NUCLEAR PHYSICS, JULY 12-27, 1948. Brookhaven National Lab. 10p. (BNL-C-4(p.27-36))

In this report an effort has been made to outline some aspects of the problem of induced structural rearrangement, especially as revealed by cytological studies of salivary gland chromosomes of *Drosophila*. The various types of induced breaks have been described, together with the patterns of recombination effected by the breakage ends. Analysis of break distribution has provided information concerning the organization of the chromosome, particularly with respect to its subdivision into euchromatic and heterochromatic regions. By using such agents as u-v and near-infrared rays in combination with x-rays, progress has been made in evaluating the breakage and recombination aspects of the process of structural alteration. These studies indicate that breaks fall into qualitatively different groups, and that the differences are reflected in the subsequent behavior of the breakage ends. Of the various types of supplementary treatment utilized, near-infrared radiation has proved most serviceable in analysis of the cycle of breakage and recombination. It has been found that this agent modifies the processes that lead to structural rearrangement of chromosomes, but not those responsible for gene mutation. Accordingly, near-infrared radiation may serve as a useful diagnostic tool, if applied to organisms in which cytological analysis is not feasible in distinguishing between genetic changes that are attributable to chromosomal alterations, and those that are not. The potentialities of this portion of the spectrum for further cytogenetic studies lie in the prospect of securing intense monochromatic radiation of known physical properties. (auth)

2060

Kaufmann, Berwind P. and Alexander Hollaender. ALTERATION OF THE FREQUENCY OF X-RAY INDUCED CHROMOSOMAL BREAKS BY USE OF ULTRAVIOLET AND NEAR INFRARED RADIATION. *Genetics* **30**, 11-12(1945).

(The following is an abstract and is reproduced here in its entirety.)

It appears possible, on theoretical grounds, to modify the capacity for reattachment of ends of chromosomes disrupted by ionizing radiation, if other types of supplementary treatment are given prior to the time that new combinations are established. *Drosophila* is well suited for experiments of this type, since the interval between irradiation of the spermatozoa and chromosome recom-

bination may be prolonged for many days by withholding the males from copulation. An extended set of experiments designed to measure such alterations in the frequency of detectable chromosomal breaks has now been largely completed. Ultraviolet and near infrared radiations were used following administration of the total x-ray dosage or in the interval between two fractional treatments. Determination of the frequency of breaks was made by analysis of salivary gland chromosomes. Ultraviolet radiation of wave length 2537Å following x-ray treatment induces a reduction in the percentage of altered sperms and in the number of breaks as compared with the controls, which received only an equivalent dose of x-rays. Similar reductions in the percentages of altered sperms and of chromosome breaks were obtained in some experiments in which the x-ray treatment was supplemented by near infrared radiation. The complete data cannot be presented here, but will form the basis of the demonstration, together with the designs of the special apparatus constructed for administering the ultraviolet and near infrared radiation.

2061

Kaufmann, Berwind P. and Alexander Hollaender. MODIFICATION OF THE FREQUENCY OF CHROMOSOMAL REARRANGEMENTS INDUCED BY X-RAYS IN *DROSOPHILA*. II. USE OF ULTRAVIOLET RADIATION. *Genetics* 31, 368-76(1946).

Ultraviolet radiation (λ 2537 Å) used subsequent to x-rays in the treatment of the spermatozoa of *D. melanogaster* effected a decrease, as compared with the controls receiving an equivalent dose of x-rays, in the frequency of chromosomal rearrangements. About 19% of the eggs failed to hatch that were deposited by females that had been inseminated by males treated with λ 2537 Å, as compared with 7% in untreated controls. The difference between the two groups is attributable to induction by the ultraviolet of the single-break type of dominant lethal. Other studies of hatchability of eggs deposited by females that had been inseminated by males treated with either 2,000 r of x-rays, or 2,000 r + λ 2537 Å suggest that the effect of post-treatment in reducing the frequency of chromosomal rearrangements is attributable to increased restitution rather than to an increase in the frequency of the single-break type of chromosomal derangement. (BA)

2062

Kaufmann, Berwind P., Alexander Hollaender, and H. Gay. MODIFICATION OF THE FREQUENCY OF CHROMOSOMAL REARRANGEMENTS INDUCED BY X-RAYS IN *DROSOPHILA*. I. USE OF NEAR INFRARED RADIATION. *Genetics* 31, 349-67(1946).

Modification of the frequency of x-ray-induced chromosomal rearrangements detected by analysis of the salivary gland chromosomes of *D. melanogaster* was effected by the use of near infra-red (λ ca 10,000 Å). Post-treatment of males with near infra-red accelerated the mitotic processes that make cells that were not mature sperm at the time of x-ray treatment available for transfer in copulation. Pretreatment with near infra-red increased significantly the frequency of detectable x-ray induced rearrangements as compared with the x-rayed controls. The higher frequency is not attributable to selective sensitization of any particular chromosome or portion thereof. Determination of hatchability of eggs deposited by females that had been inseminated by males exposed successively to near infrared and x-ray radiation suggests that pretreatment does not modify greatly the frequency of dominant lethals. Various possible modes of action of the near infrared radiation were considered. (BA)

2063

Kaufmann, Berwind P. and Katherine Wilson. MODIFICATION OF THE FREQUENCY OF CHROMOSOMAL REARRANGEMENTS INDUCED BY X-RAYS IN *DROSOPHILA*. IV. POST-TREATMENT WITH NEAR INFRARED RADIATION. *Genetics* 34, 425-36(1949).

Drosophila melanogaster males of the Swedish- b^8 stock were selected, three to five days before their emergence, and exposed to about 5,000 r of x-rays, using a Coolidge tube at 85 kv. They were then mated with virgin females and discarded; half of the females were subjected to ultraviolet radiations and the frequency of chromosomal rearrangements was determined. There was no increase in the frequency of the rearrangements due to the application of the ultraviolet rays after x-irradiation. A comparison between these results and those obtained in similar experiments is made and a theory is postulated. 28 references. (NSA)

2064

Kirby-Smith, J. S. EFFECTS OF INFRARED IRRADIATION ON THE FREQUENCY OF X- AND GAMMA-RAY-INDUCED CHROMOSOMAL ABERRATIONS IN *TRADISCANTIA* POLLEN TUBES. *Genetics* 36, 558-9(1951).

Tradescantia pollen has been treated with 250 kv X rays and 1.3 mev gamma rays in combination with near infrared radiation in the 9500-30,000 Å region. The temperature of the material during infrared radiation has been closely controlled to eliminate the possibility of thermal effects. Measurements of the infrared absorption spectra of *Tradescantia pollen* show that, in the present experiments, an appreciable amount of infrared energy is reaching the nuclei. Typical near-infrared absorption curves will be presented. The chromosomal aberration frequency in the pollen tube division following irradiation has been studied. No significant difference in the aberration frequency, including interchanges, has been observed between material treated with X or gamma rays alone and material given near infrared radiation immediately before or after exposure to X rays or gamma rays.

2065

Knowlton, Norman P., Jr. and Louis H. Hempelmann. THE EFFECT OF X-RAYS ON THE MITOTIC ACTIVITY OF THE ADRENAL GLAND, JEJUNUM, LYMPH NODE, AND EPIDERMIS OF THE MOUSE. *J. Cellular Comp. Physiol.* 33, 73-91(1949).

The effects of 250 KV x-rays on mitotic activity of the adrenal gland, lymph node, jejunum, and epidermis of the mouse have been investigated. The data obtained are summarized in seven curves and four tables. In general a quantitative response to irradiation was observed although there is a lack of correlation between the sensitivity of the mitotic activity to ionizing radiation and the radio-sensitivity of different tissues. The mitotic activity of most radio-sensitive tissues apparently responds less to irradiation than that of tissues showing a lower degree of histologic response to the radiations. In several tissues "overcompensation" was observed in the response of the mitotic index to irradiation; the possible mechanism for this is discussed. An attempt has been made to explain the abortive rise in the mitotic indices of the adrenal gland and the jejunum by the use of the direct and indirect concept of radiation injury previously reported by Hance (*J. Morphology*, 66, 409-422, 1940). The possibility of using the depression in mitotic activity subsequent to irradiation as a measure of the biological effects of radiations of different types is suggested. (NSA)

2066

Koller, P. C. and I. A. R. S. Ahmed. X-RAY INDUCED STRUCTURAL CHANGES IN THE CHROMOSOMES OF *DROSOPHILA PSEUDO-OBSCURA*. J. Genet. 44, 53-72(1942).

Males were treated with 4,500 r units. Salivary glands of 425 larval offspring were then examined for induced chromosomal breaks. Changes were found in 40% of the treated sperms. The frequency of breaks per sperm is not significantly different from that found following similar treatment of *D. melanogaster*. No 1-break aberrations were found. Sperms with an odd number of detected breaks were less frequent than expected in comparison to those with an even number of breaks, probably because of the effects of proximity and competition on reunion. The ratio of inversions within a single arm to interchanges between arms is higher than expected on the assumptions of equal arm lengths, equal chromosome breakability, and random distribution of breaks. This is probably due to the greater inviability of interarm rearrangements. Multiple breaks within the same sperm tend to produce several independent rearrangements rather than a single complex exchange involving all the altered chromosomes. The relative scarcity of duplications and deficiencies is attributed to their lower survival value. The XR chromosome has a lower and chromosome 4 a higher frequency of breaks than would be expected were breaks proportional to unit chromosome length. There was no significant difference in the breaks in successive broods from treated males over the age period of 10 to 25 days. (BA)

2067

Kosin, I. L. SOME ASPECTS OF THE BIOLOGICAL ACTION OF X-RAYS ON COCK SPERMATOOZOA. Physiol. Zoöl. 17, 289-319(1944).

The fertilizing capacity of cock spermatozoa, as indicated by the available methods of detection, is adversely affected by the soft type of x-ray irradiation. It is completely lost between 5,544 and 6,488 r. The inverse type of relationship between the fertilizing capacity and the x-ray dose can be expressed by a straight line of regression. In the present case the equation for the line was calculated to be $25 - 0.3268 y$. The coefficient of correlation between the two variables is -0.9631 . The type of fertilization is not responsible for the reduced fertilizing power of treated spermatozoa. The injurious effect of x-ray radiation is meted out directly to the spermatozoa and is not mediated via the fluid portion of the semen. The pH of the irradiated semen is unaffected by the treatment. During the first 10 days following irradiation, longevity of the treated spermatozoa compares favorably with that of controls. The total functional life-span, however, is shortened. Motility and morphology of the treated spermatozoa are not altered within the biotic range of radiation. They are modified, however, by more intensive treatment. The x-ray treatment of male gametes results in a preponderance of male chicks at hatching time from zygotes fathered by such gametes. Zygotic mortality is closely related to the intensity of radiation applied to the paternal germ cells. The bulk of deaths occurs during the early part of the incubation period. Lethality of the embryos fathered by the irradiated spermatozoa is associated with increased frequency of abnormal development. Irradiation of spermatozoa with 10,000 r has no detectable effect on their QO_2 , QCO_2 , and succinic dehydrogenase system. It is concluded that the irradiation of cock spermatozoa with doses as high as 152,000 r does not produce Hertwig phenomenon in the chicken ova exposed to such spermatozoa. The reduced fertilizing capacity is due to the increasing proportion of

injured germ cells with the rising intensity of irradiation. This "dilution" of still functional gametes with functionally inert, though motile, spermatozoa eventually leads to the complete loss of fertilizing capacity by the specimen. (Author)

2068

Kostoff, Dontcho. HOMOZYGOUS TRANSLOCATION OBTAINED IN THE SECOND GENERATION FROM MATERIAL TREATED WITH NEUTRONS. Proc. Indian Acad. Sci. 30B, 259-63(1949).

Dry seed from *Crepis capillaris* were irradiated with neutrons (20,000 r). The effect on the chromosomes are reported, and compared with chromosomal damage due to x-rays. Abnormalities can be classified as follows: 1. Chromosomal dislocations. 2. Chromosomal heteroploidy. 3. Polyploidy. (NSA)

2069

Kotval, J. P. STRUCTURAL CHANGES PRODUCED IN MICROSPORES OF *TRADESCANTIA* BY ALPHA-RADIATION. J. Genet. 48, 135-54(1947).

This work represents an extension of previous x-ray and γ -ray studies reported by Catcheside, Lea, Thoday, and Kotval, using α rays as the agent for production of structural changes. Anthers of *Tradescantia* were immersed in a radon soln. of known conc. for measured periods of time. Material was prepd. for microscopic study 24 hr. after irradiation using Benda's fixative and crystal-violet iodine stain. Structural changes noted resemble those observed following x-radiation and γ -radiation. In number they increase linearly with the dose. The number of changes in which there is an incomplete fusion of broken ends, however, is far greater than observed following other types of radiation. Since the total number of aberrations primarily produced is greater following a given dose of alpha-radiation than with other types, it is suggested that alpha particles passing close to the chromatid thread may be effective in producing breaks, as well as those which pass directly through it.

2070

Kotval, J. P. and L. H. Gray. STRUCTURAL CHANGES PRODUCED IN MICROSPORES OF *TRADESCANTIA* BY ALPHA-RADIATION. J. Genet. 48, 135-54(1947).

The structural changes seen at metaphase 24 hours after the irradiation of microspores of *Tradescantia bracteata* by known doses of α -radiation have been studied. The types of structural change produced resemble those seen at the same interval after γ -ray, x-ray and neutron treatment, and have been classified as chromatid and isochromatid breaks, or chromatid exchanges, following Catcheside, Lea, and Thoday. The number of structural changes of all three types increases linearly with the dose. The proportion of structural changes in which fusion of broken chromatid ends is incomplete is considerably greater than observed previously with any other types of radiation. Even when allowance has been made for this fact the number of structural changes primarily produced by a given dose of α -radiation is estimated to be much larger than would have been anticipated from earlier studies with x-rays and neutrons, and suggests that those α -particles which pass close to the chromatid thread as well as those which pass through it have a significant probability of breaking the thread. The new experimental data direct attention to α -rays arising from the radioactivity of soil and living tissue as the possible, origin of certain types of "spontaneous" chromosome aberrations. (Authors' Summary)

2071

Lasnitzki, I. THE EFFECT OF X-RAYS ON CELLS

CULTIVATED IN VITRO. II. RECOVERY FACTOR.

Brit. J. Radiol. 16, 61-7(1943).

Material from the choroid and sclerotic of 9-11 day chick embryo was grown in a medium of fowl plasma and chick embryo extract. Cultures for test were paired on a basis of mitotic activity; one of each pair was irradiated, the other used as control. Exposures of 100 r of 160 kv x-rays were made singly, twice separated by 48 hrs. and twice separated by 96 hrs.; exposures of 1000 r were made singly or twice separated by 10 days. Changes were observed for 10 days — 5 sub-cultures. Irradiation was followed by a marked fall in normal cell division with a temporary small wave of abnormal mitosis. Subsequently there was some reoccurrence of cell division, the appearance of degenerate cells, and then a 2nd wave of abnormal mitosis. Recovery occurred in 48 hrs. after a dose of 100 r, and in 10 days after 1000 r. If previously irradiated cultures were subjected to a 2nd dose equal to the first as soon as the cultures showed apparent recovery, the effect of the 2nd dose was greater than that of the first. If the interval was prolonged, the effects of the 1st and 2nd doses were apparently equal. (BA)

2072

Lasnitzki, I. THE RESPONSE OF CELLS IN VITRO TO VARIATIONS IN X-RAY DOSAGE. Brit. J. Radiol. 16, 137-41(1943).

Cells from the choroid and sclerotic of 9-11 day old chick embryos, grown in equal parts of fowl plasma and chick embryo extract, were irradiated with 160 kv lightly filtered x-rays, and subsequently fixed. The cells in several fields just inside the periphery were counted and classified as resting, degenerative, and mitotic. For doses from 100-1000 r, temporary inhibition of mitosis was observed; for 2500, 5000, and 10,000 r there was no mitotic recovery, but large numbers of degenerated cells. The time at which these latter appear indicates that the degeneration is due to the breakdown of cells in the resting condition. (BA)

2073

Lasnitzki, I. RECOVERY OF CELLS FROM RADIATION INJURY, p.163 of INTERNATIONAL CONGRESS OF RADIOLOGY, 6th Congress, London. 1950.

The restoration of normal cell counts does not necessarily mean full recovery has occurred. A second dose, identical with the first, given as soon as mitotic activity reaches normal, sometimes produces a greater effect than the first, suggesting that the cells are still damaged at the time the second dose is given. Thus, recovery of chick fibroblasts exposed in vitro to a dose of 100 r x-rays is apparently complete 48 hours after radiation. A second dose of 100 r units given at this point when the cell counts have returned to normal produces a greater effect than the first one. Complete recovery, as indicated by a response to the second dose similar in all respects to that obtained after the first, is observed only if the interval between the exposures is extended to 96 hours. The rate of recovery depends not only on the dose given but also on the dose-rate used and whether cells are irradiated in vivo or in vitro. Doses of 30 to 60 r units given at the rate of 1 r, 4 r and 15 r per day failed to produce any effect on chick fibroblasts exposed in vitro, suggesting that at these low dose rates of recovery keeps pace with the rate at which the radiation changes are produced within the cells. Cells exposed to doses of 100 r and 2,500 r given at 9 r, 30 r and 100 r/minute show a rate of recovery which varies directly with the dose-rate after the smaller dose and inversely with the dose-rate after the higher dose. Tumour cells exposed in vivo recover more quickly after a small dose

which does not involve the vascular system than similar cells exposed in vitro. If the dose is sufficient to damage the blood circulation, recovery is delayed in vivo as compared with the same type of tumour cells irradiated in vitro.

2074

Lea, D. E. and D. G. Catcheside. THE MECHANISM OF THE INDUCTION BY RADIATION OF CHROMOSOME ABERRATIONS IN *TRADESCANTIA*. J. Genet. 44, 216-45(1942).

Experimental data from x-ray and neutron experiments are used to develop a quantitative theory of the production of chromosome aberrations in *Tradescantia* by irradiation during mitotic prophase or resting stage. The data available show that neutrons are more efficient than x-rays for equal numbers of ionizations in the tissue. From the data it is calculated that approximately 17 ionizations must occur within the chromatid to produce a break, 5 rays become important if hard radiation is used. Isochromatid breaks are produced, according to this theory, by simultaneous breakage of sister chromatids traversed by the same ionizing particle. Hence, as the data show, they are produced with far less frequency by x-rays than by an equivalent dose of neutrons, it being relatively unlikely that a given electron trail will traverse both chromatids plus the space, if any, between them. It is calculated that probably 45% of the isochromatid breaks are detectable, but only 10-15% of the primary chromatid breaks and only about 5% of the primary chromosome breaks. The remainder rejoin or form interchanges not detectable cytologically. The period of rejoining is variable but averages about 3-½ minutes. The distance between breaks that take part in the same interchange may be as great as 1 or 2 μ , the probability of interchange varying inversely with the initial distance between the breaks. With x-rays the two breaks are usually caused by separate ionizing particles; with neutrons by the same one, although at high dosages the proportion of 2-hit interchanges becomes of importance. On the basis of the theory, x-rays of 4.4 A should be a maximum efficiency in producing chromatid breaks, with a decrease of relative efficiency to one half at approximately 5.2 A and 2.5 A. (BA)

2075

Lindemann, B. INVESTIGATION OF X-RAY HAEMOLYSIS BY THE ELECTRON MICROSCOPE, p.166 of INTERNATIONAL CONGRESS OF RADIOLOGY, 6th Congress, London. 1950.

Two interpretations of X-ray haemolysis are possible; either the erythrocyte membrane is denatured by the rays, or the membrane is sensitised against active ions. This problem has been investigated by electron-microscopic observations of irradiated erythrocytes. It has been found that radiation produces changes in the membrane similar to those produced when proteins are denatured. X-ray haemolysis is an osmotic, i.e., a diffusion phenomenon. Investigations with the electron microscope show that this haemolysis can be measured not only by the number of cells affected but also by the amount of haemoglobin liberated from each individual red cell. The "all or nothing" law, therefore, does not apply to an osmotic haemolysis. The threshold dose for X-ray haemolysis is of the order of 6,000 r. Calculating from cell volume on the basis of the target theory, the amount of absorbed irradiation necessary to cause haemolysis leads to the conclusion that haemoglobin loss in an individual red blood cell is not due to a "direct hit" but is an expression of the biological variation among the cells of the population exposed.

2076

Longley, A. E. CYTOLOGICAL ANALYSIS OF TRANS-

LOCATIONS IN CORN CHROMOSOMES RESULTING FROM IONIZING RADIATION OF THE TEST ABLE ATOMIC BOMB AND X-RAYS AND OF TRANSLOCATIONS FROM OTHER SOURCES. Naval Medical Research Section, Joint Task Force One. June 10, 1950. 60p. (NP-3072)

Of the 588 chromosome translocations in corn described, 220 came from various sources, 179 from seeds treated with measured dosages of x rays, and 172 from seeds exposed to ionizing radiations of the Test Able bomb. The nonrandom distribution of the Bikini-induced translocations was different from that of the x-ray-treated controls. Chromosome arms staining heavily adjacent to the fiber attachment had more breaks than expected when treated with x-rays and fewer breaks than expected when exposed to the Bikini radiation. Chromosome arms staining lightly throughout their length had fewer breaks than expected when treated with x rays and more than expected when exposed to Bikini radiations. A comparison of the position of breaks resulting from low, medium, and high dosages of x rays indicates that the proportion of breaks in heavily staining areas is greatest when the dosage is highest, and in lightly staining areas is greatest after low dosages. The position of the breaks in Bikini-treated material indicates that the dosage intensity was intermediate between the low and medium x-ray dosages studied. Among the whole population of translocations there was a tendency for breaks the same distance from the fiber attachment to be associated more frequently than expected on a random basis.

2077

Marinelli, L. D., B. R. Nebel, N. Giles, and D. R. Charles. CHROMOSOMAL EFFECTS OF LOW X-RAY DOSES ON FIVE DAY TRADESCANTIA MICROSPORES. *Am. J. Botany* 29, 866-74(1942).

Quantitative studies have been made on the chromosome aberrations, i.e. dicentrics (D), rings (R), and isodiametric fragments (I. F.) produced by x-radiation on the microspores of *T. canaliculata*. The material was rayed at interphase previous to the onset of nuclear enlargement and observations were made at metaphase and anaphase. The time factor was investigated by delivering different doses of radiations at constant intensity or in constant time and by delivering a given dose at different intensities. The results obtained as well as some of the data of other authors, are consistent with assumption that each D. R. or I. F. is the result of 2 chromosome breaks and that each break has a definite probability of healing. This probability seems to be independent of the radiation dose. In the course of the mathematical analysis it is shown that 2 irradiations at high intensity separated by a variable rest period will yield the most direct information of the rate of recovery. (Authors)

2078

Marquardt, Hans. THE DISTRIBUTION OF X-RAY INDUCED CHANGES IN THE CHROMOSOMES OF *BELLEVALIA ROMANA*. *Ber. deut. botan. Ges.* 60, 98-124(1942).

Roman hyacinth was x-rayed several days before nuclear division, and 2,700 of the subsequent mitoses studied. The chromosomes are large and easily studied. All chromosomes are equally liable to alteration by x-rays, except that the frequency of breaks and translocations is proportional to the length of the chromosomes. Breaks tend to occur more often in the commissure-to-subterminal end than in the subterminal-to-median region. Similarly, translocations increase in frequency from the subterminal end to the commissure, in all four chromosomes. Exchange of similar regions between homologous chromosomes is more likely than are translocations within a chromosome. (BA)

2079

Marshak, A. ALTERATION OF CHROMOSOME SENSITIVITY TO X-RAYS WITH NH_4OH . *Proc. Soc. Exptl. Biol. Med.* 38, 705-13(1938).

Seedlings of *Vicia faba* and *Allium cepa* were treated with different concn. of NH_4OH before and during irradiation with x-rays. The % chromosome abnormalities in anaphase at 3 hrs. after irradiation was greatly reduced. Curves for % abnormalities as a function of ammonia concentration had a plateau in the middle range although the curves for abnormalities produced by ammonia alone did not show any. The maximum % abnormalities after treatment with ammonia alone was observed in $\frac{1}{2}$ hr., while with x-rays alone the maximum was observed in $2\frac{1}{2}$ -3 hrs. after irradiation. Generalized swelling of chromosomes and "unraveling" of chromonemata were not found. CO_2 in concns. up to 80 vols. % produced no alteration in the % abnormalities induced by x-rays. Abnormalities were apparently produced by x-rays through the action of electrons on positively charged groups of the separating surfaces of the dividing histories. From the ammonia curves it might be possible to determine the amino groups involved in the x-ray response. (BA)

2080

Marshak, Alfred. RELATIVE EFFECTS OF X-RAYS AND NEUTRONS ON CHROMOSOMES IN DIFFERENT PARTS OF THE "RESTING STAGE". *Proc. Natl. Acad. Sci. U. S.* 28, 29-35(1942).

The per cent normal anaphase chromosomes is a negative exponential function of the dose of neutrons or x-rays in different parts of the nuclear cycle. Chromosome abnormalities are, if allowance is made for multiple hits, therefore directly proportional to the dose at all stages studied. 2. The ratio of neutron to x-ray efficiency (n/x) is constant for different species at the onset of the prophase, but increases by a factor of at least two during the nuclear resting stage of single species. 3. Increase in n/x during the resting stage indicates: Conditions for chromosome response are not constant during resting stage. The intrachromosomal structure responding to ionization may be different for the different parts of the nuclear cycle and resting stage; a theory invoking a single mechanism for the production of chromosome abnormalities is not adequate. The relative effect of neutrons on chromosomes in the resting nucleus is greater than with x-rays. Neutron therapy may produce regression in tumors which do not respond to x-rays. The daily "safe dose" for exposure to neutrons may be considerably less than x-rays. 4. The use of neutrons and x-rays as described furnishes a method for identifying the functional stages which cannot otherwise be identified. (BA)

2081

Marshak, A. and M. Bradley. X-RAY INHIBITIONS OF MITOSIS IN RELATION TO CHROMOSOME NUMBER. *Proc. Natl. Acad. Sci. U. S.* 30, 231-37(1944).

The authors report evidence that inhibition of mitosis is dependent upon the number of chromosomes in the cell. Root tips of three species of *Triticum* (*T. monococcum*, *T. dicoccum*, and *T. vulgare*) and two species of *Bromus* (*B. carinatus* and *B. arizonicus*) were used. Source of x-rays was an oil-cooled tube with a tungsten target in G. E. Company Maximar apparatus, operated at 220 kvp and 15 ma. The beam was filtered through 1 mm Al, and a lead diaphragm 1 cm thick and with a 10×10 cm aperture was used at the base of the cone which was 17.5 cm in length. The target distance was 85 cm. Irradiation was given at the rate of 43 r/min. Results show that inhibition of mitosis by x-rays is inversely proportional to the number of chromosomes in the species studied; inhibition of

mitosis is neither directly nor inversely proportional to the chromosome length. The evidence indicates that inhibition of mitosis by x-rays occurs through action upon the centromeres. The significance of these findings in connection with sensitive volume calculations is discussed. (S.V.S.)

2082

Marshak, A. and W. S. Malloch. THE EFFECT OF FAST NEUTRONS ON CHROMOSOMES IN MEIOSIS AND ITS BEARING ON PACHYTENE PAIRING. *Genetics* **27**, 576-83(1942).

Microsporocytes of *Vicia faba* were treated in pachytene with various doses of neutrons and the frequency of chromosome abnormalities in anaphase I determined. A method of estimating the duration of the different meiotic stages is described. The log per cent cells, with no chromosome abnormalities, is a negative exponential function of the dose. The slope of this "survival curve" is the same within the statistical limits of error as for mitotic chromosomes at the onset of prophase. Comparison with previous results shows that the ratio of neutron to x-ray sensitivity is approximately 6 for somatic chromosomes of several spp. but varies by more than a factor of 2 in the same sp. depending on the stage of mitosis treated. Since the ratio is approximately 6 for both meiotic and mitotic chromosomes of *V. faba*, it is concluded that a similar functional condition with respect to ionizing particles exists in the chromosomes at pachytene and at the onset of the mitotic prophase. This condition may be the presence of closely approximated chromonematic surfaces at both these stages. In seeking explanations of chromosome pairing and crossing-over, consideration should be given to forces appropriate for structures of these dimensions. (BA)

2083

Mikaelsen, Knut. THE PROTECTIVE EFFECT OF GLUTATHIONE AGAINST RADIATION INDUCED CHROMOSOME ABERRATIONS. Brookhaven National Lab. [nd] 8p. (BNL-1111)

Cuttings of *Tradescantia paludosa* were grown in solutions of different concentrations of reduced glutathione during a 48-hour exposure to continuous γ -radiation from a 3-curie Co^{60} source at a dose of 25 r per day. The results illustrated clearly that there was a positive correlation between increased glutathione concentrations and decreased fragment frequency between 1×10^{-5} and 3×10^{-4} M. The latter concentrations reduced the number of fragments produced to about 50 per cent of that in the irradiated controls. (NSA)

2084

Mottram, J. C. VARIATIONS IN THE SENSITIVITY OF THE CELL TO RADIATION IN RELATION TO MITOSIS. *Brit. J. Radiol.* **8**, 643-51(1935).

Tumor cells vary greatly in sensitivity to radium irradiation when submitted to conditions which affect cellular respiration, exposure to cold or to HCN increasing the radiosensitivity, and N or CO anaerobiosis decreasing it. The mitotic activity of the cells has been observed under these controlled conditions to determine whether there is any correlation between sensitivity and state of mitosis at the time of irradiation. None was found. HCN and anaerobiosis both cause great decrease in the number of dividing cells; cold has no effect on this number. (BA)

2085

Nabours, Robert K. and Florence M. Stebbins. CHROMOSOME ABERRATIONS AND VIABILITY IN *APOTETIX EURYCEPHALUS* HANCOCK. *Genetics* **25**, 129-30(1940).

The X-ray induced translocations of chromatin have been reported, one with the exchange between first and fourth

autosomes, with depletion in amount of chromatin for the former and augmentation for the latter (1933); the other between a first autosome and a sex-chromosome, with increase in chromatin and probably an extra traction fiber attachment for the latter. The autosome of this translocation was lost (1935 and unpublished). The three surviving aberrators are designated tentatively as 1. donor(al), 2. receptor(a4), and 3. receptor(X). The genetic and cytological data correlate (Robertson, 1935, and unpublished). Zygotes carrying donor(al), and otherwise normal, hatch but rarely survive to 3-4 instar when they are recorded (14 donor(al): 2443 normals). Receptor(a4) are 13 percent, and receptor(X) 14 percent, less viable than controls. Donor(al) +receptor(X) are 38.5 percent below normal. Donor(al) +receptor(a4) +receptor(X) fall 17 percent below controls. The data comprise approximately 50 other items of comparison of 15,088 aberrators with 49,000 normal, and with each other. In practically all cases augmentation of chromatin is accompanied by less mortality among males than females, and vice versa when there is a depletion of chromatin. There is indication, but not yet definite proof, that the XO(absence of Y) chromosome condition in grouse locusts is responsible for the significantly lower viability, and perhaps for the much smaller size, of the males among the controls in grouse locust breeding. (G)

2086

Nebel, B. R., G. B. Wilson, and L. Marinelli. X-RAY DOSAGE CURVES IN *TRADESCANTIA*. *Genetics* **27**, 158 (1942).

Three independent dosage curves have been plotted for the action of X-rays on *Tradescantia* microsporocytes observed 4-5 days after raying. The first set of exposures was made by G. B. Wilson in Geneva, N. Y. early in 1940 and scored in Montreal in 1941. The second set of data was collected by B. R. Nebel also in Geneva from plants grown in constant environment. The third set of data was collected from radiation applied to cut heads of *Tradescantia* at the Memorial Hospital by L. Marinelli. Within the limits of the three experiments environmental differences were found to be unimportant. The method of radiation is held responsible for the results obtained. At Geneva the radiation was intermittent the off period being from 30'' to 90'' with the on period of equal or shorter duration. The intensity of the on period varied between 50 and 200 r/m, 100 r/m being the most common intensity used.—The Wilson-Geneva and the Nebel-Geneva data are identical. They were scored independently. For rings and dikinetid translocations above 100 r the Geneva data show a straight line (K^1) for the relationship between dose and effect. For isodiametric fragments the independent data of Wilson and Nebel show a more than linear rise for dose and effect— $K^{\text{appl.}^2}$. A more than linear rise ($K^{1.5}$) for rings and dikinetid translocations plotted against dosage was obtained from the Nebel-Memorial Hospital experiment. The same experiment showed a value of K^2 for isodiametric fragments. These results were obtained by applying 110, 200, 300 and 400 r with varying intensity and continuous exposure over a total time of two minutes for every application. (G)

2087

Newcombe, H. B. THE ACTION OF X-RAYS ON THE CELL. II THE EXTERNAL VARIABLE. *J. Genetics* **43**, 237-48(1942).

A study of x-ray induced chromosomal changes in the pollen-grain mitosis of *Tradescantia* shows that simple chromosome breaks (fractures) vary as the square of the dose or above; while 2-break changes (new reunions) vary only as the 1.5 power, approximately. Minute fragments, which from the evidence include a large proportion of small rings behave in an intermediate fashion. All the ob-

served types vary at a higher power of the dose when the duration of the dose is kept constant than when the intensity is constant. The intensity effect, since it applies to both 1- and 2-break changes, cannot be due simply to healing of broken ends or to competition between restitution and reunion. It is attributed to an inhibition of both the restitution and the new reunions of broken ends by the irradiation, the inhibitory effect increasing with dosage more rapidly when the dose is administered more rapidly. (BA)

2088

Nichols, Charles, Jr. THE EFFECTS OF AGE AND IRRADIATION ON CHROMOSOMAL ABERRATIONS IN ALLIUM SEED. *Am. J. Botany* **29**, 755-9(1942).

Chromosomal aberrations appearing in the primary divisions of root tip cells of five variations of *A. cepa* were analyzed. Aging of the seed was found to result in an increase in the number of aberrant cells. Irradiation of dry seed also caused an increase in the number of aberrations. No correlation was found between the age of the seed and its radio-sensitivity. Delayed germination of seeds following irradiation caused a significant increase in the number of aberrations except in cases where fresh seed were used. The number of aberrations was found to be greater when the moisture content of the seed was increased during the period of delayed germination. In addition to x-rays, physiological factors such as age of seed and moisture content are of importance in bringing about structural changes in the chromosomes. (BA)

2089

Parker, D. R. OBSERVATIONS ON CROSSING OVER INDUCED BY X-RAYS IN MALES OF DROSOPHILA. *Genetics* **33**, 304-10(1948).

Relationship between dosage and frequency of induced crossing over was shielded. Inducing crossing over in the male was found quite restricted in that only a short region of the chromosome can be involved at any time. This is indicated by the preponderance of doubles involving adjacent regions of crossing over, as well as by the occurrence of clusters of crossovers involving adjacent regions. The frequency of double crossing over failed to increase greatly with increased dose. This is to be expected if crossing over is restricted to a region shorter than one marked region. The occurrence of several crossovers in the progeny of others is correlated with the presence of growth stages in some testes and absence from the testes of other males of similar age. The cluster effect may be correlated with the similarity of stage of maturation of all cells in a cyst. All cells in one cyst might be similar in their crossing over restrictions at any time. Induced crossing over may be interpreted as a result of chromosome breakage by X-rays, with the frequency/dose relationship indicating that both breaks involved in one exchange are produced by a single particle. The absence of lethal position effects does not rule out the explanation of direct breakage by X-rays if both chromatids are broken at the same locus. (NSA)

2090

Rasch, Ellen Myrberg. NUCLEAR AND CELL DIVISION IN ALLIUM CEPA AS INFLUENCED BY SLOW NEUTRONS AND X-RAYS. *Botan. Gaz.* **112**, 331-48(1951).

Bulbs of *Allium cepa*, variety Ebenezer, were exposed to x-ray dosages of 100 r, 1000 r, or 10,000 r or to slow neutrons produced in the Argonne heavy-water pile. The neutron-treated material was exposed to an average neutron flux of 5.8×10^{10} slow neutrons/sq cm/sec for periods of 2, 4, 8, or 16 minutes. Plants from treated bulbs in both series were markedly retarded in growth with respect to control plants. All plants from bulbs treated with slow neutrons died as did also those treated with the highest

dosage of x-rays. Bulbs from control and treated series were sprouted in soil. Cytological analysis of root tips collected at 48-, 52-, and 96-hour intervals showed that the effects of both types of treatment followed a pattern that was chronologically determined: a general, but temporary, inhibition of mitosis; abnormal nuclear division necessitated by structural chromosome aberrations; abnormal cell division directly following aberrant nuclear division; and, lastly, degeneration of nuclei and cells which had been severely damaged either by the original treatment or by disorientation in normal cell processes during the preceding stages. Chromosomal aberrations of all types—dicentric, centric and acentric rings, acentric fragments, and dot deletions—were observed in root-tip cells from both treatments. Dosage had no apparent effect on type of aberrancy induced. Pycnosis of many nuclei at the higher dosages was of common occurrence. Aberration frequency induced by 2-, 4-, or 8-min. exposures to slow neutrons was higher in all cases than that produced by either 100 r or 1000 r. Frequencies in the 10,000-r series approximated those found for the 16-minute dosages with slow neutrons. (Author's Summary)

2091

Rick, Charles, M. X-RAY INDUCED CHROMOSOME DELETIONS IN RELATION TO MUTATION RATE IN TRADESCANTIA. *Genetics* **25**, 132(1940).

Small spherical fragments, independent of other chromosome aberrations, result from X-radiation of *Tradescantia* microspores. Evidence from size and shape indicates most of these to be interstitial deletions of ring structure. Their frequency within the dosage range of 100 r to 600 r indicates that they are conditioned mostly by 2 hits and that they are produced at random. X-ray treatment at 3°C induces significantly more deletions than the same dose at 30°C. The effect of X-radiation during the interkinesis preceding and the one following meiosis on the size of subsequently developed pollen grains was studied. Variability following both treatments is significantly greater than in controls. Variability at low temperature exceeds that at high temperature. Pollen size is interpreted as, at least in part, genetically self-determined. Since minute deficiencies are inseparable in genetic behavior from point mutations, the close parallel between fragment frequency and variability in pollen size suggests that the latter is a measure of mutation rate. (G)

2092

Rick, C. M. ON THE NATURE OF X-RAY INDUCED DELETIONS IN TRADESCANTIA CHROMOSOMES. *Genetics* **25**, 466-81(1940).

Small spherical fragments, independent of other chromosome aberrations, result from x-radiation of *Tradescantia* microspores. Evidence from size and shape indicates most of these to be interstitial deletions of ring structure. Then frequency within the dosage range of 100 r to 600 r indicates that they are conditioned mostly by 2 hits and that they are produced at random. X-ray treatment at 3°C. induces significantly more deletions than the same dose at 30°C. The effect of x-radiation during the interkinesis preceding and the one following meiosis on the size of subsequently developed pollen grains was studied. Variability following both treatments is significantly greater than in controls. Variability at low temperature exceeds that at high temperature. Pollen size is interpreted as, at least in part, genetically self-determined. Since minute deficiencies are inseparable in genetic behavior from point mutations, the close parallel between fragment frequency and variability in pollen size suggests that the latter is a measure of mutation rate. (G)

2093

Rick, Charles. CYTO-GENETIC CONSEQUENCES OF X-RAY TREATMENT OF POLLEN IN PETUNIA.

Botan. Gaz. 104, 528-40(1943).

Pollen of petunia ($2n = 14$) treated with 10,000 to 100,000 r x-rays was applied to stigmas of untreated plants. Pollen exposed to 50,000 r functioned to produce viable seed. The half-kill dose for the number of plants produced per flowers pollinated was ca. 9,000 r. Tests applied to X_1 and X_2 showed no evidence of pseudogamous development of the egg or of diploid individuals from eggs in which a doubling of the chromosome number had occurred. Thirty-three X_1 plants exhibited gross chromosomal aberrations; $\frac{1}{3}$ of these were root-shoot chimeras, the difference usually involving the presence or absence of a fragment chromosome. Of three monosomics obtained the odd chromosome behaved as a univalent in one and was usually associated in a trivalent in the other. The trivalent pairing is attributed to duplication in the normal complement of Petunia. (BA)

2094

Riley, Herbert Parkes and Norman H. Giles, Jr. THE EFFECT OF OXYGEN ON THE FREQUENCY OF X-RAY INDUCED CHROMOSOMAL ABERRATIONS IN TRADES-CANTIA MICROSPORES. Genetics 35, 131-2(1950).

A study has been made of the effect of oxygen on the frequency of X-ray induced chromosomal aberrations (interchanges and interstitial deletions) observed at the four-to-five-day interval following irradiation of microspores. Initial comparative exposures made in air, in nitrogen, and in oxygen demonstrated that aberration frequencies were markedly reduced in nitrogen and increased in oxygen as compared with air. Further test exposures in a vacuum and in other gases such as helium and argon also resulted in greatly reduced aberration frequencies, indicating that the availability of oxygen has a marked effect in increasing the radiosensitivity of *Tradescantia* chromosomes. Additional experiments have been performed comparing the aberration frequencies in two sets of inflorescences — one kept in a vacuum both during and following irradiation and the other irradiated in a vacuum with pure oxygen being introduced under pressure immediately following the radiation exposure. The failure to find any increased aberration frequency in the second set, to which oxygen was added after irradiation, suggests that the effect of oxygen in increasing aberration frequency is exerted on the initial breakage mechanism rather than on the recovery process. (G)

2095

Riley, Herbert Parkes, Norman H. Giles, Jr. and Alvin V. Beatty. THE OXYGEN EFFECT ON X-RAY-INDUCED CHROMATID ABERRATIONS IN TRADESCANTIA MICROSPORES. Genetics 36, 572-3(1951).

Comparative X-ray dosage curves for the various types of chromatid aberrations (microspores examined at 24 hours following irradiation) have been obtained following exposures of inflorescences in atmospheres of pure oxygen and of pure helium. A constant X-ray intensity of 300 r per minute was used, and four dosages were administered — between 25 and 150 r in oxygen, and between 50 and 450 r in helium. A linear relationship between aberration frequency and dose was obtained for both isochromatid and chromatid aberrations in both the presence and the absence of oxygen. Aberration frequencies were higher in oxygen in both instances, but the magnitude of the difference was much greater for isochromatid types (2.6 x) than for chromatid types (1.4 x). Nonlinear relationships were obtained for chromatid interchanges in both the presence

and the absence of oxygen, the exponents of the dosage curves being approximately the same (1.7) in both cases. For equivalent dosages, chromatid interchanges were almost four times as frequent in oxygen as in helium. Experiments have also been performed on the effect of intensity on aberration yield in the presence and in the absence of oxygen. In oxygen, a constant dose of 150 r was administered in $\frac{1}{2}$ minute, 3 minutes, 15 minutes, and 30 minutes. In the absence of oxygen (in nitrogen), the same times of exposure were used, but a constant dose of 400 r was given in order to obtain comparable levels of biological response. There was no effect on intensity on the frequencies of chromatid and isochromatid aberrations. Chromatid exchanges decreased in frequency at lower intensities, generally similar types of curves being obtained for the two exposures. The results to date of the intensity experiments suggest that the average restitution time for broken ends is the same in the presence and in the absence of oxygen, and thus support the view that oxygen exerts its effect by increasing the initial frequency of breaks rather than by modifying the behavior of broken ends during the recovery process.

2096

Rothfels, K. H. SPONTANEOUS AND INDUCED CHROMOSOME ABERRATIONS IN THE GRASSHOPPER CHLOEAL-TIS CONSPERSA. Genetics 35, 687(1950).

An abstract of this paper appeared in Genetics, 35: 687 687(1950) Nov. and is reproduced here in its entirety.

The incidence of spontaneous chromosome aberrations in first meiotic metaphases of *Chloealtis* males is estimated to be 0.1 incomplete breaks, 0.01 complete breaks, and 0.01 interchanges per cell. After an x-ray dose of 100 r the following classes of induced chromosome aberrations come successively into maximum: (1) incomplete breaks (24 hr), (2) "stickiness" (5 days), (3) complete breaks (10 days), (4) interchanges (15 days), (5) incomplete nuclei (17 days). Over the range 2 to 300 r, 0.05 incomplete breaks are obtained per nucleus per r. If the dose-effect curve remains linear at even lower doses, natural ionizing radiations cannot account for more than 1% of the spontaneous abnormalities of this type. Similar conclusions were obtained with regard to the complete breaks and interchanges. These findings were tested directly by exposing grasshoppers at various distances from a Co^{60} source for 20 days. A dose rate of 500 x background was required to produce a clearly significant increase in chromosome aberrations over control animals. (NSA)

2097

Rugh, Roberts. THE IMMEDIATE AND DELAYED MORPHOLOGICAL EFFECTS OF X-RADIATIONS ON MEIOTIC CHROMOSOMES. J. Cellular Comp. Physiol. 36, 185-203(1950).

The mitotic and meiotic stages in spermatogenesis of the Japanese fire salamander, *Triturus pyrrhogaster*, were studied immediately and after an interval of 48 hours following x-radiation at 5,000 r and 50,000 r. The chromosomes of this salamander are among the largest known, and, since spermatogenesis is a rather continuous cyclic process, it is possible to observe the effect of x-irradiation on chromosomes at various stages of their synthesis. X-irradiation immediately affects the formed chromosomes in that it makes them less viscous, more fluid, and sticky. Their fluid nature is seen in the fact that they tend to flow out along the attached spindle fibers, losing their identity in shape. Their sticky nature is seen in the fact that the chromosomes become clumped together. The spindle fibers are normally very difficult to locate and identify but following x-irradiation and the Feulgen test

for thymonucleic acid, they are heavily stainable due to the fact that they are coated by the very fluid chromosomal material to which they are attached. The chromosomes, once formed, seem to show movement, even following x-irradiation, because the end point of the post-irradiation damage in most cells is the pycnotic nucleus. This is most frequently seen in the secondary spermatocytes. There is no evidence that chromosomes, x-irradiated to 5,000 r or more, even return to the premeiotic or non-discrete phase. Stages in spermatogenesis which show no formed chromosomes at the time of irradiation show some fragmentation of the linin network, but this is difficult to quantitate or evaluate. It is the contention of this author that since the intermitotic stages never enter mitosis, following x-irradiation to 5,000 r or more, that they must also be radio-sensitive, as are the mitotic (e.g., metaphase) stages, and the criterion of visible chromosome damage is not exclusive evidence that the non-discrete phases in chromosome synthesis are not also radio-sensitive. (NSA)

2098

Sax, Karl. AN ANALYSIS OF X-RAY INDUCED CHROMOSOMAL ABERRATIONS IN *TRADESCANTIA*. Genetics **25**, 41-68(1940).

Irradiation of *Tradescantia* microspores produces 1-hit and 2-hit aberrations in the chromatids and chromosomes. The chromosomes in the resting stage react as single threads; those in prophase react as double threads. The frequency of 1-hit aberrations shows a linear relation to dosage; 2-hit aberrations increase exponentially with dosage. When dosage is increased by lengthening the time of exposure the equation for frequency of 2-hit aberrations is $(D/K)^{1.5}$, but when dosage is increased with time of exposure constant the equation is $(D/K)^2$. The time-intensity factor is important because the 2-hit aberrations are dependent upon 2-independent breaks limited in both time and space. The frequency of initial breaks induced by x-rays is relatively independent of temperature but the frequency of aberrations is greater in cells subjected to low temperatures during or following irradiation due to greater re-union of broken ends in the original position at high temperatures. (BA)

2099

Sax, Karl. X-RAY INDUCED CHROMOSOME ABERRATIONS AND THEIR SUBSEQUENT BEHAVIOR. Genetics **25**, 134(1940).

Both chromosome and chromatid aberrations are produced by X-rays. The frequency of aberrations produced by single breaks shows a linear relation to dosage, while those dependent upon two breaks increase as the square of the dosage. Many of these aberrations produce single or double chromatid bridges at anaphase. When these bridges break new fusions of broken ends occur, although some of the broken ends appear to behave as normal ends. (G)

2100

Sax, K. TYPES AND FREQUENCIES OF CHROMOSOMAL ABERRATIONS INDUCED BY X-RAYS. Cold Spring Harbor Symposia Quant. Biol. **9**, 93-103(1941).

Irradiation of *Tradescantia* microspore chromosomes with x-rays produces only chromatid aberrations during the first 25 hours after raying, when the period of nuclear cycle is at a minimum. Between 27 and 31 hours both chromatid and chromosome breaks are found in considerable numbers, and from 34 hours to 5 days after raying only chromosome aberrations appear in the division figures. Single chromatid deletions are most frequent shortly after raying when the sister chromatids are further apart at late prophase, while double deletions are most frequent following irradiation of early prophase when the sister

chromatids are closely associated. However, a single hit can break both sister chromatids throughout prophase, even when the chromatids are easily differentiated in microscopic preparations. The relation between x-ray dosage and aberration frequency depends on the nature of the aberration and the intensity of the radiation. The relation between dosage and the frequency of one-hit aberrations is linear regardless of the time-intensity factor. With short exposure times, the two-hit aberrations increase in frequency as the square of the dosage, but as radiation intensity is decreased the aberration frequency declines and the dosage curve approaches linearity at 2.7 r/min. The effect of the time-intensity factor is due to restitution of broken ends so that fewer adjacent breaks occur within the critical limits of time and space. The evidence from varying intensity and from fractional dosage indicates that breaks can remain open for only 26-60 minutes. Due to limitations in time and space only a small proportion of the original breaks must be involved in the production of aberrations. Broken ends usually fuse and if illegitimate fusion does not take place, restitution occurs so that there is no evidence of previous breakage. (Author's Summary)

2101

Sax, Karl. THE BEHAVIOR OF X-RAY INDUCED CHROMOSOMAL ABERRATIONS IN *ALLIUM* ROOT TIP CELLS. Genetics **26**, 418-25(1941).

Irradiation of allium root tip cells with x-rays produces a "primary" effect which results in fusion bridges. The "secondary" effect produces breaks usually followed by the union of broken ends to produce rings, dicentrics, inversions, translocations, and interstitial deletions. Terminal deletions are produced when a break is not followed by union of broken ends of sister chromatids. The ring and dicentric chromosomes tend to persist for several cell generations but are soon eliminated, and only cells with normal or balanced genomes survive. The elimination of ring and dicentric chromosomes appears to be due to the deleterious effect of the deletions associated with these aberrations so that they are unable to compete with normal or balanced cells. Delayed germination of irradiated onion seed increases the frequency of chromosomal aberrations due to a physiological effect similar to the effects of age or heat, but delayed germination of irradiated onion bulbs has no effect on aberration frequency. (Author's Summary)

2102

Sax, Karl. THE MECHANISMS OF X-RAY EFFECTS ON CELLS. J. Gen. Physiol. **25**, 533-7(1942).

Irradiation of resting nuclei of *Tradescantia* microspores did not increase the sensitivity of the same nuclei when they reached the prophase stage. The frequency of x-ray induced chromosomal aberrations at prophase was slightly reduced by previous irradiation at the resting stage, due to the production of acentric chromosome fragments which were less sensitive to subsequent irradiation. So far as the individual cell was concerned the deleterious effect of x-rays was effected by a "direct hit" mechanism, but the reaction of tissues might be more dependent upon more indirect physiological factors. (BA)

2103

Sax, Karl. THE DISTRIBUTION OF X-RAY INDUCED CHROMOSOMAL ABERRATIONS. Proc. Nat. Acad. Sci. U. S. **28**, 229-33(1942).

The relative frequencies of various types of chromosomal aberrations indicate that secondary factors play an important part in determining the frequency of effective breaks induced by x-rays. These secondary factors include (1) the spatial relations of the chromosomes, (2) the

stresses imposed by the centromere in maintaining polarity and (3) the stage of chromosome development in the nuclear cycle. (BA)

2104

Sax, Karl. TEMPERATURE EFFECTS ON X-RAY INDUCED CHROMOSOME ABERRATIONS. *Genetics* **32**, (1) 75-8(1947).

The frequency of ring and dicentric chromosomes was more than doubled when *Tradescantia* microspores were irradiated at 3°C. compared with the same x-ray dosage at 36°C. Temperature differences had little or no effect on the frequency of rod deletions. The subjection of microspores to high and low temperatures before and after irradiation produced no consistent differences in x-ray induced aberrations. (BA)

2105

Sax, Karl. THE EFFECT OF X-RAYS ON CHROMOSOME STRUCTURE. *J. Cellular Comp. Physiol., Suppl.* **1**, 35, 71-81(1950).

Chromosomal breaks in the *Tradescantia* caused by x-radiation and the union of broken ends are described. Breaks induced during the resting stage produce chromosome aberrations, while those induced during prophase produce chromatid aberrations. The relation between x-ray dosage and aberration frequency depends upon the stage of nuclear development and the type of aberration involved. The intensity of the dosage is also considered. The effect of temperature and infrared and ultra-violet radiation during x-ray exposure is discussed. Comparison is made with the effects of neutron radiation. (NSA)

2106

Sax, Karl. THE CYTOLOGICAL EFFECTS OF LOW-INTENSITY RADIATION. *Science* **112**, 332-3(1950).

The effects of long-continued exposure to low-intensity radiation have been studied by exposing potted plants of *Tradescantia paludosa* to low intensities of γ radiation for several months. Exposure to 1.7 r/day increased the aberration frequency up to the end of three weeks exposure, after which time there was no continued increase. At the end of 22 weeks the plants had received 262 r of γ radiation, but showed only 0.5% breaks in the microspore chromosomes. This dose of x-rays, given in a few minutes at the prophase stage, would have produced more than 30% breaks. The fact that both chromosome aberrations and pollen sterility level off after a few weeks of exposure indicates that the plants can survive and reproduce after months, or perhaps even years, of exposure. Unfortunately, these results cannot be expected to apply to the higher animals, including man. The factors of determinate growth, high sensitivity of critical tissues, the absence of haploid mitosis in gametophytic development, and the lack of rapid somatic divisions preceding egg formation, should render animals much more vulnerable to low intensities of ionizing radiation. (NSA)

2107

Sax, Karl and Robert T. Brumfield. THE RELATION BETWEEN X-RAY DOSAGE AND THE FREQUENCY OF CHROMOSOMAL ABERRATIONS. *Am. J. Botany* **30**, 564-70(1943).

The frequency of simple chromosomal deletions induced in *Tradescantia* microspores by x-rays tends to increase in direct proportion to dosage while aberrations involving two chromosomes or two loci of the same chromosome tend to increase as the square of the dosage if the time of exposure is constant, and the x-ray intensity is high. The relation between aberration frequency and x-ray dosage for meiotic division in *Tradescantia* is approximately linear, apparently due to the prevalence of 1-hit aberrations. The frequency of 2-hit aberrations in root-tip cells in *Vicia*

tends to increase in direct proportion to dosage. The difference in the dosage curve relations in *Tradescantia* microspores and *Vicia* root-tips is attributed to differences in the physiological response to x-rays in the two types of cells. (BA)

2108

Sax, Karl and E. V. Enzmann. THE EFFECT OF TEMPERATURE ON X-RAY INDUCED CHROMOSOME ABERRATIONS. *Proc. Natl. Acad. Sci. U. S.* **25**, 397-405 (1939).

Tradescantia microspores x-rayed at low temperatures show more chromosome aberrations than those irradiated at high temperatures. At high temperatures fusion of broken ends is accelerated and many of the breaks are reunited in the original position, while at low temperatures fusion is delayed and broken ends may fuse in illegitimate unions to produce many chromosome aberrations. This interpretation applies to nuclei irradiated at the resting stage and at mid-prophase, but the reversed temperature effect on early prophase chromosomes is difficult to explain. The temperature effect is maximal at a critical temperature which appears to vary with the seasonal effect on the nuclear cycle. The varied response of different types of cells to temperature effects during irradiation can be attributed to the relative effects of physiological and genetic factors. (Authors' Summary)

2109

Sax, Karl and C. P. Swanson. DIFFERENTIAL SENSITIVITY OF CELLS TO X-RAYS. *Am. J. Botany* **28**, 52-9(1941).

Cell sensitivity to x-rays was measured by the frequency of induced chromosomal aberrations. In *Tradescantia* microspores the sensitivity is greatest shortly before mid-prophase. Of the various types of cells in *Tradescantia* the microsporocytes are most sensitive and the generative cell is most resistant to x-rays. Haploid microspores are more sensitive than diploid microspores. Differential sensitivity is attributed to differences in chromosome structure and freedom of chromosome movement. (BA)

2110

Schjeide, Ole Arne and Bennet M. Allen. THE RELATION OF MITOSIS TO THE MANIFESTATION OF X-RAY DAMAGE IN HEMATOPOIETIC CELLS OF TADPOLES. *J. Cellular Comp. Physiol.* **38**, 51-68(1951).

This work is a quantitative test of the concept that hematopoietic cells of the tadpole of *Rana catesbeiana* show visible damage from previously administered 500 r hard x rays only upon entering into mitosis. The mitotic inhibitor colchicine is utilized as an index of the rate of division in tadpole tissue. Comparison is made between total cells entering mitosis during a given period and the number of cells developing x-ray damage in the same length of time following exposure. Tadpoles are subjected to several accurately controlled body temperatures for these determinations. Hematopoietic cell destruction following 500 r x rays is found to be directly correlated with rate of cell division during this same time. Rate of mitosis, as well as rate of cell destruction by 500 r x rays is proportional to temperature. However, at 10,000 and 20,000 r the rate of hematopoietic cell destruction exceeds the amount of cell division. Hematopoietic cells appear to sustain initial invisible damage by 500 r x rays during the resting state and perhaps all cellular phases. The visible cell destruction is, however, apparently expressed as a secondary characteristic of the initial damage and seems to appear only at the time of cell division. The mitotic phase at which the first visible indications of damage occur is probably the prophase. Hematopoietic cells held in the late prophase by colchicine are destroyed by 500 r x rays. (NSA)

2111

Schmermund, H. J., H. Bleck, and H. L. Heinrich. CHROMOSOME MODIFICATIONS PRODUCED IN BARLEY SEEDLINGS BY FAST ELECTRONS OF A 6-MEV BETA-TRON. *Strahlentherapie* **81**, 177-86(1950).

A comparative study was made of fast electrons and x-rays as radiobiological agents. Various doses of 4-Mev electrons obtained in a 6-Mev betatron, and of x-rays whose half-value layer was 0.25 mm Cu, produced changes in the mitosis pictures of the end cells in the roots of barley seedlings. These changes are fragmentations of the chromosomes plus a sticking together of the latter to form a bridge between the two chromatin masses of the dividing nucleus in its ana- and telo-phases. The frequency of such changes among the dividing cells was taken as a measure of the extent of the lesion produced by the irradiation. It was found that with both kinds of rays the structural changes grow with the dose, the fast electrons being somewhat less active, per dose unit, than x-rays. This difference is explained by the inequalities in the differential ionization and in the size of the ion groupings produced by the two kinds of rays. If the ion groupings are considered the "hits" or "events" of the target theory of ray action, the lesion curves for both kinds of rays show that the number of "hits" involved in the reaction studied here is 3 to 5. (NSA)

2112

Sieburth, Louise R. THE INTERACTION OF NUCLEIC ACID AND X-RADIATIONS ON THE CHROMATIN OF RYE AND PEA. *Northwest Sci.* **25**, 132-6(1951).

Rye and pea seeds in the energetic stage were treated with x radiation and/or sodium ribose nucleate. Cells treated with 5000 r showed pycnosis and multinucleoli. The nucleolus had such dense clumping of the chromatin as to be solid in outline. The nucleolus of the rye cells was much larger than in the pea cells, but the nature of the pycnosis of the rye and pea cells was observed to be the same. The material treated with 200 r was similarly affected except that the nucleolus in rye cells showed the chromatin in distinct "bands," whereas pea cells were normal. Normal prophase of mitosis was observed in rye and pea cells treated with nucleate and followed by 200 r. The cells of rye and pea treated with 200 r and followed by nucleate showed different characteristics. In the rye cells, the chromatin was evenly dispersed but was somewhat pycnotic in nature. No nucleolus differentiation was observed. The pea cells on the other hand showed normal granular chromatin, except that the nucleolus showed distinct even clumping of the chromatin. (NSA)

2113

Simon-Reüss, I. and F. G. Spear. EFFECT OF GAMMA RADIATION ON MITOSIS IN VITRO. I. *Brit. J. Radiol.* **20**, 63-70(1947).

Cells from the choroid and sclerotic of chick embryos in culture were irradiated with doses from 55 to 1,320 r at the rate of 22 r/min, and the subsequent effect on mitosis was observed by photographic methods. At 55 r there was little alteration in cell behavior. At 88 r about half the observed dividing cells were affected. After 1,320 r mitosis was very scanty, no cells completing division normally. There was little recovery after one hour. The chief difficulty in studies of this type is to determine the beginning of the prophase. In the present study timing was begun at the beginning of metaphase to avoid this difficulty. (R)

2114

Singleton Ralph W. GENETIC EFFECTS OF RADIATION, p.40-50 of CONFERENCE ON BIOLOGICAL APPLICATIONS OF NUCLEAR PHYSICS. Brookhaven National Laboratory. July 1948. 10p. (BNL-C-4(p.40-50))

Studies have been made (with Lea collaborating) on the effects on the chromosomes of *Tradescantia* at the first and second microspore division of a) different doses and intensities of X-rays and γ rays at various temperatures, b) different wave lengths of x-rays, and c) neutrons and α -rays. The main results are as follows: Neutrons are more efficient than x-rays in producing breaks. Two-break aberrations, e.g., interchanges, are proportional to the first power of the dose in the case of neutrons, but to the square of the dose in the case of x-rays and γ -rays. Interchanges produced by x-rays are therefore due mainly to two separate hits by ionizing particles, while those produced by neutrons are mainly one hit. The neutron work enables one to show that a fairly considerable number of ionizations, spread across the chromosome, are necessary to break it; and that x-ray breakage is due mainly to the densely ionized tail of the electron track. This agrees with the finding that soft x-rays are more efficient than medium and hard ones, there being an optimum of about 4 A. About 90% of chromatid breaks primarily produced by x-rays, undergo restitution, their lives as free breaks averaging about 4 minutes at 20°C. The separation at the time production of breaks which take part in the interchanges is in the order of one micron or less. This pretty well sums up the work on exchanges produced by ionizing radiations. (Author's Summary)

2115

Slizynski, B. M. PARTIAL BREAKAGE OF SALIVARY GLAND CHROMOSOMES. *Genetics* **35**, 279-87(1950).

Low dosage x-ray treatment (400 to 600 r units) of *Drosophila melanogaster* embryos when applied in early development stages produces in the salivary gland chromosomes partial structural changes affecting only a few of the chromonemata of which the chromosome is composed. Partial structure changes include deficiencies, inversions, translocations and ring chromosomes; partial structural changes may also appear in mutual combination. Structural changes in which a few fibrils are thus separated *in vivo* from the remaining mass of the chromonemata form confirmatory experimental evidence of the polytene nature of salivary gland chromosomes of Diptera. 13 references. (NSA)

2116

Smith, Luther. A COMPARISON OF THE EFFECTS OF HEAT AND X-RAY ON DORMANT SEEDS OF CEREALS, WITH SPECIAL REFERENCE TO POLYPLOIDY. *J. Agr. Research* **73**, 137-58(1946).

Diploids were as tolerant of high temperatures as polyploids, whether the duration of treatment was a few hours or several days. Polyploids showed greater tolerance to x-rays. Seeds of diploid wheat given heat treatments after irradiation were injured slightly more than those given irradiation only. Comparable seeds given heat treatments before irradiation were injured less than those given irradiation only. Data from such combination treatments on diploid barley were not conclusive, but indicated similar results. Heat had little if any effect on the frequency of chromatinic bridges in root-tip cells of diploid, tetraploid, and hexaploid wheat, and diploid and autotetraploid barley. X-ray treatment of the same stocks resulted in a marked increase in the frequency of bridges in root-tip cells. Heat treatment of seeds of diploid and tetraploid wheat had little if any effect on the frequency of translocations. X-ray treatments, on the other hand, produced a marked increase in the frequency of translocations. Heat treatments of seeds of diploid wheat did not appreciably affect the mutation rate, whereas x-rays distinctly increased it. (CA)

2117

Smith, W. W. EFFECT OF THYROID HORMONE AND

RADIATION ON THE MITOTIC INDEX OF MOUSE EPIDERMIS. J. Cellular Comp. Physiol. **38**, 41-9(1951).

Thyroid administration caused an increase in the mitotic index of mouse ear epidermis sampled in midmorning, which reached full development at the same time as other manifestations of thyroid action. Thyroid administration did not affect the response of mitotic activity, as measured by the mitotic index of the mouse ear epidermis, to sublethal whole-body irradiation. Conversely, radiation did not affect the response of mitotic activity to thyroid administration. (Author's Summary)

2118

Sparrow, A. H. RADIATION SENSITIVITY OF CELLS DURING MITOTIC AND MEIOTIC CYCLES WITH EMPHASIS ON POSSIBLE CYTO-CHEMICAL CHANGES. Ann. N. Y. Acad. Sci. **51**, 1508-40(1951) (AECU-160)

Original data on sensitivity changes to x-rays during the nuclear cycle in *Trillium erectum* are presented. They show late prophase and metaphase to be highly sensitive to x-ray breakage and early interphase to be of low sensitivity. The tendency of broken ends to rejoin seems to be inversely related to the amount of fragmentation per unit dosage. The general significance of these conclusions is discussed in the light of other work on sensitivity changes during nuclear division. The distribution of chromosome breaks within chromosomes and the relationship of breakage to mutation are also discussed. The factors affecting nuclear radiosensitivity are considered under the following topics: morphological and structural differentiation within the nucleus; sub-microscopic, cytochemical and cytophysiological factors; effects of mitotic inhibitors, mitotic poisons and other miscellaneous substances; and effects of physical factors. It appears that the condensed state of the chromosome (late prophase, metaphase, anaphase) is one of high sensitivity to breakage and that the diffuse stages such as telophase, interphase, and early prophase are relatively much less sensitive. Possible reasons for these differences are considered and possible mechanisms whereby the processes initiated by ionizations produce effective chromosome breaks are presented and discussed. (NSA)

2119

Sparrow, Arnold H. A CYTOLOGICAL AND CYTO-CHEMICAL APPROACH TO AN UNDERSTANDING OF RADIATION DAMAGE IN DIVIDING CELLS. Brookhaven National Laboratory. [nd] 2p. (AECU-821)

The document is in abstract form; it is reproduced below in its entirety.

Analysis of induced chromosome fragmentation following irradiation at different stages in the nuclear cycle (mitosis) of *Trillium erectum* indicates that major changes in the radiation sensitivity of the chromosomes occur. Two types of fragments have been observed and scored: (a) those which become visible at the metaphase or anaphase immediately following prophase irradiation, and (b) those which are detectable only after the chromosomes have passed through an interphase and entered the succeeding metaphase. When both types are considered, it is found that irradiation at late prophase (diplotene-diakinesis) and metaphase stages yields a very large number of fragments, and irradiation at late telophase and early interphase produces relatively few fragments. Since loss of nuclear material is proportional to the induced fragmentation, it may be assumed that the amount of chromosome fragmentation is a fair index of eventual cell lethality (and probably also of mutation). It therefore becomes of considerable significance to try to determine the factors controlling the degree and manner in which the chromosomes react to ionizing radiation. Morphological changes and physical

factors (stress, repulsion, etc.) are known to be important. Submicroscopic, cytochemical, and cytophysiological changes are also very important but, unfortunately, less well known.

Measurements of desoxypentose nucleic acid (DNA) at stages of high and low sensitivity indicate that total DNA is not related to radiation sensitivity; however, its rate of synthesis or its distribution within the nucleus may be. Other factors known to influence radiation effect such as oxygen tension and sulfhydryl oxidation also will be briefly discussed, as well as evidence of disturbances in nuclear metabolism following irradiation.

Results of continuous exposure of bacteria to beta and of various species of higher plants to γ radiation will be reported briefly. (NSA)

2120

Sparrow, Arnold H. CONSIDERATION OF THE RELATIONSHIP BETWEEN CHROMOSOME BREAKAGE AND MITOTIC INHIBITION INDUCED BY IONIZING RADIATION. Brookhaven National Lab. [nd] 1p. (AECU-822)

The document is in abstract form; it is reproduced below in its entirety.

Cells irradiated in mid to late prophase are known to show a high degree of mitotic inhibition. This is also a stage of very high sensitivity to radiation-induced chromosome breakage. Subsequent loss of chromatin resulting from fragmentation leads to the production of a secondary mitotic inhibition. Two distinct mechanisms of inhibition seem to be involved. The question then arises as to whether the two stem from a common initiating phenomenon. If they do, it should be possible to relate the mechanisms of primary inhibition and chromosome fragmentation. The following working hypothesis is proposed.

Ionizing radiations are known to depolymerize DNA and denature proteins. Either of these changes in the nucleoprotein complex comprising chromosomes (or genes) can be visualized as sufficient to inhibit self-reproduction of the complex. Further, such changes seem sufficient to presume increased susceptibility of the complex to destruction by enzymatic processes. Denatured proteins are known to be more susceptible to proteolysis, and alkaline phosphatase is known to attack only the partly depolymerized form of nucleic acids. The preventing of self-reproduction is synonymous with mitotic inhibition and breakdown of changed chromatin, through attack by physiological processes, with resultant chromosome breakage. Thus it appears that both inhibition and breakage may be related to the same primary changes produced in the nucleoprotein by ionizing radiation. (NSA)

2121

Sparrow, Arnold H. SOME CYTOLOGICAL AND MORPHOLOGICAL CHANGES INDUCED IN PLANTS BY IONIZING RADIATION. Brookhaven National Lab. [nd] 1p. (AECU-1645)

The report is reproduced here in its entirety.

Several species of plants have been exposed to chronic γ irradiation from Co^{60} for periods up to four months. There was considerable variation in the radiosensitivity of different species, but in one instance no significant effect was detectable after 2000 r per day for six weeks. Generally, however, much lower dosages were sufficient to produce one or more characteristic morphological responses. These included, in addition to growth inhibition, some fasciation and various unusual shapes and sizes of leaves of reproductive structures. Hypertrophic growth in certain structures was frequently produced in some species. In others tumor-like growths as well as somatic mutations were observed. In *Tradescantia paludosa* a dramatic increase in the number of both vegetative and

flower buds was noted after chronic irradiation of about 30 r per day.

Cytological observations were made on both meiotic and somatic cells of irradiated *T. paludosa*. The expected types of chromosomal aberrations were found and their frequency in both tissues determined. Meiotic chromosomes were shown to be much more radiosensitive than chromosomes of somatic cells. This agrees with the observation that pollen sterility and morphological abnormalities in the anthers occur at dosages which have relatively little gross effect on somatic tissue.

Dosages which caused marked morphological changes also produced a considerable amount of chromosomal aberration. However, since recovery to a normal growth pattern occurred in many plants which had previously shown severe radiation damage, it would seem that most of the morphological aberrations were not of a genetic nature. It is considered that they were probably the result of radiation induced physiological changes, although the possibility that they are somehow related to chromosomal aberrations cannot yet be excluded. (NSA)

2122

Sparrow, Arnold H. X-RAY SENSITIVITY OF MEIOTIC AND MICROSPORE CHROMOSOMES OF TRILLIUM. Records Genet. Soc. Am. 12, 54-5(1943).

Trillium erectum is favorable material for studying chromosome sensitivity to X-rays at various stages, because at low temperatures meiosis proceeds very slowly. It was thus possible to irradiate at known stages and subsequently to determine the number of aberrations. The number of fragments induced by a given dosage was used as an index of the X-ray sensitivity of the stage rayed. Early results indicated that plants rayed at first metaphase and first anaphase were highly resistant, as they showed very few chromosome breaks in meiotic stages. However, a large number of tetraploid and diploid pollen grains appeared following irradiations of first metaphase and first anaphase respectively. Examinations of these revealed a very large number of fragments, indicating that the great majority of X-ray "hits" on meiotic metaphase and anaphase chromosomes do not induce visible breaks until the following microspore division. Their high sensitivity is then apparent. The least sensitive stages were early meiotic prophase (leptotene-zygotene) and pollen grain resting stage. These were of about equal sensitivity. There was an increase at pachytene to a little less than twice the number of fragments. First metaphase was still more sensitive, with about 6 times as many fragments; and anaphase was even higher, giving 9 times the number found after leptotene-zygotene raying. This large change in sensitivity cannot be correlated with known length changes of the chromonemata, but it is suggested that it may be related to the nucleic-acid and spiralization cycles. The above results indicate that colchicine treatment preceding irradiation could be used to increase tissue sensitivity. (RG)

2123

Sparrow, Arnold H. X-RAY SENSITIVITY CHANGES IN MEIOTIC CHROMOSOMES AND THE NUCLEIC ACID CYCLE. Proc. Natl. Acad. Sci. U. S. 30, 147-55(1944).

The relative effects of x-rays on different stages of meiosis and on microspore resting nuclei have been investigated in *Trillium erectum*. The ratio of chromosome aberrations was roughly 1 : 2 : 6 : 9 : 1 for early meiotic prophase, pachytene, metaphase, anaphase, and post-meiotic resting nuclei respectively. It is argued that since stages of high sensitivity to x-rays also have a high content of desoxyribose nucleic acid and v. v., sensitivity to

radiation may be correlated with nucleic acid metabolism. The relationship of the findings to tumor sensitivity is discussed.

2124

Sparrow, Arnold H. REDUCED CHROMONEMA ELONGATION AND ABNORMAL SPIRALIZATION FOLLOWING X-RAY TREATMENT OF MEIOTIC CHROMOSOMES. Genetics 30, 23(1945).

In *Trillium*, the formation of the major coil between early diakinesis and first anaphase is normally accompanied by an elongation of the chromonema estimated to be not less than threefold. However, in pollen mother cells x-rayed at meiotic prophase the major spiral in many cells is very poorly developed even as late as second anaphase. Measurements of chromonema length at first and second anaphase in such cases indicate that elongation has been reduced to considerably less than half that found in control material. Reduced spiralization in other cases is known to be associated with low nucleic acid concentrations, e.g., in negatively heterochromatic chromosomes or regions and in cold-induced "differential reactivity". It is also shown that x-rays inhibit the formation of desoxyribose nucleic acid. It is therefore suggested (1) that the abnormal spiralization and reduced chromonema elongation following x-ray treatment may be associated with an x-ray induced deficiency of desoxyribose nucleic acid, and (2) that the normal prophase increase in desoxyribose nucleic acid may play an important role in the mechanics of spiralization.

2125

Sparrow, Arnold H. TOLERANCE OF TRADESCANTIA TO CONTINUOUS EXPOSURES TO GAMMA RADIATION FROM COBALT⁶⁰. Genetics 35, 135(1950). (AECU-681)

Plants of a clonal line of *Tradescantia paludosa* were exposed under field conditions to continuous γ radiation (1.1 and 1.3 Mev) of approximately 122, 30.4, 7.5, 1.8, 0.41, and 0.084 r per day, for 8, 16, 32, and 64 days. Dosage rates of 122 and 30.4 r per day permitted little or no growth, while fairly normal growth occurred at 7.5 r per day or less. Complete pollen abortion was produced after 16 days at 122 r per day. Chromosome breaks as such were not scored, but micro-nuclei at the microspore resting stage were counted. These are assumed to represent acentric fragments which lagged and remained in the cytoplasm at second telophase. A significant increase in the frequency of micronuclei was obtained with as low as 84 mr per day after 32 days of exposure (total dose 2.69 r). Dosage curves for various exposure times will be presented. An attempt will be made to relate growth-inhibiting and lethal doses to the percentage of microspores containing micro-nuclei. (NSA)

2126

Sparrow, Arnold H. and E. Christensen. NON-RANDOM DISTRIBUTION OF CHROMOSOME FRAGMENTATION IN UNIRRADIATED TRILLIUM. Genetics 35, 135(1950)

An unusual type of spontaneous fragmentation has been found in a plant of *Trillium erectum*. There is considerable variation from another to another though some appear normal. In the most extreme case about 4% of the microsporocytes show aberrations. However, within this small group of cells chromosome fragmentation reached an extreme of about 30 breaks per cell. This is equivalent to that produced by a dose of at least 100 r at a highly sensitive stage or of not less than 5,000 r at a stage of low sensitivity. Statistical analysis shows the distribution of break frequency in the abnormal cells to differ significantly from that expected in irradiated material. The reason for this difference is not understood. Other ab-

normalities such as "fused" microsporocytes indicate that a physiological disturbance may be responsible. The seriousness of this type of spontaneous fragmentation in radiation experiments involving the use of chromosome breaks as a measure of radiation effect is obvious. (G)

2127

Sparrow, Arnold H. and Marc Maldawer. DIFFERENTIAL REJOINING AS A FACTOR IN APPARENT SENSITIVITY OF CHROMOSOMES TO X-RAY BREAKAGE. *Proc. Natl. Acad. Sci. U. S.* **36**, 636-43(1950) (AECU-989)

Differential rejoining has been studied in microspores of *Trillium erectum* following x irradiation at stages of high and low apparent sensitivity to breakage. The stages irradiated were meiotic first metaphase and early post-meiotic interphase. Fragments, dicentrics, and rings were scored at microspore anaphase. The numbers of dicentrics and rings observed were used as a measure of rejoining. The data indicate a significantly higher amount of rejoining in cells irradiated at early interphase than in those irradiated at meiotic metaphase. However, the increase in rejoining is not sufficient to account for the observed decrease in fragmentation. It is, therefore, concluded that the observed difference in sensitivity of the two stages studied is due in part to a difference in number of primary breaks (or potential breaks) and in part to a difference in the amount of rejoining which subsequently occurs. In the material studied a high sensitivity to primary breakage is associated with a low frequency of rejoining and vice versa. Certain implications of these conclusions on calculations of mutation rate and gene size are discussed. (NSA)

2128

Sparrow, Arnold H., M. J. Moses, and R. Steele. A CYTOLOGICAL AND CYTOCHEMICAL APPROACH TO AN UNDERSTANDING OF RADIATION DAMAGE IN DIVIDING CELLS. *Brit. J. Radiol.* **25**, 182-9(1952) (AECU-1438)

The amount of chromosome fragmentation induced by a dosage of 50 r of x radiation has been determined at various stages in the meiotic nuclear cycle of *Trillium erectum*. Diplotene seems to be the most sensitive, and early interphase least sensitive. (Diakinesis and first metaphase are also highly sensitive.) The sensitivity change is at least 60-fold. Higher rejoining is apparently a significant factor in reducing the amount of definitive fragmentation at the least sensitive stage, but does not account for the whole difference in sensitivity. Desoxypentose (DNA) and pentose (PNA) nucleic acid determinations show that the DNA per pollen-mother-cell increases up to diplotene and remains constant thereafter until early post-meiotic interphase. Synthesis starts again during later interphase. PNA remains constant from pachytene through second division to early interphase. The sharp rise in the sensitivity curve during the periods when DNA content increases indicates that increasing sensitivity may be associated with synthesis of DNA. However, the fall in breakage sensitivity between first metaphase and early post-meiotic interphase when DNA content does not change indicates that DNA content does not determine cellular radiosensitivity. (NSA)

2129

Sparrow, Arnold H. and L. F. Nims. A CYTOLOGICAL AND CYTOCHEMICAL APPROACH TO AN UNDERSTANDING OF RADIATION DAMAGE IN DIVIDING CELLS, p.47 of INTERNATIONAL CONGRESS OF RADIOLOGY, 6th Congress, London. 1950.

Since loss of nuclear material is proportional to the induced fragmentation, it may be assumed that the amount of chromosome fragmentation is a fair index of eventual

cell lethality (and probably also of mutation). It therefore becomes of considerable significance to try to determine the factors controlling the degree and manner in which the chromosomes react to ionising radiation. Morphological changes and physical factors (stress, repulsion, etc.) are known to be important. Submicroscopic, cytochemical and cytophysiological changes are also very important but unfortunately, less well known. Measurements of desoxypentose nucleic acid (DNA) at stages of high and low sensitivity indicate that total DNA is not related to radiation sensitivity. Other factors known to influence radiation effect such as oxygen tension and sulphhydryl oxidation are also discussed, as well as evidence for disturbances in nuclear metabolism following irradiation. Results of continuous exposure of bacteria to beta and of various species of higher plants to γ radiation are briefly reported.

2130

Spear, F. G. and A. Glucksmann. THE EFFECT OF GAMMA RADIATION ON CELLS IN VIVO. PART III. SPACED RADIATION. *Brit. J. Radiol.* **14**, 65-76(1941).

The experiments described here were conducted to determine whether the amount of degeneration seen after exposure could be increased by delivering the second of the two exposures at the moment when mitosis was least active as a result of the first exposure. In addition, "spread over" irradiations were delivered at such lowered intensity as would give the same total dose. Tadpoles were used three to six weeks after hatching. Two sources of radiation were used: (1) radium needles containing a total of 175.5 mg, and (2) 90 thin-walled, 2 mg Ra needles (total Ra content, 360 mg). The methods of irradiation were: (a) dose of 268 r delivered over 70.5 minutes at an intensity of 3.8 r/min.; (b) spread-over dose of 536 r delivered in 1,581 minutes at an intensity of 0.34 r/min.; (c) spread-over dose of 536 r delivered in 261 minutes at an intensity of 2.05 r/min.; (d) two exposures of 70.5 minutes at 3.8 r/min, separated by an interval of 24 hours; (e) two exposures of 70.5 minutes at 3.8 r/min., separated by an interval of 20 minutes; (f) single irradiation of 536 r delivered over 141 minutes at 3.8 r/min; and (g) two exposures of 70.5 minutes at 3.8 r/min, separated by an interval of 10 days. In every experiment the effect of radiation is to reduce mitotic activity. The following sequence of biological response is seen: Very small doses: no recognizable change in behavior of irradiated cell. Threshold dose: some cells prevented from dividing, but normal mitosis occurs later on. No degenerate cells produced. Larger doses: some cells reach prophase and then break down. ? some slowing-up of prophase. Maximum dose (536 r) delivered as one exposure: temporary arrest in prophase, subsequent breakdown of cells. Increase in number of differentiating cells. Maximum dose delivered in two exposures at optimum spacing: mitosis reduced almost to zero. Large amounts of degeneration. (S. V. S.)

2131

Speidel, Carl Caskey. AN EXPERIMENTAL STUDY WITH THE AID OF CINE-PHOTOMICROGRAPHY OF NUCLEAR CHANGES IN IRRADIATED AND INJURED CELLS IN LIVING FROG TADPOLES. *Anat. Records* **103**, 560(1949).

(The following is an abstract and is reproduced here in its entirety.)

Histological observations have been made on the nuclei of cells in frog tadpoles, as the animals are subjected to various kinds of injury. The changes have been watched in moribund cells, also in cells that recover. A few similar observations have been made on dividing cells. Illustrative motion pictures of both the normal and fast-motion type have been obtained. Among the injurious agents used are treatments with alcohol, metrazol, colchicine, podophyllum,

nitrogen mustard, electric shocks, potassium citrate, various other chemicals, and mechanical wound inflictions. Changes in the nucleus include marked swelling in some cases, marked contraction in others, coarse ring formations, and disintegrations into coarse or fine granules. Some of the kinds of naturally occurring degeneration that accompany tail reduction during tadpole metamorphosis have also been photographed. Long drawn trophic injuries of cells have been induced by destroying the relationship between two structures that normally function as a unit, such as the lateral-line sense organs and their specific nerves. The sensory cells of nerveless organs undergo atrophy, dedifferentiation, and degeneration. Organless nerves also degenerate. Sheath cells that remain permanently stranded on such nerves likewise atrophy and degenerate.

2132

Swanson, C. P. THE EFFECTS OF ULTRAVIOLET AND X-RAY TREATMENT ON THE POLLEN TUBE CHROMOSOMES OF *TRADESCANTIA*. *Genetics* 27, 491-503(1942).

In addition to extending information on the capacity of ultraviolet to produce simple breaks in pollen tube chromosomes, the present study has brought out the following new evidence: The frequency of chromatid breaks induced by ultraviolet at 2537A is directly proportional to dosage. A similar situation appears to hold for the longer wave lengths (2967 and 3022), but the scantiness of the data permit of no definite conclusion. A non-random distribution of chromatid breaks was found when nuclei in the pollen tubes were treated with ultraviolet and x-rays. Breaks were more frequent in the medial and distal regions contrary to that previously reported in *Tradescantia* and *Gasteria*. A delayed series of uv treatments show that the prophase chromosomes became progressively more resistant as judged from breakage data. In the 2- to 4-hour period after germination, the chromosome appears to become more susceptible to x-ray breakage, but with uv, the reverse was true. Following heavy doses of short wave length uv treatment at prophase, the metaphase chromosomes showed a marked shortening accompanied by the appearance of a hyaline sheath surrounding them. Longer wave lengths produced no such change. (Author's Summary)

2133

Swanson, C. P. DIFFERENTIAL SENSITIVITY OF PROPHASE POLLEN TUBE CHROMOSOMES TO X-RAYS AND ULTRAVIOLET RADIATION. *J. Gen. Physiol.* 26, 485-94 (1943).

This study indicates that the pollen tube chromosomes of *Tradescantia* show a varying sensitivity to both x-rays and ultraviolet as they pass through prophase stages, using the rate of induced breaks as a criterion of sensitivity. Following ultraviolet (nearly monochromatic 2537 A), a rise in sensitivity is indicated up to two hours after the pollen grains are sown on an artificial medium, after which a steady decline follows. However, since the generative nucleus at the 0 and 1-hour stages were irradiated through the pollen wall which absorbs strongly, it appears likely that the resting stage is more sensitive than are the succeeding prophase stages. Following x-radiation, a rise in total chromosome breaks continues to the 4-hour period after which a decline sets in. Each type of break varies in sensitivity at different periods. At late prophase stages, neither x-rays nor ultraviolet leads to an increased production of breaks over the spontaneous rate. The uptake of water and the movement of the chromosomes (due to spiralization and readjustments within the nucleus) readily account for the observed differential sensitivity to x-rays, the most active stages being the most sensitive. Differ-

ential breakage to ultraviolet is probably related to one or more of three factors: 1) nucleic acid accumulation on the chromonema, 2) development of the matrix, and 3) subdivisions of the chromonema. Their relative importance to this problem is conjectural. (BA)

2134

Swanson, C. P. X-RAY AND ULTRA-VIOLET STUDIES ON POLLEN TUBE CHROMOSOMES. I. THE EFFECT OF ULTRAVIOLET ON X-RAY INDUCED CHROMOSOMAL ABERRATIONS. *Genetics* 29, 61-8(1944).

A study of the effect of short wave length uv (2537A) on the production of x-ray breaks in the pollen tube chromosomes of *Tradescantia* test to the following conclusions. Pre-treatment one hour before x-raying, leads to an inhibition of all types of visible x-ray breaks. Single deletions and translocations are more affected than are double deletions. The degree of inhibition depends upon the dosage of ultraviolet used, although the exact proportionality is not known. Post-treatment has no inhibitor effect on double deletions regardless of time of application. Translocations show considerable inhibition if the post-treatment is given immediately after X-radiation, slight inhibition if given one-half hour later, no inhibition if given one hour later. Single deletions are inhibited even after the one hour post-treatment suggesting that the ultraviolet facilitates restitution. It is suggested that the action of ultraviolet is not immediate, but that a certain time interval is required before it becomes effective. A further suggestion is made that the inhibition caused by the ultraviolet results from an effect produced on the chromosome matrix which leads to its greater resistance to X-ray breakage. (Author's Summary)

2135

Swanson, C. P. and A. Hollaender. THE FREQUENCY OF X-RAY-INDUCED CHROMATID BREAKS IN *TRADESCANTIA* AS MODIFIED BY NEAR-INFRARED RADIATIONS. *Proc. Natl. Acad. Sci. U. S.* 32, 295-302(1946).

The frequency of x-ray-induced chromatid breaks in *Tradescantia* can be significantly increased by treatment of the inflorescences with near infrared radiation. Pre-treatment with near infrared radiation for seven hours prior to x-radiation increased the frequency of single deletions, double (isochromatid) deletions, and translocations between and within chromosomes; post-treatment increased only single deletions and translocations. A delay of 21 hours between treatment with infrared and x-rays did not appreciably decrease the effectiveness of the infrared, suggesting that the changes within the cell induced by the infrared were of a relatively permanent nature. At the present time, the nature of the effect of infrared is not clearly understood.

2136

Swanson, C. P. and Henry T. Yost, Jr. THE ACTION OF INFRARED RADIATION ON THE CHROMOSOMES OF *TRADESCANTIA*. *Genetics* 36, 579(1951).

By analogy with certain physical phenomena such as phosphorescence it seems possible that infrared might act by raising the molecular structures of the chromosome to a metastable condition, in which state these structures, as yet unidentified, react with increased frequency to subsequent doses of x-rays. This was tested by subjecting infrared-treated buds to heat shock (48°C. for 30 sec.), a treatment designed to return a metastable state back to an original ground state. We have shown that such heat treatments, interposed between infrared and x-rays, remove the infrared effect, the chromosomes behaving to x-rays as though no infrared had been given. A similar effect was obtained when the order of treatment was x-rays - heat -

infrared. From these two types of experiments, plus additional studies which revealed that the effectiveness of infrared was a function of the temperature of the buds at the time of infrared treatment, we have concluded that the primary action of infrared is to induce metastable states in the chromosomes. Such chromosomes react more readily with the free radicals released in the surrounding area by the ionizing radiation to yield a higher frequency of primary breaks per given dose of x-rays. (G)

2137

Tahmisian, Theodore N. **THE EFFECT OF X-RADIATION ON THE METABOLIC PROCESSES OF THE RESTING CELL.** J. Exptl. Biol. 112, 449-64(1949) (AECU-539;J-539) UAC-128)

It is reported that x-radiation dosages ranging from 10,000 r to 200,000 r do not completely inhibit respiration in the diapause grasshopper embryo (Melanoplus differentialis). Respiratory, morphological, and cytological studies revealed that anabolic enzymes are associated with the nuclear material and are more susceptible to x-irradiation damage than the catabolic enzymes. In a resting cell a nucleus was necessary for maintenance of the status quo of the cell. Following x-irradiation a resting nucleus was found not to have to undergo mitosis to become pycnotic. Pycnosis of the resting nucleus depended upon the x-ray dosage, upon the state of metabolism, and upon time. Repression of irradiation damage to the cell was obtained by subjecting the cells to submetabolic temperatures. The integrity of the nuclear chromatin material was dependent upon its functional potency. (NSA)

2138

Tahmisian, Theodore N. and Dorothy M. Adamson. **A PHASE CONTRAST MICROSCOPY STUDY OF X-RAY-INDUCED PYCNOSIS IN THE LIVING CELL.** Anat. Record 108, 572-3(1950). (ANL-4488(p.54))

This section of the report is in abstract form, and is reproduced here in its entirety.

The effect of x radiation ranging from 25,000 to 200,000 r can be kept latent in Melanoplus differentialis embryos for 6 months by maintaining them at submetabolic temperatures. If diapause eggs are irradiated and left at 25°C, pycnosis of the nuclei takes place by 8 days. When the eggs are irradiated and placed immediately at 0°C and kept at this temperature for 6 months, no morphological or physiological changes are observed upon returning them to 25°C. However, pycnosis occurs by 8 days at 25°C depending not only on the radiation dosage but also on the metabolic activity of the cell. Pycnosis in the living cell, as observed by phase-contrast microscopy, resembles fixed material morphologically. Physiologically there is a difference in the physical state of the nuclei when observed in the living condition. Most nuclei show a drop in viscosity at the time of pycnosis, as judged by the increase in Brownian movement. Vital staining with Janus green indicates that the mitochondria usually clump as a separate body, whereas the chromatin material becomes pycnotic, containing lipid-impregnated bodies. (NSA)

2139

Tahmisian, Theodore N. and Jean Gasvoda. **MORPHOLOGICAL AND RESPIRATORY CHANGES INDUCED IN MELANOPLUS DIFFERENTIALIS BY BETA IRRADIATION.** Argonne National Laboratory. Feb. 1951. 1p. (AECU-1258; UAC-350)

The report is reproduced here in its entirety.

Prediapause eggs of the grasshopper, Melanoplus differentialis, were exposed to β radiation emanating from P^{32} of Sr^{89} solutions to determine the morphological and respiratory changes that occur during and following such irradiation. Total dosages delivered to the embryos ranged

from 3.07 to 1215 r. Extensive damage was seen in the cells at all exposure levels. Respiration was increased during irradiation but was inhibited immediately thereafter. By use of Flemming's triple stain it was shown that β irradiation caused pyknotic chromatin to appear as though it were in the metaphase condition. An osmophilic material, associated with the chromosomes, was observed following exposure. This material is a lipid that undoubtedly is a degradation product of lipoproteins known to be present in chromosomes.

2140

Thoday, J. M. **THE EFFECT OF IONIZING RADIATIONS ON THE BROAD BEAN ROOT. PART IX. CONCLUDED.** Brit. J. Radiol. 24, 622-8(1951).

A technique is shown by which estimations can be made of the percentage of expected deficient daughter cells of a certain number of cells in mitosis. Estimates of the number of singly and doubly deficient cells in Vicia faba root meristems per 100 cells after various dosages of x radiation and of α particles and percentages of fragmented nuclei are tabulated. Various mitotic stages are considered. The ratio of relative efficiencies of highest doses of α particles and of x rays in producing chromosome deficiencies is shown to be about homogeneous and both are also roughly equivalent in their inhibiting effects on tissue growth of root tips. This may support the hypothesis that the structural changes produced by ionizing radiations in Vicia root-tip cells contribute largely to inhibition of root growth caused by these radiations, for these doses are not equivalent in their effects on mitotic rate and probably not in their effect on gene mutation. (NSA)

2141

Thoday, J. M. and D. E. Lea. **THE EFFECTS OF IONIZING RADIATIONS ON THE CHROMOSOMES OF TRADES-CANTIA BRACTEATA. A COMPARISON BETWEEN NEUTRONS AND X-RAYS.** J. Genetics 43, 189-210(1942).

Neutrons produce the same types of chromosome aberrations as x-rays, but are more effective per ionization produced. The ratio of x-ray dose to neutron dose (in roentgens), required to produce an equivalent effect, is not the same for the several types of aberrations: 2.4 for chromatid breaks, 3.6 for isochromatic rejoins, 4.5 for chromosome breaks, and between 5 and 10 for interchanges. Many of the latter, when produced by neutrons, are caused by single "hits", i.e., single ionization paths. Neutrons and x-rays differ in effect insofar as the former, with a denser ionization path and with fewer paths per unit volume than equivalent doses of x-rays, produce a greater number of primary breaks having a different distribution. Since neutrons produce more primary breaks per ionization than x-rays > 1 ionization is needed to break a Trades-cantia chromosome thread. (BA)

2142

Thoday, J. M. and John Read. **EFFECT OF OXYGEN ON THE FREQUENCY OF CHROMOSOME ABERRATIONS PRODUCED BY X-RAYS.** Nature 160, 608(1947).

Groups of beans, with their roots in a "perspex" cell of water through which nitrogen was bubbled, were irradiated with x-rays. Other groups were treated in the same manner except that air replaced nitrogen. Growth curves demonstrated that there was a definite decrease in radiosensitivity when nitrogen was employed. This decreased radiosensitivity was accompanied by a parallel decrease in the proportion of cells exhibiting mitotic aberrations. A similar reduction in radiosensitivity as measured by growth after irradiation occurred when nitrous oxide, carbon dioxide, and hydrogen were substituted for nitrogen.

Since anaerobiosis reduces the radiosensitivity of tumors, it is suggested that the increased radiosensitivity in the presence of oxygen is the result of the larger number of mitotic aberrations which are induced. (AWM)

2143

Thoday, J. M. and John Read. EFFECTS OF OXYGEN ON THE FREQUENCY OF CHROMOSOME ABERRATION PRODUCED BY ALPHA RAYS. *Nature* 163, 133-4(1949).

Four graded doses of α radiation were given to groups of 8 beans (*Vicia faba*) in oxygen-free water, and four in water containing 12 cc. O per liter, and the mean growth of the roots compared. O has a much greater effect on the effect of x-rays than on the effect of α -rays, the dose ratios for equal growth "without/with oxygen" being ~ 2.5 and ~ 1.3 respectively.

Cytological studies of root-tips treated in a similar manner show that while there is a somewhat larger yield of aberrations in the presence of oxygen than in its absence, the increase is far less than when x-rays are used. These effects of O parallel its effect in promoting the decomposition of water, and in view of the ability of α -rays to produce H_2O_2 whether oxygen is present or not, suggest that H_2O_2 has some influence on the processes involved in chromosome structural change. (VE)

2144

Whiting, Anna R. X-RAY SENSITIVITY OF FIRST MEIOTIC PROPHASE AND METAPHASE IN HABROBRACON EGGS. *Genetics* 27, 174-5(1942).

Hatchability percentages of unfertilized eggs X-rayed in late prophase I with dosages up to 400 r are significantly higher than of controls. Above 400 r dosage-hatchability curve indicates that death depends upon the concurrence of two or more events the chance of which increases disproportionately with increased radiation. The lethal dose is about 35,000 r. In contrast, dosage-hatchability curve of eggs X-rayed in late metaphase I indicates that death results from one event. It is unchanged by time-intensity differences or by fractionated dosages. These eggs are sensitive to 50 r and the lethal dosage is about 1250 r. After 1864 r all suitable stages show fragments (terminal deletions ?) within the telophase I spindle or between equatorial plates at metaphase II. With 500 r, 750 r and 1000 r, percentages without visible fragments form a curve parallel to and somewhat higher than dosage-hatchability curve. Mean fragment number per egg increases with dosage. No eggs treated in prophase I with 1864 r show fragments. Eggs treated in metaphase I with 2500 r pass at once into telophase I when laid (like controls). 97.5 ± 1.35 percent complete meiosis and begin cleavage at approximately normal rates. When egg-laying is temporarily restrained to keep chromosomes relatively inactive after treatment hatchability is not significantly changed. If stresses peculiar to metaphase I chromosomes sensitize this stage to irradiation, treated prophase I chromosomes, which later undergo these stresses, must receive but slight injury at dosages lethal to former or recover almost completely before entering metaphase I. Data indicate that metaphase injury, like prophase, is due to chromosome breaks correlated with ionizations and not to "physiological" causes, stickiness and clumping of chromosomes. (G)

2145

Whiting, Anna R. HATCHABILITY AND CHROMOSOME CHANGES OF HABROBRACON EGGS X-RAYED IN PROPHASE I AND METAPHASE I. *Genetics* 28, 94-5(1943).

Dosage-hatchability curve of unfertilized eggs X-rayed in metaphase I indicates that death results from one event. (Lethal dosage 1250 r.) There is no evidence for recovery.

Absence of a low dosage threshold for injury and of a high one for chromosome clumping and retardation (up to 15,000 r) eliminates chromosome stickiness as a factor. After treatment, fragments (double, terminal deletions?) are found in telophase I spindle or between metaphase II plates; occasionally smaller ones (single?) are found in one or both telophase II spindles. No bridges have been observed before cleavage. Percentages of eggs without fragments are higher than corresponding hatchability percentages. The two curves are roughly parallel. Fragments per treated nucleus vary as the 1.59 power of dosage for 250 r and 500 r. This decreases with each increase in dosage, but data are not statistically significant. These phenomena suggest that broken metaphase chromosomes, like those in spermatozoa, undergo neither restitution nor recombination while condensed. — Eggs X-rayed between synapsis and diakinesis (prophase I) have lethal dosage of about 40,000 r. Chromosomes in these stages do not react with Feulgen. Dosage-hatchability curve, almost identical in three independent experiments, depends upon unknown combinations of I-hit and multiple-hit events, is complex and has not been analyzed. No cytological effects appear at low dosages. This removes possibility that high resistance depends upon extensive elimination of dicentric in division I. At high dosages bridges have been seen in divisions I and II. — Cleavage of eggs treated in either stage may show bridges or may show fragments produced by two breaks in a bridge. (G)

2146

Whiting, Anna R. EFFECTS OF X-RAYS ON HATCHABILITY AND ON CHROMOSOMES OF HABROBRACON EGGS TREATED IN FIRST MEIOTIC PROPHASE AND METAPHASE. *Am. Naturalist* 79, 193-227(1945).

Because of their definite order in the ovariole, *Habrobracon* eggs may be treated at specific meiotic stages and then allowed to develop parthenogenetically. Those treated at metaphase I give hatchability percentages which show a linear decline with dosage from 50 to 1,400 r, but with no changes following aging after treatment, time-intensity differences, or fractionation of dose. The eggs treated in prophase I give hatchability percentages equal to or higher than controls for doses from 50 to 750 r. At medium doses, a linear relationship is apparent between dosage and hatchability but this relationship becomes obscured at the higher doses. The lethal dose for prophase I is about 44,800 r. For prophase I, hatchability increases with fractionation of dose but does not change following time-intensity changes. Eggs treated at either stage with lethal doses will continue meiosis and early cleavage at normal rates. Those treated in metaphase I lack bridges in Division I, but otherwise eggs treated at both stages show fragments and bridges at both division I and II and also in cleavage. Fertilization with untreated spermatozoa does not change the hatchability percentages of eggs treated at either stage. The correlation of cytological aberrations with hatchability percentages seems to prove that death is caused by single hit chromosome breaks. The high sensitivity of the metaphase I eggs indicates that ionization effects may depend upon chromosome tension. Other explanations for differential sensitivity at various stages are discussed and found not to apply. (BA)

2147

Whiting, Anna R. DOMINANT LETHALITY AND CORRELATED CHROMOSOME EFFECTS IN HABROBRACON EGGS X-RAYED IN DIPTOTENE AND IN LATE METAPHASE. *Biol. Bull.* 89, 61-71(1945).

Unlaid *Habrobracon* eggs x-rayed in diplotene (lethal dose about 45,000 r) and allowed to develop parthenogenetically, show fragments, bridges or both in division I; either or both in division II. Bridges in division I may be permanent. Unlaid eggs x-rayed in late metaphase I (lethal dose about 1,400 r) show fragments but no bridges in division I; bridges, fragments or both in division II. An explanation of difference in cytological effects of x-rays on these stages and of differences between them in sensitivity and in nature of survival curves is attempted through comparison with studies on forms with larger chromosomes. (BA)

2148

Wilbur, Karl M. THE RADIOSENSITIVITY OF EGGS OF *ARBACIA PUNCTULATA* IN VARIOUS SALT SOLUTIONS. Biol. Bull. 85, 193-200(1943).

Treatment of *Arbacia* eggs with 0.35 M K citrate inhibited the retarding action of x-radiation on cell division. However, the inhibition by citrate was slight, and appeared mainly with high x-ray doses (30,400 and 53,200 r). The radiosensitivity was unaffected by increasing the Ca or Mg content of the sea-water medium. The K citrate treatment increased the viscosity of the unfertilized egg. The viscosity was decreased slightly in the sea-water solutions of increased Ca and Mg content. The data presented indicate that changes in the ionic composition and viscosity of the protoplasm may occur without altering the sensitivity of the egg to x-radiation. Doses of x-radiation which markedly altered the rate and normal course of cell division produced no detectable change in the viscosity of the unfertilized egg. (BA)

2149

Wilson, G. B. and B. R. Nebel. CHANGES IN CHROMOSOME SENSITIVITY TO X-RAYS. Genetics 25, 140(1940).

Microspores of *Tradescantia reflexa* Raf. were rayed at various stages preceding first pollen-grain metaphase. Sensitivity was measured by the degree of chromosome alteration at first pollen-grain metaphase. Results indicate a positive correlation between the speed of mitotic development and the degree of response called "sensitivity." Several agents which either stop or retard division are being tested; first, for their own effect on chromosome and cell morphology and second, for their effects on sensitivity to X-rays as judged by comparisons with normal sensitivity curves. (G)

2150

Yamashita, H., K. Mori, and M. Miwa. THE ACTION OF IONIZING RAYS ON SEA-URCHINS. V. THE MITOTIC OBSERVATIONS ON THE EFFECTS OF ROENTGEN RAYS UPON THE UNFERTILIZED EGGS AND SPERM. Gann 34, 239-45(1940).

The difference in the mitotic events between normal and irradiated eggs in the developing cycle from fertilization to first cleavage has been investigated numerically in histological studies. Irradiations were made with roentgen rays of moderate intensity. It was found that delay in time of the first cleavage of irradiated eggs occurred essentially in the nuclear streak phase and prophase. Considering these facts in connection with previous studies (Yamashita, H., Mori, K., and Miwa, M., Gann, 33, 117-121, 1939) that the radiological susceptibility of the fertilized eggs is highest in the phase of nuclear streak, we suggest that this particular mitotic phase is importantly involved in the damaging of living cells by irradiation. (Author's Summary)

2151

Yost, H. T., Jr. AN ANALYSIS OF COMBINED INFRARED

AND X-RAY EFFECTS ON *TRADESCANTIA* CHROMOSOMES. Genetics 35, 700(1950).

X-rayed *Tradescantia* microspores have been given pre- and post-treatments with infra-red radiations. In all cases, percentage increases of 50—120% in chromosomal aberrations were observed in the infra-red-treated cells. Post-treatments have been given as late as 96 hours after X-radiation with no apparent decrease in the effectiveness of the infra-red radiations. From these data the conclusion may be drawn that the determination of the type of aberration recovered (chromosome or chromatid) is independent of the time of recombination, and dependent solely upon the singleness or doubleness of the chromosomes at the time of X-radiation. Studies of *Tradescantia* chromatid aberrations indicate that the infra-red-induced increases show a non-linear relationship to the dosage of infra-red given. These studies and other concerned chiefly with X-ray dosage relationships and spectral dependency permit some conclusions concerning the mechanism by which infra-red radiations produce their effect. (G)

2152

Yost, Henry T., Jr. THE FREQUENCY OF X-RAY INDUCED CHROMOSOME ABERRATIONS IN *TRADESCANTIA* AS MODIFIED BY NEAR INFRARED RADIATION. Genetics 36, 176-84(1951).

From the data presented on the effects of infrared radiations when used as supplementary treatments with x radiation, the following conclusions have been made: (1) pretreatment and posttreatment with infrared radiations increase the frequency of chromosome aberrations induced by x radiation; (2) the posttreatment may be delayed 93 to 96 hr after x radiation with no decrease in the effectiveness of the infrared radiations; (3) the type of aberration induced is dependent upon the time at which the x radiation is administered, and is independent of the time of infrared radiation and the time of recombination. The various hypotheses which have been advanced to explain the effect of infrared treatment are discussed. The potential break hypothesis is supported by this data. (NSA)

2153

Zirkle, R. E. SOME EFFECTS OF ALPHA RADIATION UPON PLANT CELLS. J. Cellular Comp. Physiol. 2, 251-74(1932).

α rays from polonium retard and inhibit, but never accelerate, 3 distinct processes in the germination of the spores of *Pteris longifolia*: cracking of the spore wall, development of chlorophyll, and cell division. The doses producing 50% inhibition of these processes are, respectively, 33,000; 13,000; and 4000 α particles per protoplast, which correspond to somewhat smaller amounts of energy per unit volume than those used by others to produce hemolysis and 50% inhibition of cell division in yeast. When 4000 α -particles per protoplast are used, about 7% of the protoplast is liable to direct alteration by ionization. All 3 processes are more easily inhibited in germinating than in air-dry spores, but increase in inhibition of cracking appears earlier in germination than that of greening or of division. Irradiation of definite fractions of the protoplast indicates the following conclusions: cracking, greening, and division may each be inhibited by extranuclear injury, but all are much more easily inhibited if the nucleus is irradiated; the extranuclear injury which inhibits greening is not direct injury to plastids or protoplasts; imbibition is inadequate for production of normal cracking; and extranuclear irradiation produces a high frequency of a type of induced twinning. (BA)

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NUMERICAL INDEX

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The non-Project reports referred to herein are generally available from their issuing sources.

GLOSSARY

MDDC-	A code assigned to declassified reports released by the Manhattan Engineer District and USAEC before March 1, 1948.	NM-	Naval Medical Research Institute, Bethesda, Maryland.
AECD-	A code assigned to declassified reports released by the USAEC after February 29, 1948.	NP-	A file designation assigned by the Technical Information Service, USAEC, to nonproject reports whose codes, if present, are not practical for TIS use.
AECU-	A code assigned to AEC unclassified reports.	NYO-	USAEC, New York Operations Office
AD-	Naval Radiological Defense Laboratory.	ORNL-	Oak Ridge National Laboratory.
AERE-	Atomic Energy Research Establishment, Harwell, Berks (England).	ORO-	USAEC, Oak Ridge Operations Office
AMRL-	Army Medical Research Laboratory, Fort Knox.	RAD-	Rand Corporation
ANL-	Argonne National Laboratory.	TID-	Technical Information Service
BNL-	Brookhaven National Laboratory.	UCLA-	University of California, Los Angeles
CH-	Metallurgical Laboratory, University of Chicago.	UCRL-	Radiation Laboratory, University of California, Berkeley
HW-	Hanford Engineer Works.	UR-	Atomic Energy Project, University of Rochester
LA-	Los Alamos Scientific Laboratory.	USAF-	United States Air Force School of Aviation Medicine.
M-	TIS USAEC file number.	UWFL-	University of Washington Applied Fisheries Laboratory
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ACD Abstracts of Classified Documents (Technical Information Service, USAEC)
ADD Abstracts of Declassified Documents (Technical Information Service, USAEC)
AJR American Journal of Roentgenology and Radium Therapy
AP Archives of Pathology
AR Anatomical Record
AWM Abstracts of World Medicine
BA Biological Abstracts
BCPA British Chemical and Physiological Abstracts
BEMP The British Encyclopedia of Medical Practice, Surveys and Abstracts
BJR British Journal of Radiology
CA Chemical Abstracts
CR Cancer Research
EM Excerpta Medica
G Genetics
GPR Guide to Published Research in Atomic Energy (Technical Information Service, USAEC)
N Nucleonics
NSA Nuclear Science Abstracts
PA Physics Abstracts
R Radiology
RG Records of the Genetic Society of America
TIS Technical Information Service, USAEC, Oak Ridge Extension
YBR Year Book of Radiology