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Argonne National Laboratory

MONTHLY PROGRESS REPORT

APRIL 1952

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ARGONNE NATIONAL LABORATORY
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MONTHLY PROGRESS REPORT

APRIL, 1952

Report of the Work of the
BIOLOGICAL and MEDICAL RESEARCH,
RADIOLOGICAL PHYSICS, and HEALTH SERVICES DIVISIONS
for the Quarterly Period ending
March 31, 1952

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ARGONNE NATIONAL LABORATORY
MONTHLY PROGRESS REPORT
FOR APRIL, 1952

The monthly progress report from the Argonne National Laboratory includes material from one-third of the Laboratory. The three divisions into which the work has been divided are: (1) Reactor Engineering, Physics, Instrument Research and Development, and Electronics, (2) Biological and Medical Research, Radiological Physics, and Health Services, and (3) Chemistry and Chemical Engineering, Metallurgy and Remote Control Engineering. The present monthly report covers the work in Biological and Medical Research, Radiological Physics, and Health Services for the quarterly period ending March 31, 1952.

Three of five persons available for study of the rate of disappearance of RaSO_4 from the human lung have been measured for total-body and lung content after a four- to five-month interval. Although preliminary, these data indicate that the rate of elimination from the lung may vary significantly from patient to patient and that the patient showing the lowest lung elimination rate exhibits the lowest Rn to total Ra ratio. It also seems clear that, within the observational period reported, the rate of elimination from the lung is definitely faster than that from the whole body. (6310-01)

Plasma glucose determinations in newly-hatched chicks at one, three, and five hours after X irradiation (1000 r at 43 r per minute) showed no significant changes in mean value from control levels. Individual animals, however, showed a hyperglycemia of 50 to 100 mg per cent over control values three and five hours following irradiation. Such hyperglycemia was usually found in sick birds and was commonly associated with liver hemorrhages. The effect of X irradiation in the young chicken has been shown to be dependent on dose rate. Data now available permit a comparison of the radiation sensitivity of chickens of different ages up to maturity (six months after hatching). The mature chicken showed a response to variation in X-ray dosage rate similar to that reported in newly-hatched birds. Survival following 1000 r at 6 r or 43 r per minute indicated that there was little or no change in radiosensitivity within the first six months. (6400-01)

Control and experimental mice were injected intravenously with different amounts of bone marrow (1.5 mg and 0.75 mg) before exposure to 900 r X radiation. In both groups recovery was approximately the same, and the circulating blood picture was not significantly different, indicating that recovery was not dependent on dose. Further experiments reveal that excellent protection results when the time interval between bone marrow injection and X irradiation is increased from 4 to 48 hours. Some protection is afforded after 72 hours. Sufficient data have been accumulated to show that intravenous homologous bone marrow injections are also effective in

chronic irradiation anemia. Preliminary studies in which CF#1 female mice were exposed to 900 r total-body X radiation after intravenous injections of homologous bone marrow indicate that the 21-day survival of this strain is approximately 50 per cent.

Two groups of mice were exposed to divided doses of X radiation (225 r weekly for four weeks), one group with spleen protection. In a third spleen-shielded group a single dose of 900 r was given. Results suggest that prolonged depression of hematopoietic activity may be a factor in producing lymphoid tumors. Four age groups of CF#1 mice younger than 12 weeks were tested to determine the effect of age on survival following X irradiation (1025 r) with spleen protection. Survival was higher in mice between the ages of six to twelve weeks of age. (6400-02 and -14)

Preliminary experiments on the toxicity of C^{14} (mouse dose = 20 μ c per g; rat dose = 2.5 μ c per g) reveal that longevity in rats and mice was not different from that in the control animals. The incidence of disease among the injected rats was no different from that encountered regularly in control rats. At the present state of the analysis of the experimental data, it appears that a total dose of 500 μ c of C^{14} given to rats or mice has little if any effect upon longevity and morbidity. (6400-03)

The radiation chamber being constructed for the neutron radiobiology program will have a source of fast neutrons at one end and a source of γ rays at the other. With this chamber it will be possible to expose nine units of the gamma source (Co^{60}) while the other nine remain shielded. (6400-04)

The effect of photoperiodism on floral and fruit development is being studied. Experiments with Xanthium reveal that with a 14-hour dark induction period 20 to 22 hours are required for the production and translocation of the flowering substance in amounts sufficient for floral initiation. The data also indicate that the substance is not destroyed by light while it is still in the leaf, a point that had not been clarified to date. That temperature affects the movement of the flowering substance is indicated by experiments in which one-leafed Xanthium plants were induced to flower with a single 14-hour dark period at 75-80°F. Plants held at 80°F flowered, but no flowering occurred in those transferred to a room held at 50°F. Floral initiation in time appears to be dependent both on the time required for movement of the flowering substance from the sites of formation in the leaf to the stem and meristem regions and on the time required for synthesis of an effective amount in the dark period.

In the red kidney bean (Phaseolus vulgaris), long photoperiods (15 hours or longer) inhibited floral bud development, and a number of vegetative growth responses were also observed to be correlated with variable duration of photoperiod treatment. Generally, photoperiods that inhibited

floral bud development significantly promoted increased length of both primary and lateral plant axes and resulted in a greater number of both lateral axes or shoots and number of expanded compound leaves. The observed correlation of increasing degree of vegetative growth with a decreasing or complete arresting of floral growth for kidney bean plants in response to increasing photoperiod duration suggests the possibility that a photoperiodic control of both the physiological level of auxin and the flowering stimulus may be operative in this plant species.

As part of a study of the influence of physiological factors on sensitivity to ionizing radiation and to radiomimetic substances, with particular reference to effects on cell division, a series of experiments has been performed on the ciliate, Tetrahymena geleii. Proteose-peptone-suspended Tetrahymena irradiated with 5000 r have a growth delay about 45 minutes more than nonirradiated control animals, compared with a five-hour longer delay following 40,000 r. No killing was observed with the doses employed. (6400-05)

Attempts are being made to determine the choline acetylase content of irradiated and control postdiapause grasshopper embryos. Although the data are incomplete they suggest that there is no immediate radiation effect on the choline acetylase content of the embryo. The acetylase content seems to depend on neural differentiation as well as on functional activity of the differentiated tissues. The anabolic processes that are affected by 25,000 r X radiation in turn affect the anabolism of the choline acetylase. That originally present in the embryo does not diminish in amount for 18 days after exposure.

A very large nucleus has been observed in the premature ovum of M. differentialis. Prior to the meiotic division leading to the secondary oöcyte the nucleus attains a diameter greater than 50 μ . In the more mature ovum the nucleus appears to move in an oscillatory rotational fashion. This activity has been photographed by time lapse motion pictures. (6400-06)

In the series of reactions in which tryptophan is converted to indoleacetic acid, the immediate precursor is considered to be indoleacetaldehyde. The radiosensitivity of the reaction sequence leading to the aldehyde was therefore examined. A study of indoleacetaldehyde levels in the mung bean immediately following low doses of X radiation (25 to 50 r) showed a significant increase in the aldehyde in contrast with nonirradiated control plants. The simplest interpretation of these results is that a major locus of the radiosensitivity lies in the lability of the enzyme controlling the conversion of indoleacetaldehyde to indoleacetic acid.

The activity of crystalline alcohol dehydrogenase is readily inhibited by X irradiation, the degree of inactivation being directly proportional to X-ray dosage. Protection of the enzyme against X-ray inactivation has

been achieved by the addition of 0.01M glutathione or cysteine prior to irradiation. Addition of glutathione after irradiation gave only partial protection. The mechanism of inactivation seems to be due to oxidation of the -SH groups by the OH and O₂H radicals produced by irradiation of water. In this inactivation H₂O₂ plays no role, for 10⁻⁴ M had no effect. The enzyme was inhibited 23 per cent by 10⁻³ M H₂O₂.

Since adenosine and 3-adenylic acid have been shown to decrease the blood pressure of rats to a greater extent than any other nucleic acid derivative, it appeared that postirradiation hypotension might be partially explained by the appearance in the circulating blood of adenosine derivatives as a result of destruction of nucleic acids or possibly of adenosine triphosphate. There was not a consistent difference between normal and irradiated rats in respect to total plasma pentose. There was no significant correlation between plasma histamine and blood pressure measured on the same animal. Benzimidazole, which competitively inhibits the utilization of purines by certain microorganisms, modified very slightly the response of the rat vascular system to adenosine or adenylic acid; however, this dose (100 mg per kg) greatly attenuated the action of histamine. (6400-07)

An experiment was initiated to attempt to answer some of the questions arising from the use of food containing aureomycin. Two groups of CF#1 mice were fed two brands of food, Derwood pellets and Lab-Blox, the latter of which contained 1/4 mg per pound of aureomycin. Results suggest that such an amount of aureomycin has no growth-stimulating effect on five- to eleven-week CF#1 female mice. Similarly, the sudden exclusion of this antibiotic from the diet of animals that received it had no detrimental effect. Some diarrheas occurred in both groups of mice. (6400-08)

Re-examination of the data describing three biological effects (vegetative death, suppression of division, and death after autogamy) in Paramecium aurelia after increasing time of exposure to methyl bis (β-chloroethyl) amine hydrochloride that over the period of a year there was a gradual shift in the quantitative relationships between two of these effects and dose, and that the direction of shift was different for each of the effects measured. At equivalent doses death after autogamy increased and suppression of division decreased, while death before cell division remained about the same. Modification of these responses has been accomplished by varying temperature, and while it is not possible to explain these shifts in responses at the present time, it does appear that death after autogamy is not easily modified by environmental changes. (6400-10)

Electromigration has been used to study the phosphorus constituents of neutron-activated rat bone. Four zones were found for dried bone, for bone treated with ethylene diamine, for CaHPO₄, and for NaH₂PO₄; three zones for apatite; and two for Na₄P₂O₇ and for muffled bone. On the basis of half lives and β energy, all of these anions were phosphorus compounds. (6400-11)

An experiment was undertaken to study the diminution in specific activity of bone carbonate that occurs during manipulations preceding analyses. The findings indicate that bone carbonate recently exchanged in vivo is more susceptible to removable by chemical and physical agents than older carbonate. Ground samples of this bone were fractionally acidified to determine whether time-dependent behavior results from diffusion through the bone matrix or from heterogeneity of carbonate within the bone salts. The CO_2 evolved first had a high specific activity that diminished with each successively liberated fraction. (6400-11)

Rats and mice on stock diets were continuously exposed to air containing a constant low partial pressure of C^{14}O_2 . Within two weeks the radioactivity of the total liver carbon reached a constant level. This constant specific activity was also found in the livers of mice born and raised in labeled atmosphere. Such agreement is evidence that the total fixed carbon of the liver had become isotopically saturated. A survey of the distribution of C^{14} revealed that fixed carbon distribution differs considerably from that reported after isotope exposures of shorter duration. (6400-12)

Carbon 14-labeled dextran has been used in a series of experiments designed to determine its metabolic fate. For man a six per cent isotonic solution was used ($6 \mu\text{c}$ per g); for animals the dextran was tagged with $110 \mu\text{c}$ of C^{14} per g. Tentative conclusions indicate that: dextran is metabolized similarly by the rat, dog, and man; the rates of dextran excretion and metabolism depend on the metabolic needs of the animal; about 50 per cent of injected dextran is excreted as such during the first three days, while a large part of that remaining in the animal is oxidized to CO_2 over a longer period of time; and after intravenous administration neither dextran nor any of its metabolic products is excreted by way of the intestinal tract. (6400-13 and 20)

The protective effects of pretreatment with cysteine followed by spleen implantation after irradiation with 1025 r were found to be additive in a small group of mice. Cysteine failed to produce any beneficial effect on survival when given six hours after 1100 r total-body irradiation with or without protection of the exteriorized spleen during exposure.

Earlier studies have revealed that the protection afforded rats by cysteine shows some proportionality to the dosages of cysteine and X radiation. A standard dose of cysteine (1200 mg per kg, I.V.) was given to CF#1 female mice after a fraction of the total radiation dose was delivered. The total radiation dose was given in successive fractions. On the assumption that cysteine did not influence the radiation fraction preceding it, the following protective ratio was computed:

$$\text{Protective ratio} = \frac{(\text{postcysteine } r) - (\text{effective } r - \text{precysteine } r)}{\text{postcysteine } r}$$

The data suggest that cysteine neutralizes a fairly constant percentage of the radiation dose. (6400-13 and -14)

The effectiveness of ATA (aurin tricarboxylic acid) is believed to be due in part to prolonged retention of the dye around beryllium particles in the tissues. It was therefore considered important to determine the length of time a single, therapeutically effective dose would remain distributed among the body tissues in effective concentrations. Rats and dogs were given intravenous injections of C^{14} -methyl-labeled ATA. Autoradiographs of rat liver, lung, and spleen show a fairly uniform distribution of C^{14} throughout these tissues, but in the kidney there is some cortical localization. The periosteum and marrow of the femur and humerus appear to be uniformly active, while the inorganic bone matter is devoid of activity. (6400-16 and -20)

It is likely that the ortho-carboxyl-hydroxy groups on the aurin tricarboxylic acid molecule are responsible for increasing the survival of mice poisoned acutely with Be. Other compounds containing these groups have been tested. The following did not prevent death of Be-poisoned mice: anthranilic acid, eriochrome cyanine, mandelic acid, aspartic acid, and sodium malate. However, dosages of 30 to 40 mg of sulfosalicylic acid permitted 80 to 100 per cent survival, while with a dosage of 20 mg there was only 60 per cent survival. (6400-16)

A study was undertaken to determine whether the salicylic acid portion of the aurin tricarboxylic acid molecule is comparably effective in reversing experimental beryllium intoxication. An LD_{95} of $BeSO_4$ (0.7 mg per kg of Be) was injected intravenously into CF 1 female mice, and the compounds tested for antidotal properties were similarly administered one hour later. Sodium salicylate proved to be effective when given in adequate doses. Analogs of salicylic acid were tried and those without the ortho-hydroxy-carboxylic acid group were uniformly ineffective. Sodium p-amino-salicylate gave only equivocal results. Sodium gentisate was unsuccessful. Disodium catechol sulfonate was successful only in prolonging the time to 50 per cent death. Sodium salicylate afforded protection when treatment was delayed 8 hours but not when postponed 24 hours. Pretreatment eight hours before beryllium was administered was ineffective. Antidotal action is believed to result from the chelating action of the ortho-hydroxy-carboxylic acid structure, which reduces the availability of the toxic ionized beryllium by the formation of ionized complexes. Whether lake formation is required in addition to chelation in the treatment of chronic beryllium granulomatosis is a problem for future investigation. (6400-16)

Consideration is given to the development of a theory of the growth of organisms that will be satisfactory in application to radiation effects. In ANL-4745 a simple case is developed and applied to normal growth and to the effects of continuous X-ray exposure; the desirability of studying

laboratory models of tissue-like systems is stressed, and some results of a theoretical analysis of such models are mentioned. (6400-17)

Labeled 3-indoleacetic acid 2-C¹⁴ (IAA), which had been oxidized during storage either by exposure to moist air or P₂O₅, has been repurified by paper chromatography. (6400-19)

Carbon 14 was used in an experiment designed to tag fibrin, albumin, and the globulins in order to give significant C¹⁴ counting levels following the administration of labeled glycine in the female rat. After an injection of 10 mg of carboxyl-tagged glycine (0.5 μ c per g) there was a rapid increase in the level of tagged CO₂ in the exhaled air during the first 30 minutes after injection, but after 30 minutes the rapid formation of tagged CO₂ ceased abruptly. It appears that injected free glycine as such is no longer present in the animal after 30 minutes. (6400-20)

A calorimeter has been designed for absolute fast neutron dosimetry employing tissue equivalent material in a calorimeter bomb. The energy available will give a temperature rate of change of about 10⁻⁶°C per second, but the equilibrium temperature rise will be about 10⁻³°C. The measurement must be corrected for an energy loss of perhaps 10 per cent which is due to chemical reactions. An accurate measure of this energy loss will be obtained by using a calibrated source of α rays in a mercury calorimeter under construction. (6510-01 and 6400-04)

A preliminary investigation was carried out to determine if self-absorption occurred in scintillating terphenyl-xylene solutions. Radiation corresponding in wave length to the scintillation was passed through the solutions. Absorption was observed, increasing with increasing concentration of the terphenyl. The absorption peak shifted toward longer wave lengths at higher concentrations. When certain non-quenching solvents were added, absorption decreased by an amount corresponding to the dilution of the terphenyl. On the basis of these results, self-absorption apparently does occur in these solutions. (6510-01)

The reaction of 3-aminophthalhydrazide (luminol) with hydrogen peroxide is accompanied by chemiluminescence, and an alkaline solution plus hemin, a catalyst, emits light when irradiated with X rays, γ rays, β rays, α particles, and neutrons, presumably through the intermediate formation of peroxide of oxidizing radicals. An alkaline solution of luminol has been prepared in order that the possibilities of using it as an aqueous system dosimeter of the scintillating type can be investigated. (6520-01)

Studies on a fast neutron detector are continuing. A formula relating the maximum pulse heights of the layer counter to the energy of the incident neutrons and to the thickness of the scintillating layers has been developed.

The variation of pulse height for monoenergetic 14-mev neutrons with different thickness of scintillating layers has been tested.

The construction of an instrument that will continuously record and analyze the carbon dioxide and oxygen concentrations in respired air has been completed. (6541-01)

The larger shield required for the new grid wall ionization chamber was built. In order to reduce the variations of the observed currents to a usable level, it was found necessary to keep air movements within the shield to a minimum. This has been accomplished by stiffening the walls of the shield and by establishing a thermal gradient so as to eliminate convection currents. (6541-01)

Two models of the ionization type halide detector have been set up in the radiological physics section of the permanent physics building and are now being operated. It has become increasingly apparent that the response of this type of detector depends very strongly on surface effects. Electrode surfaces have been varied in a number of ways, e.g., by applying solid materials, by electrical discharges, by washing with water or acids, by flaming, or by adding gaseous materials continuously. The results have been evaluated in terms of stability, speed of response, and sensitivity. (6541-02)