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**LABORATORY OF NUCLEAR MEDICINE
AND
RADIATION BIOLOGY**

**UNIVERSITY OF CALIFORNIA
900 VETERAN AVENUE
LOS ANGELES, CALIFORNIA**

MASTER

DOE CONTRACT DE-AM03-76-SF00012

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UNIVERSITY OF CALIFORNIA
LABORATORY OF NUCLEAR MEDICINE AND RADIATION BIOLOGY
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LOS ANGELES, CALIFORNIA 90024

This work was supported by Contract DE-AM03-76-SF00012 between the U.S. Department of Energy and the University of California.

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ANNUAL PROGRESS REPORT

FOR THE PERIOD

JULY 1, 1979 - JUNE 30, 1980

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LABORATORY OF NUCLEAR MEDICINE AND RADIATION BIOLOGY

UNIVERSITY OF CALIFORNIA

LOS ANGELES

DIRECTOR

O. R. Lunt

ASSOCIATE DIRECTORS

David E. Kuhl
James F. Mead
William J. Moffitt
Evan M. Romney

FACULTY ADVISORY COMMITTEE
TO THE LABORATORY

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Chairman, Department of Radiological Sciences

Frederick Allen
School of Engineering and Applied Science

Donald J. Jenden
Chairman, Department of Pharmacology

F. Harlan Lewis
Associate Dean, Life Sciences/Biology

Sherman Mellinkoff
Dean, School of Medicine

John D. O'Connor
Chairman, Department of Biology

John G. Pierce
Department of Biological Chemistry

EX-OFFICIO MEMBER

Albert A. Barber
Associate Vice Chancellor - Research

REPORT OF THE DIRECTOR

The research staff has published about 170 technical papers, received numerous honors and made important teaching contributions during the last year. From my perspective the Laboratory is vigorous and healthy. Attention is directed to appropriate sections of this report for details on our activities.

The foregoing notwithstanding, the combination of rising costs and reduced or relatively static budgets is requiring reductions and adjustments in administrative and support areas to maintain research programs. With the dedication of our staff we expect to maintain necessary administrative functions.

The "International" program is developing slowly but on a sound basis. During the past year we have had three Latin American scientists training with our staff and colleagues.

We are indebted to the Office of Health and Environmental Research of the Department of Energy, Office of Environment for financial support for our programs, and to the Chancellor and his staff and to the Advisory Committee to the Laboratory for advice and guidance.

A new name for the Laboratory has been proposed to the Chancellor which, if approved, will more accurately reflect our activities.

STATISTICAL SUMMARY OF LABORATORY OPERATIONS

I. Budgeted Operating Expenditures FY 1980 (\$1,000's)

D.O.E. Base Funding	
Division of Biomolecular and Cellular Science	\$1,137
Division of Environmental Biology	1,447
Division of Nuclear Medicine	1,509
Other	<u>151</u>
	\$4,324
Non-D.O.E. Base Funding	<u>1,139</u>
Total	\$5,463

II. Space Resources (square feet)

Net assignable, Warren Hall	63,000
Assigned to Laboratory for research, Center for Health Sciences	7,000
Net assignable, Biomedical Cyclotron	<u>3,000</u>
Total	73,000

III. Staff (June 30, 1980)

Principal Investigators	26
Professional Scientific Support	15
Total Employees	180

IV. Teaching Activities (Academic Year 1979-1980)

Graduate students working under supervision of Laboratory staff	45
Postdoctoral trainees	22
Visiting scientists	6
Courses to which Laboratory staff have made significant contributions	53
Number of departments in which these courses were offered	9

PROFESSIONAL STAFF
GRADUATE STUDENTS
VISITORS

PRINCIPAL INVESTIGATORS

GEORGE V. ALEXANDER, M.S.
Distribution of tracer elements in biological systems, development of spectrometric methods and equipment; computer applications

JORGE BARRIO, Ph.D.
Development of new radiopharmaceutical indicators for diagnostic imaging and physiologic study

JEAN S. de VELLIS, Ph.D.
Developmental neurotoxicology

ARMAND J. FULCO, Ph.D.
Control of lipid biosynthesis

OLIVER HANKINSON, Ph.D.
Genetic control of carcinogen metabolism

ISAAC M. HARARY, Ph.D.
Control of mammalian cell development and specific function

ESTHER F. HAYS, M.D.
Leukemia; etiology and pathogenesis; cadmium effects on host defenses

HARVEY R. HERSCHMAN, Ph.D.
Regulation of cell division and gene expression by endogenous factors and environmental agents

EDWARD J. HOFFMAN, Ph.D.
Development of new radionuclide instrumentation for diagnostic imaging and physiologic study

HENRY HUANG, D.Sc.
Mathematical modeling for radionuclide imaging of physiologic systems

DAVID E. KUHL, M.D.
Development of new radionuclide techniques for diagnostic imaging and physiologic study of local organ function

ACADEMIC DEPARTMENT

Radiological Sciences
Pharmacology

Anatomy
Psychiatric and Bio-
behavioral Sciences

Biological Chemistry

Pathology

Biological Chemistry

Medicine

Biological Chemistry

Radiological Sciences

Radiological Sciences

Radiological Sciences

PRINCIPAL INVESTIGATORS

ACADEMIC DEPARTMENT

ROBERT G. LINDBERG, Ph.D.
Physical ecology of desert rodents;
environmental effects of solar thermal
power systems

Environmental Science
and Engineering

NORMAN S. MAC DONALD, Ph.D.
Development of new cyclotron-produced
radionuclides for diagnostic imaging and
physiological studies

Radiological Sciences

JAMES F. MEAD, Ph.D.
Lipid metabolism in normal, aging, and
malignant tissue; membrane peroxidation

Biological Chemistry
Public Health

LAWRENCE S. MYERS, JR., Ph.D.
Damage of DNA and its consequences

Radiological Sciences

KENNETH A. NAGY, Ph.D.
Vertebrate physiological ecology

Biology

HIDEO NISHITA, Ph.D.
Assessment of heat transfer fluids used
in solar thermal power systems; SO₂
sorption by soils

PARK S. NOBEL, Ph.D.
Plant physiological ecology, photosynthesis,
and plant distribution

Biology

AMOS NORMAN, Ph.D.
Cell biology

Radiological Sciences

MICHAEL E. PHELPS, Ph.D.
Development of new radionuclide instrumentation
for diagnostic imaging and physiologic study

Radiological Sciences

GERALD D. ROBINSON, JR., Ph.D.
Development of new radiopharmaceutical indicators
for diagnostic imaging and physiologic studies

Radiological Sciences

EVAN M. ROMNEY, Ph.D.
Radionuclide and stable element cycling in
plants and soils

PRINCIPAL INVESTIGATOR

HEINZ SCHELBERT, M.D.
Development of new radionuclide techniques
for diagnostic imaging and physiologic
study of local organ function

FREDERICK B. TURNER, Ph.D.
Biology of desert vertebrates; environmental
effects of solar thermal power systems

ARTHUR WALLACE, Ph.D.
Plant physiology particularly nitrates
and trace elements in nutrition

ROBERT A. WOOD, B.S.
Radiochemistry

SENIOR PROFESSIONAL STAFF

ROBERT ANDERSEN, Ph.D.

JUDITH BERLINER, Ph.D.

WADE L. BEKRY, Ph.D.

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CLIVE SHIFF, Ph.D.

DAVID SIMPSON, Ph.D.

ROBERT A. STEIN, Ph.D.

GARN A. WALLACE, Ph.D.

GUEY-SHUANG WU, Ph.D.

ACADEMIC DEPARTMENT

Radiological Sciences

DIVISION

Biomolecular and Cellular Sciences

Biomolecular and Cellular Sciences

Environmental Biology

Biomolecular and Cellular Sciences

Environmental Biology

Biomolecular and Cellular Sciences

Biomolecular and Cellular Sciences

Biomolecular and Cellular Sciences

Nuclear Medicine

Nuclear Medicine

Environmental Biology

Biomolecular and Cellular Sciences

Biomolecular and Cellular Sciences

Biomolecular and Cellular Sciences

Biomolecular and Cellular Sciences

POSTDOCTORALS

JOSEPH P. BRESSLER, Ph.D.
DANIEL CAWLEY, Ph.D.
DAVID GELMONT, M.D.
RANDALL HAWKINS, M.D.
EBERHARD HENZE, M.D.
SHINICHI KITADA, Ph.D.
SHALINI KUMAR, Ph.D.
HOA KU, Ph.D.
FRANK J. LOMBARDI, Ph.D.
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AHMAD NAJAFI, Ph.D.
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STEPHEN SWANSON, Ph.D.
EVELYN TIFFANY-CASTIGLIONE, Ph.D.
DANIEL P. WEINGARTEN, Ph.D.
ROBERT WOODHOUSE, Ph.D.

GRADUATE STUDENTS

ALARIC ARENANDER, B.S.
STEPHEN BARUCH, M.P.H.
BRUCE BIRREN, B.A.
KENNETH BERGER, M.S.
DALE BRENTNUP, B.A.
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SPONSOR

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Harvey R. Herschman
James F. Mead
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Robert G. Lindberg

GRADUATE STUDENTS

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GARY KEOUGH, M.S.
DAVID KERK, B.A.
STEVEN LAVINGER, M.A.
STEVEN T. LEADON, B.S.
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Harvey R. Herschman
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Jean S. de Vellis

VISITING SCIENTISTS

ERNESTO AEERHARD, Ph.D.
Reaction of membrane-bound
enzymes with membrane lipids

MARTINE CHESSEBEUF, D.E.Sc.
Development of monoclonal
antibodies to brain protein

BRIAN GREEN, Ph.D.
Ecological energetics of
vertebrates

M. M. HEIKAL, Ph.D.
Effect of salinity and trace
elements on plant growth

UNIVERSITY

University of Rio Cuarto
Cordoba, Argentina

University of Dijon
Dijon, France

CSIRO Wildlife
Canberra, Australia

Assiut University
Assiut, Egypt

VISITING SCIENTISTS

DAVID J. LONGSTRETH, Ph.D.
Environmental effects on
leaf anatomy

RENATO DOS SANTOS MELLO, Ph.D.
Cytogenetic effects of radiation
and contrast agents

UNIVERSITY

Department of Botany
Louisiana State University
Baton Rouge, Louisiana

University of Brazil
Brasilia, Brazil

FACULTY PARTICIPANTS IN SOLAR PROGRAM

JOHN H. BALDWIN, Ph.D.
Environmental planning for
community applications

CLIMIS DAVOS, Ph.D.
Environmental management and
policy decision making strategies

WILLIAM DRITSCHLO, Ph.D.
Ecology and environmental
assessment

LEONA M. LIBBY, Ph.D.
Physics and chemistry of
energy systems, isotope dating

DUNCAN D. PATTEN, Ph.D.
Environmental Biology of desert
ecosystems

RICHARD L. PERRINE, Ph.D.
Chemical, thermal, nuclear
engineering and environmental
assessment

BART B. SOKOLOW, D.Env.
Environmental Assessment of
alternate energy sources

MICHAEL K. STENSTROM, Ph.D.
Water resources and reclamations

UNIVERSITY

School of Architecture and
Urban Planning, UCLA

School of Public Health, UCLA

Environmental Science and
Engineering, UCLA

Environmental Science and
Engineering, UCLA

Arizona State University
Tempe, Arizona

School of Engineering and Applied
Science and Chairman of Inter-
departmental Program in Environ-
mental Science and Engineering, UCLA

Environmental Science and
Engineering, UCLA

School of Engineering and Applied
Science, UCLA

<u>FACULTY PARTICIPANTS IN SOLAR PROGRAM</u>	<u>UNIVERSITY</u>
ALAN Z. ULLMAN, Ph.D. Chemical, thermal, nuclear engineering	School of Engineering and Applied Science, UCLA
WALTER E. WESTMAN, Ph.D. Ecology and environmental policy development	Department of Geography, UCLA

RESEARCH HIGHLIGHTS

ABSTRACTS

DIVISION OF BIOMOLECULAR AND CELLULAR SCIENCES

RESEARCH HIGHLIGHTS

The research efforts of the Division of Biomolecular and Cellular Sciences in the past year have been reported in 22 published papers, 13 manuscripts currently "in press" and 29 abstracts of presentations at a variety of professional meetings. Principal Investigators and their professional associates have also presented seminars at a number of educational and research institutions throughout the United States, Europe, and Israel during the past year.

The major thrust of research in the division continues to be the elucidation of biochemical and cellular mechanisms of growth, differentiation and specialized function. Particular attention is directed to the interactions of these processes with endogenous (hormones, growth factors) and exogenous (carcinogens, promoters, temperature, heavy metals, noxious gasses, irradiation) agents which can influence these biological functions.

Among the major research accomplishments and/or observations reported are the following: (1) The development of routine, reliable procedures for the culture of separated populations of astrocytes, oligodendrocytes and neurons from the central nervous system. These cultures will serve as substrates to distinguish differential cell-type response and sensitivity to carcinogens, promoters and heavy metals. (2) The demonstration of a new pathway for membrane lipid biosynthesis in bacteria. (3) The observation that the cytochrome P-450 hydroxylation system of B. megaterium can epoxidize certain unsaturated fatty acids. (4) Demonstrations that growing lymphomas (in mice) lead to the presence of a serum-borne lipid mobilizing factor. The activity is also present in the culture fluids of lymphoma cell lines. Purification efforts are underway. (5) The establishment of a procedure for sensitizing E. coli B to ionizing irradiation. The method involves conversion of hydrated electrons and hydroxyl-free radicals, produced by radiolysis of intra- and intercellular water to $\cdot\text{Br}_2^-$ radical anion, and attack by $\cdot\text{Br}_2$ or its decay products on the bacteria. This procedure enhances radiation sensitivity nine-fold (three times greater than the largest previous enhancement factor). The applicability of the method to mammalian cells is under current study. (6) Development of rapid methods, based on the polarization of fluorescein or carboxyanion fluorescence, for the identification of the mitogen responding fraction of human lymphocytes. (7) The observation of a defect in immune complex clearance in mice exposed to a prolonged intake of oral cadmium. (8) Preparation of a culture system which separates normal hematopoietic cells from leukemic cells. (9) Construction of a computer video-digitizer and written program to measure the rate and force of contraction of beating cultured heart cells. The computer-aided analysis permits measurement of velocity and acceleration of single-cell contraction and relaxation. The system will permit state-of-the-art evaluation of hormones, heavy metals, and pharmacologic

reagents on cardiac function. (10) Identification of the inhibitory action of lead on muscle cell fusion. The production and/or secretion of a high molecular weight factor is blocked. (11) Development of the chemical methodology for the preparation of "magic bullets" -- toxic chimeric proteins composed of a receptor binding protein (hormone, antibody, growth factor) and the killing subunit of a toxic lectin or bacterial toxin. Such conjugates will be used for receptor-specific cell killing. (12) Isolation of variant cell lines in which the biological response to the tumor promoter TPS is eliminated. (13) Demonstration of a new tumor marker in cultured human melanoma cells.

ABSTRACTS

1. Aharonov, A., Goodman, R., Walker, P., Weichsel, Jr., M.E. and Herschman, H.R.: Decreased Nerve Growth Factor (NGF) Concentration in Submaxillary Glands (SMG) and Heart of Dystrophic (dy/dy) Mice. Seventh International Meeting of the International Society of Neurochemistry, Jerusalem, Israel, September (1979).

Several studies have indicated abnormalities in sympathetic nerves of 129 ReJ dy mice, a strain with congenital muscular dystrophy. Also, SMG from homozygous dy/dy mice has been reported to contain significantly less NGF than control mice. Because NGF is important in maturation and maintenance of peripheral sympathetic nerves, we measured NGF concentration in SMG, heart, muscle, brain, and liver of 10 adult male homozygous 129 ReJ dy mice and 10 phenotypically normal littermates using a specific radioimmunoassay for β -NGF. No significant differences were noted for muscle, brain, or liver NGF levels. SMG (3.5 ± 0.4 μ g/mg protein; mean $\pm$ S.E.M.) and heart (133.1 ± 8.0 pg/mg protein) of dy/dy mice contained significantly less NGF than did control SMG (7.2 ± 0.3 μ g/mg protein; $p < 0.001$) and heart (159.9 ± 5.7 pg/mg protein; $p < 0.05$) suggesting that NGF metabolism is significantly altered in dy/dy mice. Since sialectomy in mice results in reduced tyrosine hydroxylase activity in the superior cervical ganglion (SCG), the decreased NGF level in SMG of dy/dy mice may be associated with diminished sympathetic innervation of the heart, thus accounting for the decreased cardiac NGF levels. Conversely, the primary abnormality may reside in the SCG with diminished NGF concentrations in both target organs, SMG and heart. The normal NGF levels in affected skeletal muscle suggests a limited role of NGF in skeletal muscle pathology in this disorder. Levels of tyrosine hydroxylase activity in the SCG and the adrenal glands are currently being measured.

2. Arenander, A.T. and de Vellis, J.: Glial-Released Proteins in Clonal Cultures and Their Modulation by Hydrocortisone. Brain Res. in press (1980).

Rat glial C6 cells release into the culture medium a reproducible spectrum of soluble proteins of 12 major peaks over a broad molecular weight range as determined by fractionation on SDS-gel electrophoresis. Exposing C6 monolayers to hydrocortisone (HC) results in a selective alteration in the pattern of glial-released protein (GRP). The selective HC-induced increase or decrease in GRP peaks is specific: to HC in that 17 β -estradiol, dibutyl cyclic AMP, isoproterenol and melatonin exert either no detectable or a qualitatively different influence on the GRP pattern. The HC influence is dose dependent over a physiological range of concentrations from 10^{-9} to 10^{-6} M. Differences in culture age and in subclones of

C6 can influence both the normal and the HC-induced pattern of GRP. The origin of the GRP is unknown, but pattern reproducibility, viability tests, surface labelling studies and metabolic labelling studies of soluble and particulate compartment proteins and glycoproteins support the position that cell lysis is not an important source of GRP. More importantly, these studies indicate that GRP and HC-induced changes in GRP pattern are physiologically significant aspects of glial cell behavior.

3. Arenander, A.T. and de Vellis, J.: Hormonal Regulation of Glial Released Protein in Cell Culture. Soc. Neuroscience, Abstracts, 5:753 (1979).

Glial cells synthesize and release a variety of macromolecular factors including glycosaminoglycans, proteins (e.g., Nerve Growth Factor), glycoproteins and polypeptides, some of which are capable of influencing the morphological and/or biochemical differentiation of various neuronal populations. There has been little analysis of the range of potential protein factors or of the control mechanisms which modulate their production and release.

We report here that monolayers of rat clonal and primary glial cells release into the culture medium a reproducible, broad spectrum of soluble macromolecules. Furthermore, a number of these glial-released proteins (GRPs) are shown to be regulated in a specific manner by a variety of hormonal agents. Conditioned medium was collected from C6 glioma cell monolayers after being incubated for 24 hr in serum-free medium and labelled during the last 6 hr with either [^3H] or [^{14}C]leucine. SDS-polyacrylamide slab gel electrophoresis of soluble GRPs revealed 20 major peaks of labelled protein distributed over a molecular weight (MW) range of 10,000 to 300,000. Gel radiolabelled patterns were reproducible both within and between experiment based on visual examination of plots, $^3\text{H}/^{14}\text{C}$ isotope ratios and label reversal. Exposure of the cells to hydrocortisone (HC, 1-2 μM) for 24 hr altered the pattern of GRP in a selective and specific manner. Six major GRP peaks were consistently observed to either increase or decrease based on plots of isotope ratios. The effect could be observed at 0.02 $\mu\text{g/ml}$ (5.4×10^{-8} M) but not at 0.002 $\mu\text{g/ml}$. Treatment of cells with 17- β -estradiol (2 μM) gave no observable change in pattern of GRP. Dibutyryl cyclic AMP (1 mM) and isoproterenol (10 μM) were also capable of selectively influencing the GRP patterns but in a manner different from HC. A number of the GRP peaks are glycoproteins based on metabolic labelling with [^{14}C]gluco-samine. Pure primary cultures of astroglia and oligodendroglia obtained from newborn rats generated a spectrum of GRP closely resembling that of C6, differing mainly in the high MW region. HC treatment also influenced the GRP pattern from mixed glial cultures.

Thus, both clonal and primary glial cultures released a wide MW range of proteins (GRP) that were under specific hormonal control. The origin and possible role in neuronal-glial coupling of GRPs is being investigated.

4. Bogin, E., Massry, S.G. and Harary, I.: Effect of Parathyroid Hormone (PTH) on Heart Cells. Association of American Physicians (1979).

Myocardiopathy is common in uremia but its cause is unknown. It has been shown that excessive entry of Ca in heart cells by catecholamines causes necrosis of myocardium. The high blood levels of PTH in uremia may also enhance entry of Ca into heart cells and exert deleterious effects on the heart. We examined the effect of PTH on heart cells grown in culture. Both N-terminal (1-34) PTH and intact (1-84) PTH produced immediate and sustained significant rise in beats/min and the cells died earlier than control. The effect is reversed if PTH is removed from media. There was a dose-response relationship between both moieties of PTH and the rise in heart beats but the effect of 1-84 PTH was significantly greater than that of 1-34. PTH stimulated cAMP production within one minute from 4.3 ± 2.4 to 15.6 ± 1.6 /mol/mg protein and cAMP remained elevated thereafter. The effect of PTH required Ca, was mimicked by Ca-ionophore, prevented by verapamil and was not abolished by α or β adrenergic blockers. PTH action was additive to phenylephrine and synergistic with isoproterenol. Sera from uremic-PTX rats did not affect heart beats but sera from uremic rats with intact parathyroid glands or from uremic-PTX rats treated with PTH had similar effects as PTH. Data indicate 1) heart cells have PTH receptors, 2) PTH increases heart beats and cause early death of cells, 3) PTH effect is due to Ca entry into heart cells, 4) the locus of action through which PTH induces Ca entry is different from that for catecholamines, 5) uremic serum has no effect unless it contains PTH. Data suggest that myocardial damage may occur in uremia due to prolonged exposure to very high blood levels of PTH and assign new dimensions to PTH toxicity in uremia.

5. Bony, S., Subramanian, C., Mead, J.F. and Dhopeswarkar, G.A.: Dietary Eggs and Changes in Plasma, Liver and Brain Lipids in Rats. Nutrition Reports International 21:77-86 (1980).

A study was undertaken to determine the effect of feeding cooked whole eggs on the lipid metabolism of adult female rats and their progeny. The results showed that there was a significant elevation of total lipids, cholesterol esters and triglycerides in the livers of female rats at the end of 45 days on the egg diet. The addition of vitamins and minerals to the egg diet did not prevent this

accumulation of liver lipids. The progeny born to the dams on the egg diet grew poorly and showed high mortality. Examination of brain lipids of the pups showed an unusual accumulation of sterol esters in the brain. Addition of vitamins and minerals corrected all the abnormalities. Accumulation of sterol esters in the brain, generally found only in demyelinating diseases, is discussed in relation to the diet.

6. Bressler, J., Cole, R. and de Vellis, J.: The Neoplastic Progression of Oligodendrocytes: An In Vivo-In Vitro Model. Fed. Proc. 39:863 (1980).

Previously our laboratory has established procedures enabling the preparation of pure oligodendrocytes or astrocytes. In this report we have applied this technique to develop a model to study the neoplastic progression of the oligodendrocyte. Oligodendrocytes were prepared from pups treated with ethylnitrosourea (ENU) or phosphate buffer saline (PBS) during gestation. During the first 90 d both groups of cells grew at a slow pace, then a marked increase in cellular proliferation was observed in the ENU-derived cultures. After 150 d, the PBS-derived cells also proliferated rapidly. All the cell lines retained oligodendrocyte properties, such as 5-100 protein, 2':3'-cyclic nucleotide phosphorylase, and a mechanism to induce lactate dehydrogenase levels after dibutyryl 3':5'-adenosine monophosphate (cAMP) treatment. However, the cell lines lost the ability to increase glycerol phosphate dehydrogenase levels after hydrocortisone stimulation, and to increase cAMP levels after beta-agonist stimulation. The cells were similar to oligodendrocytes as observed by both light and electron microscopy. All cell lines grew in soft agar and grew tumors *in vivo*. Only some of the cell lines displayed marked fibrinolytic activity, or agglutination after concanavalin A treatment. Further studies in progress will characterize the preneoplastic oligodendrocytes, as well as attempt to modulate their progression.

7. Butler-Gralla, E. and Herschman, H.R.: Variants of 3T3 Cells Lacking Mitogenic Response to the Tumor Promoter Tetradecanoyl Phorbol Acetate (TPA). J. Supramol. Struct. Suppl 4:157 (1980).

One of our laboratory's basic aims has been to understand the series of events by which a previously non-dividing cell enters the cell division cycle. Our approach has been to isolate cell lines that do not respond to specific mitogens, and to determine what lesion causes the nonresponsiveness. TPA is a potent mitogen for 3T3 cells, as well as being a tumor promoter. Four independent variants of 3T3 cells that do not divide or reach an increased saturation density in response to TPA have been isolated. All variants retain response to elevated levels of fetal calf serum. Three variants retain

response to Epidermal Growth Factor (EGF); one does not. This is interesting in view of the reported effects of TPA on EGF binding. EGF binding studies are being done on all the cell lines. The cell line that does not respond to EGF has no measurable EGF binding. The others bind EGF in varying amounts. In these lines, EGF binding in the presence and absence of TPA has been measured at 37°. In all cases, TPA decreases the affinity of the EGF receptor for EGF to approximately the same degree as it does in the parent 3T3. Thus we have isolated cell lines that retain some response to TPA (i.e. modulation of EGF binding), but have lost the mitogenic response. These variants will be useful for the study of the nature of the mitogenic response, the mechanism of tumor promotion, and the interrelation between these two phenomena.

8. Cawley, D.B., Simpson, D.L. and Herschman, H.R.: Toxicity of an Asialofetuin-Ricin A-Chain Chimera on Cultured Cells Is Mediated by the Asialoglycoprotein Receptor. Fed. Proc., 1980 ASBC Meeting, New Orleans (1980).

Ricin, a toxic castor bean lectin which can be designated A-B, binds to cells through its B chain. The A chain subsequently enters the cytoplasm and enzymatically inactivates ribosomes. Desialylated fetuin (asialofetuin: ASF) was derivatized with N-succinimidyl-3(2-pyridyldithio)propionate (SPDP). The derivative, ASF-PDP, was conjugated to ricin A chain by disulfide exchange and ASF-A was purified on G-100 Sephadex. The ASF-A "chimera" inhibits protein synthesis in primary cultures of rat hepatocytes. We have demonstrated that these cultures degrade ASF but not fetuin. The toxic effect exerted by ASF-A is inhibited by ASF but not by fetuin, suggesting that ASF-A is internalized by the asialoglycoprotein (ASGP) receptor, which binds and removes asialoglycoproteins from blood. The liver-specific ASGP receptor is not present in mouse 3T3 cells and, as expected, ASF-A is not toxic to 3T3 cells. The concentration of ASF-A (100 ng/ml) required to inhibit protein synthesis by 50% in 1.5×10^6 hepatocytes in 24 hr is similar to the amount of ricin (80 ng/ml) required to exert the same effect. Thus, it is possible to construct "chimeras" which are (i) capable of utilizing cell-type specific receptor-mediated endocytotic systems, and which are (ii) biologically as potent as the "parent" toxin.

9. Chandler, C.E. and Herschman, H.R.: Modulation of Epidermal Growth Factor (EGF) and Nerve Growth Factor (NGF) Induced Adhesion and Growth Factor Binding of PC-12 Pheochromocytoma Cells by Tumor Promoter Tetradecanoyl Phorbol Acetate (TPA). J. Supramol. Struct. Suppl. 4:59 (1980).

NGF has previously been shown to increase the adhesion of PC-12 cells to cell culture dishes. We now report that EGF is also able to elicit increased adhesion of PC-12 cells. The dose response curve for EGF is bell shaped in contrast to the more classical dose response curve obtained with NGF. EGF does not cause neurite outgrowth although the increase in adhesion is of the same magnitude as that induced by NGF. Thus, an increase in cell adhesion is not sufficient to cause neurite formation.

TPA is able to block the EGF induced adhesion of PC-12 cells. TPA does not, however, alter the NGF-induced adhesion of these cells. TPA shifts the EGF binding curve to the right but does not alter maximal EGF binding at saturating concentrations of growth factor. NGF binding is not affected by TPA.

TPA is able to alter the expression of phenotypic characteristics in a number of cell culture systems. Process outgrowth of serum-deprived neuroblastoma cells and NGF exposed chick embryonic ganglia cells in culture have been reported to be delayed by TPA. NGF induced neurite formation by PC-12 cells, however, is unaffected by TPA.

TPA is able to block the decrease in short microvilli caused by EGF but not the decrease caused by NGF as seen by scanning electron microscopy. Long microvilli which are formed in response to both EGF and NGF are blocked in both cases by TPA.

10. Chandler, C.E. and Herschman, H.R.: Tumor Promoter Modulation of Epidermal Growth Factor and Nerve Growth Factor Binding of PC-12 Pheochromocytoma Cells. J. Cell Physiol. in press (1980).

Nerve growth factor (NGF) has previously been shown to increase the rate of adhesion of PC-12 pheochromocytoma cells to cell culture dishes. This increase in the rate of adhesion was postulated to be important in NGF-mediated neurite outgrowth. We now report that epidermal growth factor (EGF) is also able to increase the rate of adhesion of PC-12 cells to cell culture dishes, but does not elicit neurite outgrowth. The dose response curve for EGF is bell shaped, in contrast to the more classically shaped dose response curve obtained with NGF.

Tetradecanoyl-phorbol-acetate (TPA), a potent tumor promoter, blocks the EGF-induced increase in adhesion rate of PC-12 cells, but does not alter the NGF-induced increase in adhesion rate. TPA shifts the EGF binding curve to the right for PC-12 cells, but does not alter maximal EGF binding at saturating concentrations of EGF. The binding of NGF to PC-12 cells is not affected by TPA. NGF-induced neurite formation by PC-12 cells is unaffected by TPA, in contrast to the previously reported delay of neurite outgrowth of serum-deprived neuroblastoma cells and NGF-exposed chick embryonic ganglia cells.

NGF and EGF both cause a decrease in the number of short microvilli and an increase in the number of long microvilli on PC-12 cells. TPA blocks the decrease in the number of short microvilli in EGF treated cells, but not in NGF treated cells. Long microvilli formation is blocked by TPA in both conditions, suggesting the latter are not involved in the increased adhesion rates.

11. Fulco, A.J.: The Regulation of Membrane Lipid Biosynthesis in Bacilli. Proceedings of the International Symposium on Frontiers in Lipid Research, p. 21 (1980).

In response to changes in environmental temperature, bacilli adjust the fluidity of their membrane lipids by altering the chain-lengths, branching and degree of unsaturation of the component fatty acids. To elucidate the mechanisms regulating one of these processes, the inverse relationship between growth temperature and unsaturated fatty acid composition, we selected *Bacillus megaterium* 14581 to study in detail. At growth below 30°, *B. megaterium* contains an O₂-dependent desaturase that converts phospholipid-bound palmitate to *cis*-5-hexadecenoate. *In vivo*, the half-life of this enzyme is inversely proportional to temperature. Desaturase inactivation follows first-order kinetics at all temperatures and its rate is determined solely and instantaneously by the incubation temperature. A more complex temperature-mediated control process involves the regulation of desaturase synthesis. Cultures growing at 35° contain neither unsaturated fatty acids nor the desaturase necessary for their production. When culture temperature is lowered rapidly to 20°, however, synthesis of desaturase begins after a brief lag and attains a maximum rate shortly thereafter. This hyperinduction process, so-called because the rate of desaturase synthesis after culture transfer from 35° to 20° far exceeds the rate found in cultures growing from inoculum at 20°, requires new protein and RNA synthesis. Hyperinduction is followed by a period of rapid attenuation until the rate of desaturase synthesis is at or below that of comparable cultures growing at 20° from inoculum. The shut-down of hyperinduction at 20° in transfer cultures as well as the lower rate of desaturase synthesis in cultures growing from inoculum at 20° appear to result from the action of a temperature-sensitive modulator protein. In the absence of modulator (i.e., during hyperinduction) the rate of desaturase synthesis is simply proportional to the overall rate of protein synthesis. Modulation, however, is an exponential function of protein synthesis. The modulator, which may be an oligomeric protein in equilibrium with an inactive monomer, seems to act at the level of transcription by selectively inhibiting the synthesis of the messenger RNA coding for desaturase. Finally, the first-order inactivation of desaturase as well as the hyperinduction and modulation

of its synthesis is directly mediated by temperature. Neither the state of membrane fluidity nor wide variations in O₂-tension affect these parameters.

12. Gaynor, R., Irie, R., Morton, D. and Herschman, H.R.: S100 Protein is Present in Cultured Human Malignant Melanomas. Nature in press (1980).

S100 protein, so called because of its solubility in 100% saturated ammonium sulphate is an acidic cytoplasmic protein specific for the nervous system. It is localized primarily to glial elements of the brain, Schwann cells in the peripheral nervous system and satellite cells in sympathetic ganglia. This brain-specific protein shows a close immunological relationship among a wide variety of vertebrates, as measured by a quantitative complement fixation technique. Although strict serological conservation and tissue localization have been maintained among different species, no function for S100 protein has been determined. However, the appearance of S100 protein in brain is correlated with maturation of the nervous system in both rat and man. Previous *in vitro* studies on the production and regulation of S100 protein in the C6 cell line derived from a rat astrocytoma indicated that cell contact and cessation of division induced S100 protein. Neuroblastoma cell lines lack this protein although it is found in other astrocyte cell lines. We are unaware of any reports of cell lines, other than those of glial origin, which produce S100 protein. Melanocytes are derived from neuroectodermal elements, and this common origin of glial cells and melanocytes prompted us to study whether S100 protein might be present in cell lines from human malignant melanomas. We now report the presence of S100 protein in five of seven continuous cell lines of human malignant melanoma.

13. Golde, D.W., Herschman, H.R., Lusk, A.J. and Groopman, J.E.: Growth Factors. Annals of Internal Medicine 92:650 (1980).

Humoral regulation of somatic and hematopoietic cell growth has been intensely investigated during the past decade. Growth hormone is unique because it regulates the size of the person within the constraints of the genetic program. The somatomedins and insulin growth factors are low molecular weight polypeptides believed to mediate some functions of growth hormone. Epithelial growth factor and nerve growth factor are well-characterized polypeptides that influence the growth and differentiation of epithelial and neural tissues and interact with specific cell surface receptors. The hematopoietins are a family of polypeptide hormones that specifically regulate the proliferation and differentiation of stem cells giving rise to erythrocytes, granulocytes, monocytes, megakaryocytes, and B and

T lymphocytes. Platelet-derived growth factor modulates the proliferation of fibroblasts *in vitro* and may have a role in the development of atherosclerosis and myelofibrosis. New knowledge on the biochemistry and physiology of growth factors will probably have a substantial impact on our understanding of human diseases involving abnormal cell growth.

14. Goodman, R. and Herschman, H.R.: Tyrosine Hydroxylase Induction in Response to Protein and Steroid Factors in Clonal Cell Lines. Seventh International Meeting of the International Society of Neurochemistry, Jerusalem, Israel, September (1979).

Clonal cell lines have been isolated from a rat pheochromocytoma tumor in which either protein factors, such as nerve growth factor, or a glucocorticoid hormone, such as dexamethasone, elicit a specific induction of the adrenergic enzyme tyrosine hydroxylase (TH). The responses are independent; the steroid responsive line (PC-G1s) does not respond to the protein factors, and the protein responsive line (PC-G2) responds only marginally to the steroids. These responses are dose dependent. The time course of these reactions will be presented as well as data on the specificity of the responses. A comparison of the induction of TH in the PC-G1s cells, the PC-G2 cells, and the PC-12 cells will be presented.

15. Goodman, R., Slater, E. and Herschman, H.R.: Epidermal Growth Factor Induces Tyrosine Hydroxylase in a Clonal Pheochromocytoma Cell Line, PC-G2. J. Cell Biol. 84:495-500 (1980).

We have previously described the isolation of a clonal cell line (PC-G2) in which the level of tyrosine hydroxylase (TH), the rate-limiting step in the synthesis of the catecholamine neurotransmitters, is induced by nerve growth factor (NGF). We now report that epidermal growth factor (EGF) also induces TH in the PC-G2 cell line. Although EGF has been shown to be mitogenic for many cultured cells, no neuronal function has been previously reported for this protein. The TH response to EGF is elicited in a dose-dependent fashion at concentrations as low as 0.1 ng/ml and is maximal at 10 ng/ml EGF. The maximal response is observed after 3-4 d of exposure to 10 ng/ml EGF. The induction by NGF and EGF is inhibited by their respective antisera. Dexamethasone, a synthetic glucocorticoid which we have previously shown modulates the response of PC-G2 cells to NGF, also modulates the TH induction elicited by EGF.

16. Hankinson, O.: Mutants of Cultured Hepatoma Cells Deficient in Aryl Hydrocarbon Hydroxylase. In Microsomes, Drug Oxidations, and Chemical Carcinogenesis, Coon, M.J., Conney, A.H., Estabrook, R.W., Gelboin, H.V., Gillette, J.R. and O'Brien, P.J. eds., New York: Academic Press, Vol. II, pp. 1149-1152 (1980).

BP-resistant, aryl hydrocarbon hydroxylase (AHH)-deficient clones have been isolated from a mouse hepatoma line. Their frequency is increased by a number of mutagens. Complementation tests show that they arise by mutations in at least two loci.

17. Hankinson, O.: Unstable Aryl Hydrocarbon Hydroxylase-Deficient Variants of a Rat Hepatoma Line. Somatic Cell Genetics in press (1980).

The H-4-II-E-C3 line has high aryl hydrocarbon hydroxylase (AHH) activity. It was also found to be very sensitive to benzo(a)pyrene (BP) toxicity, and a single-step selection procedure for isolating BP-resistant (BPR) clones was designed. All the BPR variants tested had reduced AHH activities under both inducing and non-inducing conditions. As H-4-II-E-C3 was propagated, it gradually declined in AHH activity and increased in cloning efficiency in BP. The spontaneous rate of origin of the BPR variants gradually increased in AHH activity, and decreased in cloning efficiency in BP as they were propagated. Partially resistant variants also generated, at an appreciable rate, cells with even greater degrees of resistance to BP. The instabilities of the wild-type and variant cultures suggest that the variants arose by an epigenetic mechanism or by changes in gene dosage, rather than by point mutations.

18. Harary, I. and Berliner, J.: Electron Microscopic Examination of Lead Treated L₆ Skeletal Muscle Line Cells in Culture. J. Environmental Pathology and Toxicology in press (1980).

A study has been made of the effects of lead on developing muscle using a cell culture system. When the L₆ clonal cell line was treated with lead acetate in culture during the first or second day after plating (but not at later times) fusion of cells to form skeletal muscle straps was inhibited. This inhibition was not due to a general toxic effect of lead on the cells since cell division continued at a normal rate during the first 10 days of culture after lead addition. When cells were examined ultrastructurally using stereology, the only apparent effect of lead was a change in mitochondrial size and configuration. Five times as many partially condensed mitochondria were seen in lead treated cells and mitochondrial size was also significantly increased. Lead appears to effect a very early event in cell fusion since gap junction formation (a necessary event in fusion) and some synthesis of myofibrils occurs even in the presence of lead.

19. Hays, E.F. and Hale, L.: Separation of Normal Hemopoietic Stem Cells from Leukemia Cells by Long-Term Culture of Mouse Bone Marrow. J. Supramolecular Structure Suppl. 4 (1980).

AKR mice with early and advanced spontaneous and virus-accelerated T cell lymphoma (leukemia) were studied. Bone marrows which contained 50-95% lymphoma cells were placed in long-term cultures and evaluated at weekly intervals for 1-12 weeks for persistence of lymphoma cells, totipotent stem cells (CFUs), granulocyte-monocyte progenitors (CFUc) and granulopoiesis. The contents of a femur and tibia were flushed into 10 cc of Fischer's Medium with 25% horse serum and hydrocortisone 0.5 µg/ml. The cultures were incubated at 33°C, 5% CO₂. At weekly intervals 1/2 of the medium was removed and replaced with fresh medium. At week 4, 25% fetal bovine serum replaced the horse serum. Cell counts, cell morphology and stem cell assays were performed on selected samples. After 2 weeks in culture no leukemic cells could be seen. The cultures consisted of attached cells with progranulocytes and maturing granulocytes in suspension. In the non-adherent cells at week 6-7 CFUc (500-700/ml) and CFUs (15-17/ml) were present. Cell counts revealed that proliferation was occurring. There was a peak in cell number at week 5-6. The spleen colonies formed were erythroid, granuloid or mixed. No lymphoma cell colonies were seen and 10⁶ cells from 6-week cultures did not produce lymphomas when inoculated into syngeneic mice. Preliminary studies suggest that inoculations of stem cells from 5, 6, and 7 week cultures could reconstitute 950 r treated syngeneic animals. These experiments show that the culture conditions used favor normal hemopoietic stem cell proliferation and granulocyte maturation. They selectively deplete leukemic blasts thus providing normal hemopoietic progenitor cells for transplantation to syngeneic hosts.

20. Herschman, H.R.: Prostatic Acid Phosphatase and Prostatic Cancer. Trends in Biochemical Science March:82-84 (1980).

The enzymatic determination of serum prostatic acid phosphatase has been used for nearly 40 years as a confirmatory test for extra-capsular prostatic cancer. A specific radioimmunoassay for this protein may now be of value in detecting intracapsular prostatic cancer and in assessing the progress of the disease.

21. Herschman, H.R.: Radioimmunoassay for Serum Prostatic Acid Phosphatase and the Detection of Prostatic Cancer. Joint Congress on Clinical Chemistry, Montreal, Canada (1979).

American Cancer Society statistics suggest that 20,000 men died of prostatic cancer in the U.S. in 1977. Prostatic cancer is third only to lung and colorectal carcinoma in cancer-related deaths.

The disease is most often detected by digital rectal examination of the prostate and is frequently confirmed in more advanced cases by the enzymatic detection of elevated levels of a unique acid phosphatase, synthesized by prostatic cells, in the sera of afflicted individuals. Accurate measurement of low levels of prostatic acid phosphatase (PAP) in serum is hampered, however, by the presence of a number of other acid phosphatases; in normal serum PAP amounts to only about 10% of the total acid phosphatase activity. In addition, the enzyme activity of serum PAP is sensitive to increases in both temperature and pH.

Because of specificity, enzymatic stability and sensitivity limitations in the enzymatic termination of PAP we have developed serologic methods for the measurement of the enzyme mass in serum. We have chosen radioimmunoassay (RIA) procedures because of their reproducibility and sensitivity. PAP was purified by column chromatography from the prostatic fluid of normal males. Antisera were prepared in rabbits; each animal received approximately 250 micrograms of antigen in two injections. Purified antigen was labelled for RIA with ^{125}I by the chloramine T method. Initial RIA studies of the PAP system utilized the double-antibody method of separating free from bound antigen. However, a solid phase assay in which antibody was bound to disposable polypropylene tubes gave more rapid, reproducible, inexpensive and efficient results. The working range of the assay is 1-30 ng PAP/ml. Utilizing this assay, analysis of 150 samples require less than eight hours of labor. The specificity of the RIA for PAP was analyzed by examining cross-reactivity in twelve tissues. The maximum tissue level of cross-reactive material was only 0.1% of the activity present in a prostate extract. The PAP levels of 50 control individuals, 113 patients with prostatic cancer, 36 with benign prostatic hyperplasia (BPH) 83 with other cancers, 20 with gastro-intestinal disorders and 28 with total prostatectomies were determined by RIA and enzyme assay. When the upper limit was set at 8.0 ng/ml, the RIA diagnosed prostatic cancer in 33, 79, 71, and 82 percent of patients with Stage I, II, III, and IV disease. In contrast, the enzyme assay detected elevations of enzyme in the serum of 12, 15, 29, and 60 percent respectively. No false positives were detected by either assay in normal controls; RIA was positive in two patients with BPH and one with total prostatectomy. The RIA identified over half the cases of intracapsular prostatic cancer. Preliminary screening data and logitudinal studies will also be described.

22. Herschman, H.R., Goodman, R. and Chandler, C.: Pheochromocytoma Cell Lines as Models of Neuronal Gene Expression. Seventh International Meeting of the International Society of Neurochemistry's Bat-Sheva Seminar on Biochemical Development of Nervous Tissue in Culture, Rehovot, Israel, August (1979).

We have developed new cell lines derived from a rat pheochromocytoma, for use in studying the regulation of adrenergic expression in neuronal tissue. These cell lines are complementary to the PC-12 cell line isolated by Greene and Tischler. In experimental animals Nerve Growth Factor causes both hypertrophy of the sympathetic ganglia and elevation of the specific activity of tyrosine hydroxylase (TH), the rate limiting step in norepinephrine synthesis. Glucocorticoid hormones are able to enhance this stimulation of TH by NGF. We have now isolated a new cell line, PC-GIS, in which glucocorticoid hormones induce TH. Dose-response, time course, and specificity data will be presented. We have also utilized a tyrosine-deficient medium to select for a clonal line of pheochromocytoma cells in which TH levels are modulated by NGF. Dose-response, time course, and specificity data for induction of TH in PC-G2 cells will be presented. We have confirmed the observation of Schubert and Whitlock that NGF is able to increase adhesion of PC-12 cells to plastic substrates. We have now shown that Epidermal Growth Factor (EGF) is also able to increase adhesion of PC-12 cells, but does not cause process extension -- in contrast to NGF. These observations have led to an examination of EGF and NGF receptors and ligand-receptor processing in PC-12 cells. EGF is rapidly degraded by PC-12 cells. In contrast, degradation of NCF occurs only slowly.

23. Kamberi, I.A., de Vellis, J., Baclean, E.S. and English, D.: Hormonal Patterns of the Hypothalamo-Pituitary-Gonadal Axis in the Rat during Postnatal Development and Sexual Maturation. Endokrinologie 559 (1979).

Protein or steroid hormonal levels in male and female rats from birth to adulthood were measured by radioimmunoassay. Animals were sacrificed by decapitation at 15.00 to 16.00 h (unless otherwise noted). Neonates (1 to 3 days of age) had high levels of serum gonadotropins (LH and FSH) which declined by days 5 to 7, rose sharply again at days 10 and 15, and declined a second time until the peri-pubertal period. The developmental patterns of FSH and LH were qualitatively similar in both sexes, but were quantitatively less in the males. Furthermore, the male serum FSH continued to increase slightly after day 30 and throughout the peri-pubertal period. Hormonal levels of gonadotropin-releasing hormone or gonadoliberin (Gn-RH) in the hypothalamus were detectable at day 5 in both sexes and increased rapidly between days 7 and 15. In males, this increase continued, attaining maximal values at adulthood, but the female hypothalamic Gn-RH content after day 15 was not significantly increased until the peri-pubertal period and the day of vaginal opening. The Gn-RH content in the cerebral cortical tissue of both sexes was undetectable, and the serum Gn-RH was also not detectable until a significant

increase occurred in both sexes on day 15. The male serum Gn-RH continued to increase and attained maximal values at adulthood. Female maximal values were attained by day 20 and did not show any significant changes until the day of vaginal opening. In both sexes, the serum estradiol-17 β (E₂) levels were high at birth, but they declined significantly by day 24. The E₂ levels rose again between days 10 and 20 but to a level lower than the birth value, and by day 25 they again decreased. They continued to be low in males throughout adulthood, and in females they were low until the peri-pubertal period and increased at the start of the estrus cycle. Prolactin levels in both sexes dropped slightly after birth and remained low until day 15; at day 20, a sharp increase occurred and continued to day 35 in females and to day 30 in males. Thereafter, the levels continued to decrease in males, whereas, the female levels varied with the stage of estrus cycle. Serum progesterone levels were low in both sexes. In males, an increase in progesterone occurred by day 10 followed by another slight rise until day 40. By day 60, male levels were slightly lower than at days 30 to 40. Female progesterone levels increased by day 15, followed by a slight increase until days 20 to 25 and a sharp rise at days 30 to 35. Low progesterone levels were observed at the peri-pubertal period and throughout the day of vaginal opening. Hormonal levels in females at the day of vaginal opening (day of functional proestrus), and three days thereafter varied greatly. The morning of vaginal opening was characterized by a significant increase in serum E₂ levels, and the cells in the vaginal smear were cornified. The gonadotropin surge, occurring in the afternoon, was always preceded by an E₂ rise. Shortly after the gonadotropin surge, a sharp progesterone increase occurred which continued until the following day. Variations in the hypothalamic content and in the serum concentration of Gn-RH were also evident on the day of vaginal opening. The slight yet significant decline in the hypothalamic content of Gn-RH on the afternoon of proestrus was immediately reflected in a slight increase in serum Gn-RH. These changes occurred before the gonadotropin surge. The variety of hormonal changes that occurred from birth to adulthood suggests that the factors that cause the onset of puberty are very complex.

24. Karin, M., Andersen, R., Slater, E., Smith, K. and Herschman, H.R.: Metallothionein mRNA Induction in HeLa Cells in Response to Zinc or Dexamethasone Is a Primary Induction Response. Nature in press (1980).

Metallothioneins are low molecular weight, heavy metal binding proteins unique in their high cysteine content and high affinity for Zn⁺⁺, Cd⁺⁺, Hg⁺⁺, Ag⁺, and Cu⁺. The synthesis of MT is induced by zinc or cadmium in the liver and kidney and in cultured cells. More recently MT induction by the steroid hormone dexamethasone has been demonstrated

in HeLa cells and adrenalectomized rats. Because glucocorticoid hormones lead to an intracellular accumulation of zinc the question arises whether the induction of MT gene expression by steroids is a "primary induction response" or is due to elevated intracellular Zn^{++} . The glucocorticoid induced elevated transport of Zn^{++} is dependent on concurrent protein synthesis. We now show that, in contrast to glucocorticoid stimulated Zn^{++} transport, the Zn^{++} and dexamethasone induction of translatable MT-mRNA is independent of concomitant protein synthesis but not RNA synthesis; i.e., MT induction by either agent is a "primary induction response."

25. Karin, M. and Herschman, H.R.: Characterization of the Metallothioneins Induced in HeLa Cells by Dexamethasone and Zinc. Eur. J. Biochem. in press (1980).

The metallothioneins induced by HeLa cells by dexamethasone and Zn^{2+} were labeled with [^3H]cysteine and [^{35}S]cysteine respectively. The labeled metallothioneins from dexamethasone and zinc-induced HeLa cells were compared to one another and to metallothioneins from human liver by (i) gel permeation chromatography on G-75 Sephadex columns, (ii) ion-exchange chromatography on DEAE Sephadex A-25 columns, (iii) electrophoresis on non-denaturing polyacrylamide gels, and (iv) electrophoresis of reduced and alkylated proteins on dodecylsulfate-polyacrylamide gels. The dexamethasone-induced metallothioneins of HeLa cells, the Zn^{2+} -induced metallothioneins of HeLa cells, and the metallothioneins of human liver were indistinguishable by these four criteria.

26. Karin, M. and Herschman, H.R.: Dexamethasone Stimulation of Metallothionein Synthesis in HeLa Cell Cultures. Science 204:176-177 (1980).

HeLa cells in culture synthesize metallothionein. To investigate the effects of glucocorticoids on metallothionein synthesis we adapted HeLa cells to growth in a defined medium lacking hydrocortisone. In this defined medium, containing $1.5 \times 10^{-6}M$ Zn^{2+} , dexamethasone ($10^{-6}M$) caused a five- to sixfold increase in the synthesis of metallothionein. Progesterone ($10^{-5}M$), a known antagonist of glucocorticoids, inhibited this response by 50 percent.

27. Karin, M. and Herschman, H.R.: Glucocorticoid Hormone Receptor Mediated Induction of Metallothionein Synthesis in HeLa Cells. J. Cell. Physiol. in press (1980).

HeLa cells grown in chemically defined medium lacking glucocorticoids synthesize metallothioneins, low molecular weight heavy metal binding proteins. Dexamethasone and hydrocortisone increase the rate of metallothionein synthesis five to ten fold. Maximal induction is

achieved with 10^{-8} M dexamethasone and 10^{-7} M hydrocortisone. Half-maximal induction is achieved at 5×10^{-9} M dexamethasone and 5×10^{-8} M hydrocortisone. Although carried for many generations in the absence of any glucocorticoids, HeLa cells (clone S) contain 25,000 specific ^{3} H-dexamethasone receptors that translocate into the nucleus after one hour of incubation. ^{3} H-dexamethasone binds to a single class of receptors with an apparent $K_d = 18.8$ nM. A variety of steroids can be classified into four classes, based on their effect on metallothionein synthesis: (a) full agonists (optimal inducers), (b) intermediate effectors which have either partial agonist or antagonist activities, and (c) inactive steroids. There is a correlation between the effects on metallothionein synthesis of different steroids and their ability to compete with ^{3} H-dexamethasone binding. We conclude that metallothionein is induced in HeLa cells by a glucocorticoid receptor mediated mechanism.

28. Karin, M., Herschman, H.R. and Weinstein, D.: Primary Induction of Metallothionein by Dexamethasone in Cultured Rat Hepatocytes. Biochem. Biophys. Res. Comm. 92:1052-1059 (1980).

Dexamethasone or Zn^{++} increase the rate of synthesis of the metal-binding protein metallothionein in hepatocyte cultures. Dexamethasone induction of the capacity to synthesize metallothionein is not blocked by cycloheximide. In contrast, the dexamethasone stimulated increase in Zn^{++} uptake is inhibited by cycloheximide. Like Zn^{++} , dexamethasone is a "primary inducer" of metallothionein. The glucocorticoid induction of metallothionein in primary cultures of rat hepatocytes is not mediated through elevation of Zn^{++} uptake.

29. Keough, W.G. and Myers, Jr., L.S.: The Repair of γ -ray Induced DNA Strand Breaks in CHO Cells after Hyperthermia at 45°C. Abstracts, Annual Meeting of the Radiation Research Society, New Orleans, Paper Cd-5, June (1980).

Radiation dose survival curves were determined for CHO cells exposed to hyperthermia (45°C for 15 min) then incubated at 37°C for either 0, 24, 48, 72, or 96 hours before being irradiated. Results from these experiments indicate an increase in the shoulder of D_0 of the 48 and 72 hour survival curves. The alkaline elution technique was used to examine repair of DNA strand breaks in cells irradiated with 300 rads at 0, 24, 48, 72 and 96 hours post hyperthermia treatment. This was accomplished by incubating the cells at 37°C for either 0, 7.5, 15, 30 or 60 minutes after irradiation. Preliminary results indicate a change in the repair capability of hyperthermia treated cells with time post heating. The results also indicate a correlation between repair capability and an increase in the shoulder of the radiation survival curves of hyperthermia

treated cells. The possible contribution of cell cycle synchronization to the radiation response of heat treated cells is being investigated.

30. Kerk, D.K., Myers, C.P. and Hays, E.F.: Parametric Analysis of CFUs Self-Renewal. Exp. Hemat. Suppl. 6 7:28 (1979).

The self-renewal capacity (SR) of CFU-S has been studied in C57B16/J mice employing the double transplantation technique. Results are customarily expressed as a ratio: $SR = (\bar{x}_2 \cdot M) / \bar{x}_1$, where $\bar{x}_2$ = mean of observed secondary colony counts, M = reciprocal of the dilution factor employed in the secondary transfer, and $\bar{x}_1$ = mean of observed primary counts. This report describes a procedure that reduces these ratios to a normally distributed form suitable for parametric statistical analysis. Initially, colony counts were corrected for crowding overlap by the method of Till. Linear regression of the variance on the mean of observed counts produced slopes characterizing the distribution of 1' and 2' colonies. The former are negative binomial, confirming the report of Mossman. Interestingly, the 2' colonies are Poisson. The transform $y' = \log(y + (k/2))$ was used to approximate normality and equality of variance. The value of k was predicted by the slope of the regression of var/mean on mean ($1/k$). A linear expression was derived involving the assay parameters, $\bar{x}_1$, $\bar{x}_2$, k_1 , k_2 , $\bar{x}_1$, $\bar{x}_2$, and M . The result, for each experiment, is an unbiased estimate of the mean SR and its variance. An inverse transformation may be applied to obtain the estimated mean on the original untransformed scale. Studies were performed with cells suspended in neutral PBS(NPBS) (pH=7.2) and acid PBS(APBS) (pH=5.2). The distributional characteristics of both 1' and 2' counts appear to be unaffected by pH. However the SR of APBS treated CFU-S was significantly reduced as compared to that of NPBS (40 vs 100) ($P < .05$). An interesting source of bias occurred in APBS expts. Those with appreciable mortality prior to 2' cell transfer or before 2' count yielded significantly higher SR (50) than those in which no such death occurred (35) ($P < .05$). These results suggest that two distinct mechanisms may be operating to increase SR: selection of 2' cell donors, and increased $\bar{x}_2$ from loss of animals with lowest counts. These mechanisms may not be responsible for heterogeneity of SR under less stringent conditions. Nevertheless the ability of this analysis to distinguish small differences between populations is demonstrated. Incubation of marrow cells with the organic dye Merocyanin 540 has been previously shown to exert a suppressive effect on spleen colony formation. We have confirmed this observation. Preliminary data suggests, further, a heterogeneous response of the CRU-S pool. We are currently examining the SR of CFU-S as a function of exposure time to this membrane-active agent.

31. Kitada, S., Hays, E.F. and Mead, J.F.: A Lipid Mobilizing Factor in Serum of Tumor-Bearing Mice. Lipids 15(3):168-174 (1980).

There is considerable evidence that the growing tumor requires a source of unsaturated fatty acids, but the nature of this source and the mechanism of mobilizing the fatty acids from it are obscure. These experiments make use of AKR mice with implanted adipose tissue labeled with $1\text{-}^{14}\text{I}$ inoleic acid. With this experimental animal, it has been found that: (a) in the normal, fed mouse, fat is mobilized slowly and appears largely as respiratory CO_2 , following oxidation, (b) in the normal, fasted mouse, fat is mobilized rapidly and appears largely as respiratory CO_2 ; (c) in the tumor-bearing, fed mouse, fat is mobilized rapidly and appears largely in the tumor; and (d) the serum from tumor-bearing mice, when injected into normal mice, produces an immediate massive fat mobilization that does not respond to feeding, whereas the serum from normal, fed mice does not. It is concluded that a mobilizing factor of unknown nature is present in the serum of tumor-bearing AKR mice.

32. Kitada, S., Hays, E.F. and Mead, J.F.: Characterization of a Lipid Mobilizing Factor (LMF) from Tumors. Proceedings of Golden Jubilee International Congress on Essential Fatty Acids and Prostaglandins, Minneapolis, May 5-7, in press (1980).

Using a new *in vivo* technique for measuring mobilization from adipose tissue, it has been found that growing lymphomas in AKR mice produce a factor that causes mobilization of fatty acids from adipose tissue to lymphoma lipids. This factor has been found in serum from lymphoma-bearing mice and human cancer patients, extracts of lymphoma and culture medium from a growing lymphoma cell line. LMF has been concentrated by chromatography on Biogel P6 and appears to be a small molecular weight protein which is a direct product of tumor cells.

33. Kumar, S., McGinnis, J.F. and de Vellis, J.: Catecholamine Regulation of Lactate Dehydrogenase in Rat Brain Cell Culture. J. Biol. Chem. 255(6):2315-2321 (1980).

The mechanism of catecholamine induction of the soluble cytoplasmic enzyme lactate dehydrogenase (EC 1.1.1.27) was studied in the rat glial tumor cell line, C6. Lactate dehydrogenase was partially purified from extracts of $[^3\text{H}]$ leucine-labeled cells by affinity gel chromatography and quantitatively immunoprecipitated with anti-lactate dehydrogenase-5 IgG and with anti-lactate dehydrogenase-1 IgG. The immunoprecipitates were dissociated and electrophoresed on sodium dodecyl sulfate polyacrylamide gels. Using this methodology, the increased enzyme activity of lactate dehydrogenase in norepinephrine-treated C6 cells was observed to be concomitant

with the increased synthesis of enzyme molecules. Despite the continued presence of norepinephrine, the specific increase in the rate of synthesis of lactate dehydrogenase was transient. It was first detected at 4 h, was maximum at 9 h, and returned to basal levels by 24 h. The half-life of lactate dehydrogenase enzyme activity was 36 h during the induction and 40 h during deinduction. The half-life for decay of ^3H -labeled lactate dehydrogenase was 41 h. These observations suggest that the increase in lactate dehydrogenase activity in norepinephrine-treated cells does not involve any change in the rate of degradation. Norepinephrine increased the specific rate of synthesis of both lactate dehydrogenase-5 (a tetramer of four M subunits) and lactate dehydrogenase-1 (a tetramer of four H subunits), although to different extents. Since these subunits are coded for by two separate genes on separate chromosomes, it suggests that the regulatory mechanism involves at least two separate sites of action.

34. Leveille, P.J., McGinnis, J.f., Maxwell, D.S. and de Vellis, J.: Immunocytochemical Localization of Glycerol-3-Phosphate Dehydrogenase in Rat Oligodendrocytes. Brain Research 200:000-000 (1980).

In this study, two indirect immunoperoxidase staining procedures were used to investigate the cellular localization of rat brain glycerol-3-phosphate dehydrogenase (EC1.1.1.8; GPDH). At the light and electron microscopic level, we found that the use of monospecific rabbit antibodies to GPDH consistently resulted in the specific staining of only one glial cell population. GPDH-positive cells in perineuronal, interfascicular and perivascular positions were identified as oligodendrocytes by classical morphological criteria. The specificity of GPDH antigen-antibody reaction was determined by qualitative and quantitative immunochemical methods and by immunocytochemical controls of immunologic and methodologic sources of non-specific reaction product. The illustrative data from this study serve to qualitatively define GPDH as a biochemical marker for oligodendrocytes in rat central nervous tissue. In view of the fact that the synthesis of rat brain GPDH is specifically regulated by glucocorticoids, the positive results obtained in this study further warrant the interpretation that rat oligodendrocytes are target cells for glucocorticoids.

35. Levy, L., Vredevoe, D., Knutson, D., China, D. and Hays, E.: The Effect of Oral Cadmium Administration to Mice on Their Ability to Affect Administered Aggregated IgG. ASPET Meeting, Portland, OR, August 19-23 (1979).

Cadmium (Cd) toxicity due to chronic oral ingestion has been reported in man and laboratory animals. In experiments to be reported CBA mice were given Cd in their drinking water in doses of 1-300 ppm

for periods up to six months. At various times up to six months animals were examined *in vivo* and *in vitro* to determine the removal of ^{125}I labeled AgIgG from the blood or medium and the subsequent appearance in organs or isolated cells. Similar studies were also done using ^{125}I monomeric IgG. Injection of ^{59}Fe labeled mouse cells were administered to determine whether blood or organ values of IgG reflected changes in blood flow. When Agg IgG was given I.V. to control (no Cd) mice, the biological half life ($t_{1/2}$) was 4.3 ± 0.17 (SEM) and in those animals receiving 300 ppm Cd for six months it was 9.4 ± 0.7 (SEM). Different doses (10, 1 ppm) yielded decreasing half times approaching control. The persistence of Agg IgG in chronic high dose Cd mice may ultimately be reflected in immune complex deposition diseases in target organs such as the kidney, heart and lungs.

36. Lombardi, F.J., Chen, S.L. and Fulco, A.J.: A Rapidly Metabolizing Pool of Phosphatidylglycerol as a Precursor for Phosphatidylethanolamine and Diglyceride in Bacillus Megaterium. J. Bacteriology 141(2):626-634 (1980).

Pulse-chase experiments in Bacillus megaterium ATCC 14581 with $[\text{U-}^{14}\text{C}]$ -palmitate, L- $[\text{U-}^{14}\text{C}]$ serine, and $[\text{U-}^{14}\text{C}]$ glycerol showed that a large pool of phosphatidylglycerol (PG) which exhibited rapid turnover in the phosphate moiety (PG_t) underwent very rapid interconversion with the large diglyceride (DG) pool. Kinetics of DG labeling indicated that the fatty acyl and diacylated glycerol moieties of PG_t were also utilized as precursors for net DG formation. The $[\text{U-}^{14}\text{C}]$ glycerol pulse-chase results also confirmed the presence of a second, metabolically stable pool of PG (PG_s), which was deduced from $[\text{P-}^{32}]$ phosphatide studies. The other major phospholipid, phosphatidylethanolamine (PE), exhibited pronounced lags relative to PG and DG in ^{14}C -fatty acid, ^{14}C -glycerol, and $[\text{P-}^{32}]$ -phosphate incorporation, but not for incorporation of L- $[\text{U-}^{14}\text{C}]$ serine into the ethanolamine group of PE or into the serine moiety of the small phosphatidylserine (PS) pool. Furthermore, initial rates of L- $[\text{U-}^{14}\text{C}]$ serine incorporation into the serine and ethanolamine moieties of PS and PE were unaffected by cerulenin. The results provided compelling *in vivo* evidence that *de novo* PG_t , PS, and PE syntheses in this organism proceed for the most part sequentially in the order $\text{PG}_t \rightarrow \text{PS} \rightarrow \text{PE}$ rather than via branching pathways from a common intermediate and that the phosphatidyl moiety in PS and PE is derived largely from the corresponding moiety in PG_t , whereas the DG pool indirectly provides an additional source for this conversion by way of the facile $\text{PG}_t \leftrightarrow \text{DG}$ interconversion.

37. Lombardi, F.J. and Fulco, A.J.: Temperature-Mediated Hyperinduction of Fatty Acid Desaturation in Pre-Existing and Newly Formed Fatty Acids Synthesized Endogenously in Bacillus Megaterium. Biochimica et Biophysica Acta 618:359-363 (1980).

^3H -labeled fatty acids synthesized endogenously by Bacillus megaterium ATCC 14581 growing at 35°C in the presence of L-[G- ^3H]valine exhibited the same time-course of hyperinduced desaturation following a temperature decrease to 20°C as was observed previously with exogenously supplied ^{14}C -labeled fatty acids. Radioactive fatty acids synthesized in the presence of [1- ^{14}C]glucose during hyperinduction at 20°C following a shift-down from 35°C were desaturated at the same relative rate as ^{14}C -labeled fatty acids synthesized previously at 35°C, suggesting that the newly synthesized fatty acids equilibrate with a large portion of the preexisting moieties before becoming susceptible to desaturation.

38. Lombardi, F.J. and Fulco, A.J.: Two Distinct Pools of Membrane Phosphatidylglycerol in Bacillus Megaterium. J. Bacteriology 141(2):618-625 (1980).

The predominant membrane lipid in Bacillus megaterium ATCC 14581, phosphatidylglycerol (PG), is present in two distinct pools, as shown by [^{32}P]phosphate incorporation and chase experiments. One pool (PG_T) undergoes rapid turnover of phosphate moiety, whereas the second pool (PG_S) exhibits metabolic stability in this group. The phosphate moiety of the other major phospholipid, phosphatidylethanolamine, is stable to turnover. [^{32}P]phosphate- and [2- ^3H]glycerol-equilibrated cultures yielded the following glycerolipid composition: 56 mol% PG (34 mol% PG_T and 22 mol% PG_S), 21 mol% phosphatidylethanolamine, 1 to 2 mol% phosphatidylserine, 20 mol% diglycerides, less than 0.5 mol% cardiolipin, and 0.2 to 0.4 mol% lysophosphatidylglycerol. Accumulation of PG was halted immediately after the addition of cerulenin, an inhibitor of *de novo* fatty acid synthesis, whereas phosphatidylethanolamine accumulation continued at the expense of the diglyceride and PG pools. Strikingly, initial rates of [^{32}P]phosphate incorporation into PG were unaffected by cerulenin. In control cultures at 35°C, incorporation of [^{32}P]phosphate into PG exhibited a biphasic time course, whereas incorporation into phosphatidylethanolamine was concave upward and lagged behind that of PG during the initial rapid phase of PG incorporation. Finally, levels of lysophosphatidylglycerol expanded rapidly after cerulenin addition at 20°C, but not at 35°C. Moreover, incorporation of [^{32}P]phosphate into lysophosphatidylglycerol lagged behind incorporation into PG in both the presence and absence of cerulenin at 20 and 35°C.

39. McCarthy, K.D. and de Vellis, J.: Preparation of Separate Astroglial and Oligodendroglial Cell Cultures from Rat Cerebral Tissue. J. Cell Biology 85:890-902 (1980).

A novel method has been developed for the preparation of nearly pure separate cultures of astrocytes and oligodendrocytes. The method is based on (a) the absence of viable neurons in cultures prepared from postnatal rat cerebra, (b) the stratification of astrocytes and oligodendrocytes in culture, and (c) the selective detachment of the overlying oligodendrocytes when exposed to sheer forces generated by shaking the cultures on an orbital shaker for 15-18 h at 37°C. Preparations appear >98% pure and contain $\sim 1-2 \times 10^7$ viable cells (20-40 mg of cell protein). Three methods were used to characterize these two culture types. First, electron microscopic examination was used to identify the cells in each preparation (mixed and separated cultures of astrocytes and oligodendrocytes) and to assess the purity of each preparation. Second, two oligodendroglial cell markers, 2',3'-cyclic nucleotide 3'-phosphohydrolase (EC 3.1.4.37) and glycerol phosphate dehydrogenase (EC 1.1.1.8) were monitored. Third, the regulation of cyclic AMP accumulation in each culture type was examined. In addition to these studies, we examined the influence of brain extract and dibutyryl cAMP on the gross morphology and ultrastructure of each preparation. These agents induced astroglial process formation without any apparent morphological effect on oligodendrocytes. Collectively, the results indicate that essentially pure cultures of astrocytes and of oligodendrocytes can be prepared and maintained. These preparations should significantly aid in efforts to examine the biochemistry, physiology, and pharmacology of these two major classes of central nervous system cells.

40. McGinnis, J.F. and de Vellis, J.: Glycerol-3-phosphate Dehydrogenase Isoenzymes in Human Tissues: Evidence for a Heart-Specific Form. Journal of Molecular and Cellular Cardiology 11:795-802 (1979).

Incubation of homogenates, from human heart, brain, liver and skeletal muscle, with excess antiserum against purified rat skeletal muscle glycerol phosphate dehydrogenase (1-glycerol-3-phosphate:NAD⁺ oxidoreductase, EC 1.1.1.8) demonstrated the presence of two immunologically distinct forms of the enzyme. The major form of the enzyme in heart tissue does not react with the antibody and is very heat labile. Anion exchange chromatography resulted in the separation of heart glycerol phosphate dehydrogenase into three peaks, each of which was distinguishable from the others by heat lability and immunological reactivity. The isoenzymes appear to represent combinations of two different subunits to produce HH, HL and LL forms with HH representing the major heart isoenzyme and LL the liver. The data suggests that the detection of the HH isoenzyme in serum may be used as an indicator to diagnose cardiac infarctions in humans.

41. Masse, M.J.O. and Harary, I.: Primary Cultures of Embryonic Rat Heart Cells. In Vitro in press (1980).

In contrast to neonatal rat heart cells in culture, embryonic myocardial cells form colonies. They also differ from neonatal cells in their appearance and behavior - i.e., fewer striations, fewer binucleated cells, their loose packing and sorting from non-muscle cells and most of all in their capacity to divide.

42. Masse, M.J.O. and Harary, I.: The Use of 5-Bromodeoxyuridine and Irradiation for the Estimation of the Myoblast and Myocyte Content of Primary Rat Heart Cell Cultures. J. Cell Physiology in press (1980).

A method for killing dividing cells (Puck and Kae, 1967) was adapted for the elimination of dividing heart muscle cells (myoblasts) in cultures. We have used this method to demonstrate their presence and to estimate their number as well as the number of non-dividing heart muscle cells (myocytes) in the neonatal rat heart. Cells were cultivated in BUdR 10^{-4} for three days and then irradiated with long UV light. The selective elimination of dividing cells led to a loss of myosin Ca^{2+} activated ATPase in the cultures. This indicates the presence of dividing cells which contain myosin. The percent of ATPase left after irradiation was 32% of the control in cultures derived from 1 day post-natal rats and 48% in cultures from 4 day post-natal rats. This reflects an *in vivo* shift of myoblasts to myocytes in the muscle cell population as the rat ages.

43. Masse, M.J.O. and Harary, I.: The Use of Fluorescent Antimyosin and DNA Labelling for the Estimation of the Myoblast and Myocyte Population of Primary Rat Heart Cell Cultures. J. Cell Physiology in press (1980).

Cell division in heart muscle cells progressively ceases during the development of the rat heart, leading to an adult stage with muscle cells incapable of cell division. We have quantitatively determined the number of dividing and non-dividing heart muscle cells in cultures derived from different stages of the developing rat heart with the use of ^3H TdR continuous labelling and fluorescent anti-myosin staining. The cultures were derived from 14 and 17 day post-coital (dPC) rat embryos and from 1 and 4 day post-natal (dPN) rats. The percent non-dividing cells increased with development and the age of the post-natal rat. The percent non-dividing cells in 14dPC equalled 21%, 17 dPC equalled 25%, 1 dPN equalled 44% and in 4dPN equalled 60%. This method for the quantitative determination of dividing and non-dividing cells in the developing rat heart provides a model which is useful for the study of the mechanism of the loss of cell division capacity.

44. Mead, J.F.: The Essential Fatty Acids - Past, Present and Future. Proceedings of the Golden Jubilee International Congress on Essential Fatty Acids and Prostaglandins, Minneapolis, May 5-7, in press (1980).

Following the pioneering work of Burr and his colleagues, studies were initiated on the metabolism of the polyunsaturated fatty acids. Using the alkaline isomerization technique, information was obtained that could not be readily interpreted in terms of mechanism at the time. Studies with ^{14}C -labeled suspected precursors and intermediates revealed the pathways of conversion of the PUFA and *in vitro* enzyme studies have amplified and clarified those results.

Another pioneer in the field, Smedley-MacLean, postulated that cancer cells would also require a source of essential fatty acids but was unable to carry out studies to test the theory. We continued with this idea and have now shown not only that cancer cells utilize EFA for cell membrane synthesis, but have discovered the mechanism by which they are able to obtain them from the host. This is by release of a lipid mobilizing factor that mobilizes fatty acids from adipose tissue and in some way, preventing the oxidation of these fatty acids as an energy source.

45. Menon, N.K. and Dhopeswarkar, G.A.: Essential Fatty Acid Deficiency and Lipid Metabolism of the Developing Brain. Proceedings of the Golden Jubilee International Congress on Essential Fatty Acids and Prostaglandins, Minneapolis, May 5-7, in press (1980).

EFA deficiency produced by excesses of certain fatty acids (FA) in the presence of limited amounts of 18:2 is not uncommon in human populations. We have shown earlier that large amounts of 18:1 in the diet interferes with the utilization of 18:2. To study the effect of such a nutritional stress on the developing brain, pregnant rats were maintained on a 5% 18:1 diet starting at 14 days after impregnation and the offspring continued on the diet up to 120 days. Even though the pups looked normal throughout the study, their growth fell below the controls starting at birth. The lipid:protein ratio was lower in the brain microsomes and mitochondria. Elevated triene/tetraene ratio, characteristic of EFA deficiency, was found in all the lipid classes of serum and liver at 21 days. 20:3 ω 9 appeared in the brain PL at that time. This reached index values (>0.4) in the individual PL of whole brain, myelin and microsomes during the later developmental period. The amount of 20:3 ω 9 in the male rats was almost double that of the female. A 11.5% decrease in 18:1 was also noted in the brain but not in the serum or liver. On the contrary, in a similar study using 5% hydrogenated coconut oil (CO) diet, there was no change in the FA of the brain even after 90 days; in contrast the triene/tetraene ratio increased to index values in the serum and liver lipids. This study shows that excess

of 18:1 competing for scarce EFA in the diet produces EFA deficiency in the developing rat brain. Lack of such an effect by dietary CO may be due to non-competitive nature of the saturated FA.

46. Michaels, B.C. and Fulco, A.J.: Characterization of a Fatty Acyl Epoxide Hydrase from Bacillus Megaterium. Fed. Proc. 39(6):2084 (1980).

A soluble hydrase which acts on long-chain epoxy fatty acids and esters has been purified more than 100-fold from cell-free preparations of B. megaterium ATCC 14581. In general, the trans-9,10-epoxides are hydrated more efficiently than the corresponding cis-isomers and the methyl esters are more active as substrates than are the free acids of equivalent chain lengths. Using trans-9,10-epoxypalmitic acid as the substrate, the rate of enzymatic hydration was insensitive to pH changes over the range of 5-9 and to a variety of metal ion chelators and sulfhydryl-complexing reagents. Anionic and non-ionic detergents did not affect activity but the cationic detergent, hexadecyltrimethylammonium bromide, at $1 \times 10^{-3}M$, caused a 92% inhibition. The molecular weight of the epoxide hydrase was estimated, by chromatography on Sephadex G-75, to be about 50,000. Specific activity of the hydrase decreased with increasing protein concentration, however, suggesting reversible inactivation by enzyme polymerization.

47. Michaels, B.C., Ruettinger, R.T. and Fulco, A.J.: Hydration of 9,10-Epoxypalmitic Acid by a Soluble Enzyme from Bacillus Megaterium. Biochem. and Biophys. Res. Comms. 92(4):1189-1195 (1980).

In a recent publication from this laboratory, a soluble, cytochrome P-450-containing preparation from Bacillus megaterium, shown previously to catalyze the (ω -2) monohydroxylation of long-chain fatty acids (including palmitoleate) was shown to also convert palmitoleic acid to 9,10-epoxypalmitate and 9,10-dihydroxypalmitate. We now wish to report the results of experiments to determine whether this preparation contained epoxide hydrase activity that could account for the formation of 9,10-dihydroxypalmitate from epoxypalmitate, and if so, whether this activity could be dissociated from the monooxygenase complex.

48. Moore, C.E. and Dhopeswarkar, G.A.: Placental Transport of Trans Fatty Acids in Rats. IFS/AOCS World Congress, New York, JAACS 57 (1980).

Transport of elaidic (18:1t) and linoleaidic (18:2t,t) acids was demonstrated from maternal plasma to placental and fetal tissues

in rats. On the 18th day of gestation, a ^{14}C -labeled albumin complex of elaidic or linoelaidic acid was injected into the maternal circulation. All animals were sacrificed 1 hr after injection. Lipid composition and distribution of label were determined in placenta, fetal tissues and maternal plasma. Differences in specific activities of plasma, placental and fetal total lipids suggested that a maternal-fetal concentration gradient of elaidic and linoelaidic acids exists. Specific activity (cpm/mg) of maternal plasma total lipids was 4 to 7 times greater than specific activity of placental total lipids, which was several fold greater than specific activity of fetal total lipids. Distribution of radioactivity in various lipid components was determined by TLC. Irrespective of the label, the highest percentage of total radioactivity was carried by the triglyceride fraction in maternal plasma (~60-80%) and was incorporated primarily in phospholipids of fetal tissue (~50-60%). A nearly equal distribution of the label was found between phospholipids and triglyceride fractions of placental lipids (~40%). Radioactivity of fatty acid methyl esters (FAMES) determined by Radio-GLC indicated that after injection of linoelaidate, radioactivity of maternal plasma, placenta and fetal tissue FAMES was associated only with 18:2t,t. Following injection of elaidate, all radioactivity in placental FAMES was associated with 18:1t. However, the label in fetal tissues was distributed between 16:0 and 18:1t. These findings suggest that by the 18th day of gestation, rat fetal tissue can metabolize elaidic acid via β -oxidation.

49. Myers, Jr., L.S.: Free Radical Damage of Nucleic Acids and Their Components: The Direct Absorption of Energy. In Free Radicals in Biology, Pryor, W.A. ed. New York: Academic Press, Vol. IV, pp. 95-114 (1980).

This study is an attempt to extract from the vast literature on radiation effects on solid compounds information relevant to processes which may actually occur when living organisms are irradiated. Topics covered include: i) initial radical products; ii) reactions of initial products and identification of secondary products; iii) effects of LET, light, and metal ions on radical structure and stability; and iv) interactions such as charge and radical transfer between bases when stacked in various conformations.

50. Myers, Jr., L.S. and Kay, E.: Radiolysis of LmNA and Other Biopolymers. Int. J. Radiat. Oncology, Biol. and Phys. 5:1055-1060 (1980).

Studies of radiolysis of biopolymers serve the dual purposes of giving information on a) chemical mechanisms by which radiation modifies life processes and b) structure-function relationships

in macromolecules. Conditions in living cells are such that both direct and indirect depositions of energy in biopolymers are possible. Direct effects in chromatin components result in formation of specific radical products, many highly reactive. In irradiated DNA the cationic radical, $\cdot\text{Gua}^+$, and the anionic radical, $\cdot\text{Thy}^-$, make large contributions to the ESR spectrum. Secondary reactions of the cationic radicals are largely unknown. Indirect effects occur when energy is deposited in water or other components in a solution, and radiolysis products such as eag^- and $\cdot\text{OH}$ react with the biopolymer under investigation. Studies carried out half a century ago show that this process is effective in inactivating enzymes. Conversion of $\cdot\text{OH}$ to the less reactive inorganic radical-anion $\cdot\text{Br}_2^-$ has made it possible to determine the role of tyrosine in functional and structural integrity of several proteinase inhibitors. Both eag^- and $\cdot\text{OH}$ react rapidly with DNA, but only $\cdot\text{OH}$ initiates reactions which damage DNA. Radiolysis of double-stranded DNA leads to an increase in optical absorption. The $\cdot\text{OH}$ is believed to attack the deoxyribose moiety, causing strand breaks and partial denaturation, thus reducing the hypochromic effect. After the DNA is partially denatured, or single-stranded, $\cdot\text{OH}$ attacks the bases also. Three kinds of strand breaks have been observed: 1) immediate, 2) those appearing post-irradiation, and 3) those appearing on postirradiation treatment with alkali. Radiolysis of chromatin results in DNA strand breaks, base damage, and protein-DNA cross links. Yields for strand breaks and base damage are lower in chromatin than in purified DNA, and lower still in intact cells. A general hypothesis for radiation damage of chromatin is outlined.

51. Myers, Jr., L.S., Warnick, A. and Kay, E.: Enhancement of Lethal Effects of Ionizing Radiation on *E. coli* by Bromide Ion. Abstracts, Annual Meeting of the Radiation Research Society, New Orleans, Paper Cb-11 (1980).

The presence of bromide ion in aqueous media converts the hydroxyl free radical, produced by radiolysis of water, into the less reactive but more specific reagent, the dibromide radical anion, $\cdot\text{Br}_2^-$. We have examined the consequences of this conversion on the radiation sensitivity of *E. coli* B under a variety of conditions. The bacteria were suspended in an inorganic medium with or without 0.1 M KBr, saturated with N_2 , O_2 , or N_2O and exposed to Co-60 radiation. Survival was determined by colony assay. The presence of bromide markedly decreased survival under all conditions tested. Dose reduction factors as compared with anoxic conditions were: O_2 2.5, N_2O 1, N_2 + KBr 1.7, O_2 + KBr 4.6 and N_2O + KBr 9.2 for 10% survival. Preliminary results indicate that similar sensitization occurs at survival levels as low as 0.01%. These results, combined with results of experiments using DNA and DNA components in similar

chemical systems a) have shown that mechanisms exist for increasing the lethal effects of radiation to levels well above the usual oxygen enhancement ratio, b) have led to an understanding of how to increase the contribution of indirect effects to cell damage, and c) have obvious implications for radiation therapy which are being investigated by experiments with mammalian systems.

52. Myers, Jr., L.S., Warnick, A., Kay, E. and Keough, G.: Sensitization of *E. Coli* to Ionizing Radiation by Exposure in the Presence of N_2O and KBr. Abstracts, 146th National Meeting, AAAS, San Francisco, p. 126 (1980).

The presence of 0.1 M KBr in an N_2O -saturated solution containing *E. coli* results in an extraordinarily great sensitization of the bacteria to ionizing radiation. Radiation doses of 1000 and 3000 rads, lethal to 2 and 8% of the bacteria in the absence of KBr, are lethal to 20 and 50% respectively in its presence. The sensitization appears to be even greater at higher doses. In the N_2O /KBr system, hydrated electrons are converted to $\cdot OH$ (hydroxyl free radicals), and these in turn to $\cdot Br_2^-$ radical anions. Experiments with model compounds show that under these conditions, bases in single and double stranded DNA, and protein amino acid residues such as tyrosine, tryptophan, and cysteine are destroyed, but the deoxyribose moieties of DNA and aliphatic amino acid residues of proteins are not attacked. These results suggest that the sensitization is the result of conversion of $\cdot OH$ to a relatively unreactive species which reacts relatively specifically with sensitive targets in *E. coli*. Experiments are being carried out to determine whether the sensitization also occurs in mammalian cells.

53. Pedersen, S., Haseltine, W.A. and Hays, E.F.: Replication of Inoculated Virus in AKR Mouse Lymphomas Accelerated by AKR MCF 247 Virus. Virology in press (1980).

Mice of the AKR strain develop thymic lymphoma at a high incidence between six months and one year of age. The development of this disease is correlated with the expression of a polymorphic group vertically inherited endogenous retroviruses. Viruses that have a host range restricted to mouse cells (ecotropic) and are positive in an XC fusion test are produced after two weeks of age and can be isolated from animals of all ages. Viruses capable of replication on cells derived from animals other than mice (xenotropic) can be detected in older mice. A number of other viruses can be isolated from the lymphoid tissues of preleukemic and leukemic mice. These include viruses that are negative in the XC fusion assay and are ecotropic, as well as viruses that have a broad host range, including

both mink and mouse, and that are also negative in the XC fusion test (polytropic or MCF viruses).

The age related changes in retrovirus expression may represent early events in the disease process. To test this hypothesis, viruses derived from the preleukemic and leukemic tissues of AKR have been injected into newborn animals to determine if they accelerated the onset of disease. Results of such tests indicate that whereas the ecotropic XC⁺ virus that can be isolated from young animals does not accelerate the onset of disease, several other viruses do. These include some of the cloned polytropic isolates such as MCF-247 and some of the viruses produced by cell lines derived from spontaneously occurring thymic lymphoma (SL viruses). With virus acceleration the median age of onset is decreased from 269 days to 90-135 days.

Although injection of certain strains of virus accelerate the onset of disease in the AKR mice, a question remains as to whether or not the injected virus replicates in the tumor cells. To test this possibility, newborn AKR mice were injected with the MCF-247 polytropic strain of virus, and a cell line established from one of the thymic tumors that arose five months later.

We report that the virus produced by the cells used to establish this line retained its polytropic host range; that the virus produced by the cell line is identical to the strain used for infection as judged by a high resolution analysis of the ribonuclease T₁ resistant oligonucleotides of the RNA genome; and that the DNA of the tumor cell line contained novel sequence indistinguishable from MCF-247 proviral DNA.

54. Pruss, R.M. and Herschman, H.R.: Cholera Toxin Stimulates Division of 3T3 Cells. J. Cell. Physiol. 98:469-474 (1979).

Cholera toxin was used in an attempt to inhibit epidermal growth factor stimulated 3T3 cell division. Instead, cholera toxin alone at low concentrations (10⁻¹⁰M), was able to stimulate cell division and could augment EGF stimulated cell division. The mitogenic effect of cholera toxin can occur despite a dramatic increase in the intracellular levels of cAMP in 3T3 cells. Cholera toxin stimulated mitogenesis could not be mimicked by choleragenoid, the binding but inactive subunit of cholera toxin, or by other agents which elevate cAMP levels in 3T3 cells.

55. Pruss, R.M. and Herschman, H.R.: Mitogenic Effects of Murine Serum and Fibroblast Growth Factor on EGF Non-Proliferative Variants of 3T3. J. Supramol. Struct. in press (1980).

The enhanced ability of murine serum to support growth of 3T3 cells, when compared with fetal calf serum, is also evident on variants of 3T3 cells lacking the ability to bind epidermal growth factor. Variant 3T3 cell lines unable to bind EGF also retain a mitogenic response to fibroblast growth factor.

56. Rudd, C.J. and Herschman, H.R.: Characterization of Metallothionein in a Human Cell Line. 18th Annual Meeting of the Society of Toxicology, New Orleans, March, (1979).

Synthesis of metallothionein (MT) can be induced in the liver and kidney by cadmium or zinc salts and MT has been found in a number of other organs. MT synthesis was also induced in a clonal rat liver cell line (RLC-GAI). MT synthesis was investigated in a human cell line, HeLa-S, derived initially from a cervical carcinoma. Cells were grown in a serum free medium containing $1.5 \times 10^{-6}M$ Zn^{++} . Confluent cells were labeled with $^{65}ZnCl_2$, $^{109}CdCl_2$, or ^{35}S -cystine + Zn acetate ($5 \times 10^{-5}M$) and $CdCl_2$ (10^{-8} - $10^{-5}M$) for 18-24 hours. Soluble proteins were chromatographed on a Sephadex G-75 column. Up to 4.7 nmol Cd^{++}/mg total protein was found associated with MT. Concentrations of 10^{-6} and 10^{-5} Cd^{++} stimulated the incorporation of ^{35}S -cystine into MT. Addition of $5 \times 10^{-5}M$ Zn^{++} produced 3.6 nmol of Zn^{++}/mg protein in MT and stimulated the incorporation of ^{35}S -cystine. That cyclohexamide did not completely inhibit ^{109}Cd binding indicates that MT is normally present in the cell line. The results indicate that the induction of MT synthesis by Cd^{++} and Zn^{++} is not limited only to cells originating from the liver.

57. Salem, R. and de Vellis, J.: Phosphorylation of Plasma Membrane Proteins Dependent on Adenosine 3',5'-Monophosphate in Rat-Glial C6 Cells. Eur. J. Biochem. 107:271-278 (1980).

The presence of protein kinase(s) dependent on adenosine 3',5'-monophosphate (cyclic AMP) and their endogenous substrates were demonstrated in a glial plasma-membrane preparation. Three proteins, C, D and E, are the major substrates for a cyclic-AMP-regulated phosphorylation system in the plasma membrane of C6 cells, a glial tumor cell line. Plasma-membrane fractions were isolated by a modification of the $ZnCl_2$ -method of Warren et al. and were endogenously phosphorylated *in vitro* in the presence of [γ - ^{32}P] ATP. Phosphorylated proteins were separated by electrophoresis in 7, 9 and 12% discontinuous gradient polyacrylamide gels. Phosphorylated protein bands were visualized by autoradiography. The time course of phosphorylation and dephosphorylation of protein bands C, D and E was regulated by cyclic AMP. The approximate molecular weights of these proteins are 51000, 47000 and 38000, respectively. Quantitative microdensitometry of the autoradiograms showed that

the endogenous phosphorylation of the three proteins was affected by the concentration of cyclic AMP, cyclic GMP, ATP and divalent cations. The concentration of cyclic AMP required for optimal stimulation of the endogenous phosphorylation of the three proteins was in the range of 0.1 to 1 μ M. Cyclic GMP gave maximal stimulation above 10 μ M. Mg^{2+} was a more effective metal ion than either Mn^{2+} or Co^{2+} . The optimal concentration of those divalent cations was in the range of 10 - 24 mM. When Mg^{2+} was replaced by Ca^{2+} , Cu^{2+} or Zn^{2+} , little or no phosphorylation was observed. However, two proteins, A and B, were specifically phosphorylated in the presence of Cu^{2+} and Zn^{2+} respectively, but not in the presence of Mg^{2+} , Mn^{2+} or Ca^{2+} . We propose that such cyclic-AMP-dependent phosphorylation of plasma-membrane proteins may mediate cyclic AMP action in regulating membrane functions, such as amino acid transport in C6 cells.

58. Sevanian, A., Stein, R.A. and Mead, J.F.: Preferential Phospholipase A_2 Activity Against Oxidized Phosphatidylcholine. ISF/AOCS World Congress - Abstracts of Papers, Abstract 380B (1980).

There has been considerable speculation concerning the fate of damaged lipids in biomembranes. It has been suggested that the processes leading to membrane damage and leakage may involve either loss of integrity via lipid peroxidation, or that such events may accelerate enzyme mediated lipolysis resulting in membrane destruction. The possibility that oxidized fatty acids in membranes may be recognized and preferentially removed by lipolytic enzymes such as phospholipase A_2 (PL A_2) has been difficult to demonstrate directly. Part of this difficulty resides in the instability of lipid peroxidation products and hence in the unavailability of suitable substrates. There is now evidence that lipid peroxidation in membranes may yield products unlike those found in other lipid systems; in many instances lipid epoxides represent the major isolable products of peroxidation. The isolation and characterization of phospholipid epoxides from peroxidized liposomes, microsomes and whole organs, and their relative stability in aqueous preparations prompted an analysis of PL A_2 activity using phospholipid epoxides as substrates representing peroxidation products. Using 1-palmitoyl-2-epoxy-stearoyl phosphatidylcholine (PCE) prepared from 1-palmitoyl-2-oleoyl phosphatidylcholine (PC), we were able to demonstrate that PL A_2 was at least twice as active against PCE than PC in either pure enzyme (snake venom) or microsomal preparations. The major products of the PC/PCE-PL A_2 reaction were lyso PC, free fatty acid or fatty acid epoxide. The fatty acid epoxide, but not PCE, was rapidly hydrated in the absence of an epoxide hydratase inhibitor.

What these experiments demonstrate is an additional group of enzymes protecting the tissues from oxidative damage. First, phospholipase

(A₂) increases the rate of hydrolysis of the oxidized fatty acid. Second, epoxide hydrolase reacts many times more rapidly with the free fatty acid than with the bound fatty acid. Present experiments are concerned with similar findings with phospholipase C which results in the formation of a diglyceride, a product that could be readily converted to the epoxide-containing triglycerides found in the lung following exposure to NO₂.

59. Shine, H.D., Hertz, L., de Vellis, J. and Haber, B.: Preferential Localization of γ -Glutamyl Transpeptidase in Glia. Society for Neuroscience Abstracts, 5:416 (1979).

γ -glutamyl transpeptidase (γ -GTP) is an enzyme which may have a role in transport of amino acids and peptides across biological membranes. High levels of γ -GTP activity found in the brain suggest that this enzyme may well have such transport functions within neural tissues. We observe that in the central nervous system levels of enzymatic activity are greatest in the capillaries, followed by white matter and are significantly lower in gray matter. The higher levels of γ -GTP activity in white matter suggest a preferential association of γ -GTP with glia. To determine the cellular localization of γ -GTP in neural tissues we have employed cultured cells of neuronal and glial origin as models of neurons and glia *in vivo*. γ -GTP activity was measured using a highly sensitive fluorometric assay which employed the synthetic substrate 7- γ -glutamylamido-4-methyl coumarin and high liquid chromatography or fluorescent spectroscopy. Enzymatic activity in clonal cell lines of glial origin uniformly expressed greater activity than did a variety of neuroblastoma cell lines. Furthermore the γ -GTP activity of normal non-transformed rodent astrocytes and oligodendrocytes was also higher than neuronal levels. No significant difference in γ -GTP activity was found between the normal astroglia and oligodendroglia. Taken together this data strongly suggest that the bulk of CNS γ -GTP activity is primarily associated with astroglia, oligodendroglia and CNS capillaries.

60. Sorrentino, J.M., Brankow, D.W. and Herschman, H.R. Selection of an Epidermal Growth Factor Non-Responsive 3T3 Variant Cell Line Which Retains EGF Receptors. J. Cell Biol. 83:246a (1979).

Epidermal Growth Factor (EGF), a potent mitogen for murine embryo cell lines, is capable of stimulating quiescent 3T3 cells to resume a proliferative state. We have now selected a clonal 3T3 cell line which is no longer capable of giving a mitogenic response to EGF, but which still possesses the ability to bind and internalize the hormone. This selection has been accomplished by the addition of EGF (10 ng/ml) and colchicine (1.2 μ g/ml) to confluent, quiescent

monolayers of 3T3 cells for a period of 3 days. The cells which are capable of responding to EGF are arrested in mitosis and removed by washing the plates. The cells remaining demonstrate a greatly diminished mitogenic response to EGF. This selection protocol was repeated six times before clones were isolated by dilution to single cells in multiwell cloning plates. The resulting clones have yielded a cell line, 3T3-136A, which does not have a proliferative response to EGF but which possesses a full complement of EGF binding activity (receptors), internalizes EGF and demonstrates receptor down regulation. Autoradiographic analysis utilizing either ^3H -thymidine or ^{125}I -deoxyuridine shows that these cells no longer synthesize DNA in response to EGF treatment, but will do so when challenged by other mitogens.

61. Sorrentino, J.M. and Herschman, H.R.: Characterization of Cell Lines Established with Mutations in the EGF Proliferative Response. J. Supramol. Struct. Suppl. 4:150 (1980).

Cellular mitogenesis consists of a complex and, as yet, primarily unknown series of events. Its study is facilitated considerably by the use of defined "growth factors" whose mechanism of action can be studied. We have been utilizing epidermal growth factor (EGF) to characterize the proliferative response in Swiss 3T3 mouse embryo cells. EGF addition will stimulate quiescent cultures of 3T3 cells to reinitiate proliferation. In view of this, one approach to the study of mitogenesis is to establish variant cell lines which no longer manifest a proliferative response to EGF and then to characterize these cells as to whether they (i) continue to respond to other known mitogenic compounds, (ii) have any alterations in either the quantity or affinity of EGF receptors, and/or (iii) are blocked in biochemical or physiological steps distal to receptor occupancy in the proliferative response. We have established such cell lines, and the delineation of the characteristics of one variant, 136A, which possesses EGF binding and degradation ability - but does not have a mitogenic response to epidermal growth factor - is the basis of this report.

62. Strong, D.D. and Herschman, H.R.: Identification and Characterization of a Brain-Specific Antigen Enriched in Neonatal Brain. II. Antigenic Stability, Species Cross-Reactivity and Tumor Cell Association. Brain Res. 184:271-282 (1980).

NABSA is a brain-specific antigen enriched in neonatal brain. Micro-complement fixation was used to determine the extent of serological stability of NABSA towards heat denaturation and freeze-thaw denaturation. NABSA antigenic activity was progressively lost from neonatal and adult brain solutions incubated at temperatures above 40°C. All activity was lost above 65°C. Dilute solutions of NABSA

were stable at 80°C for at least two weeks and could be frozen and thawed in Tris-phosphate buffer at concentrations above 2 mg/ml with little loss of activity.

NABSA was found in every vertebrate species tested. An unusually close structural similarity (a frequent characteristic of both brain-specific antigens and fetal antigens) was demonstrated by serological methods among the mammalian and avian NABSAs.

NABSA was detected by microcomplement fixation analysis in 4 out of 16 rat and murine neural clonal tumor cell lines. There was no clear limitation of NABSA to particular class of neural cell (as defined by the phenotypes of these tumor cell classes) or to rapidly dividing or stationary phase cells. NABSA may be a brain-specific oncofetal antigen (OFA-associated), since it is present in tumor cells of the nervous system and high levels are found in immature brain.

63. Weingarten, D. and de Vellis, J.: Selective Inhibition by Sodium Butyrate of the Glucocorticoid Induction of Glycerol Phosphate Dehydrogenase in Glial Cultures. Biochem. and Biophys. Res. Comm. 93(1):1297-1304 (1980).

We examined the effect of millimolar concentrations of the short chain fatty acid, n-butyrate, on the induction of two cytoplasmic enzymes in the C6 rat glioma cell line. Hydrocortisone addition to the culture medium produced a 2- to 3.5-fold induction of glycerol phosphate dehydrogenase after 24 h, and norepinephrine produced a 2-fold increase in lactate dehydrogenase activity in this time period. Five mM sodium butyrate completely abolished the glucocorticoid-mediated response, while the catecholamine-mediated response was unaffected. This selective inhibition was rapid and reversible, and did not affect the level of cytoplasmic steroid binding. Furthermore, high doses of hydrocortisone did not overcome the inhibition. Finally, this phenomenon was also seen in primary cultures of pure oligodendrocytes.

64. Wu, G.-S., Stein, R.A. and Mead, J.F.: Rates and Products in Autoxidation of Phosphatidylcholine Liposomes. ISF/AOCS World Congress - Abstracts of Papers, Abstract 225 (1980).

Small phosphatidylcholine (PC) vesicles have been chosen as a model to study autoxidative processes in biomembranes. The autoxidation of pure soybean PC (containing 12% 18:1, 70% 18:2, and 6% 18:3 as major unsaturated fatty acids) at 40°C was found to give mainly hydroperoxides, consisting of 45% 13-hydroperoxy and 33% 9-hydroperoxy fatty acids in the total product isolated. The disappearance of both 18:2 and 18:3 follows the classical autocatalytic type

kinetics. When a large quantity of dipalmitoyl PC was incorporated into soybean PC liposomes, the rate of autoxidation was depressed considerably and both kinetics and product pattern were changed from those of pure soybean PC with the comparable extent of conversion. The major products include epoxy, hydroxyepoxy, dihydroxy and trihydroxy fatty acids in the proportions of 5%, 13%, 10% and 45%, respectively. The production of hydroperoxide was found to be very much suppressed, with 13-hydroperoxide being only 10%, and 9-hydroperoxide only 16% of the total product. The structures of all the products were unequivocally established by GC/MS. Previously we also observed a similar effect in autoxidation of linoleic acid monolayers with added saturated fatty acid.

The explanation for the change in mechanism of peroxidation may stem from the inability of the initially formed hydroperoxide to transfer an oxygen to a near neighbor containing a double bond. This forces the transfer to occur intramolecularly with production of hydroxy epoxides and their hydrolysis products, the trihydroxy fatty acids. This is a likely mechanism for the reaction occurring in the lung or in other membranes in which saturated and unsaturated fatty acids are intermixed.

DIVISION OF ENVIRONMENTAL BIOLOGY
RESEARCH HIGHLIGHTS

In November 1979, the division sponsored an international symposium on trace element stress in plants in which representatives from 34 other nations in addition to those from the U.S.A. presented over 60 papers. This symposium helped to integrate and correlate work world-wide with that done here at the laboratory on problems related to excess trace elements in the environment. Of considerable importance are this Laboratory's contributions to understanding and definitions of stress for single and multiple elements operating simultaneously. The data are important for several energy technologies.

Studies of environmental effects of coal combustion wastes have shown changes in native annual floras exposed to precipitator ash from a power plant in southern Nevada. Numbers of species and individuals have been reduced in treated areas--to only 3-4% of controls in plots receiving 30 and 100 metric tons of ash per hectare.

After the mirror field for the Barstow pilot solar thermal power plant was cleared and graded, about 160 metric tons of sand were blown away and deposited in an arc east of the clearing. This arc extended about 100 m downwind of the field. Changes in states of animal populations near the margin of the field between 1979 and 1980 were paralleled in areas 600 m farther east.

Investigation of the status of the flat-tailed horned lizard in southeastern California showed that this species is not presently endangered. However, like many other desert animals, this lizard is in jeopardy because of unrelenting alteration and development of desert areas.

Development of the doubly labeled water method for measuring resource requirements of wild animals was continued by analyzing the potential errors in the technique. Sufficient information has been gathered to permit formulation of predictive models for the resource (food, energy and water) requirements of one major group of vertebrates--lizards. Current work centers around mammals and birds.

Our overall objective is to develop predictive capability for the response of desert plants to the environment. Within this framework, we have studied seedling establishment for *Agave deserti* and found that only one year in the last seventeen was suitable in the western Sonoran desert. The northern distributional limit of cacti was dictated by the spines and pubescence near the apex as well as the presence of nurse plants. The desert grass *Hilaria rigida* was discovered to have the highest rate of photosynthesis known for any plant, which makes it an interesting candidate for revegetation as well as biomass production in the desert.

Chemical extractability of transuranic elements (^{237}Np , ^{239}Pu , ^{241}Am and ^{244}Cm) from widely different kinds of soils as a function of pH has been studied. The relative magnitudes of the distribution coefficient, K_d , values around the pH levels of the soils were $^{237}\text{Np} < ^{239}\text{Pu} < ^{241}\text{Am}$, ^{244}Cm . A comprehensive review of the physical and chemical reactions of Pu in soils and other geologic materials has also been prepared.

ABSTRACTS

1. Alexander, G.V. and McAnulty, L.T.: Multielement Analysis of Plant-Related Tissues and Fluids by Optical Emission Spectrometry. In Proceedings International Symposium on Trace Element Stress in Plants, November 1979, in press (1980).

The application of a multielement analytical system designed for the analysis of dry biological tissues is described. The sample is analyzed as a dry tissue without adulteration or preashing. The method is presented in sufficient detail to permit an evaluation of advantages and limitations. A new system designed for the direct analysis of fluids at the trace and ultra trace level is described briefly.

2. Berry, W.L. and Ulrich, A.: Interactions of Environmental Factors. In Controlled Environment Guidelines for Plant Research, Tibbitts, T.W. and Kozlowski, T.T. eds., Academic Press (1979).

Many controlled environment studies have been desirred to very carefully control and monitor one or at most a few environmental factors while paying relatively little attention to others. It is becoming increasingly important, however, to carefully control a number of additional factors in order to assess the impact on plants of numerous interactions among such factors. Such interactions may be synergistic, additive, independent, or antagonistic.

This paper will discuss interactions among environmental factors and will emphasize interactions of mineral supply with water, temperature, air pollution, light intensity, and nutritional preconditioning.

3. Berry, W.L., Wallace, A. and Lunt, O.R.: Utilization of Municipal Wastewater for the Culture of Horticultural Crops. HortScience 15:11-13 (1980).

The use of municipal wastewater for horticultural production on the surface appears to be a very simple concept. In its simplest form it is the use of a waste product of one process as the raw material for a second process. However, if the best use of the combination of the two systems is to be made, it will be necessary to maximize the sum of the two systems rather than of each individual system. These two systems, horticulture and municipal wastewater, are interfaced by a number of mutual components which are mineral nutrients, CO₂, water and heat. The heat and CO₂ can only be taken advantage of under controlled environmental conditions, with a bare minimum being greenhouse conditions, while all horticultural operations can utilize the nutrients and water.

4. Bickler, P.E. and Nagy, K.A.: Effects of Parietalectomy on Energy Expenditure in Free Ranging Lizards. Copeia, in press (1980).

The parietal (pineal or "third") eye of lizards is presumed to function as a solar radiation dosimeter, limiting the amount of time a lizard spends abroad each day. If this is true, then parietalectomized lizards should spend more time active than intact lizards. Since 80-90% of a lizard's daily energy expenditure (DEE) occurs during its activity period, parietalectomized lizards should have significantly greater daily energy expenditures than intact animals. We measured DEEs in intact and parietalectomized lizards in the field (using doubly labeled water), and found no significant effect of parietalectomy, suggesting that the "third" eye of lizards does not regulate the duration of their daily activity period. This is the first application of the doubly labeled water method to an experimental question.

5. El Ghonemy, A.A., Wallace, A. and El Din, H.K.: Economic Potentiality of Thymelaea hirsuta (Endle.), A Perennial Shrub in Egyptian Desert Lands. In Advances in Desert and Arid Land Technology and Development, Vol. 1, Chur-London-New York: Harwood Academic, pp. 425-448 (1979).

Paper pulp is in great shortage not only in Egypt but also in other nations in arid regions of the world. A perennial desert shrub, Thymelaea hirsuta, which grows abundantly along the Mediterranean coast of Egypt, has characteristics which make it a candidate for a source of paper pulp. The pericycle of this plant is composed of numerous large groups of long fibers measuring 3000 to 10,000 microns in length and 14 to 22 microns in diameter. Xylem tissues have lignified fibers varying in length from 700 to 2500 microns with diameters of from 15 to 23 microns. The plant can be partially harvested on a rotational basis from the 2.5 million acres in Egypt where it is a dominant species without harm to the plant and to the ecosystem. Plants can be so handled about every fourth year. Studies have been made of the technical suitability of the species for paper pulp production and these will be reported. The results are very encouraging. With planning and care most of the need for paper pulp in Egypt could be met from this source.

6. Hunter, R.B., Romney, E.M. and Wallace, A.: Lithium Toxicity in Amsinckia Tessellata Gray at the Nevada Test Site. J. Plant Nutrition 2:73-74 (1980).

Three years after an application of 454 g of $\text{LiSO}_4 \cdot \text{H}_2\text{O}$ in a trench around a pair of shrub clumps at West Frenchman Flat of the Nevada Test Site, several Amsinckia tessellata Gray annual plants growing near the trenches showed symptoms of leaf burn while seedlings of

the same species away from the trenches were free of symptoms. No other species in the area had such symptoms. Leaves of plants with symptoms contained 525 μg Li/g leaf while control plants had around 1 μg /g. Stems contained 54 μg Li/g dry weight. Calcium and Li distributed similarly between leaves and stems.

7. Jordan, P.W. and Nobel, P.S.: Infrequent Establishment of Seedlings of Agave Deserti (Agavaceae) in the Northwestern Sonoran Desert. Amer. J. Bot. 66(9):1079-1084 (1979).

Survival of seedlings of the common desert succulent, Agave deserti, required unusually wet years and the protection afforded by nurse plants or other shelters. The characteristics of seed germination and of seedlings showed that water stress in the seedling stage may be the most important factor affecting establishment. Leaves wilted irreversibly at an osmotic potential of -1.6 MPa (-16 bars). Survival of seedlings required the generation of enough biomass during the first wet season to survive drought periods when the water potential of the soil was below -1.6 MPa. Lengths of individual growing seasons and subsequent droughts were obtained from rainfall records for 1961 through 1978 for a site in the western Colorado desert. The length of the first major drought following germination apparently limited establishment of Agave deserti to only one year in the last 17. The favorable year, 1967, was consistent with the estimated year of germination of the six smallest Agave deserti observed in 1,500 m² at the field site.

8. Kawasaki, T. and Wallace, A.: Ca, Na, and Mg Interactions in Corn. J. Plant Nutrition 2:221-224 (1980).

Corn (Zea mays L. cv. Golden Cross Bantam) was grown in solution culture for 15 days to determine interactions among Ca, Na, and Mg. Sodium and Mg intensified Ca deficiency symptoms and decreased Ca concentrations slightly in blades. Negative correlations between Ca and shoot concentrations of Zn, Mn, Cu and Fe were observed. Negative correlations were also observed between root Ca and root Mn and Fe.

9. Kawasaki, T. and Wallace, A.: Effect of Chelating Agent GEDTA on the Mineral Nutrient Status of an Mg-Efficient and an Mg-Inefficient Corn Inbred. J. Plant Nutrition 2:181-185 (1980).

Two corn (Zea mays L.) inbreds, B57 and OH40B, were grown in nutrient solution with and without the chelating agent GEDTA (enough to chelate all the Ca in the nutrient solution) to determine if the effects on mineral nutrient status could reveal more of the nature of the inefficiency of the OH40B to Mg. The GEDTA increased plant concentrations of both Ca and Mg, but more so in the efficient than in the inefficient

inbred. The chelator depressed Cu transport to shoots of both inbreds and served to induce an Fe deficiency at the highest level of application. The inefficient inbred shoots generally contained more Zn and Mn than the efficient inbred in all treatments and for Mn the effect was expressed in both shoots and roots.

10. Longstreth, D.J., Hartsock, T.L. and Nobel, P.S.: Mesophyll Cell Properties for Some C₃ and C₄ Species with High Photosynthetic Rates. Physiol. Plant. 48:494-498 (1980).

Leaves of twelve C₃ species and six C₄ species were examined to understand better the relationship between mesophyll cell properties and the generally high photosynthetic rates of these plants. The CO₂ diffusion conductance expressed per unit mesophyll cell surface area ($g_{CO_2}^{cell}$) was determined using measurements of the net rate of CO₂ uptake, water vapor conductance, and the ratio of cell surface area to leaf surface area (A_{mes}/A). A_{mes}/A averaged 31 for the C₃ species and 16 for the C₄ species. For the C₃ species $g_{CO_2}^{cell}$ ranged from 0.12 to 0.32 mm s⁻¹, and for the C₄ species it ranged from 0.55 to 1.5 mm s⁻¹, exceeding a previously predicted maximum of 0.5 mm s⁻¹. Although the C₃ species Camissonia claviformis did not have the highest $g_{CO_2}^{cell}$, the combination of the highest A_{mes}/A and highest stomatal conductance resulted in this species having the greatest maximum rate of CO₂ uptake in low oxygen, 93 $\mu\text{mol m}^{-2} \text{s}^{-1}$ (147 mg dm⁻² h⁻¹). The high $g_{CO_2}^{cell}$ of the C₄ species Amaranthus retroflexus (1.5 mm s⁻¹) was in part attributable to its thin cell wall (72 nm thick).

11. Longstreth, D.J. and Nobel, P.S.: Nutrient Influences on Leaf Photosynthesis. Plant Physiol. 65:541-543 (1980).

The net rate of CO₂ uptake for leaves of Gossypium hirsutum L. was reduced when the plants were grown at low concentrations of NO₃⁻, PO₄⁴⁻, or K⁺. The water vapor conductance was relatively constant for all nutrient levels, indicating little effect on stomatal response. Although leaves under nutrient stress tended to be lower in chlorophyll and thinner, the ratio of mesophyll surface area to leaf area did not change appreciably. Thus, the reduction in CO₂ uptake rate at low nutrient levels was due to a decrease in the CO₂ conductance expressed per unit mesophyll cell wall area ($g_{CO_2}^{cell}$). The use of $g_{CO_2}^{cell}$ and nutrient levels expressed per unit of mesophyll cell-wall provides a new means of assessing nutrient effects on CO₂ uptake of leaves.

12. Nagy, K.A.: CO₂ Production in Animals: Analysis of Potential Errors in the Doubly Labeled Water Method. American Journal of Physiology 238:R466-R473 (1980).

Laboratory validation studies indicate that doubly labeled water (³HH₂¹⁸O and ²HH₂¹⁸O) measurements of CO₂ production are accurate to within ± 8% in nine species of mammals and reptiles, a bird, and an insect. However, in field studies, errors can be much larger under certain circumstances. Isotopic fraction of labeled water can cause large errors in animals whose evaporative water loss comprises a major proportion of total water efflux. Input of CO₂ across lungs and skin caused errors exceeding +80% in kangaroo rats exposed to air containing 3.4% unlabeled CO₂. Analytical errors of ±1% in isotope concentrations can cause calculated rates of CO₂ production to contain errors exceeding ±70% in some circumstances. These are 1) when little decline in isotope concentrations has occurred during the measurement period, 2) when final isotope concentrations closely approach background levels, and 3) when the rate of water flux in an animal is high relative to its rate of CO₂ production. The following sources of error are probably negligible in most situations: 1) use of an equation that does not correspond to the pattern of change in total body water, 2) variations in rates of water or CO₂ flux through time, 3) use of H₂¹⁸O dilution space as a measure of body water volume, 4) exchange of ¹⁸O between water and organic compounds in animals (including excrement), 5) incomplete mixing of isotopes in the animal, and 6) input of unlabeled water via lungs and skin. Errors in field measurements of CO₂ production can be reduced to acceptable levels (<10%) by appropriate selection of study subjects and recapture intervals.

13. Nagy, K.A. and Costa, D.P.: Water Flux in Animals: Analysis of Potential Errors in the Tritiated Water Method. Am. J. Physiol. 238:R454-R465 (1980).

Laboratory studies indicate that tritiated water measurements of water flux are accurate to within -7 to +4% in mammals, but errors are larger in some reptiles. However, under conditions that can occur in field studies, errors might be much greater. Influx of environmental water vapor via lungs and skin can cause errors exceeding ±50% in some circumstances. If water flux rates in an animal vary through time, errors approach ±15% in extreme situations, but are near ±3% in more typical circumstances. Errors due to fractional evaporation of tritiated water may approach -9%. This error probably varies between species. Use of an inappropriate equation for calculating water flux from isotope data can cause errors exceeding ±100%. The following sources of error are either negligible or avoidable: use of isotope dilution space as a measure of body water volume, loss of nonaqueous tritium bound to excreta,

binding of tritium with nonaqueous substances in the body, radiation toxicity effects, and small analytical errors in isotope measurements. Water flux rates measured with tritiated water may be expected to be within $\pm 10\%$ of actual flux rates in most situations.

14. Nagy, K.A. and Montgomery, G.C.: Field Metabolic Rate, Water Flux, and Food Consumption in Three-Toed Sloths (Bradypus Variegatus). J. Mamm. 61(3):465-472 (1980).

Metabolic rates (CO_2 production) and water fluxes were measured using doubly labeled water in free-living three-toed sloths (Bradypus variegatus) on Barro Colorado Island, Panama Canal Zone. Feeding rates were calculated from metabolic rates using natural tracer estimates of energy assimilation efficiency. Field metabolic rates averaged about $147 \text{ kJ (kg day)}^{-1}$ and did not differ significantly among nonreproductive females, lactating females, and males. This rate is only about 74% of the predicted mammalian basal metabolic rate, but is about 1.8 times the actual basal rate of these animals. Field water fluxes, ca. $38 \text{ ml H}_2\text{O (kg day)}^{-1}$, were also comparatively low and can be accounted for by dietary water input and metabolic water production alone. This indicates that sloths probably did not drink, even though rain fell during the study. The two lactating females allocated 5% and 11% of their water and assimilable energy intake, respectively, to producing milk for their offspring. We estimate that a 4-kg sloth consumes 60 g dry-mass of food per day, and that the three-toed sloths on Barro Colorado Island eat 138 kg dry mass of food per ha per year. This is about 2% of the yearly leaf production.

15. Nishita, H.: A Review of Behavior of Plutonium in Soils and Other Geologic Materials. U.S. Nuclear Regulatory Commission NUREG/CR-1056 UCLA 12-1193 (1979).

Available information on the physical and chemical reactions of Pu in soils and other geologic materials is reviewed. The primary intent of this review was to bring together information that may be helpful in assessing the movement and biological availability of Pu in terrestrial environment. The review is divided into two general categories, e.g. studies of chemical reactions of Pu in aqueous solutions and studies of Pu reactions in the more complex systems of soils and other geologic materials. The latter category is further divided into studies of Pu in materials that were freshly contaminated in the laboratory and of Pu in materials that had been contaminated in natural environments and had resided there for varying number of years. After the discussion of physical and chemical reactions of Pu, several reported examples of the actual movement of Pu in terrestrial environments are given.

16. Nishita, H.: Thermoluminescence. In The Encyclopedia of Soil Science, Part I, Fairbridge, R.W. and Finkl, Jr., C.W. eds. Stroudsburg, PA: Dowden, Hutchinson and Ross, Inc., pp. 562-564 (1979).

This is a review of thermoluminescence in soils. Thermoluminescence is the emission of light produced by heating a solid to a temperature below that of incandescence. To exhibit thermoluminescence, a substance must have an ordered structure such as is found in crystals or a semiordered structure as in glasses. In addition, it must be electrically an insulator or a semiconductor. Soils show a variety of thermoluminescent characteristics. In general, the soils that are high in lime content show high thermoluminescence, while those very high in free iron oxides or organic matter show only little or no thermoluminescence. Most soils show only little, if any, natural thermoluminescence below the threshold temperature of around 200° C. The exposure of soils to high energy ionizing radiation increases their thermoluminescence. The distinctive characteristics of the development of induced thermoluminescence has been put to practical application of using soils as ionizing radiation dosimeters.

17. Nishita, H., Wallace, A., Romney, E.M. and Schulz, R.K.: Effect of Soil Type on the Extractability of ^{237}Np , ^{239}Pu , ^{241}Am and ^{244}Cm as a Function of pH. NUREG/CR-0997, UCLA 12-1192, 32 pp (1979).

The extractability of ^{237}Np , ^{239}Pu , ^{241}Am and ^{244}Cm from widely different kinds of soils as a function of pH was determined using an equilibrium batch technique. Hydrochloric acid or NaOH was used to adjust the pH. The sorption and extractability of the transuranics studied varied considerably with pH and the kind of soil. A general pattern of extractability that is common to all of the transuranics studied was exhibited to a varying degree by each mineral soil (except the calcareous soil). Typically the extractability was relatively high under strongly acidic condition, particularly below pH2. Then, as the pH increased, there was a zone of rapid decrease, which was followed by a zone of relatively low extractability. Above the latter zone, there was an increase to a peak with increasing pH and then a decline. The organic soil used differed from this general pattern in that it showed a progressive increase of extractability in the alkaline pH range instead of peaking and declining. Among the mineral soils, the extractability of ^{237}Np was markedly greater than those of ^{239}Pu , ^{241}Am , or ^{244}Cm in the pH range below pH 6. Above this pH, the relative extractability of the radionuclides depended on the soil. The extractability of ^{244}Cm was practically the same as that of ^{241}Am over the entire pH range. The relative magnitudes of the distribution coefficient, K_d , values around the pH levels of the soils were $^{237}\text{Np} < ^{239}\text{Pu} <$

²⁴¹Am, ²⁴⁴Cm. Soil organic matter and hydros oxides of Al, Fe, and MN appeared to influence the sorption and extractability of the transuranics studied.

18. Nobel, P.S.: Morphology, Nurse Plants, and Minimum Apical Temperatures for Young Carnegiea Gigantea. Bot. Gaz. 141(2):000-000 (1980).

The northern limit of Carnegiea gigantea (Engelm.) Britton and Rose apparently depends on minimum apical temperatures. Diameters, apical spine coverage, and effects of nurse plants on incoming long-wave (infrared [IR]) radiation, all of which affect apical temperatures, were therefore determined for stems of C. gigantea up to 4 m tall at four sites along a north-south transect in Arizona. A simulation model indicated that the increase in diameter accompanying stem growth raised the minimum apical temperature more than 3 C. Thus, plants with the shortest stems would be expected to be the most vulnerable to freezing damage; indeed, freezing damage on stems <0.5 m tall without nurse plants was fairly common at the colder sites. Nurse plants obstructed a greater portion of the sky for C. gigantea at the colder sites; e.g., the effective environmental temperature for IR radiation at such locations was raised more than 10 C for stems under 1 m tall. If the northern limit of C. gigantea reflects wintertime survival of juveniles, nurse plants could extend the range by offering some protection against freezing.

19. Nobel, P.S.: Morphology, Surface Temperatures, and Northern Limits of Columnar Cacti in the Sonoran Desert. Ecology 61(1):1-7 (1980).

Interspecific morphological differences and intraspecific morphological changes with latitude were evaluated to help examine the distributional ranges of Carnegiea gigantea, Lemaireocereus thurberi, Lophocereus schottii, Pachycereus pecten-aboriginum, and P. pringlei in the Sonoran Desert (USA and Mexico). A computer model, which predicted the average surface temperature of the stem within 10 C of that measured hourly throughout a 24-h period, was particularly useful in studying the thermal relations of the stem apex, where the lowest surface temperature occurred.

Under the same environmental conditions the minimum apical temperatures were 7.70 C, 5.90 C, and 3.90 C for C. gigantea, Lemaireocereus thurberi, and immature stems of Lophocereus schottii, respectively, which is the same relative order as their northernmost limit (34°56'N, 32°38'N, and 31°55'N, respectively). The northern limit for these three species, but not for Pachycereus pecten-aboriginum and P. pringlei, may well be determined by the low temperatures occurring at the stem apex.

20. Nobel, P.S.: Water Vapor Conductance and CO₂ Uptake for Leaves of a C₄ Desert Grass, Hilaria Rigida. Ecology 61(3):000-000 (1980).

Availability of soil water was the major influence on seasonal stomatal activity of Hilaria rigida (Thurb.) Benth. ex Scribn. over a 2-yr study period in the Colorado desert section of the Sonoran desert. Major stomatal opening (water vapor conductance >2 mm/s) occurred for 4.6 mo in the relatively cool winter-spring (maximum daytime temperatures averaging 17°C) and for 1.7 mo in the late summer-early fall (maximum daytime temperatures averaging 31°C). The temperature optimum for CO₂ uptake was generally above daytime temperatures, particularly in the winter. When the daytime growth temperature was raised from 16° to 49°C in laboratory experiments, the temperature optimum for CO₂ uptake shifted from 29° to 43°C. Besides the rather high temperature optimum for CO₂ uptake, H. rigida displayed other typical C₄ characteristics including Kranz anatomy, a low CO₂ compensation point (12 µl/l), and a lack of light saturation of CO₂ uptake at full sunlight. Under optimal field conditions, the CO₂ uptake rate can be 67 µmol·m⁻²·s⁻¹ (106 mg CO₂·dm⁻²·h⁻¹), higher than has been reported for any other species. The accompanying high water use efficiency (mass CO₂ taken up by leaf blades/mass H₂O lost) may help explain the success of this hardy grass in both the Mojave and Sonoran deserts.

21. Parsa, A.A. and Wallace, A.: Differential Partitioning of Boron and Calcium in Shoots of Seedlings of Two Pistachio Cultivars. J. Plant Nutrition 2:263-266 (1980).

In a greenhouse pot culture experiment, uniform seedlings of two Iranian pistachio cultivars (Pistacia vera L.) previously established in sand were transferred into pots containing Moreno soil from California and treated with 0, 1, 2, 4 and 8 µg B per g soil on the soil basis. Analysis of plant parts revealed that uptake by all parts increased with increasing rates in both soils and more B was retained by senescent parts, but differentially by the two cultivars. None of B levels had any adverse effect on vegetative growth in eight weeks even with shoot B concentrations of over 300 µg/g in the old leaves. Calcium partitioned like B did.

22. Parsa, A.A. and Wallace, A.: Effect of Strength of Nutrient Solution on the Growth and Nutrient Uptake of Pistachio Seedlings. J. Plant Nutrition 2:257-261 (1980).

In an effort to find the most appropriate nutrient solution for the growth of pistachio seedlings, three major Iranian pistachio cultivars, Badami and Fandoghi (Pistacia vera L.) and Benesh (Pistacia terebinthus L.) seedlings were grown in an automated sand culture system in a glasshouse for 8 weeks. Treatments included 0, 1/8,

1/4, 1/2, 1, 2, 4, 8, and 10 strength Hoagland solution. Aerial and root growth as well as the uptake of P, Na, K, Ca, Mg, Zn, Cu, Fe, Mn, and B were determined. Highest growth of aerial and root portions were associated with dilute (1 strength nutrient solution or lower) and tolerance of media salinity was higher by Badami and Fandoghi than by Benesh.

23. Parsa, A.A., Wallace, A. and Martin, J.P.: Enhancement of Iron Availability by Some Organic Materials. J. Agric. Sci. 93:115-120 (1979).

In a preliminary laboratory experiment in Iran, not reported here, 5 out of 30 plant materials incorporated into a highly calcareous soil had a positive effect on increasing the DTPA- (diethylenetriaminepentacetic acid)-extractable Fe and all except one significantly increased the vegetative growth of sorghum. The plant materials included Lawsonia inermis L., Malva silvestris L., Zyzyphus nummularia Wak. and Lavandula carnopifolia L. A glasshouse study was repeated with two California soils pretreated with 0.5% Fe₂O₃ to determine if these organic materials have practical value in making Fe available to plants. A calcareous, Fe-deficient Hacienda (fine-silty, mixed, non-acid, thermic typic xerothents). The previously mentioned organic materials and Laminaria saccharina L. (Lamour) were incorporated into the soils at two rates, 15000 and 20000 µg/g, as air dry and in ash form. An adequate supply of major and micronutrients other than Fe was ensured. Other treatments included 5 µg Fe/g as FeSO₄, Fe-138 chelate and control. All of the plant materials with the exception of L. carnopifolia significantly increased dry-matter yield and Fe, Zn, Cu and Mn uptake by sorghum in the Hacienda soil. In the Yolo soil the above were not significant. Thin-layer chromatography of the extracts of the plant materials revealed the presence of significant quantities of phenolic substances.

24. Parsa, A.A. and Wallace, A.: Organic Solid Wastes from Urban Environment as Iron Sources for Sorghum. Plant and Soil 53:455-461 (1979).

Sorghum (Sorghum bicolor L. Moench) which is susceptible to Fe deficiency was grown in two different soils in a glasshouse with two different organic urban wastes (sewage sludge and dog manure) to ascertain their ability to supply Fe and other micronutrients to plants. One soil was calcareous with a history of Fe deficiency. Sewage sludge and dog manure at an application rate of 15,000 µg/g to this soil effectively supplied Fe to plants. This effect was not present when the ash rather than the organic matter was used. Ferrous sulfate and Fe-EDDHA (Fe ethylenediamine di-O-hydroxyphenylacetate) likewise were not effective. Infrared spectra revealed

differences in the fulvic acid for the two sources of solid wastes. The results imply that some sources of organic wastes may be useful in prevention or correction of Fe deficiency in calcareous soils.

25. Patel, P.M. and Wallace, A.: Effect of Trace Metal Applications on Emergence of Bromus Rubens in Desert Soil. J. Plant Nutrition 2:65-66 (1980).

Bromus rubens L. seeds in calcareous desert soil which was brought from the Nevada Test Site to UCLA for pot tests with differential excess trace metal treatments gave differential emergence in response to the trace metal experiments. Zinc up to 5300 µg/g soil did not impair emergence. Cadmium at 1200 µg/g soil impaired emergence but 800 µg/g did not. Nickel at 500 µg/g soil did not impair emergence but 1000 and 2000 did. There was no emergence at 3000 µg Ni/g soil.

26. Patel, P.M., Wallace A. and Alexander G.V.: Transfer Values to Fruits of Li in Tomato and Cd in Bush Beans. J. Plant Nutrition 2:87-91 (1980).

Different levels of Li (10^{-5} , 10^{-4} , $5 \times 10^{-4}M$ and Cd (2×10^{-6} , 10^{-5} , $10^{-4}M$) were studied in solution culture in a glasshouse to evaluate the effects on growth and fruit transfer values in tomato (Lycopersicon esculentum mill. cv. Marglobe) and bushbeans (Phaseolus vulgaris L. cv. Improved Tendergreen). No effect on yield was observed for up to $10^{-4}M$ Li levels; after that yields were significantly decreased. The yield of bushbeans was significantly reduced by the Cd levels added. The Li in solution culture significantly increased the Li concentration in tomato roots, leaves, and fruits. The Cd had an increasing effect on Cd concentration only in bushbean roots and a nonsignificant effect was observed in leaves and pods. Considerable amounts of Li were translocated to leaves and fruits while very little Cd was found in fruit pods. The exact amount was unknown due to limits of method.

27. Patel, P.M., Wallace, A., Alexander, G.V. and Romney, E.M.: Effects of Coal Fly Ash Mixed in Desert Soil on Successive Crop Yields and Mineral Composition of Lycium andersonii and Ambrosia dumosa in Pot Tests in a Glasshouse. J. Plant Nutrition 2:135-145 (1980).

Lycium andersonii A. Gray and Ambrosia dumosa (A. Gray) Payne cuttings were grown for 15 months in desert soil in which had been mixed, 0.0, 0.2, 0.5, 1.0, 5.0, 10.0 and 20% fly ash with periodic sampling of the leaves. The very high levels of fly ash resulted in leaf yield depressions which persisted for the 15 months. Boron in leaves was elevated especially in the early cuttings. Increases in Mo in plants may be the result more of increased soil pH than of fly ash. Increases in leaf Sr were not as great as expected from its concentration in fly ash. Trace metals did not become more available with time. Fly ash induced P deficiency.

28. Patel, P.M., Wallace, A., Hartsock, T. and Romney, E.M.: Zinc, Nickel, and Cadmium Uptake and Translocation to Seed Pods and Their Effects on Gas Exchange Rates of Bush Bean Plants Grown in Calcareous Soil from the Northern Mojave Desert. J. Plant Nutrition 2:67-72 (1980).

Bush bean plants (*Phaseolus vulgaris* L. cv. Improved Tendergreen) were grown in highly calcareous desert soil with high levels of Zn, Ni, and Cd added to them. The purposes were to compare growth and uptake with desert plants grown in the same soil, to assess translocation to fruits, and to measure gas exchange rates. All three trace metals produced toxicity in the highly calcareous soil and the bush beans were less tolerant than previously grown desert plants. The levels used at various points produced 50% or more yield decrease. Zinc and Ni were transported to fruits at concentrations considerably less than in leaves. The transport was greater for Ni than for Zn. Cadmium was not translocated to fruits in detectable quantities. Zinc and nickel supplied in excess restricted Cu movement to fruit. The levels of Zn and Ni had no influence on photosynthesis and transpiration, but the gas exchange rates were decreased by Cd on the dry weight basis.

29. Patel, P.M., Wallace A., Romney, E.M. and Alexander, G.V.: A Collander-Type Experiment in Large Tanks of Solution Culture. J. Plant Nutrition 2:127-133 (1980).

Several different plant species were grown together in large (400 l) tanks of solution culture in the pattern of the original Collander experiment (Plant Physiol. 16:691) except in the present one, plants were spaced far enough apart that roots could not become entangled so that root-shoot partitioning could be studied. Two sets of plants were grown in the tanks. One set was with agricultural species and the other was with native desert plants. One tank contained a standard nutrient solution and the second contained the same solution with addition of several cations: Na, Cd, Li, Ni, Cr, Pb, Sr, Ba. Plant species behaved differently to the mixture of cations with differential partitioning among plant parts. Exclusion phenomena discussed in the original Collander paper are mostly retention in roots with little translocation to shoots. The extra cations in some cases increased yields, in some cases decreased yields with no differences in others. Several nutrient element interactions were indicated. The Ca vs Sr is not exactly like that suggested by Collander.

30. Patel, P.M., Wallace, A., Romney, E.M. and Alexander, G.V.: Effect of Added Zn, Ni and Cd on Desert Shrubs Grown in Desert Soil. J. Plant Nutrition 2:55-64 (1980).

Desert shrubs - Ambrosia dumosa, Lycium andersonii, Larrea tridentata, and Ephedra nevadensis were grown in a glasshouse in desert (calcareous) soil with different levels of added Zn, Ni, and Cd. The objective was to study effects of the metals on growth and yield and uptake and translocation of metals in desert plant species which are common in the Mojave Desert (areas of Nevada and southeast California). Zinc and Cd considerably decreased yields of all four species. Yields of E. nevadensis were increased by Ni at 250 and 500 mg/kg applied to desert soil. Ephedra nevadensis was more tolerant of Ni than were the other three desert shrubs. Some interactions were observed among various elements: manganese concentration was increased in shrubs by Zn. Particularly, application of Ni reduced the concentrations of Zn and Mn over the control.

31. Procopiou, J., Haritou-Andriotaki, A., Papanicolaou, X. and Wallace, A.: Effects of Sulfuric Acid Added in Calcareous Soil in Leaf Fe Concentration of Several Plant Species. In Mineral Nutrition of Plants, Proceedings of First International Symposium on Plant Nutrition, Varna, Bulgaria, Vol. 1, pp. 165-170 (1980).

The leaf Fe concentration of several plants, including citrus and olive, commercially grown in calcareous soils in Greece was in some cases increased after addition of sulfuric acid to the soil. It was added in early summer in 4 to 8 holes per tree or in the irrigation basin (not touching the tree trunk), in quantities of about 3-4 kg per mature tree, usually followed by irrigation. Higher rates were in some cases applied in 2 or 3 doses. Trees tolerated high levels of H_2SO_4 in the calcareous soils. Some trees regreened and had normal leaf composition. No changes were indicated for trees already green.

32. Procopiou, J. and Wallace, A.: Elemental Composition of Leaves from Polluted and Nonpolluted Areas. J. Plant Nutrition 2:119-121 (1980).

Leaves of different plant species grown in the polluted center of Athens and nonpolluted Vari Rhodes, or Holargos, were analyzed. Leaves from Athens had, in some cases, higher concentrations of Pb. There was evidence of Cu deficiency in Rhodes. The other elements examined showed no differences in their concentration.

33. Romney, E.M., Wallace, A., Alexander, G.V. and Lunt, O.R.: Effect of Beryllium on Mineral Element Composition of Bush Beans. J. Plant Nutrition 2:103-106 (1980).

Bean plants were grown in solution culture with either 0, 4, 8, 16 μg Be/ml. Most Be remained in roots. Leaf concentrations of P, Ca, Mg, Zn, Cu, Fe, Mn, B, Al, Si, Mo, Sr, Ba were decreased by high Be application.

34. Romney, E.M., Wallace, A. and Hunter, R.B.: *Revegetation Studies Pertinent to the Barstow 10 MWe Solar Thermal Power Station and to Potential Installations Elsewhere in the Mojave Desert*. UCLA 12-1224, 44 pp (1979).

Revegetation of disturbed arid land is one of the great challenges of a desert. It is not an impossible task, however, if the natural and manmade resources available are utilized and managed. Because of unfavorable moisture and temperature conditions, the natural revegetation processes in the Mojave Desert require periods of time that are much longer than practical for meeting environmental protection standards. While solar facilities are generally considered as ecologically benign, we have no experience in this country with the consequences of constructing and operating large solar thermal power plants with extensive mirror fields. At least, one must expect total destruction of the ecosystem resulting from clearing of vegetation and land preparation within the area of the mirror field. The Barstow 10 MWe STPS affords an opportunity to examine accurately the environmental costs associated with large solar thermal power systems. Because the STPS site is scheduled to be restored at the conclusion of the demonstration project, the objectives of this study are to understand the abiotic and biotic processes influencing revegetation, and to experiment with techniques capable of enhancing the reestablishment and growth of native plants at that site.

This report presents findings from three different aspects of experimental efforts. A ready-made restoration experiment already exists in the area on which the STPS is to be located as the result of the land being cleared for agricultural use in 1953, and then being abandoned in 1956. We are investigating those factors involved in the natural revegetation which have occurred during the 23 year period since that earlier disturbance. A field trial experiment using transplanted shrubs was established near the proposed mirror field site in order to investigate the extent to which the transplanted shrubs might be destroyed by grazing rabbits, and how they would respond to irrigation. Initial results indicate that shrubs can be transplanted successfully on site, if supplemental irrigation and protection from grazing rabbits is provided. Work is underway at the UCLA plant propagation facilities to prepare specimens of desert shrubs for future transplanting experiments. Experimental facilities and some recently cleared and abandoned land made available to us at the Nevada Test Site has allowed work to proceed on a newly disturbed site without being encumbered with construction activities and delays. We are proceeding in our work with the assumption that our ability to control the factors related to restoration of deserts is proportional to how well we understand the processes governing crown sprouting from sheared-off root systems, seed germination, and how we can best manage the disturbed system to assure the survival of new desert plant

seedlings. Environs of the study site at NTS are typically Mojave Desert, so findings therefrom should be generic to the Barstow 10 Mile STPS site and also relevant to vegetation restoration needs of potential STPS sites elsewhere in desert areas.

35. Romney, E.M., Wallace, A. and Kinnear, J.E.: Plant Uptake of Pu and Am Through Roots in Nevada Test Site Soils. In Selected Environmental Plutonium Research Reports of the NAEG, June 1978, NVO-192, Vol. 1, Nevada Applied Ecology Group, USDE, Las Vegas, Nevada, pp. 109-120 (1979).

Plant uptake experiments were conducted under controlled conditions in order to eliminate external contamination of plant foliage by resuspended materials. This was done to determine plant uptake of $^{239,240}\text{Pu}$ and ^{241}Am through roots and translocation to aboveground parts of plants grown on soils from "safety-shot" fallout areas at the Nevada Test Site (NTS) and Tonopah Test Range (TTR). Experimental details and initial results were reported earlier (Romney et al, 1977). Additional interpretations of findings from these experiments indicate the following:

- a. Vegetation to soil concentration ratios (C.R.), which serve as an index of root uptake, varied from 10^{-5} to 10^{-3} for $^{239,240}\text{Pu}$ and from 10^{-4} to 10^{-1} for ^{241}Am , depending upon the kind of soil involved and the agricultural amendments applied.
- b. On the relative basis, Am was taken up at a faster rate than Pu as indicated by mean Am C.R./mean Pu C.R. values (4.2 for barley, 9.9 for alfalfa, and 21.6 for soybeans).
- c. DTPA chelate increased root uptake of both Pu and Am when added in conjunction with nitrogen, organic matter, or sulfur amendments. This enhancement effect of chelate on root uptake was more pronounced in soils from Areas 11 and 13 of the Nevada Test Site than it was in soils from different locations on the Tonopah Test Range. Differences in soil characteristics might be influential, but the residence time of the fallout debris in the soils also might have influenced availability from the high-fired oxide source materials deposited in 1956-57 at NTS and in 1963 at TTR.
- d. C.R. values were lower for fruit than for vegetative parts of soybeans.
- e. Am was slightly more mobile for transport from shoots to fruits of soybeans than was Pu.
- f. The correlation coefficients between Pu and Am in shoots and fruiting parts of soybeans were +0.988 for Pu and +0.983 for Am.

36. Turner, F.B. ed.: Ecological Base Line Studies at the Site of the Barstow 10 MWe Pilot Solar Thermal Power System, Annual Report to the U.S. Department of Energy, UCLA 12-1223, 53 pp (1979).

Base line ecological measurements and observations were made in 1979 at the site of the Barstow pilot 10 MWe solar thermal power system. The station will be constructed on Southern California Edison's Cool Water property, just east of the Cool Water Generating Station.

Surface soils of the site are sandy, but soils below 3 m are generally well graded sand with some silt and gravel. Some of the soils are highly saline, to an extent precluding plant growth. All soils are alkaline, with pH values as high as 9. Soils become saturated down to 20 cm shortly after winter rains, but soil moisture contents at 50 to 100 cm lag well behind rainfall events.

The prospective mirror field was cleared of vegetation in 1953 and some crops were grown until 1956, so shrubs occupying the field today are 23 years old or younger. Over 130 species of plants have been identified on the site, 18 of which are non-native. The three principal shrubs are creosotebush (*Larrea tridentata*), desert saltbush (*Atriplex polycarpa*), and bur-sage (*Ambrosia dumosa*). Estimated aggregate densities of annual plants range from around 600 to almost 9000 m⁻², depending on sampling locale. Aggregate densities of perennials (including herbaceous species) range from as low as 0.02 to 4.4 m⁻². Cover by shrubs is low in the areas cleared in 1953 (<6%), but increases to as high as 18% in areas to the east.

Creosotebush supports a varied assemblage of sap-feeding and defoliating insects, principally homopterans and orthopterans. Some 300 different kinds of arthropods were distinguished in samples from the site.

The most common rodents are kangaroo rats, pocket mice and ground squirrels. Over 60 kinds of birds were observed around the site, many associated with evaporating ponds adjoining the generating station. The most abundant in the prospective mirror field were horned larks, with estimated densities as high as 540 km⁻² in September 1978. The most commonly counted lizards on the site were gridiron-tailed lizards and western whiptail lizards.

37. Turner, F.B.: Environmental Issues and Solar Thermal Power Systems. In Proceedings 26th Annual Meeting, Institute of Environmental Sciences, Philadelphia, PA, pp 430-434 (1980).

Central receiver solar thermal power systems require about 3 ha of land per MWe power output. Large systems (100 MWe) will require, then, more than one square mile for heliostats and associated

structures. Because of efficiency and cost considerations solar thermal systems will probably use wet cooling towers. Water requirements for wet cooling are substantial--on the order of 15-20 acre-feet per MWe per year. Land availability and waste heat and water losses from cooling towers are presently seen as the major environmental problems. Other issues are noise, misdirected beams from heliostats, and possible escapes of high temperature working fluids (e.g., molten salts, hydrocarbon and silicone oils). Modeling studies of very large solar thermal power systems predict some mesoclimatic changes in the vicinity of the station, brought about by loss of water from cooling towers. Microclimatic changes of uncertain ecological consequence may be expected in the immediate vicinity of smaller (<100 MWe) stations.

38. Turner, F.B., Rorabaugh, J.C., Nelson, E.C. and Jorgensen, M.C.: A Survey of the Occurrence and Abundance of the Flat-Tailed Horned Lizard (*Phrynosoma mcallii*) in California. Report to the U.S. Bureau of Land Management, 28 pp (1980).

The occurrence of the flat-tailed horned lizard (*Phrynosoma mcallii*) in California was investigated in 458 sections (each 1 mi²) in Riverside, San Diego and Imperial Counties, and the present overall distribution of the species in California was reviewed. Areas of favorable habitat in Imperial and San Diego Counties were identified. In all sections 40 *P. mcallii* (0.09 per man-hours) and 2,191 horned lizard scats (4.8 per man-hour) were counted. When sections were grouped in twelve general areas, mean numbers of horned lizards ranged from 0.40/hr (north of Benson Dry Lake), 0.13/hr (near Ogilby), and ca. 0.1/hr (Superstition Mountain, Kane Spring area, southeastern Yuha Basin) to as low as 0.02/hr (Riverside County), and 0.00/hr (northern East Mesa, Coyote Wells area).

Neither counts of *P. mcallii* nor of scats of horned lizards in 11 areas were statistically correlated with counts of any other kind of lizard. Counts of horned lizards were significantly correlated ($p = <0.05$) with counts of nests of the harvester ant, *Veromessor pergandei*, but not with counts of nests of harvester ants of the genus *Pogonomyrmex*. Counts of horned lizard scats were uncorrelated with counts of ant nests, and counts of horned lizards were uncorrelated with counts of scats.

We examined the proposed Yuha Basin geothermal lease area and four sand and gravel lease areas in Imperial County. Observations were made in 12 sections in the geothermal lease area. Five *P. mcallii* (0.10/man-hour) and 354 scats (7.4/man-hour) were recorded. From one to three sections were inspected in the other areas and numbers of scats counted ranged from zero to 2.6/man-hour; of horned lizards from 0.0 to 0.25/man-hour. As a result of these investigations it

was recommended by BLM that no surface occupancy occur in eight sections and that surface occupancy be limited in other parts of the southeast Yuha Basin.

P. mcallii is not an endangered species. However, the original geographic range of this lizard has been diminished, and the species is not as abundant in certain parts of its range as it once was. Such changes have almost certainly been brought about by human activities. P. mcallii, like many other desert species, is not in immediate danger of extinction, but stands in jeopardy because of continued alteration or destruction of its habitat.

39. Turner, F.B. and Volimer, A.T.: Ecological Effects of Precipitator Ash on Desert Plants. Annual Report to Southern California Edison, Research and Development Series 80-RD-94 (1980).

A field experiment was established in Jackass Flats, Nevada, to test possible effects of precipitator ash from the Mohave Generating Station on native vegetation. Twenty-eight 15 x 15 m plots were set up in seven blocks of four, with each block containing one untreated plot and three treated plots. Target treatment levels were 10, 30, and 100 metric tons of ash per hectare. Field tests with neutron-activated ash have shown that when ash is distributed over the soil surface some of it is displaced by wind. About 1/3 of the distributed ash was displaced within 6 months. After 33 months about 58% of the remaining ash was detected 1.4-2.5 centimeters (cm) below the surface, and about 7% between 2.6-3.8 cm below the surface.

Counts and identifications of annual plants growing in 500 quadrats were made in March, April and May 1979. March density was 291/m², lower than in two previous springs (cf. 464/m² in 1977 and 1323/m² in 1978). Numbers of species identified were also less than in previous years. However, in all blocks the general pattern manifested in 1978 persisted: numbers of species observed were highest in untreated plots and declined in treated plots. Numbers of annual plants in plots receiving 30 and 100 mt/ha of ash have been conspicuously reduced--to only 3-4% of that in controls in the heavily treated plots. Some species are more resistant to ash than others. Bromus rubens (a non-native grass), Camissonia kernensis, Eriogonum reniforme and Monoptilon bellidiforme have sustained remarkable numbers even in plots receiving 30 mt/ha of ash. Aggregate survival of annual plants between March and May 1979 ranged from 50-69%. As in previous years, aggregate survival of those annuals germinating was unaffected by treatment. However, individual species show differences in survival, as a function of treatment. Bromus rubens, Eriophyllum pringlei, Camissonia kernensis, Chaenactis fremontii and Monoptilon bellidiforme exhibited comparable March-May survival in untreated plots and plots receiving 10 and 30 mt/ha of ash. Survival

of other species (e.g., Cryptantha micrantha, Eriogonum reniforme, Linanthus jonesii) was similar in the most lightly treated and untreated plots, but declined in more heavily treated plots. The grass Festuca octoflora appeared quite sensitive to ash, and survival was reduced in even the most lightly treated plots.

We carried out experiments on the effects of precipitator ash on seed germination. Seeds of Bromus rubens, Chaenactis fremontii, Malacothrix glabrata, Monoptilon bellidiforme, Camissonia munzii and Cryptantha nevadensis were pre-treated by aeration in water, then planted in soil containing no ash and mixtures of up to 50% ash by weight. Germination in controls ranged from 8% (M. bellidiforme) to 100% (Cryptantha nevadensis).

Rates of germination generally declined with increasing amounts of ash in soil, but germination of M. bellidiforme seeds increased (to 28%) in soils containing up to 25% ash. Germination of seeds of Bromus rubens, Camissonia munzii and Cryptantha nevadensis was fairly well sustained (relative to controls) in 10% ash-soil mixtures. Hardly any seeds germinated in 50% ash-soil mixtures, but 24% of seeds of C. nevadensis did.

40. Wallace, A.: Effect of Chelating Agents on Uptake of Trace Metals When Chelating Agents are Applied to Soil in Contrast to When They are Applied to Solution Cultures. J. Plant Nutrition 2:171-175 (1980).

When metal chelates were applied to soil the concentrations of several trace metals were increased in plants. Similar additions to nutrient solutions usually result in plant reductions in trace metals such as Cu, Zn, Mn, Ni, and Cd. Hypotheses for differential effects between soil and solution are discussed.

41. Wallace, A.: Effect of Excess Chelating Agent on Micronutrient Concentrations in Bush Beans Grown in Solution Culture. J. Plant Nutrition 2:163-170 (1980).

Bush bean plants (Phaseolus vulgaris L. cv. Improved Tendergreen) were grown for 18 days in 3700 ml nutrient solutions in a glasshouse in the presence of $2 \times 10^{-5}M$ $NiSO_4$, at two different pH levels (4.3 and 7.5) and at 0, 10^{-4} and $10^{-3}M$ NaDTPA. The objective was to determine which micronutrients were changed in uptake by DTPA. Iron in leaves was increased slightly by $10^{-4}M$ DTPA ($2 \times 10^{-5}M$ FeEDDHA was applied in all treatments) but decreased slightly by the highest levels of DTPA. Nickel accumulation was absent in all plant parts as result of DTPA much unlike the effect observed in soil. The two highest levels of DTPA decreased plant yields which was probably the result of Cu deficiency at the low pH and Zn, Cu,

and Mn deficiencies at the high pH (no Zn and Cu added to the solutions except as contaminants). The Mo in plant parts was decreased by DTPA at the low pH. In a similar experiment with EDTA and EDDHA (10^{-4} and $5 \times 10^{-4}M$ each) but with no Ni added and with plants grown for 17 days, and yields were decreased by the high level of EDTA with leaf decreases in Fe and Cu and also in Zn to a slight extent. The highest level of EDDHA had relatively little effect.

42. Wallace, A.: Trace Metal Placement in Soil on Metal Uptake and Phytotoxicity. J. Plant Nutrition 2:35-38 (1980).

Corn plants (*Zea mays* L. cv. Golden Cross H.C.) were grown for 21 days in Yolo loam soil to which a mixture of trace metals had been blended and applied to the soil in compartments. The treatments were control, all contaminated, top 1/2 control - bottom 1/2 contaminated, top contaminated -bottom control, and 1/2 contaminated with 1/2 control uniformly mixed. The trace metals involved were applied as sulfates and in $\mu g/g$ were 200 Zn, 200 Cu, 75 Co, 100 Ni, 100 Cd, and 13 Li. Treatments having 1/2 noncontaminated soil whether top or bottom grew plants without stress. The same quantity of trace metals uniformly mixed with all soil gave some indications of phytotoxicity and the treatment with all contaminated soil (two times more trace metals than the other three treatments receiving trace metals) showed severe toxicity symptoms most of which were probably due to Cd. The Zn, Mn, Co, Ni, Li, and Cd concentrations in leaves were highest for this treatment. When the bottom half of soil was contaminated, Li concentrations of leaves were decreased compared with other treatments. Roots tended to concentrate in the noncontaminated part of the soil when only part of the soil was contaminated.

43. Wallace, A., Alexander, G.V., Soufi, S.M. and Mueller, R.T.: Micronutrient Supplying Power of Pyrite and Fly Ash. J. Plant Nutrition 2:147-153 (1980).

Bush bean plants (*Phaseolus vulgaris* L. cv Improved Tendergreen) were grown in nutrient solution with added waste mine tailings pyrite and coal fly ash to test their ability to supply micronutrients to plants. The ability of fly ash to supply K was also tested. The pyrite was a satisfactory source of Fe, Mn, Zn, B and Cu to the solution cultures. The pyrite also supplied Ca. The fly ash supplied inadequate Fe and Mn but adequate quantities of Zn, B and Cu. It supplied adequate Ca and inadequate K. Both pyrite and fly ash supplied some Cd (when solution was acid), Cr and Pb to roots but not in detectable amounts to shoots. In another experiment, fly ash also failed to supply K to bush bean plants and failed to supply Zn. Iron, B, Si, Cu, Mo, Sr, Ba and some Ni and Cr were supplied

to leaves; Si, Sr, Ba, Ni and Cr were supplied to roots by the fly ash. None of these elements seemed to result in the phytotoxicity. A suggestion is made that fly ash and pyrite could be blended for soil application of some micronutrients where soil pH change is not needed.

44. Wallace A., Cha, J.W. and Mueller, R.T.: Effect of NaCl on Some Trace Metals in Bush Beans. J. Plant Nutrition 2:115-117 (1980).

When bush bean plants (*Phaseolus vulgaris* L. cv. Improved Tendergreen) were grown in nutrient solution, yields were depressed by levels of NaCl up to 100 me/l. When trace metals Li, Sr and Co were applied, only the treatment with 100 me/l NaCl had decreased yields for the trace metals but not significantly higher than control. The NaCl increased shoot concentrations of Zn, Cu and Si in roots. When Sr, Li and Co were applied, NaCl tended to decrease their concentrations in shoots and also in roots except for Li.

45. Wallace, A., Kawasaki, T., Romney, E.M. and Clark, R.B.: Trace Metal Interactions in Corn Inbreds Differing in Efficiency of Mg Uptake. J. Plant Nutrition 2:231-235 (1980).

The Mg-efficient corn (*Zea mays* L.) inbred B57 and the Mg-inefficient inbred Oh40B were grown in solution culture with moderate levels of some trace metals to test their relative interactions since previous studies had indicated that excess trace metals may be part of the Mg-inefficient syndrome. At the levels used only Co depressed yields and that for the Mg-inefficient inbred only. Distribution of minerals in the plants was mostly as reported in the literature. At both a high and low level of Mg, Mg concentration was lower in the shoots of the Mg-inefficient inbred than in the efficient one. In roots the reverse held especially at the low Mg level. The P concentration was higher in both roots and shoots of the inefficient inbred. The Zn was always higher in the inefficient inbred and this was more pronounced for roots than for shoots. Such effects with Mn were even more pronounced. Where extra Cu was supplied less was associated with roots of the inefficient inbred than with the efficient. When Ni was supplied it was distributed somewhat similarly. More K was in both shoots and roots of the inefficient inbred than in the efficient one. The reverse held for Ca in roots only. But at the high Mg level Oh40B shoots had more Ca than did B57 shoots. The low level of Mg resulted in more Ca in both roots and shoots of both inbreds but the increase in roots was far greater for the efficient inbred than for the inefficient inbred. Mg deficiency symptoms appeared only on the Oh40B inbred and iron chlorosis appeared on the Mg-inefficient inbred with Zn, Cu, and Ni additions but on the Mg efficient inbred only with Cu addition.

46. Wallace, A., Kinnear, J., Cha, J.W. and Romney, E.M.: Effect of Washing Procedures on Mineral Analyses and Their Cluster Analyses for Orange Leaves. J. Plant Nutrition 2:1-9 (1980).

Fifty mature orange leaves were divided into groups of 10 and each group received a different washing procedure (control, wipe only with cloth, wipe plus detergent and acid (1/10N HCl) wash, acid wash, wiping and acid wash followed by deionized water). The objective was to determine if the so-called dust elements (Fe, Al, Si, Ti) clustered together when dust was cleaned from leaves. The clustering was changed by washing procedures. Calcium, Na, Cu, and Mn concentrations were not changed by washing. Phosphorus, Mg, and K were lost from leaves by leaching with severe washing. Dust or contaminating Fe, Al, Si, Ti, and Pb were removed by all washing procedures but wiping with acid tended to decrease the coefficient of variation among samples.

47. Wallace, A. and Mueller, R.T.: Calcium Uptake and Distribution in Plants. J. Plant Nutrition 2:247-256 (1980).

Calcium uptake and distribution in plants are influenced by many factors. Root uptake seems to be independent of metabolic inhibitors but transfer to shoots is drastically reduced by such inhibitors. K uptake increases with root temperature which in turn results in depressed Ca uptake. Plant species differences in the proportion of K vs Ca uptake are often related to root cation exchange capacity. The cations K, Mg, Na, NH_4^+ , and H^+ directly and indirectly depress Ca uptake and distribution. Their effects are more pronounced at low Ca concentrations than at high. Lime-induced chlorosis is associated with depressed Ca levels in leaves and tests under controlled conditions indicate that bicarbonate results in root retention of Ca and a decrease of Ca in leaves. Nitrate as a complementary ion promotes Ca uptake by plants. Trace metals in excess inhibit calcium uptake. Aluminum in particular greatly depresses Ca retention by roots as well as Ca uptake and transport to shoots. Leaves generally increase in Ca with age. Magnesium can result in phytotoxicity when Ca levels are low and this may be involved in crop Ca disorders. Leaf fruit or seed transfers of Ca can be related to concentration of Ca in leaves.

48. Wallace, A. and Mueller, R.T.: Effects of Iron Level on Trace Metal Stress in Bush Bean Plants Grown in Solution Culture. J. Plant Nutrition 2:99-102 (1980).

Bush beans (*Phaseolus vulgaris* L. cv. Improved Tendergreen) were grown in nutrient solutions with levels of Cu, Zn, Ni, Cd, Co, and Mn at or near the stress point and with a high and a low level of Fe supplied as the chelate Fe EDTA. No Fe deficiency was present

on the control plants at the low Fe level. The Cu resulted in severe stress at low Fe and none at high Fe. The Zn resulted in severe stress at the low Fe level and in considerable stress at the high Fe level. The Ni resulted in a slight stress at the low Fe level and in no stress at the high Fe level. The Cd resulted in severe stress at both Fe levels. The Co resulted in severe stress at low Fe and in moderate stress at the high Fe level. The Mn resulted in considerable stress at the low Fe level and in no stress at the high Fe level. Thus no two metals behaved similarly at the levels used. The Cu, Zn, Cd, and Co resulted in low Fe concentrations in trifoliolate leaves on plants supplied low Fe but only Cd resulted in low Fe concentrations in plants grown with high Fe. These results with Fe were also quite similar for primary leaves. The high Fe level suppressed Ni, Cd, Cu, and Mn concentrations in leaves but not those of Co and Zn. Manganese was the only element in excess which accumulated in primary leaves to a large extent. Trace metals often decreased Ca levels in leaves which resulted in some increase in K.

49. Wallace A. and Mueller, R.T.: Effect of Nitrogen Rates on Iron Chlorosis in P154619-5-1 Soybeans. J. Plant Nutrition 2:199-201 (1980).

The Fe inefficient P154619-5-1 soybean (*Glycine max* L.) was grown in calcareous Hacienda loam soil with different applied N levels, i.e., 0, 100, 200 and 400 μ g soil applied as NH_4NO_3 . One set was grown without Fe addition and other with 0.25 μ g Fe/g soil as the FeEDDHA chelate. When no Fe was applied, the zero N resulted in no Fe chlorosis symptoms and symptoms became more pronounced with increasing N. Leaf analysis indicated a syndrome of true Fe deficiency resulting from the high N which was accompanied with increased P, Cu and Al. When Fe was applied, all the N treatments resulted in green plants with highest vegetative yield at 100 μ g N/g soil. Zero N, 200 and 400 μ g N/g soil resulted in close to similar yields. Nitrogen promoted increased Fe uptake in this experiment when Fe was added as a chelate. Leaf mineral analyses were unlike those not supplied with Fe.

50. Wallace A. and Mueller, R.T.: Effect of Steam Sterilization of Soil on Plants Susceptible to Iron Deficiency. J. Plant Nutrition 2:197-198 (1980).

When soybeans efficient and inefficient for Fe were grown in sterilized and nonsterilized Yolo loam (pH 6) soil, the inefficient P154619-5-1 soybean became Fe deficient because increased Mn uptake decreased Fe uptake. In efficient Hawkeye soybean, Fe was not depressed enough for Fe deficiency. The Fe inefficient YSI

corn inbred was chlorotic whether or not soil was sterilized and Zn and Cu concentrations were elevated. Increased Mn did not further depress Fe. The efficient WF9 inbred was green for both soil treatments.

51. Wallace A. and Mueller, R.T.: Effect of Steam Sterilization of Soil on Trace Metal Toxicity in Bush Beans. J. Plant Nutrition 2:123-126 (1980).

Bush beans (Phaseolus vulgaris L. cv. Improved Tendergreen) were grown in steam sterilized soils and in control soils with and without added Ni, Cd, and Cu. The objective was to determine if steam sterilization had interaction with the availability of trace metals to plants. The increased availability of Mn and possibly Cu to plants following sterilization depressed uptake of at least Ni and resulted in yield improvement. Steam sterilization increased Mo uptake by plants.

52. Wallace, A. and Mueller, R.T.: Nutrient Solution pH Resulting from Growing Fe-Efficient and Fe-Inefficient Soybeans. J. Plant Nutrition 2:203-204 (1980).

Hawkeye and PI54619-5-1 soybeans (Glycine max L.) were grown in nutrient solution at a low iron level ($10^{-5}M$ FeEDDHA) and at initial pH of near 4.0 and 7.0. The solution pH was monitored regularly and it was observed that the Fe-inefficient cultivar PI54619-5-1 at the high pH resulted in a further increase in solution pH while growing yellow Fe deficient plants with decreased yields. The Hawkeye soybean gave similar results but less pronounced.

53. Wallace, A. and Mueller, R.T.: Recovery from Acute Silver Toxicity by Bush Beans Grown in Solution Culture. J. Plant Nutrition 2:93-95 (1980).

Bush bean plants (Phaseolus vulgaris L. cv. Improved Tendergreen) that had been severely damaged by application of silver nitrate to nutrient solution, recovered at least partially after the Ag had been removed from the nutrient solution. A transition period of about 2 weeks was necessary before plants were growing normally. Silver, which usually accumulates in roots rather than in shoots, was detectable in slight amounts in stems of recovered plants and remained in or on roots even when no longer toxic.

54. Wallace, A. and Mueller, R.T.: The Effect of DTPA on Leaf/Stem Ratios of Some Trace Elements in Soybean Plants Grown with Different Soil Amendments. J. Plant Nutrition 2:189-192 (1980).

DTPA (diethylene triamine pentaacetic acid) (100 µg/g soil) increased the leaf/stem ratio of Ni, Zn, Cu, and Mn in PI54619-5-1 soybeans (*Glycine max* L.). The greatest increase for Ni was at the lowest soil pH values while that for Zn was at the highest pH values. The results add strength to the concept that under some conditions chelating agents are absorbed by plants and translocated to shoots at least at moderately high levels of DTPA.

55. Wallace, A., Mueller, R.T., Alexander, G.V. and Soufi, S.M.: Effect of Soil pH on Iron Uptake and Its Specific Activity by Two Cultivars of Soybeans Differing in Ability to Accumulate Iron and by Oleander. J. Plant Nutrition 2:205-211 (1980).

PI54619-5-1 and Hawkeye soybeans (*Glycine max* L.) were grown in Yolo loam soil with different amendments to alter the soil pH (5, 6, 7.4, and 8.2). High specific activity ^{59}Fe had been equilibrated with the soil before transplanting. The numbers of plants per pot varied to create competition (8 or 2 for each variety plus 4 of each variety together). The PI54619-5-1 soybeans were Fe deficient at pH 7.2 and both varieties were deficient at pH 8.5. The Hawkeye accumulated the most Fe except at pH 8.5. Iron accumulation and specific activity otherwise increased with soil pH, but varietal difference was most pronounced at pH 8.5. No stress effects were noted for growing the two soybean varieties together in these same pots. A high level of hydroquinone (10^{-3}M) in the nutrient solution increased both Fe level and specific activity of ^{59}Fe in PI54619-5-1 soybeans. The DTPA (diethylene triamine pentaacetic acid) did not always extract the same specific activity of ^{59}Fe as was present in soybeans and oleander (*Nerium oleander*).

56. Wallace, A., Mueller, R.T. and Cha, J.W.: Will High Usage of Synthetic Chelating Agents Eventually Harm Soils? J. Plant Nutrition 2:177-179 (1980).

To test the hypothesis that long-usage of metal chelates on soils will eventually result in abnormal plant nutrition, bush bean plants (*Phaseolus vulgaris* L. cv. Improved Tendergreen) were grown in Yolo loam soil which had been equilibrated with high levels of DTPA and EDDHA as Na salts; the levels were 500 and 1000 µg/g for each. Two crops of plants were grown at different points in the leaching stages. Yields were not affected by the treatments. Several trace elements were elevated in leaves after partial leaching and, after apparent complete leaching, Mn was elevated in primary leaves of 3 of 4 chelate treatments but in only one of four treatments in trifoliolate leaves. There was a residual effect on Zn and P in primary leaves but not in trifoliolate leaves. There was no real indication of adverse effects of the high levels of chelating agents after they had been leached from the soil.

57. Wallace, A., Mueller, R.T. and Romney, E.M.: Variable ^{241}Am Concentration in Soil Uptake and C.R. in Barley Plants. In Selected Environmental Plutonium Research Reports of the NAEG, June 1978, Nevada Applied Ecology Group, USED, Las Vegas, Nevada, Vol. 2, NVO-192, pp. 629-635 (1979).

Barley plants (*Hordeum vulgare* L. Atlas 57) were seeded into small pots of Yolo loam soil containing different concentrations of ^{241}Am (4,000, 10,000, 20,000, and 40,000 dpm/g soil). Four successive harvests were made with the first three harvests each of one-third of the original plants, but of different ages. One set of all concentrations was without and one set with the chelator DTPA. There were four replicates. Plant uptake of ^{241}Am was related to concentration, but the C.R. decreased slightly without DTPA (about 3x) as the soil concentration was increased tenfold. With DTPA, uptake was proportional to concentration (that of concentration of DTPA supplied was constant). The effect of DTPA relative to that of no DTPA increased with increasing concentration of ^{241}Am in soil. The C.R. under these conditions was reasonably constant, but severalfold higher than without DTPA. The last harvest contained less ^{241}Am than did the first, both with and without DTPA. The value of the coefficient "Y" in the equation

$$(C_1/C_2)^Y = \text{uptake ratio}$$

was about 50% lower without DTPA compared to with DTPA. With DTPA the value of "Y" was near 1, which implies that ^{241}Am in plants was directly proportional to that in soil at all concentrations.

58. Wallace, A., Mueller, R.T. and Wood, R.A.: Arsenic Phytotoxicity and Interactions in Bush Bean Plants Grown in Solution Culture. J. Plant Nutrition 2:111-113 (1980).

Bush bean plants (*Phaseolus vulgaris* L. cv. Improved Tendergreen) were grown in solution culture with varied levels of As to ascertain levels and plant concentrations associated with phytotoxicity and to determine if there were any interactions between As and other minerals in plants. The level of 10^{-4}M arsenate in solution resulted in considerable plant damage. Plant concentrations of As at this application rate were 3.6, 18.8 and 41.7 $\mu\text{g/g}$ respectively for leaves, stems, and roots. This level of arsenate resulted in increased Fe, Cu, Mg, Al, Si, Ti and Ba in all plant parts except Mg in roots. All of the increases may be due to concentration. Simultaneously there was depressed Mn, P and Ca in all plant parts. K also was depressed in roots. These depressions were not due to dilution.

59. Wallace, A., Mueller, R.T. and Wood, R.A.: Selenate Toxicity Effects on Bush Beans Grown in Solution Culture. J. Plant Nutrition 2:107-109 (1980).

Bush beans (*Phaseolus vulgaris* L. cv. Improved Tendergreen) were grown in solution culture with 0, 10^{-5} , 10^{-4} , and $10^{-3}M$ levels of Na_2SeO_3 . Mild toxicity was obtained for $10^{-4}M$ and severe toxicity at $10^{-3}M$. At severe toxicity, leaves were stunted and had brown spots. Selenium was fairly evenly distributed in plant parts. At severe toxicity, concentrations in $\mu g/g$ were leaves 901, stems 1058, and roots 1842. The high level of Se also decreased P, Ca, Mg, Mn and K concentrations in leaves and P and Ca in roots. Silicon and Ti tended to be higher with the highest Se level.

60. Wallace, A. and Romney, E.M.: Effect of Chelating Agents on Movement of Trace Metals into Cut Stems of Bush Bean Plants. J. Plant Nutrition 2:187-188 (1980).

The ability of the chelating agents EDTA and DTPA to facilitate transport from nutrient solutions at pH 5 of trace metals to leaves of bush bean plants (*Phaseolus vulgaris* L. cv. Improved Tendergreen) through cut stems was measured. Both chelating agents resulted in increased transfer of Cu, Co and Ni to primary leaves and in Cu, Co, Ni to a lesser extent, to trifoliate leaves. Potassium in leaves decreased as result of the cutting.

61. Wallace, A. and Romney, E.M.: Effect of Powdered Coal on Plant Growth and Composition. J. Plant Nutrition 2:159-161 (1980).

Bush bean plants (*Phaseolus vulgaris* L. cv. Improved Tendergreen) were grown in two different kinds of soil to which had been blended 6% powdered coal. Growth and mineral composition of the plants were measured after 28 days to obtain an estimate of effects for coal scattered in the environment. Coal was added with and without elemental sulfur to the noncalcareous soil used in order to determine if there were any interaction of coal in an extremely acid soil. In the noncalcareous soil the coal reduced vegetative yields slightly with and without the sulfur. Coal had no effect on yield when added to the calcareous soil. Coal tended to decrease P and K concentrations of the plants. In the acidified soil coal resulted in an increase of Mn in plants. Some other interactions were indicated.

62. Wallace, A. and Romney, E.M.: Gradients of Mineral Elements in Corn Leaf Blades from Base to Top from Plants Grown in Soil with Excess Trace Metals. J. Plant Nutrition 2:97-98 (1980).

Corn plants (*Zea mays* L. cv. Golden Cross N.C.) were grown for two months in 2000 g quantities of Yolo loam soil in which had been blended in $\mu\text{g/g}$ soil, 50 Co, 150 Ni, 13 Li, 200 Zn and 200 Cu. The K, P and Fe concentrations were lowest at the base and increased part way up 8 blades except that P increased continuously with each blade going from base to top. The trace metals Zn, Cu, Mn, Co, Ni, Li and Sr were highest in the basal blade (oldest blades) and decreased going upward generally to the fourth or fifth blade. The gradient was essentially the same as was that for Ca.

63. Wallace, A. and Romney, E.M.: Has the Work of NAEG at the Safety Shot Sites Come to a Logical Conclusion? In Selected Environmental Plutonium Research Reports of the NAEG, June 1978, Nevada Applied Ecology Group, USDE, Las Vegas, Nevada, NVO-192, Vol. 1, pp. 121-126 (1979).

The five years of study by the Nevada Applied Ecology Group of Pu and other radionuclides at the old safety-shot sites in Nevada have provided much environmental information, especially as relates to the nature, distribution, persistence, and amount of the contaminants present. There is, however, much important information on resuspension and on biologic, edaphic, and hydrologic reaction mechanisms which yet needs to be obtained in order to help resolve the many questions concerning dissemination of transuranic elements into the natural environment. Several cases in point are discussed as examples. At least another five years of coordinative studies at the old safety-shot sites are highly recommended.

64. Wallace, A. and Romney, E.M.: Interactions of Nitrogen Sources and Excess Nickel on Bush Beans. J. Plant Nutrition 2:75-78 (1980).

Bush bean (*Phaseolus vulgaris* L. cv. Improved Tendergreen) plants were grown in a glasshouse in 37-0 ml nutrient solutions for 15 days with three nitrogen sources and different levels of NiSO_4 . All NH_4^+ and urea treatments received CaCO_3 (10 g/3700 ml) in the nutrient solution to protect against excess acidity. In general, plants receiving the NH_4^+ source of N had less growth than those receiving urea or NO_3^- and $5 \times 10^{-4}\text{M}$ Ni treatments greatly inhibited growth. There was, however, no indication of interactions of N source and Ni on yield. Plants receiving NH_4^+ and urea had higher Ni concentrations than NO_3^- plants. Nickel resulted in decreased Fe in trifoliate leaves but not in primary leaves and the reverse occurred in roots. There was no interaction of Ni and Fe in roots but there was a Mn-Ni-N-source interaction in roots.

65. Wallace, A. and Romney, E.M.: Retention of Trace Elements in Leaves as a Result of Aerial Deposition from Fly Ash. J. Plant Nutrition 2:155-158 (1980).

Coal fly ash was applied periodically (9 applications in 5 months) to leaves of three tree species in the field and leaf samples were analyzed 8 months after the first application to determine if any of the trace metals from the fly ash had been retained in the leaves. A similar experiment was conducted with bush beans (Phaseolus vulgaris L. cv. Improved Tendergreen) in a glasshouse and plants were analyzed after 22 days exposure. All plants were washed in 0.1N HCl and deionized water before analysis. Tree leaves retained some Fe, Al, Ti, Sr and Ba and small amounts of some of the other trace elements but not consistently. The bush bean leaves retained Fe, Al, Ti, Ba but not Sr. Element retention was related to concentration in the fly ash and could be the result of surface contamination. Silicon, however, which has high concentrations in fly ash was not elevated in leaves. The pronounced marker trace elements in fly ash, Ba and Sr, were not strongly transferred to leaves. There was no evidence of transfer of trace elements to new leaves from old leaves and stems in the bush beans.

66. Wallace, A. and Romney, E.M.: Some Problems in the Study of Simultaneous Multiple Nutrient Deficiencies in Plants. J. Plant Nutrition 2:213-216 (1980).

Two experiments were conducted to determine some of the problems associated with study of multiple nutrient deficiencies in plants. In the first experiment in which bush beans (Phaseolus vulgaris L. cv. Improved Tendergreen) were grown in solution with no added Fe, no added Mn, or with both omitted simultaneously, vegetative yields of trifoliolate leaves were depressed by 25% for no Fe, 77% for no Mn, but only 58% for both no Fe and Mn. There was a clear interaction then, that resulted in better growth for no Mn and no Fe than for Mn with Fe. In the second experiment in which bush beans were grown in solution culture with low P and K ($10^{-5}M$ each singly and together), the multiple deficiency resulted in trifoliolate leaf yields about the same of those of the individual nutrients alone indicative of the operation of the law of the minimum.

67. Wallace, A., Romney, E.M. and Alexander, G.V.: Zinc-Cadmium Interactions on the Availability of Each to Bush Bean Plants Grown in Solution Culture. J. Plant Nutrition 2:51-54 (1980).

Bush bean plants (Phaseolus vulgaris L. cv. Improved Tendergreen) were grown for 12 days in nutrient solutions in a factorial experi-

ment involving 0 and $10^{-5}M$ $CdSO_4$, two solution pH values (4.5 and 7) and 0, $10^{-4}M$ EDTA and $10^{-4}M$ DTPA. There were then 24 treatments each with four replicates. Plants were separated to primary leaves, trifoliolate leaves, stems and roots, washed in 0.1M HCl and deionized water, and assayed by emission spectrography. The low Zn level resulted in some Zn deficiencies particularly with chelating agents and at high solution pH. Although Cd tended to depress Zn uptake, Zn did not modify Cd toxicity without chelating agents. Cadmium was not strongly toxic in the presence of chelating agents at high solution pH even though there was some Cd accumulation in leaves with those treatments. High Zn tended to favor large root accumulation of Cd but only at the low solution pH.

68. Wallace, A., Romney, E.M. and Clark, R.B.: Corn Inbreds Differing in Efficiency to Zinc. J. Plant Nutrition 2:225-229 (1980).

Corn (Zea mays L.) inbreds H84 (Zn efficient) and A635 (Zn inefficient) were grown in solution culture with moderate (contaminants only) and high ($10^{-4}M$) levels of Zn and with 3 different phosphorus levels. Each of these treatments were with and without $10^{-4}M$ chelating agent EDTA. The upper shoots of the plants tended to have lower Zn concentrations in the Zn inefficient inbred than in the Zn efficient inbred, particularly at the low level of Zn application. This was independent of the P levels. In roots the opposite was observed at the low level of Zn application but at the high level of Zn the inefficient inbred had sometimes more and sometimes less than the Zn efficient inbred partly depending upon P level. The high Zn level was mildly toxic to both inbreds at the low P level and an Fe interaction was involved (induced Fe deficiency). The effect of P in increasing and decreasing Zn concentrations was not consistent. EDTA tended to decrease Zn uptake and, at the low P level, caused a much greater yield decrease for the Zn inefficient inbred than for the Zn efficient inbred.

69. Wallace, A., Romney, E.M., Kinnear, J. and Alexander, G.V.: Single and Multiple Trace Metal Excess Effects on Three Different Plant Species. J. Plant Nutrition 2:11-23 (1980).

Three crops of plants corn (Zea mays L. cv. Golden Cross N.C.), barley (Hordeum vulgare L. cv. Atlas), soybeans (Glycine max L. cv. Hawkeye and PI54619-5-1) were grown in succession in flats of Yolo loam soil which had received in $\mu g/g$ soil 0, 13 Li, 200 Zn, 200 Cu, 75 Co, 100 Ni, and 100 Cd both singly and in various combinations. The three plant species with two cultivars of soybeans reacted differently to the trace metals. Protective (competitive), additive and synergistic effects were all present. The treatments slightly modified soil pH but this did not explain all

effects. Barley was most tolerant of the trace metals and yield depression occurred only when all six trace metals were applied simultaneously and this probably because of metal induced P deficiency.

70. Wallace, A., Romney, E.M., Kinnear, J.E. and Mueller, R.T.: Metal Ratios as an Index of Plant Species Differences on Uptake Characteristics of Different Trace Metals. J. Plant Nutrition 2:25-34 (1980).

Six plant species were grown in a flat of Yolo loam soil (fine-silty, mixed, thermic Typic Xerorthents) which had been uniformly blended with 133 Cu, 50 Co, 100 Cd, 67 Ni, 13 Li and 133 Zn as $\mu\text{g/g}$ soil. The trace metals stopped new growth of bush beans (Phaseolus vulgaris L. cv. Improved Tendergreen), inhibited growth of mint (Mentha viridis), barley (Hordeum vulgare L. Atlas), or wheat (Triticum aestivum L.). Mineral analyses were made of leaves on shoots of the plants and from the data, ratios of various elements were calculated for each species by a computer program. Ratios of element pairs for different plant species and ratios of one species to another for given elements indicated common relationships among Zn, Cu, Fe, Mn and Cd.

71. Wallace, A., Romney, E.M., Mueller, R.T. and Alexander, G.V.: Calcium-Trace Metal Interactions in Soybean Plants. J. Plant Nutrition 2:79-86 (1980).

Hawkeye soybeans (Glycine max L.) were grown for 13 days in nutrient solutions in a glasshouse with differential Ca and trace metal concentrations. Yields were little affected by low Ca levels without excesses of trace metals but yield depressions for excesses of Ni, Cd, Al, Mn, and Cu generally were greater at low Ca levels than at a high level. Ca, Mg, and K levels in plants were all depressed by the trace metals. Some of the effects were expressed also in roots. The 10^{-3}M level of Al resulted in virtually no Ca in roots and in diminished transport to shoots. The trace metal concentrations in leaves generally decreased with increasing Ca.

72. Wallace, A., Romney, E.M., Mueller, R.T. and Lunt, O.R.: Influence of Environmental Stresses on Response of Bush Bean Plants to Excess Copper. J. Plant Nutrition 2:39-49 (1980).

Bush beans (Phaseolus vulgaris L. cv. Improved Tendergreen) were grown in nutrient solutions in a glasshouse at low and at potentially toxic levels of Cu. These Cu treatments were interacted with other treatments to create various types of environmental stress. In an exploratory experiment, salinity (0.05M NaCl) and phosphorus

deficiency stresses were observed to result in proportionately more plant toxicity with a high Cu level than with a low. These two factors were then further studied in additional experiments and the observations were verified. Levels of P and NaCl which resulted in no or little yield reduction with normal amounts of Cu resulted in proportionately large yield decreases at high levels of Cu. Stress resulting from no aeration of the nutrient solution was less harmful relatively at a high Cu level than at a low. Slightly increased root temperature was slightly more injurious at the high Cu level than at the low while severe shading was equally harmful of both Cu treatments. Synergistic effects were noted for salinity and phosphorus levels as they interacted with the copper levels on growth of the plants. Mineral analyses do not explain these synergistic effects.

73. Wallace, A., Romney, E.M., Wallace, G.A., Mueller, R.T. and Cha, J.W.: Pyrite as a Source of Iron for Plants. J. Plant Nutrition 2:193-195 (1980).

Soybeans (*Glycine max* L. cv. PI54619-5-1) were grown for 28 days in a glasshouse in calcareous Hacienda loam soil in pots to which had been banded in the center of 500 g pots the following iron amendments: Control, 25 g of a commercial sulfur-iron (8%) mixture*, 25 g sulfur, a 20 g sulfur+ 5 g iron sulfate, 25 g of a commercial iron oxide mixture**, 25 g iron pyrite***, 12.5 g each of iron pyrite and sulfur, 25 g iron sulfate, and 12.5 g each of iron oxide and sulfur. Most rapid and complete greening was with iron sulfate or iron oxide alone or in combinations. Sulfur and pyrite-treated plants did not become green until about the 3rd week. Banding of all amendments increased Fe concentrations of leaves. Banding of sulfur did not result in increased Mn in leaves but pyrite resulted in some Mn toxicity and in increased Zn, Cu, Al, Ni and Pb in leaves with decreased leaf growth.

* Popcorn Iron of Union Oil Co. but use of trade name does not imply endorsement

** GU 49 of Master Builders

*** Iron Sulphur of Best Chemical

74. Wallace A., Soufi, S.M. and El Gazzar, A.M.: Wastewater as a Source of Nutrients and Water for Hydroponic Crop Production in Arid Regions. In Advances in Desert and Arid Land Technology and Development, Chur-London-New York: Harwood Academic Publishers, Vol. 1, pp. 263-270 (1979).

Reclaimed water from a sewage plant at Calabasas, California was a satisfactory source of nutrients, except for iron for growing crop plants in hydroponic culture under pilot plant commercial conditions.

Commercial culture of a number of glasshouse crop plants could be done without toxicity from salt or other materials. The crops were grown at energy savings compared with standard crop culture as it was not necessary to use manufactured fertilizers. Water which was otherwise wastewater was utilized in the process. To avoid adding additional soluble nutrients to the sewage water, iron was supplied either as foliar spray or as insoluble iron oxide applied to plant roots before and after transplanting. The latter procedure was most satisfactory. After the water had been used in the hydroponic tanks, much of the copper, zinc, manganese, iron, nickel, lead, and some of the nitrogen, phosphorus, and potassium had been stripped from the water. In arid regions of the world an on-line hydroponic culture system could be a very important aspect of a water recycling program. Economic benefit and water purification could result.

75. Wallace, A., Soufi, S.M., Romney, E.M. and Alexander, G.V.: Translocation of Calcium and Other Nutrients from Potato Tubers to Sprouts. J. Plant Nutrition 2:237-243 (1980).

Calcium levels in growing sprouts on potato (*Solanum tuberosum* L.) tubers were about 1800 µg/g of dry weight. Although this level is probably adequate, or close to it, it is only one-fourth to one-half of what is considered very deficient in leaves of potatoes. The Cu concentration in the sprouts was relatively high especially for the small amount of Ca present. Iron, Mn, Zn, and Cu concentrations in the entire sprouts from one set of tubers were 35, 25, 19, 19 µg/g of dry weight, respectively. For another set the concentrations in the upper one-third of the sprouts were 47, 7, 57, and 42 µg/g respectively, while that of Ca was 943 µg/g. These tips became necrotic due to either Ca deficiency or heavy metal excess or to both. Translocation of P, K, and Mg from tubers to the growing sprouts seemed to be from surface tissue adjacent to the sprouts. Strontium and Ba were not as readily translocated to the growing sprouts as was Ca.

76. Wallace A. and Wieland, P.A.T.: Mineral Nutrition Associated with Flower Color in Hydrangea. J. Plant Nutrition 2:217-220 (1980).

Analysis of blue and pink flowers of *Hydrangea macrophylla* DC growing in gardens in Los Angeles gave poor differentiation by concentration of Al in them in contrast to the effect reported in literature. Blue flowers usually associated with acid soils contained 510 µg Al/g dry weight while pink flowers usually associated with alkaline soils contained 481 µg/g. Pink flowers contained 322, 18, 1793, 42, 1.1, 0.6 and 4.7 µg/g respectively of Fe, Mn, Si, Ti, Mo, Cr and Sn. Blue flowers simultaneously contained respectively of the same elements, 146, 27, 622, 22, 0.4, 0.3, and 2.8. Some of these dif-

ferences may relate to flower color. Hydrangea cuttings grown in a glasshouse in soils of different pH values had blue flowers at soil pH 3.5 and these flowers were higher in Al, Mn, Mg and Si than flowers which were pink or pinkish blue on plants grown at higher soil pH values.

77. Wallace A., Wallace, G.A. and Cha, J.W.: Effect of Calcium Deficiency on Stem Thickening and Mineral Composition of Stem of Bush Beans. J. Plant Nutrition 2:245-246 (1980).

Bush beans (*Phaseolus vulgaris* L. cv. Improved Tendergreen) when grown in a nutrient solution with no added Ca had dead terminal growing points and a greatly enlarged stem diameter. Mineral composition of the stems relative to that of control plants showed increases of 9.6, 3.2, 2.0, 24.0, 3.2, 14.8, 1.6, 3.6, 3.5, 32.0, 2.9, 12.8, and 12.0 times respectively for Na, K, Zn, Cu, Fe, Mn, B, Al, Si, Mo, Sr, Ba and Pb. Simultaneously the Ca concentration of the stems was decreased 30.5 times.

78. Wanger, L.E. and Turner, F.B.: Trace Elements in Vegetation Downwind of a Coal-Fired Power Plant. Water, Air, and Soil Pollution 13:99-108 (1980).

Concentrations of As, B, Br, Co, Cu, F, Ga, Li, Mo, Ni, Sr, V, and Zn were measured in samples of four different kinds of plant at distances of 8, 12, 16, 24, 40, 70, and 120 km downwind of a large coal-fired power plant in New Mexico. Concentrations of B, Br, Co, Li and Sr decreased with distance from the power plant in grasses, but not in shrubs. Fluorine concentrations decreased in stems of a shrub. These decreases, taken with concentration enrichment and solubility considerations, provide circumstantial evidence that at least B and F trends may be due to power plant stack emissions.

SOLAR PROGRAM

The following reports were prepared under the direction of Dr. Robert G. Lindberg, Manager of the Solar Program.

1. Arzt, I. and Stenstrom, M.K.: An Evaluation of Cooling Water Requirements and Availability for Solar Power Plants in the Southwestern United States. UCLA Report 12/1247 (1980).

Solar power plants are no different than other types of power plants in that they require cooling water to remove waste heat. A significant consideration with solar power plant siting is the availability of suitable supplies of cooling water. This consideration is compounded by the arid nature of proposed solar power plant sites, which provide ample sunlight and land, but little if any water for cooling.

Previous power plant siting studies were investigated to determine if cooling water supplies were available at the suitable power plant sites. Previous studies show that the southeastern desert regions of California and southwestern regions in Arizona are most suitable for solar power plant sitings, based upon criteria other than cooling water availability. Unfortunately these regions have very little surface water available for power plant cooling. The major source of surface water in this region, the Colorado River, has been previously allocated.

It was found that cooling water is potentially available from ground water and return irrigation flows; however, there exist agency regulations, laws, and other institutional barriers which must be overcome. It also appears that cooling water can be made available through innovative methods, including conjunctive use of surface and groundwater, and wastewater recycle. After mitigation of institutional problems or development of innovative techniques, sufficient cooling water will be available for a 1000 MWE solar power plant.

2. Ullman, A.Z. and Sokolow, B.B.: Worker Health and Safety in Solar Thermal Power Systems. I. Overview of Safety Assessments. UCLA Report 12/1211 (1980).

Some aspects of safety in solar thermal power systems (STPS) have been studied to ascertain ways in which worker health and safety may be protected. Unique STPS hazards are also examined. A data base and methodology for quantitative predictions of injury rate is proposed. The methodology utilizes ordered comparisons of worker activities in STPS and in current industrial practice. Generic and design-specific hazards of thermal energy storage are examined by an event and fault tree methodology. The effects of the diffuse nature of solar energy on routine hazards are assessed by establishing

strawman designs for alternative STPS. Failure rates are estimated from extant data, and preferential rankings of the alternative STPS are made. Hazards of off-normal events in which thermal mismatches exist in receiver and generating subsystems are assessed. Characteristic hazards of solar ponds are addressed.

3. Ullman, A.Z., Sokolow, B.B., Daniels, J.I.: Worker Health and Safety in Solar Thermal Power Systems. II. Data Base and Methodology for the Estimation of Worker Injury Rates. UCLA Report 12/1212 (1980).

A data base and methodology useful for the quantitative estimation of worker hazards in hypothetical technologies is proposed. The hazard to workers is partitioned into categories of accident sources and injury-types. The probability of experiencing a specified rate in each category is estimated from data on a selected group of industries. Direct comparisons between existing and hypothetical technologies are constructed based on anticipated worker activities in plant operations and maintenance. Selected examples of worker hazards in solar thermal electric power generation are developed.

4. Ullman, A.Z., Sokolow, B.B., Daniels, J. and Hurt, P.: Worker Health and Safety in Solar Thermal Power Systems. III. Thermal Energy Storage Subsystems. UCLA Report 12-1213 (1980).

The effects of the use of thermal energy storage (TES) subsystems in solar thermal power systems (STPS) on operating failures and on worker health and safety are examined. Relevant near- and medium-term designs for TES subsystems are reviewed. Generic failure events are considered by an event tree methodology. Three generic categories of initiating events are identified which can lead to release of storage fluids and other hazards. Three TES subsystem designs are selected for, and subjected to, analysis. A fluid release event tree for a sensible heat TES subsystem using mixed media organic oil/crushed rock and sand, designed for the Barstow, CA, 10 MWe pilot plant, is developed. Toxicology and flammability hazards are considered. The effect of component failures, including ullage and fluid maintenance units, on subsystem safety is considered. A latent heat subsystem using $\text{NaNO}_3/\text{NaOH}$ as the working medium is studied, and relevant failure events delineated. Mechanical equipment failures including the scraped wall heat exchangers, are examined. Lastly, a thermochemical TES subsystem using SO_2/SO_3 interconversion is considered. Principal hazards identified include mechanical failures and storage fluid release. The integrity of the system is found to depend on catalyst and heat exchanger reliability. Dynamic response to off-normal system events is considered.

5. Ullman, A.Z., Sokolow, B.B., Hill, J., Meunier, G. and Busick, III, H.: Worker Health and Safety in Solar Thermal Power Systems. IV. Routine Failure Hazards. UCLA Report 12/1214 (1980).

Routine failure events in selected solar thermal power system designs are examined, and their rates of occurrence estimated. The results are used to compare and rank the systems considered. Modules of 1 to 100 MWe are developed based on reference or other near-term designs. Technologies used include parabolic trough, parabolic dish, and central tower focusing; central and distributed power generation; and proximate and independent siting of power modules. Component counts and failure rates estimated include heat transfer system leaks, sensor failures, and mechanical and electrical component failures, such as pumps, motors, and wire and cable. Depending on the technology chosen, leak rates can approach 1000 per year per 100 MWe system capacity, while component failure rates can be several times that level. Within categories of failures, the various technologies can have rates differing by a factor of 1000 or more. A uniform weighting for the consequences of various failure types is proposed. Under this weighting, central tower systems are most favored, followed by parabolic trough, parabolic dishes with dispersed power generation, and does not account for possible variations in the technologies. A sensitivity analysis is used to bound the relative hazards of the various failure events required to invert one or more of the system rankings.

6. Ullman, A.Z., Sokolow, B.B., Pauker, S., Robinson, D. and Bussick, III, H.: Worker Health and Safety in Solar Thermal Power Systems. V. Off-Normal Events. UCLA Report 12/1215 (1980).

In addition to routine events, off-normal events can be expected to affect worker health and safety. Reflecting the distributed nature of solar energy, collector subsystem response to off-normal events may not be as controllable as, for example, the power in a fossil fueled power plant. The consequences are reflected within the receiver subsystem in the effect of mismatches in energy flows. For example, collectors are required to shut-down during an interruption of coolant flow (ICF) to the receiver, or in the event of a loss of energy sink (LES) in the coolant loop. The time allowed for this shut-down is dictated by the desire to maintain integrity in the coolant loop and other components, since their failure is both a potential hazard to workers and economically undesirable. Several methods of achieving shut-down exist, each with its own characteristic time and reliability. These times are compared to assessments of the interval before loss of integrity during an ICF and an LES in selected receivers and coolant loops.

7. Ullman, A.Z., Sokolow, B.B. and Broutman, M.: Worker Health and Safety in Solar Thermal Power Systems. VI. Solar Ponds. UCLA Report 12/1216 (1980).

The design of solar pond electric power generation systems is reviewed to delineate factors which may affect worker health and safety. Materials handling problems are identified, including brine production and circulation hazards. Toxicity of micro-organisms and of pond additives is considered, as well as salt intrusion and dispersal. Each appears to have a potential negative health effect. An effect of the water supply quality on worker health may arise from impurities in the water and from waste disposal. This is of major importance if agricultural runoff waters are used. Other hazards identified include fire and reduced visibility hazards.

Additional studies on Solar Program work

8. Romney, E.M., Wallace, A. and Hunter, R.B.: Revegetation Studies Pertinent to the Barstow 10 Mw Solar Thermal Power Station and to Potential Installations Elsewhere in the Mojave Desert. UCLA Report 12-1224 (1979).

Revegetation of disturbed arid land is one of the great challenges of a desert. It is not an impossible task, however, if the natural and manmade resources available are utilized and managed. Because of unfavorable moisture and temperature conditions, the natural revegetation processes in the Mojave Desert require periods of time that are much longer than practical for meeting environmental protection standards. While solar facilities are generally considered as ecologically benign, we have no experience in this country with the consequences of constructing and operating large solar thermal power plants with extensive mirror fields. At least, one must expect total destruction of the ecosystem resulting from clearing of vegetation and land preparation within the area of the mirror field. The Barstow 10 Mw STPS affords an opportunity to examine accurately the environmental costs associated with large solar thermal power systems. Because the STPS site is scheduled to be restored at the conclusion of the demonstration project, the objectives of this study are to understand the abiotic and biotic processes influencing revegetation, and to experiment with techniques capable of enhancing the reestablishment and growth of native plants at that site.

This report presents findings from three different aspects of experimental efforts. A ready-made restoration experiment already exists in the area on which the STPS is to be located as the result of the land being cleared for agricultural use in 1953, and then being

abandoned in 1956. We are investigating those factors involved in the natural revegetation which have occurred during the 23 year period since that earlier disturbance. A field trial experiment using transplanted shrubs was established near the proposed mirror field site in order to investigate the extent to which the transplanted shrubs might be destroyed by grazing rabbits, and how they would respond to irrigation. Initial results indicate that shrubs can be transplanted successfully on site, if supplemental irrigation and protection from grazing rabbits is provided. Work is underway at the UCLA plant propagation facilities to prepare specimens of desert shrubs for future transplanting experiments. Experimental facilities and some recently cleared and abandoned land made available to us at the Nevada Test Site has allowed work to proceed on a newly disturbed site without being encumbered with construction activities and delays. We are proceeding in our work with the assumption that our ability to control the factors related to restoration of deserts is proportional to how well we understand the processes governing crown sprouting from sheared-off root systems, seed germination, and how we can best manage the disturbed system to assure the survival of new desert plant seedlings. Environs of the study site at NTS are typically Mojave Desert, so findings therefrom should be generic to the Barstow 10 MWe STPS site and also relevant to vegetation restoration needs of potential STPS sites elsewhere in desert areas.

9. Turner, F.E., ed.: Ecological Base Line Studies at the Site of the Barstow 10 MWe Pilot Solar Thermal Power System, Annual Report to the U.S. Department of Energy, UCLA Report 12/1223 (1979).

Base line ecological measurements and observations were made in 1979 at the site of the Barstow pilot 10 MWe solar thermal power system. The station will be constructed on Southern California Edison's Cool Water property, just east of the Cool Water Generating Station.

Surface soils of the site are sandy, but soils below 3 m are generally well graded sand with some silt and gravel. Some of the soils are highly saline, to an extent precluding plant growth. All soils are alkaline, with pH values as high as 9. Soils become saturated down to 20 cm shortly after winter rains, but soil moisture contents at 50 to 100 cm lag well behind rainfall events.

The prospective mirror field was cleared of vegetation in 1953 and some crops were grown until 1956, so shrubs occupying the field today are 23 years old or younger. Over 130 species of plants have been identified on the site, 18 of which are non-native. The three principal shrubs are creosotebush (Larrea tridentata), desert salt bush (Atriplex polycarpa), and bur-sage (Ambrosia dumosa). Estimated aggregate densities of annual plants range from around

600 to almost 9000 m⁻², depending on sampling locale. Aggregate densities of perennials (including herbaceous species) range from as low as 0.02 to 4.4 m⁻². Cover by shrubs is low in the areas cleared in 1953 (<6%), but increases to as high as 18% in areas to the east.

Creosotebush supports a varied assemblage of sap-feeding and defoliating insects, principally homopterans and orthopterans. Some 300 different kinds of arthropods were distinguished in samples from the site.

The most common rodents are kangaroo rats, pocket mice and ground squirrels. Over 60 kinds of birds were observed around the site, many associated with evaporating ponds adjoining the generating station. The most abundant in the prospective mirror field were horned larks, with estimated densities as high as 540 km⁻² in September 1978. The most commonly counted lizards on the site were gridiron-tailed lizards and western whiptail lizards.

10. Turner, F.B.: Environmental Issues and Solar Thermal Power Systems. In Proceedings 26th Annual Meeting, Institute of Environmental Sciences, Philadelphia, PA, pp. 430-434 (1980).

Central receiver solar thermal power systems require about 3 ha of land per MWe power output. Large systems (100 MWe) will require, then, more than one square mile for heliostats and associated structures. Because of efficiency and cost considerations solar thermal systems will probably use wet cooling towers. Water requirements for wet cooling are substantial--on the order of 15-20 acre-feet per MWe per year. Land availability and waste heat and water losses from cooling towers are presently seen as the major environmental problems. Other issues are noise, misdirected beams from heliostats, and possible escapes of high temperature working fluids (e.g., molten salts, hydrocarbon and silicone oils). Modeling studies of very large solar thermal power systems predict some mesoclimatic changes in the vicinity of the station, brought about by loss of water from cooling towers. Microclimatic changes of uncertain ecological consequence may be expected in the immediate vicinity of small (≤ 100 MWe) stations.

DIVISION OF NUCLEAR MEDICINE

RESEARCH HIGHLIGHTS

During the one year following July 1979, members of the Division of Nuclear Medicine had 37 scientific papers published, 25 abstracts published, and 26 scientific papers accepted for publication. Compared to the previous year, this represents a volume increase of 68% in papers published and 117% in papers accepted for publication. The quality of this research effort has been recognized by others during the past year. For example, Dr. Michael Phelps received an Award of Excellence for his manuscript delivered at the 9th International Symposium on Cerebral Blood Flow and Metabolism in Tokyo, was named Distinguished Alumnus by Western Washington University, and was made fellow and member of the Council on Circulation, American Heart Association. Dr. Heinz Schelbert received an Investigative Group Fellowship Award of the American Heart Association and was made a fellow and member of the Council on Circulation, American Heart Association. Dr. Gerald Wisenberg received the First Prize Award for radiological research from the James T. Case Radiological Foundation. Dr. Donald Rose received the Special Education Award for scholarly contributions and research by the James T. Case Radiological Foundation. Dr. David Kuhl was named John Kershman Memorial Lecturer by the Eastern Association of Electroencephalographers, received the Herman L. Blumgart, M.D. Pioneer Award of the New England Chapter of the Society of Nuclear Medicine, and was named Principal Investigator of a program grant award by the National Institute of Neurological and Communicative Diseases after a national competition.

The general theme of this research is described in more detail in the enclosed abstracts. In reviewing these, it becomes apparent that individual research projects within the division are well integrated so as to reinforce each investigator's special interests but to make possible by combined efforts investigations that would be impossible without team work.

In chemistry, new short-lived tracers were introduced and remote systems were described for cyclotron production of agents necessary for physiological research. Quantification of the emission computed tomographic scan was emphasized in simulation studies to design optimum CT filters and to reduce noise levels; the effects of sampling, non-uniform resolution, and attenuation corrections were determined; electrocardiographic gating was applied to reduce the effects of heart motion. Tracer kinetics were modeled for blood volume and blood flow determinations by positron ECT. A successful model was introduced for determination of local cerebral metabolic rate by ECT, kinetic constants were determined and the model was validated in man. These basic studies were then brought to bear in applying positron ECT and single-photon ECT to clinical research. Positron ECT was applied to study the effect of drugs on heart performance at rest and exercise and the non-invasive assessment of local myocardial blood flow. Local cerebral blood volume was

evaluated in head injury using ECT. Positron ECT was applied successfully for evaluation of local perfusion and metabolism in patients with stroke and epilepsy. In patients with epilepsy considered as possible candidates for anterior temporal lobectomy, the positron ECT scan of ^{18}F FDG was established as an important indicator of the part of the brain most responsible for causing seizures. These findings in epilepsy have attracted considerable attention in the neurological community. Finally, we showed by positron ECT of ^{18}F FDG that glucose metabolic rates in the primary and associative visual cortex of man increases as the complexity of visual scenes increases. This demonstration signals the way for a new kind of assessment of normal brain function in man, a study area in the neuro-sciences previously restricted to animals.

These accomplishments reflect a healthy program here focused on the multidisciplinary investigation of local organ metabolism and circulation by means of quantitative reconstruction tomography.

ABSTRACTS

1. Barrio, J.R., Bryant, J.D. and Keyser, G.E.: A Direct Method for the Preparation of 2-Hydroxyethoxymethyl Derivatives of Guanine, Adenine, and Cytosine^{1a}. J. Med. Chem. 23:572-574 (1980).

Alkylation of 2-chloro-6-iodopurine with iodomethyl [(trimethylsilyl)-oxy]ethyl ether at -63°C and subsequent treatment of the 9-substituted chloriodopurine with K₂CO₃ in aqueous dioxane at 25°C and then with NH₃ under pressure at 150°C provided 9-[(2-hydroxyethoxy)methyl]-guanine (1a), a potent antiviral agent against Herpes simplex virus type 1, in excellent yield. Its monophosphate (1g), which is enzymatically produced from 1a in the virus-infected cell, was also synthesized. 6-Chloropurine and 4-(methylthio)pyrimidin-2-one anions were similarly alkylated with iodomethyl [(trimethylsilyl)-oxy]ether, and the products (1f and 2b) were transformed by treatment with methanolic NH₃ at 110°C into 9-[(2-hydroxyethoxy)-methyl]adenine (1b) and 1-[(2-hydroxyethoxy)methyl]cytosine (2a), respectively. The syntheses of these analogues, heretofore difficult to prepare by a simple procedure, have been conveniently accomplished.

2. Barrio, J.R., Robinson, Jr., G.D. and Najafi, A.: Remote Systems for Chemistry Using Large Amounts of Cyclotron Produced Radionuclides. J. Nuc. Med. 21:92, abstract (1980).

A reliable approach to designing systems for chemical processing of cyclotron targets and for the synthesis of organic compounds with short-lived radionuclides has been developed.

The processes, although some times complex, are broken down into the required number of unit operations (e.g., adding reagents, removing solvent, extraction, chromatography, etc.). These simple unit operations are performed on a remote, semiautomated basis where standard laboratory glassware and equipment are normally used in conjunction with solenoid valves.

Chemist interaction is entirely remote and involves addition of reagents, transfer of fluids by application of pressure or vacuum, and the initiation of each operation by actuating the appropriate switch or combination of switches.

This approach has been applied to designing systems which are now being used for target processing and preparation of the Zn-62/Cu-62 generator (20 mCi), synthesis of F-18 labeled 2-deoxy-2-fluoro-D-glucose (two runs/day, yield = 20-25 mCi/run), and synthesis of C-11 labeled palmitic acid (multiple runs/day, 25-30 mCi/run).

Advantages of this approach include: very low cost, rapid reconfiguration to accommodate new or revised syntheses, reduced radiation exposure to the chemist (< 1 mR/run), and highly reliable, routine production of large mCi amounts of clinically useful radiopharmaceuticals.

3. Bruce, D., Obrist, W., Zimmerman, R., Bilaniuk, C., Dolinkas, C., Kuhl, D. and Schut, L.: The Pathophysiology of Acute Severe Brain Swelling Following Pediatric Head Trauma. In Cerebral Blood Flow and Metabolism, Gotoh, F., Nagai, H. and Tazaki, Y. eds. Acta Neurol. Scand. Suppl. 72, 60:372-373 (1979).

The clinical history and examination of these children clearly divided them into 2 groups. In group 1, 16 children had an initial episode of unconsciousness lasting for greater than 10 minutes followed by some degree of recovery. From 30 minutes to 12 hours later there was a sudden decrease in level of consciousness associated with sweating, pallor, intermittent and frequently alternating pupillary dilatation, bradycardia, systemic hypertension and sometimes intermittent decerebration. At least 1 episode of apnea occurred in 25% of these patients. In group 2, 20 children were deeply unconscious from the time of injury and exhibited either flaccidity or bilateral decerebration. None of these 20 patients had a lucid period and this group appeared to have suffered a much greater degree of primary brain injury.

The pattern of diffuse brain swelling, which we believe is the neuro-radiological correlate of "malignant brain edema," is associated with vasodilatation and cerebral hyperaemia. This event can occur with minimal primary impact brain injury in which case supportive respiratory therapy is all that is required to insure excellent recovery, or it can occur in association with severe multifocal primary impact injury to the brain. The clinical history and examination readily differentiate between the 2 groups of patients. Group 2 patients are likely to develop a delayed increase in ICP because of the delayed development of a slowly progressive multifocal cerebral edema associated with a multifocal brain injury and the underlying hyperaemia. While further regional cerebral blood volume studies are required to prove that the cerebral blood volume is indeed elevated as well as the blood flow we believe at this point that acute brain swelling in children following head injury is produced by acute cerebral vasodilatation and cerebral hyperaemia.

4. Bruce, D.A., Raphael, R.C., Goldberg, A.S., Zimmerman, R.A., Bilaniuk, L.T., Schut, L. and Kuhl, D.E.: The Pathophysiology, Treatment and Outcome Following Severe Head Injury in Children. Child's Brain 5:174-191 (1979).

The pathophysiology and outcome following severe head injury in 85 children are presented. The commonest initial CT diagnosis was of acute brain swelling. This swelling was associated with an increased white matter density on the CT scan which decreased to normal concomitant with recovery and increased ventricular size.

CBF measurements in 6 of these patients revealed an increased blood flow despite a decreased CMRO₂ and clinical coma. This CT pattern of diffuse swelling is believed to be due to acute cerebrovascular congestion and hyperemia and not to edema. Because of this, all children were treated with endotracheal intubation and controlled hyperventilation as part of the initial management. Mass lesions were uncommon, 20%. ICP was monitored in 40 children. The ICP rose above 20 Torr despite therapy in 80% of children with decerebrate or flaccid coma and in only 20% of children with spontaneous motor function. The ICP was at its highest between the second and fifth day. Aggressive therapy to control the ICP, with barbiturates if necessary, was successful in 80% of the patients. The overall results were useful recovery in 87.5% of the children, 3.5% were left vegetative or severely disabled and 9% died.

5. Bryant, J.D., Keyser, G.E. and Barrio, J.R.: Acyclic Nucleoside Analogues: Synthesis of Open-Ring Riboside or Deoxyriboside Analogues Lacking C(3') or the C(3')-C(4') Bond. J. Org. Chem. 44:3743-3744 (1979).

2-Alkyl-1,3-dioxolanes were treated with trimethylsilyl iodide to generate iodoalkyl (trimethylsilyloxy)ethyl ethers which were used to provide acyclic nucleoside analogues lacking C(3') or the C(3')-C(4') bond.

The ready availability of substituted dioxolanes and the excellent alkylating properties demonstrated by the derived iodoalkyl (trimethylsilyloxy)ethyl ethers make this an attractive synthetic methodology. In addition, our preparation now offers the possibility of synthesizing a variety of specifically substituted compounds, many of which would be quite difficult to obtain by conventional methods.

6. Bryant, J.D., Keyser, G.E. and Barrio, J.R.: Iodomethylethers and Thioethers from 1,3-Dioxolane and 1,3-Oxathiolane: Preparation of Acyclic Nucleoside and Analogs. 1979 Annual National Meeting of the American Chemical Society, Washington, D.C., September 9-14, abstract ORGN 22 (1979).

1,3-Dioxolane and 1,3-oxathiolane react rapidly and smoothly with trimethylsilyl iodide at temperatures ranging from -78°C to 0°C to afford iodomethyl trimethylsilyloxy ethyl ether (1a) or thioether (1b), respectively. Compounds 1a and 1b are efficient alkylating agents and react with a variety of purine and pyrimidine anions at -63°C to provide nucleoside analogs (70 - 80% yields) with an acyclic side chain identical to that of 9-(2-hydroxyethoxymethyl)guanine, a compound reported to possess potent antiviral activity (ED₅₀: 0.1 µM) against Herpes simplex virus type 1. This synthetic methodology is aimed toward a variety of potential antibiotic, antitumor and antiviral agents.

7. Engel, J., Ackermann, R.F., Caldecott-Hazard, S. and Kuhl, D.E.: Epileptic Activation of Antagonistic Systems May Explain Paradoxical Features of Experimental and Human Epilepsy: A Review and Hypothesis. In Kindling, Wada, J. ed., Raven Press, in press (1980).

Evidence is presented to suggest the hypothesis that amygdaloid kindling induces hyperactivity in at least two systems, one that is responsible for mediating the ictal event (chewing, head-bobbing, clonus, rearing, ictal EEG discharge) and one that mediates post-ictal phenomena (seizure termination, catatonia, wet-dog shakes, myoclonic jerks, IISs). Many paradoxical features of experimental epilepsy might be explained if seizures could be generated independently by these two antagonistic systems. Clinically, generalized convulsions and most partial seizures may be analogous to kindled ictal events, while petit mal seizures and some auras may represent activity analogous to postictal behavior in amygdaloid kindling.

8. Engel, Jr., J., Lieb, J., Rausch, R., Kuhl, D.E. and Crandall, P.H.: Interictal and Ictal Abnormalities of the Temporal Lobe in Patients with Partial Complex Epilepsy. In Limbic Epilepsy and the Dyscontrol Syndrome, Girgis, M. ed., North-Holland: Elsevier, in press (1980).

Interictal EEG and SEEG spikes per se are unreliable for localizing the epileptogenic lesion; however, some features of interictal spike activity may prove to be of more value for this purpose.

SEEG spikes that are less activated during sleep correlate better with the epileptogenic focus than those that are more activated during sleep.

Bilaterally synchronous EEG and SEEG spikes are a poor prognostic sign for temporal lobectomy and may indicate a frontal lesion.

Some interictal EEG and SEEG spike discharges may reflect neuronal activity that reduces seizure susceptibility.

Evidence of a focal functional deficit is important for confirming the location of the epileptogenic lesion. This can be demonstrated by:

- a) attenuation of spontaneous or barbiturate induced EEG and SEEG fast activity.
- b) inability of one temporal lobe to support memory during the modified intracarotid amytal test.
- c) a zone of decreased LCMR_{glc} and CBF demonstrated by positron emission computed tomography.
- d) an increased threshold for electrically induced afterdischarge.

SEEG recorded ictal activity that has a regional onset indicates that the epileptogenic lesion is distant from the recording electrodes. Whereas the prognostic significance of regional ictal onset is poorer than focal ictal onset, this is by no means absolute.

Scalp and sphenoidal recorded ictal onset can occur contralateral to the epileptogenic lesion and should not be considered localizing unless a focal functional deficit can be demonstrated in the same area.

Chronic partial complex epilepsy is not a focal disorder. Presurgical evaluation should not be aimed at finding a single focus, but at identifying the epileptogenic lesion most responsible for the patient's habitual seizures.

9. Engel, Jr., J., Rausch, R., Lieb, J.P., Kuhl, D.E. and Crandall, P.H.: Correlation of Criteria Used for Localizing the Epileptic Focus in Patients Considered for Surgical Therapy of Epilepsy. Ann. Neurol., in press (1980).

Criteria for anterior temporal lobectomy, performed on seven patients with partial complex seizures, were derived from a battery of 14 presurgical tests. Seven tests were routine studies aimed at identifying a focus of epileptic excitability while seven were designed to reveal areas of focal functional deficit. Conflicting information was frequently obtained from the tests of epileptic excitability, suggesting that it is probably inaccurate to view patients with partial complex seizures as having a single identification of the focus most responsible for the patient's habitual seizures. Tests of focal functional deficit provided useful non-conflicting confirmatory information in each of the seven patients studied. The most reliable information was obtained from depth electrode implantation and this procedure should be considered essential, except when all evidence of surface recorded epileptic excitability, including ictal onset, and evidence of focal functional deficit agree.

10. Engel, Jr., J., Rausch, R., Lieb, J.P., Kuhl, D.E. and Crandall, P.H.: Re-evaluation of Criteria for Localizing the Epileptic Focus in Patients Considered for Surgical Therapy of Epilepsy. Epilepsia 21:184-185, abstract (1980).

Identification of the epileptic focus for purposes of surgical resection is determined primarily on the basis of interictal spike activity and/or site of seizure onset derived from scalp (EEG), cortical (ECoG), or intracerebral depth (SEEG) recordings. Since 1977, all epileptic patients evaluated at UCLA for possible temporal lobectomy have been studied with seven routine studies aimed at identifying focal epileptic excitation (measurements of interictal and ictal EEG and SEEG data) and, also, an additional

seven studies designed to demonstrate focal functional deficits (measurements of interictal EEG and SEEG data, intracarotid amytal and positron emission scans). Seven patients who have completed this protocol and received temporal lobectomies now have had 6 months or more of post-operative follow-up. All have benefited greatly from surgery and pathological lesions were found in each of the resected specimens. Fifty-five per cent of the seven measures of focal epileptic excitability correctly localized the epileptic lesion, but 26% were falsely localizing. On the other hand, 55% of the seven measures of functional deficit correctly identified the epileptic lesion and no false localization occurred. Confirmatory evidence of focal decreased function, in addition to focal epileptic excitability, should be considered essential before deciding if and where surgery is to be performed.

11. Henze, E., Marshall, R.C., Schelbert, H.R.: Radionuclide Imaging in Patients with Chronic Stable Angina. Weekly Update in Cardiology, in press (1980).

This short invited review critically evaluates the use of radionuclide procedures in patients with coronary artery disease.

12. Henze, E., Wisenberg, G., Morales, L., Kuhl, D., Schelbert, H.R.: Effects of Supine Bicycle Exercise on Blood Concentrations of In Vivo and In Vitro Labeled Red Blood Cells for Equilibrium Blood Pool Imaging. J. Nuc. Med. 21(6):48, abstract (1980).

Changes (Δ) in cardiac chamber volumes measured by multiple gated acquisition blood pool imaging during supine exercise (E) could be affected by Δ in the indicator blood concentrations (IC). Using in vitro labeled RBC's (IVT) we found E caused an increase in IC. To examine this observation we randomly employed IVT or in vivo labeled RBC's (IVV) in 19 patients. Δ in IC were measured by well counting of serial blood samples and Δ in splenic activity (SA) by gamma camera imaging and expressed as % Δ from the control value obtained 10 min. after injection. At rest, IC's fell linearly but at different rates and were after 20 min. 4.4 ± 1.3 (SD)% with IVT and 11.9 ± 4.5 (p<0.01) with IVV below control. With E, IC with IVV declined to -5.1 ± 4.3 but increased with IVT to $+3.0 \pm 4.0$ (p<0.01) while SA fell with both to -37.7 ± 17.5 and -33.4 ± 33.9 (p<0.01 in both), respectively. Five minutes after E, IC with IVT decreased to -4.4 ± 4.9 (p<0.01 compared to E) while SA rapidly rose to $+1.7 \pm 24.9$ (p<0.01 compared to E). IC with IVV continued to decline after E to -7.7 ± 5 although SA rapidly rose to -16.0 ± 6.5 (p<0.01). Δ in IC's varied considerably between individuals and between IVV and IVT. Thus, RBC's may be injured during in vitro labeling and preferentially extracted by the spleen. Splenic contraction reported in animals

may also occur in man and account for the increase in IC's during E. We conclude that Δ in cardiac chamber activity during E should be normalized for changes in IC in order to accurately determine exercise induced Δ in ventricular volumes.

13. Henze, E., Wisenberg, G. and Schelbert, H.R.: Effects of Exercise on Regurgitant Fraction and Right and Left Ventricular Function in Aortic and Mitral Insufficiency. J. Nuc. Med. 21(6):49-50, abstract (1980).

The hemodynamic response to supine exercise was studied with equilibrium blood pool imaging in 9 patients with isolated mitral (MI) or aortic (AI) insufficiency and compared to that in 9 normals. In order to calculate right ventricular (RV) ejection fractions (EF) and regurgitant fractions (RF) a technique was developed that corrects for the contribution of right atrial activity to right ventricular activity. At rest, mean LVEF in AI was 57.0 ± 7.6 (SD) and not significantly different from N (59.6 ± 4.2) but was lower in MI (51.5 ± 7.6 ; $p < 0.01$). Resting RVEF were slightly but significantly depressed in MI when compared to N (44.0 ± 10.7 vs. 52.5 ± 6.5 ; $p < 0.05$) but not in AI (51.8 ± 6.6). With this new approach RF in N at rest was negligible ($1.9 \pm 8.6\%$), but was $53.2 \pm 4.8\%$ in AI and $51.8 \pm 10.8\%$ in MI (AI vs. MI not significant). With exercise, LVEF and RVEF increased in N significantly to 70.5 ± 3.8 ($p < 0.01$) and 68.0 ± 7.3 ($p < 0.01$), respectively, without a significant change in calculated RF ($2.1 \pm 14.1\%$). However, in both AI and MI, LVEF fell to 46.8 ± 11.8 ($p < 0.05$) and 41.8 ± 6.1 ($p < 0.05$) with no significant difference between AI and MI. The RVEF response, however, was distinctly different: it decreased in MI to 33.3 ± 6.8 ($p < 0.05$) but increased in AI to 65.8 ± 8.3 ($p < 0.01$). In both AI and MI the RF declined with exercise to 31.4 ± 12.9 and 34.0 ± 12.7 , respectively ($p < 0.01$ in both). Thus, in response to exercise RF declined both AI and MI; and RVEF increased in AI but declined in MI. We conclude that exercise multiple gated acquisition blood pool imaging permits evaluation of the hemodynamic response and changes in RF in patients with valvular insufficiency.

14. Hoffman, E.J., Huang, S.C. and Phelps, M.E.: Quantitation in Positron Emission Computed Tomography: I. Effect of Object Size. J. Compt. Tomogr. 3:299-308 (1979).

The effect of object size on the capability of positron emission computed tomography to measure isotope concentrations in a cross section was studied. The relationship between the apparent isotope concentration in an image and the true concentration was measured as a function of object size for three instrument resolutions and four convolution filters. The relationship between image size and object size was also measured under the same conditions.

Depression of apparent isotope concentration in an image for objects equal in size to the instrument resolution (FWHM) was significant (50% for a cylinder and 25% for a bar). For objects larger than 1.0 FWHM, accurate object sizes can be estimated from the images. Thus, reasonably accurate and practical schemes of compensation for object size effects can be implemented for objects larger than 1.0 FWHM. Accuracy in quantitating isotope concentrations in smaller objects is seriously compromised by the loss of sensitivity to the object size and the large correction factors required to compensate for instrument response. The results of the measurements were found to be in good agreement with theoretical predictions for ideal systems of comparable resolution.

15. Hoffman, E.J., Phelps, M.E., Huang, S.C. and Kuhl, D.E.: Effect of Accidental Coincidences in Positron Emission Computed Tomography. J. Nuc. Med. 20:634 (1979).

Errors caused by detection of accidental coincidences (ACs) and techniques for removing these events from image data were investigated in terms of their effect on quantitation in Positron Emission Computed Tomography (PCT). Removal of ACs is accomplished by simultaneous measurement of total coincidence events and ACs followed by an on line subtraction of the ACs from the total coincidences. Sequential phantom studies with short-lived positron emitters, which were performed with increasing scan times to compensate for isotope decay, gave images of constant true coincidence counts and variable AC fractions (0-50%). Images of pure ACs were obtained with phantoms containing ^{99m}Tc .

Errors in measured isotope concentrations in images were linearly related to AC fractions and are a function of size and shape of cross section and isotope distribution. For a 20 cm diameter uniform distribution of activity, a 50% (24%) AC rate contributed 46% (23%) of counts at center of cylinder, giving overestimate of 85% (33%) for concentration of positron emitter. Images of pure ACs show count distributions varying 2 to 1 from center to edge of field of view with a definite geometric pattern of 10-20% oscillations superimposed. This pattern, due to differences in true and accidental detection efficiencies, is removed by the on line AC subtraction technique.

ACs were found to create significant and correlated errors in PCT, indicating a need for accurate correction techniques which take into account the nature of this source of error.

16. Hoffman, E.J., Phelps, M.E., Ricci, A.R., Huang, S.C. and Kuhl, D.E.: Optimization of System Design Parameters for Emission Computed Tomography. IEEE/EMBS 79CH/440-7:363-368 (1979).

Two design parameters (coincident detector spacing and slit shield geometry) are singled out for investigation as to their influence on two of the more intractable problems in PCT design (spatial uniformity and scatter coincidence rejection). The effect of spatial non-uniformity on the extraction of quantitative information from images is shown. The magnitude and spatial distribution of scatter coincidences and the influence of slit shield design and detector spacing on scatter coincidences is shown. A new multiplane geometry is suggested which allows the high precision of a single plane PCT system and high efficiency of a multiplane PCT system to be combined in one system.

17. Hoffman, E.J., Phelps, M.E., Wisenberg, G., Schelbert, H.R. and Kuhl, D.E.: ECG Gating in Positron Emission Computed Tomography. J. Comput. Assist. Tomogr. 3:733-739 (1979).

Electrocardiographic (ECG) synchronized multiple gated data acquisition was employed with positron emission computed tomography (ECT) to obtain images of myocardial blood pool and myocardium. The feasibility and requirements of multiple gated data acquisition in positron ECT were investigated for ^{131}I , ^{18}F -2-fluoro-2-D-deoxyglucose, and ^{11}C -carboxyhemoglobin. Examples are shown in which image detail is enhanced and image interpretation is facilitated when ECG gating is employed in the data collection. Analysis of count rate data from a series of volunteers indicates that multiple, statistically adequate images can be obtained under a multiple gated data collection format without an increase in administered dose.

18. Huang, S.C. and Cox, J.R.: Derivation of Transit Time Distributions of a Stationary Flow System from Velocity and Length Characteristics. J. Appl. Math. Modeling, in press (1980).

With a particular probability space established for a stationary flow system it is shown that transit-time distribution of non-diffusible tracers is mathematically related to the distributions of path lengths and fluid flowing velocities. Functional form of the transit-time distribution can be derived by first determining the distributions of path lengths and fluid velocities from basic structural characteristics of a system and then employing the mathematical techniques in probability theory to convert them to transit-time distribution. The procedure of deriving transit-time distribution by this method is illustrated with an example.

19. Huang, S.C., Hoffman, E.J., Phelps, M.E. and Kuhl, D.E.: Quantitation in Positron Emission Computed Tomography: 2. Effects of Inaccurate Attenuation Correction. J. Comput. Assist. Tomogr. 3(6):804-814 (1979).

Effects of inaccurate attenuation correction on quantitation in positron emission computed tomography were investigated by both computer simulation and theoretical analysis, followed by experimental verification with phantom measurements. It was found that, due to the finite width of detector responses, compensation of scan measurements by measured attenuation correction factors does not completely correct for attenuation. For FWHM > 1.8 cm, errors in object size and in activity levels of reconstructed images are more than 4%. Mismatches between true and assumed attenuation media are found to give large errors. These mismatches include object shift, incorrect size and shape, uniform and nonuniform mismatches in attenuation coefficients, and nonzero background levels. Errors as large as 14% in the reconstructed activity level can be introduced by a 5 mm shift in object position. A 5% error in the cylinder diameter can give differences between the total reconstructed activity and true value more than 12%. Strong image distortions, which could lead to incorrect interpretations of images, are created by object shift and by nonuniform mismatches in attenuation coefficient. It was also found that statistical noise in measured attenuation correction factors can significantly increase noise levels in images, resulting in lower effective total counts for the emission scan. Effective total counts can be estimated as $N_{eff} = kN_{trm}N_{em}/(N_{em} + kN_{trm})$, where N_{em} and N_{trm} are total counts in emission and transmission scans, and k is a scanner dependent factor, which accounts for configuration differences.

20. Huang, S.C., Hoffman, E.J., Phelps, M.E. and Kuhl, D.E.: Quantitation in Positron Emission Computed Tomography: 3. Effect of Sampling. J. Comput. Assist. Tomogr., in press (1980).

Effect of insufficient transverse sampling on quantitative positron emission computed tomography was investigated with computer simulation and measurements on parallel bar and line source phantoms. Aliasing artifacts were observed and were found to be dependent on both the configuration and the location of imaged objects. Images of parallel bar phantoms were found to have aliasing artifacts similar in characteristics to aliasing on one dimensional signals. In line source images, aliasing effects were manifested as variations in amplitude and full width half maximum resolution (FWHM) for sources at even slightly different locations in the field of view. It was found that employing sampling distances smaller than 1/3 of the intrinsic detector FWHM eliminated noticeable aliasing

artifacts. Image resolution was also found to be affected by the sampling distance. For a sampling distance equal to $1/2$ of the intrinsic detector FWHM, the imaging FWHM is about 10% worse than the intrinsic FWHM. Selection of sampling distance in noisy environments is discussed. Parallel bar phantoms are shown to have advantages over line sources in the evaluation of sampling and resolution performance of ECT scanners.

21. Huang, S.C., Phelps, M.E., Hoffman, E.J. and Kuhl, D.E.: A Theoretical Study of Quantitative Flow Measurements with Constant Infusion of Short-lived Isotopes. Phys. Med. Biol. 24(6):1151-1161 (1979).

Recent developments in the technique of constant infusion and in emission computed tomography have provided a new method for quantitative regional flow measurements. This paper re-examines critically the theoretical relationship between flow and radioactivity during constant infusion of short-lived isotopes. Sensitivity analysis is used to assess the accuracy of the method. Criteria for the selection of an appropriate half-life to meet accuracy requirements are also discussed. A method for the determination of the distribution volume of the tracer is proposed.

22. Huang, S.C., Phelps, M.E., Hoffman, E.J. and Kuhl, D.E.: Cubic Spline for Design of Reconstruction Filters in Emission Computed Tomography (ECT). J. Nuc. Med. 21:38 (1980).

In ECT, due to variability in photon statistics, sampling, and detector FWHM, ability to flexibly adjust reconstruction filter (RF) to reduce noise while maintaining image resolution is highly desirable. Use of cubic splines is investigated to provide design techniques for flexible ECT RF. Frequency response function (FRF) of ECT RF's should be 1) real and symmetric, 2) approximately equal to $|f|$ for $f \neq 0$, and 3) smooth, with response at high frequency adjustable to reduce noise. Thus, ECT RF's can be specified completely by defining the real part of its FRF at positive frequencies. Smoothness and low frequency requirements can be achieved by cubic splines, which are smooth curves (C^3) that pass through arbitrarily selected points (knots). An interactive computer software system was developed to generate desired FRF with cubic splines. FRF values are specified at a few (<15) frequencies. The system generates and displays cubic spline that passes through these specified knots. One examines the curve and modifies locations of knots until satisfied with curve. Applying inverse FFT to FRF, system can generate an ECT RF with desired FRF. System is convenient and generated RF's tested on simulated and real ECT data gave faithful reconstructions. No artifacts were observed. With this system, ECT RF's of various cutoff characteristics can be

generated conveniently to match ECT scanning parameters to optimize image signal to noise ratio. One such RF design was found to reduce image noise by 50% without significantly affecting image resolution. It is concluded that cubic spline is useful for convenient and flexible design of ECT RF to optimize image signal to noise ratio.

23. Huang, S.C., Phelps, M.E., Hoffman, E.J. and Kuhl, D.E.: Cubic Splines for Filter Design in Computed Tomography. IEEE Trans on Nuc. Sci., in press (1980).

Application of cubic splines is investigated to provide a convenient method of designing flexible reconstruction filters for computed tomography (CT). Cubic splines were found to be compatible with the basic requirements of CT filter's frequency response functions. An interactive computer software system was developed to implement the method of designing CT filters with cubic splines. The system was found to be convenient to use and could provide filters of various characteristics. An example is shown to illustrate the capability of the method in designing filters that can reduce noise levels in emission CT images.

24. Huang, S.C., Phelps, M.E., Hoffman, E.J. and Kuhl, D.E.: Sensitivity Analysis in Physiological Modeling. Proceedings of 2nd International Conference on Mathematical Modeling, University of Missouri, Rolla (1979).

The various steps in physiological modeling are shown to be very similar to those used in the engineering design. The critically important role of sensitivity analysis in these two processes is discussed. Two examples in tracer methods are used to illustrate the importance and usefulness of sensitivity analysis in physiological modeling. In the constant infusion technique, results of a sensitivity analysis show that the error in flow measurement is minimized if the infused isotope has a physical half life equal to 0.35 times the mean transit time through the tissue. In the tomographic method for the measurement of local cerebral metabolic rate of glucose (LCMRGlc), sensitivity analysis indicates that if the tomographic measurement of local activities is taken between 50 and 120 min. after a bolus injection of a glucose analog, the error of the results can be expected to be within 10%. These examples show that sensitivity analysis in physiological modeling can provide guidance to model formulation and to the design of experimental procedures.

25. Huang, S.C., Phelps, M.E., Hoffman, E.J. and Kuhl, D.E.: Sensitivity Analysis of the Fluorodeoxyglucose (FDG) Method for the Measurement of Local Cerebral Metabolic Rate of Glucose (MR). J. Nuc. Med. 21:21 (1980).

FDG method for measuring MR assumes the use of average normal values of 4 kinetic rate constants (k 's) of FDG transport gives accurate MR. Sensitivity of method to errors in assumed values was investigated to assess accuracy of FDG method. When true MR is in normal range, error sensitivity to k 's was evaluated analytically and found to be related to standard deviation (SD) of k 's. SD of k 's in 13 normal subjects was found to be about 30%. Corresponding SD of estimated MR was found to be about 11%, if measurement was 40 to 120 min after FDG injection. For MR's differ greatly from normal range, error sensitivity to k 's was investigated by computer simulation of FDG transport model. Wide ranges of errors in k 's that correspond to more than 3-fold changes in MR were studied. It was found that if measurement was 60 min after FDG injection, error in estimated MR was less than 0.2 (true MR - normal MR), with overestimation for high MR and underestimation for low MR. Computer simulation was also used to investigate cases in which MR changes during time interval between FDG injection and measurement. Estimated MR was found to be weighted average of MR in interval with larger weights for MR of early time. For example, if MR changes from 14 to 7mg/min/100gm at 20 min, estimated MR at 60 min would be 11mg/min/100gm. As time for first MR is lengthened, estimated MR becomes closer to MR of early time. This result is useful in interpreting MR measurements involving stimulation and intervention studies. It is concluded that FDG method must be applied with care to obtain accurate MR measurements.

26. Huang, S.C., Phelps, M.E., Hoffman, E.J. and Kuhl, D.E.: The Role of Simulation in Computed Tomography. Proceedings of the 1980 Summer Computer Simulation Conference, in press (1980).

Computed Tomography (CT) provides cross-sectional images from projection measurements. Due to its unique data collection and image reconstruction procedures, requirements of CT imaging are very different from traditional direct imaging. Computer simulation can be used to generate the projection data of objects that are composed of simple geometric figures and from these projection data to reconstruct images of the original objects. By adjusting various parameters and factors in the simulation, the technique can provide important information in the basic understanding of CT. Results of two such simulation studies are shown. The usefulness of computer simulation in the development and maintenance of CT systems is also discussed.

27. Huang, S.C., Phelps, M.E., Hoffman, E.J., Sideris, K., Selin, C.J. and Kuhl, D.E.: Noninvasive Determination of Local Cerebral Metabolic Rate of Glucose in Man. Am. J. Physiol. 238(1) E69-E82 (1980).

A method for the determination of local cerebral metabolic rates of glucose (LCMRGlc) in normal man is described. The method employs [^{18}F]2-fluoro-2-deoxy-D-glucose (FDG) and emission-computed tomography (ECT). FDG was injected intravenously as a bolus. Radioactivities in separate brain regions were measured with ECT. Plasma FDG concentration following injection was measured from blood samples. A mathematical model that describes the kinetics of FDG transports was employed to determine the transport rate constants of FDG and to convert the radioactivity measurements to metabolic rates. The model has taken into account the possible dephosphorylation reaction from FDG-6- PO_4 (FDG-6-P) to free FDG in brain tissues. Experiments were performed in 13 normal volunteers. The rate constants of FDG in man were found to be comparable to those of deoxyglucose in rat and in rhesus monkey. The average LCMRGlc in gray and in white matter were found to be 7.30 ± 1.18 (SD) and 3.41 ± 0.64 mg/min per 100 g brain tissue, respectively. The subject-to-subject variation of LCMRGlc as measured by the present method was comparable to those of other methods that measure whole-brain CMRGlc.

28. Kuhl, D.E.: Emission Tomography: A Preface to the Symposium (in) Positron and Single-Photon Tomography. In Proceedings of a Symposium Held in Chicago, Illinois, Kuhl, D.E. ed., March 20-21, New York: G & T Management, in press (1980).

We emphasize emission tomography of the brain and heart, knowing full well that the method has important application to other organ systems as well. In these discussions, we hope to cast light not only on the significant potential of this powerful study method, but also to consider such practical questions as to the likely role of emission tomography in medical practice. Some of these questions might be: Will the primary role of emission tomography be in clinical diagnosis or in clinical research? Is the tomographic examination likely to be used alone or always in conjunction with conventional radionuclide imaging? Will quantitative data retrieval be common or rare? Will the most significant contributions of emission tomography come from very expensive instrument systems restricted to a few centers or from inexpensive devices which are widely applied?

29. Kuhl, D.E., Alavi, A., Hoffman, E.J., Phelps, M.E., Zimmerman, R.A., Obrist, W.D., Bruce, D.A., Greenberg, J.H. and Uzzell, B.: Local Cerebral Blood Volume in Head-Injured Patients: Determination by Emission Computed Tomography of Tc-99m Red Cells. J. Neurosurg. 52:309-320 (1980).

Local cerebral blood volume (CBV) was mapped in 10 normal subjects and in 30 patients after head injury. In normal subjects, the mean CBV was 4.34 ml/100 gm. The coefficient of variation was 12% for the group mean, and 3% for values obtained in duplicate studies of individuals. Patients with head injuries were divided into three groups according to the stage of their illness: acute illness, early recovery, and later recovery. Averages of mean CBV were within one standard deviation of normal. In contrast, consistent changes were found in serial studies of the mean CBV in the same patient. Compared to recovery values, levels of mean CBV measured soon after injury were reduced, largely at the expense of the gray-matter compartment. In five adults with predominantly unilateral lesions, there was an average early reduction in mean CBV and cerebral blood flow of 15% and 36%, respectively. In three children with diffuse brain swelling, there was an average early mean CBV reduction of 12%; a single child had early increased mean CBV at a time when intracranial pressure was high. Greater changes were seen in local CBV on individual sections. There were mixed zones of hypervolemia and hypovolemia in regions of infarction and intracerebral hematoma. Subdural hematomas had consistent medial margins of increased local CBV, representing dilated blood vessels of the underlying cortex. The presence and displacement of this hypervolemic zone were sensitive indicators of persistent subdural collection and mass effect, even when the collection was lucent to x-ray computed tomography.

30. Kuhl, D.E., Engel, J.E. and Phelps, M.E.: Emission Computed Tomography: Applications in Stroke and Epilepsy (in) Cerebral Circulation and Neurotransmitters. Proceedings of the International Congress on Cerebral Circulation, Toulouse, France, September 27-29, Bes, A. and Geraud, G. eds., Excerpta Medica, Amsterdam, pp. 37-43 (1980).

We have applied emission computed tomography (ECT) using ^{18}F -fluorodeoxyglucose (^{18}F FDG) and ^{13}N -ammonia (^{13}N HN $_3$) as indicators of abnormalities in local cerebral glucose utilization (LCMR $_{\text{glc}}$) and relative perfusion, respectively. The ECAT positron tomography was used to scan normal control subjects, stroke patients at various times during recovery, and patients with partial epilepsy, both in the interictal and ictal states.

ECT can serve as an *in vivo* analog of quantitative autoradiography. It is a noninvasive scanning method which produces a similar, but

less detailed, cross section picture of brain radioactivity in man, following intravenous injection of a labeled indicator.

The *in vivo* ^{18}F FDG-ECT method for determination of LCMR_glc in individual brain structures is derived from the ^{14}C -DG-autoradiographic method of Sokoloff et al. ^{18}F FDG enters the brain rapidly, is phosphorylated by brain hexokinase, and the metabolic product, ^{18}F FDG-6-PO₄, remains fixed with little further metabolism. Calculations are derived from a model of the biochemical behavior of deoxyglucose and glucose in the brain. The time course of specific activity in cerebral capillary blood is estimated by measuring arterialized venous blood samples obtained while the blood is clearing of tracer, at times greater than 40 minutes there is measurement of local cerebral ^{18}F concentrations by ECT scan, and, with knowledge of predetermined rate constants and a lumped constant, LCMR_glc is calculated for each zone in the tomographic image.

We chose ^{13}N H₃ as an indicator of relative cerebral perfusion because ammonia has a cerebral uptake that varies with capillary perfusion, a static cerebral distribution which is desirable for ECT scanning, a short physical half life (10 min.) which permits use prior to an ^{18}F FDG scan without residual interference, and simple chemical preparation.

31. Kuhl, D.E., Engel, J. and Phelps, M.E.: Emission Computed Tomography of ^{18}F FDG and ^{13}N H₃ in Partial Epilepsy. In Proceedings of the 12th Research Conference on Cerebral Vascular Disease, March 2-4, Raven Press, in press (1980).

The most important finding in this project was that the interictal ^{18}F FDG-ECT scan effectively detected dysfunctional brain zones considered most likely to be responsible for seizures in patients with partial epilepsy. When the nonlinear response of ^{13}N H₃ to flow changes is considered, our data suggests that the depressed LCMR_glc and LCBF are coupled within the dysfunctional zones. In our ictal patients, the cortex alone was the site of increased radionuclide uptake.

Our results indicate that the interictal ^{18}F FDG scan is useful in localizing the responsible focus in patients considered for surgery, and should be especially useful when EEG abnormalities are bilateral or confusing. Since ^{13}N H₃ underestimates both increases and decreases in LCBF, the metabolic tracer ^{18}F FDG is the preferred indicator now. With further development, the ECT method should have potential usefulness in the study of epilepsy beyond survey of the preoperative patient. A comparison of functional mapping by ^{18}F FDG-ECT in man and ^{14}C -2DG autoradiography in animals may aid validation of experimental models of epilepsy and improve our understanding of human epilepsy.

32. Kuhl, D.E., Engel, J. and Phelps, M.E.: Emission Computed Tomography of F-18 Fluorodeoxyglucose and N-13 Ammonia in Partial Epilepsy. J. Nuc. Med. 21:21, abstract (1980).

Seventeen patients with partial epilepsy had EEG monitoring concurrent with cerebral emission computed tomography (ECT) after F-18 fluorodeoxyglucose and N-13 ammonia were given intravenously as indicators of local cerebral glucose utilization ($LCMR_{glc}$) and relative perfusion, respectively. In 12 of 15 patients who had unilateral or focal electrical abnormalities, interictal F-18 fluorodeoxyglucose scan patterns clearly showed localized regions of decreased (20-50%) $LCMR_{glc}$, which correlated anatomically with the eventual EEG localization. These hypometabolic zones appeared normal on x-ray computed tomography in all but three patients and were unchanged on scans repeated on different days. In 5 of 6 patients who underwent temporal lobectomy, the interictal F-18 fluorodeoxyglucose scan correctly detected the pathologically confirmed lesion as a hypometabolic zone, and removal of the lesion site resulted in marked clinical improvement. In contrast, the ictal F-18 fluorodeoxyglucose scan patterns clearly showed foci of increased (82-130%) $LCMR_{glc}$ which correlated temporally and anatomically with ictal EEG spike foci and were within the zones of interictal hypometabolism (3 studies in 2 patients). N-13 ammonia distributions paralleled F-18 fluorodeoxyglucose increases and decreases in abnormal zones, but N-13 ammonia differences were of lesser magnitude. We conclude that the interictal F-18 fluorodeoxyglucose-ECT scan is useful now in aiding localization of the dysfunctional cerebral zone most likely to be responsible for seizures in patients considered for temporal lobectomy. With further development, ECT may help in categorizing better the various forms of the disorder and in elucidating the basic mechanisms of epilepsy in man.

33. Kuhl, D.E., Engel, Jr., J., Phelps, M.E. and Selin, C.: Epileptic Patterns of Local Cerebral Metabolism and Perfusion in Man Determined by Emission Computed Tomography of ^{18}F FDG and ^{13}N H₃. Ann. Neurol., in press (1980).

Seventeen patients with partial epilepsy had EEG monitoring concurrent with cerebral emission computed tomography (ECT) after ^{18}F -fluorodeoxyglucose (^{18}F FDG) and ^{13}N -ammonia were given intravenously as indicators of local cerebral glucose utilization ($LCMR_{glc}$) and relative perfusion, respectively. In 12 of 15 patients who had unilateral or focal electrical abnormalities, interictal ^{18}F FDG scan patterns clearly showed localized regions of decreased (20-50%) $LCMR_{glc}$, which correlated anatomically with the eventual EEG localization. These hypometabolic zones appeared normal on x-ray computed tomography in all but three patients and were unchanged on

scans repeated on different days. In 5 of 6 patients who underwent temporal lobectomy, the interictal ^{18}F FDG scan correctly detected the pathologically confirmed lesion as a hypometabolic zone, and removal of the lesion site resulted in marked clinical improvement. In contrast, the ictal ^{18}F FDG scan patterns clearly showed foci of increased (82%-130%) LCMR_{glc} which correlated temporally and anatomically with ictal EEG spike foci and were within the zones of interictal hypometabolism (3 studies in 2 patients). ^{13}N H₃ distributions paralleled ^{18}F FDG increases and decreases in abnormal zones, but ^{13}N H₃ differences were of lesser magnitude. When the relationship of ^{13}N H₃ uptake to local blood flow found in dog brain was applied as a correction to the patients' ^{13}N H₃ scan data, local alterations in perfusion and glucose utilization were usually matched, both in the interictal and ictal states. We conclude that the interictal ^{18}F FDG-ECT scan is useful now in aiding localization of the dysfunctional cerebral zone most likely to be responsible for seizures in patients considered for temporal lobectomy. With further development, ECT may help in categorizing better the various forms of the disorder and in elucidating the basic mechanisms of epilepsy in man.

34. Kuhl, D.E., Engel, J., Phelps, M.E. and Selin, C.: Patterns of Local Cerebral Metabolism and Perfusion in Partial Epilepsy by Emission Computed Tomography of ^{18}F -Fluorodeoxyglucose and ^{13}N -Ammonia. In *Cerebral Blood Flow and Metabolism*, Gotoh, F., Nagai, H. and Tazaki, Y. eds. *Acta Neurol Scan Suppl* 72 60: 538-539 (1979).

Ten patients with partial epilepsy underwent ECAT positron tomography during continuous surface or depth EEG monitoring. ^{18}F -fluorodeoxyglucose (^{18}F FDG) and ^{13}N -ammonia were given intravenously as indicators of cerebral glucose utilization (LCMR_{glc}) and relative perfusion, respectively.

We found that the interictal ^{18}F FDG scan patterns clearly show localized regions of decreased (20%-50%) LCMR_{glc} which correlates anatomically with interictal spike foci (6 of 7 patients). These zones were not detectable by x-ray CT. The localized metabolic depressions probably represent regions of permanently damaged brain rather than transiently suppressed function since, in 4 patients, focal metabolic depressions were unchanged in interictal scans repeated on different days. The interictal ^{18}F FDG scans were not sensitive to changes in interictal focal spike activity. There were no differences between interictal scans made during periods of high and periods of low focal spike activity in paired studies of 3 patients. In all of three mentally retarded patients with diffuse or multifocal EEG abnormalities, the interictal ^{18}F FDG scans demonstrated only globally decreased LCMR_{glc}. On the other hand, the ictal ^{18}F FDG scan patterns clearly showed foci of increased

(82%-130%) LCMR_{glc} which correlated temporally and anatomically with ictal EEG spike foci (3 studies in 2 patients). In both patients, the hypermetabolic ictal focus coincided anatomically with the zone of interictal hypometabolism.

35. Kuhl, D.E., Phelps, M.E. and Engel, J.: Emission Computed Tomography in Head Injury, Stroke, and Epilepsy. In Positron and Single-Photon Tomography, Proceedings of a Symposium held in Chicago, Illinois March 20-21, Kuhl, D. ed., New York: G&T Management, in press (1980).

This paper describes our initial clinical applications of emission computed tomography (ECT) for quantitative measurements of local cerebral circulation and metabolism. From 1959 to 1966, the original ECT method evolved into a useful clinical study method at the University of Pennsylvania; physiological measurements depended on our introduction of accurate corrective reconstruction beginning in 1965, followed by the first absolute determinations of local cerebral blood volume (LCBV) and local glucose utilization (LCMR_{glc}), all by single-photon ECT methods. Subsequently, we have extended this approach to positron ECT at UCLA. In each instance, the intention has been to derive meaningful information concerning the local physiological status of the brain in terms of a cross-section picture obtained by non-invasive means.

36. Kuhl, D.E., Phelps, M.E., Kowell, A.P., Metter, E.J., Selin, C., and Winter, J.: Effects of Stroke on Local Cerebral Metabolism and Perfusion: Mapping by Emission Computed Tomography of ¹⁸FDG and ¹³NH₃. Ann. Neurol. 8:47-60 (1980).

By means of emission computed tomography (ECT), we used ¹⁸F-fluorodeoxyglucose (¹⁸FDG) and ¹³N-ammonia (¹³NH₃) as indicators of abnormalities in local cerebral glucose utilization (LCMR_{glc}) and relative perfusion, respectively. The ECAT positron tomography was used to scan normal control subjects and 10 stroke patients at various times during recovery. In normal subjects, mean LCMR_{glc} was 5.28 ± 0.76 mg per 100 gm tissue per minute (mean $\pm$ SD; N = 8). In patients with stroke, mean LCMR_{glc} in the contralateral hemisphere was moderately decreased during the first week, profoundly depressed in irreversible coma, and normal after clinical recovery.

Quantification was restricted by incomplete understanding of tracer behavior in diseased brain, but relative local distributions of ¹⁸FDG and ¹³NH₃ trapping qualitatively reflected the increases and decreases as well as coupling and uncoupling expected for local alterations in glucose utilization and perfusion in stroke. Early after cerebrovascular occlusion there was a greater decrease in local trapping of ¹³NH₃ than ¹⁸FDG within the infarct, probably because of increased anaerobic glycolysis. Otherwise, ¹⁸FDG was a

more sensitive indicator of cerebral dysfunction than was $^{13}\text{NH}_3$. Hypometabolism, due to deactivation or minimal damage, was demonstrated with the ^{18}F FDG scan in deep structures and broad zones of cerebral cortex that appeared normal on x-ray computed tomography and technetium $^{99\text{m}}$ pertechnetate scans.

In its present state of development, the ^{18}F FDG ECT method should aid in defining the location and extent of altered brain in studies of disordered function after stroke. With improved knowledge of tracer behavior in diseased brain, the method has promise for mapping the response to therapeutic intervention and increasing our understanding of how the human brain responds to stroke.

37. MacDonald, N.S., Cook, J.S., Birdsall, R.L., McConnell, L.J. and Kuhl, D.E.: Nitrogen-13-Labeled Ammonia for Multiple Daily Needs in a Nuclear Medicine Clinic. Trans. Am. Nuc. Soc. 33:928 (1979).

This report describes a system developed at the UCLA Nuclear Medicine Division to provide aqueous solutions of ammonia, labeled with 10-min half-life ^{13}N for diagnostic procedures to evaluate regional blood supply in body organs such as brain and heart.

Nitrogen-13 is produced with the UCLA compact cyclotron by bombardment of 10 ml of water in an aluminum, water-cooled target chamber with an external beam of protons, incident on the water at 21.0 MeV. The reaction is $^{16}\text{O}(p,\alpha)^{13}\text{N}$. The target is permanently fixed to one of the 7 available external beam lines and is dedicated solely to ^{13}N production. It is loaded remotely with water from the chemistry laboratory outside the cyclotron vault by means of a 35-ft length of 1/8-in. o.d. Teflon tubing. Bombardment time is 15 min at a beam current of 20 μA . The ^{13}N activity is in solution in the form of NO_3^- and NO_2^- ions. After bombardment the irradiated water is drawn from the target chamber by suction through the tubing into a glass dropping funnel, making sure to divert the nonradioactive water in the tubing to a waste container for discard. The solution is then allowed to drop into one of 6 prepared glass reaction vessels, each of which contains a mixture of dry NaOH and powdered De Vardas Alloy (46% Al, 49% Cu, 50% Zn) which serves to reduce the ^{13}N to the NH_3 form. The heat of the reaction evolves gaseous NH_3 , which, assisted by a flow of nonradioactive N_2 gas, passes through a spray trap and into 10 ml of sterile isotonic NaCl solution. This solution is then sucked through a 0.22- μm Millipore sterilizing filter directly into a sealed, sterile serum vial encased in 1/2-in.-thick lead shield. All this equipment is in a vented hood behind a 4-in. barricade with a 6-in. lead glass view window. All transfers of liquid are accomplished by hands-off techniques using solenoid-operated valves and Teflon tubing in a closed system. Six reaction vessels are prepared before the first run so the radiochemist need not reach behind the barricade for the rest of the day.

The sealed vial containing the radioactivity is inserted into the "send" station of a pneumatic tube delivery system. This commercial-type, 3-in.-diam pneumatic line runs from the cyclotron lab, up one floor level to the Nuclear Medicine Clinic hot lab, a distance of about 400 ft. The carrier arrives there about 20 s later and drops into a lead-shielded terminal. The whole procedure from the time the cyclotron beam is turned on to arrival of the product at the clinic takes 20 to 22 min. The activity delivered is 100 to 180 mCi in 8 to 9 ml of solution, ready for injection. A batch can be prepared and delivered as often as every half-hour if necessary. The radiation dose to the radiochemist is less than 1 mR, measured directly by film badges on the coat lapel and thermoluminescent dosimeters on the fingers. Quality control of the product is checked by periodic tests for pH, half-life, gamma-ray emissions, sterility, freedom from pyrogens, and freedom from metal-ion contamination.

38. Marshall, R.C., Nash, W.W., Shine, K.I., Phelps, M.E. and Ricchiuti, N.: Glucose Metabolism During Ischemia Due to Excessive Oxygen Demand on Altered Coronary Flow in the Isolated Arterially Perfused Rabbit Septum. Circ. Res., in press (1980).

The isolated arterially perfused interventricular rabbit septum was adapted for the study of glucose metabolism during ischemia produced by either increased oxygen demand or altered coronary flow. The septum, perfused at 1.5 cc/min with a stimulus rate of 72 min⁻¹ at 37°C, was shown to be a low work preparation in which glucose utilization, lactate production, oxygen consumption, and developed tension were stable for at least 90 minutes. The metabolic and functional response of the septum was evaluated during normoxic increased work produced by introducing a paired stimulus at 90 min⁻¹ and increasing flow to 3.5 cc/min, during demand-induced ischemia produced by introducing a paired stimulus at 90 min⁻¹ and maintaining flow at 1.5 cc/min, and during low flow ischemia produced by decreasing flow and maintaining stimulus rate constant at 72 min⁻¹. During normoxic increased work, glucose utilization increased (±SEM) 115±26% over control, while oxygen consumption increased 100±11%, lactate production 13±9% and developed tension 45±8%. During demand-induced ischemia, glucose utilization increased 115±24%, while oxygen consumption increased only 29±7%, lactate production rose 106±19% and developed tension declined 20±4%. These results are consistent with accelerated glucose oxidation during normoxic increased work and accelerated anaerobic glycolysis during demand-induced ischemia. During severe low flow ischemia, glucose utilization declined 44±8% while developed tension and oxygen consumption decreased by 80±8% and 74±2% respectively. These results extend to ischemia produced by exces-

sive oxygen demand previous work showing that glucose utilization is flow-dependent during oxygen deprivation due to reduced flow or anoxic perfusion.

39. Marshall, R.C., Wisenberg, G., Schelbert, H.R. and Henze, E.: Effect of Oral Propranolol on Rest, Exercise, and Post Exercise Left Ventricular Performance in Normals and Patients with Coronary Artery Disease. Circulation, in press (1980).

The effect of beta-adrenergic blockade with oral propranolol on resting, exercise, and post-exercise ventricular performance was evaluated using multiple gated equilibrium cardiac blood pool images in normal volunteers and patients with coronary artery disease. Propranolol produced no detectable effect on basal left ventricular function in normals at doses producing intermediate (160 mg propranolol/day) and maximum (434 ± 99 mg propranolol/day) beta blockade and in patients with coronary artery disease at clinically effective anti-anginal doses (162 ± 47 mg propranolol/day). In normals during exercise, a dose-related negative inotropic effect was observed: 160 mg propranolol/day produced a small but statistically insignificant decline in exercise left ventricular performance while maximum beta blockade significantly depressed the response of the left ventricle to exercise. In patients with coronary artery disease, propranolol's effect on exercise ventricular performance depended on the presence or absence of ischemic dysfunction during exercise. In patients with an ischemic functional response to exercise, propranolol significantly improved regional and global performance during exercise and in the post exercise period; in coronary artery disease patients with a normal response to exercise, propranolol had no significant effect on exercise and post-exercise ventricular function. These results imply increased sensitivity to the effects of beta blockade in ischemic myocardium. In both coronary artery disease patients with an abnormal response to exercise and normal volunteers during beta blockade, propranolol's effect on exercise left ventricular performance was observed to be independent of heart rate and blood pressure related changes in ventricular preload and afterload.

40. Phelps, M.E., Hoffman, E.J., Huang, S.C. and Kuhl, D.E.: Design Considerations in Positron Computed Tomography (PCT). IEEE, Nuc. Sci. 26:2746-2751 (1979).

PCT system design is complex and involves optimization and trade-offs in numerous design parameters. A design approach or system evaluation in terms of FWHM resolution and gross efficiency is insufficient and misleading. There are many sources of noise in PCT other than statistical which must be minimized. When they become competitive with statistical noise, then further

increases in efficiency will not produce significant improvements in performance and image signal/noise. At this time, circumferential systems are more optimal than planar arrays for PCT. The advantages and disadvantages of the hexagon and circle need to be analytically determined in more detail.

The importance of positron emission computed tomography (PCT) has grown over the past five years. The principle objectives of this technique is to combine the noninvasive, analytical measurement of tissue radionuclide concentration of labeled compounds which trace a physiologic process in a known manner, and physiologic models that allow the calculation of physiologic variables of interest. This approach is referred to as Physiologic Tomography, PT.

PT requires tomographs capable of analytical measurements in man rather than qualitative grey scale imaging of activity distributions. This requires more careful and detailed system design to both control the fundamental factors which can compromise this objective, and to maximize the image signal-to-noise ratio (S/N).

This paper will discuss some of the physical aspects, sources of noise, design factors, and design alternatives in PCT. It will deal more with general concepts than specific details and try to illuminate some of the complex issues which are considered in PCT design. Studies in brain and heart are presented to illustrate present day image quality.

41. Phelps, M.E., Huang, S.C., Hoffman, E.J. and Kuhl, D.E.: Validation of Tomographic Measurement of Cerebral Blood Volume with C-11-Labeled Carboxyhemoglobin. J. Nuc. Med. 20:328-334 (1979).

Red blood cells, tagged with C-11 by administration of ^{11}CO gas, have been used to portray the distribution of blood in the brain. To date, however, the accuracy of this approach has not been validated. We have performed in vitro measurements of regional cerebral blood volume (CBV) with red blood cells labeled with C-11 and Cr-51 in four dogs and two rhesus monkeys. These studies yielded a ratio of $\text{CBV}_{\text{C-11}}$ to $\text{CBV}_{\text{Cr-51}}$ of 1.02 ± 0.03 (s.d.) from 92 samples. A least-squares fit to these data showed $\text{CBV}_{\text{C-11}} = 1.01 \text{ CBV}_{\text{Cr-51}} + 0.037$; $P < 0.001$. The ratio of CBV in gray matter to that in white matter was 2.8 ± 0.4 ($n = 12$) and 3.1 ± 0.6 ($n = 8$). In vivo studies with emission computed tomography (ECT) and $^{11}\text{CO-RBC}$ gave coefficients of variation of $\pm 2.8\%$ and $\pm 4.8\%$ for cross-sectional CBV and regional ($\sim 4 \text{ cm}^2$) CBV over an 80-min period. The average human CBV was found to be $4.2 \pm 0.4 \text{ cc}$ blood per 100 g tissue. Clear tomographic delineation of the distribution of CBV in human subjects is achieved with ECT, which provides a "live" measurement of this parameter of cerebral

hemodynamics. These data demonstrate that ^{11}CO administered by single-breath inhalation is a reliable and accurate blood tracer for measurement of CBV with ECT.

42. Phelps, M.E., Huang, S.C., Hoffman, E.J., Schelbert, H.R., Barrio, J.R. and Kuhl, D.E.: Cerebral Extraction of N-13 Ammonia: Its Dependence on Cerebral Blood Flow and Capillary Permeability. Stroke, in press (1980).

^{13}N -labeled ammonia was used to investigate 1) the cerebral extraction and clearance of ammonia, ii) the mechanism by which capillaries accommodate changes in cerebral blood flow (CBF) and iii) its use for the measure of CBF. The single pass extraction of $^{13}\text{NH}_3$ in rhesus monkeys was measured during PaCO_2 induced changes in CBF and dog studies were performed using in vitro tissue counting techniques to examine $^{13}\text{NH}_3$ extraction in gray and white matter, mixed tissue and cerebellum during variation in CBF produced by combinations of embolization, local brain compression, and changes in PaCO_2 . The single pass extraction fraction of $^{13}\text{NH}_3$ varied from about 70 to 20% over a CBF range of 12 to 140cc/min/100gms. Capillary permeability-surface area product (PS) estimates with a Renkin/Crone model show PS increasing with CBF. The magnitude and rate of increase in PS with CBF was highest in gray matter > mixed tissue > white matter. Tissue extraction of $^{13}\text{NH}_3$ vs CBF relationship was best described by a unidirectional transport model in which CBF increases by both recruitment of capillaries and by increases of blood velocity in open capillaries. This saturable-recruitment model provides a possible explanation for the mechanism of flow changes at the capillary level. Glutamine synthetase, which incorporates $^{13}\text{NH}_3$ into glutamine appears to be anatomically located in astrocytes in general and specifically in the astrocytic pericapillary end feet that are in direct contact with gray and white matter capillaries. The net $^{13}\text{NH}_3$ extraction, subsequent to an i.v. injection increases nonlinearly with CBF. Doubling or halving basal CBF produced from 40 to 50% changes in the ^{13}N tissue concentrations with further increases in CBF associated with progressively smaller changes in ^{13}N concentrations. $^{13}\text{NH}_3$ appears to be a good tracer for the detection of cerebral ischemia with positron tomography but exhibits a poor response at high values of CBF.

43. Phelps, M.E., Huang, S.C., Hoffman, E.J., Selin, C.E. and Kuhl, D.E.: Tomographic Measurement of Local Cerebral Glucose Metabolic Rate in Man with (^{18}F) Fluorodeoxyglucose: Validation of Method. Ann. Neurol. 6:371-388 (1979).

Tracer techniques and quantitative autoradiographic and tissue counting models for measurement of metabolic rates were combined

with positron computed tomography (PCT) and (F-18)2-fluoro-2-deoxy-D-glucose (FDG) for the measurement of local cerebral metabolic rate for glucose (LCMRGlc) in humans. A three-compartment model, which incorporates hydrolysis of FDG-6-PO₄ to FDG, was developed for the measure of kinetic constants and calculation of LCMRGlc. Our model is an extension of that developed by Sokoloff et al. Although small, hydrolysis of FDG-6-PO₄ was found to be significant. A PCT system, the ECAT, was used to determine the rate constants, lumped constant, and stability of the model in human beings. The data indicate that cerebral FDG-6-PO₄ in humans increases for about 90 minutes, plateaus, and then slowly decreases. After 10 minutes, cerebral blood FDG activity levels were found to be a minor fraction of tissue activity. Precursor pool turnover rate, distribution volumes, and red blood cell-plasma concentration ratios were determined. Reproducibility (precision) of LCMRGlc measurements (~ 2 cm² regions) was $\pm 5.5\%$ over a 5-hour period. The replacement of arterial blood sampling with venous sampling was validated.

44. Phelps, M.E., Huang, S.C., Hoffman, E.J., Selin, C., Sokoloff, L. and Kuhl, D.E.: Tomographic Measurement of Local Cerebral Glucose Metabolic Rate in Humans with (F-18)2-Fluoro-2-Deoxy-D-Glucose: Validation of Method. Ann. Nuerol. (1979).

Tracer techniques and quantitative autoradiographic and tissue counting models for measurement of metabolic rates were combined with positron computed tomography (PCT) and (F-18)2-fluoro-2-deoxy-D-glucose (FDG) for the measurement of local cerebral metabolic rate for glucose (LCMRGlc) in humans. A three-compartment model, which incorporates hydrolysis of FDG-6-PO₄ to FDG, was developed by Sokoloff et al. Although small, hydrolysis of FDG-6-PO₄ was found to be significant. A PCT system, the ECAT, was used to determine the rate constants, lumped constant, and stability of the model in human beings. The data indicate that cerebral FDG-6-PO₄ in humans increases for about 90 minutes, plateaus, and then slowly decreases. After 10 minutes, cerebral blood FDG activity levels were found to be a minor fraction of tissue activity. Precursor pool turnover rate, distribution volumes, and red blood cell-plasma concentration rates were determined. Reproducibility (precision) of LCMRGlc measurements (~ 2 cm² regions) was $\pm 5.5\%$ over a 5-hour period. The replacement of arterial blood sampling with venous sampling was validated.

45. Phelps, M.E., Huang, S.C., Kuhl, D.E., Hoffman, E.J. and Selin, C.: Cerebral Extraction of N-13 Ammonia: Its Dependence on Cerebral Blood Flow and Capillary Permeability. Stroke, in press (1980).

^{13}N -labeled ammonia was used to investigate i) the cerebral extraction and clearance of ammonia, ii) the mechanism by which capillaries accommodate changes in cerebral blood flow (CBF) and iii) its use for the measure of CBF. This was investigated by measuring the single pass extraction of $^{13}\text{NH}_3$ in rhesus monkeys during PaCO_2 induced changes in CBF and with dog studies using *in vitro* tissue counting techniques to examine $^{13}\text{NH}_3$ extraction in gray and white matter, mixed tissue and cerebellum during variations in CBF produced by combinations of embolization, local brain compression, and changes in PaCO_2 . The single pass extraction fraction of $^{13}\text{NH}_3$ varied from about 70 to 20% over a CBF range of 12 to 140 cc/min/100gms. Capillary permeability-surface area product (PS) estimates from this data and the dog experiments with a Renkin/Crone model show PS increasing with CBF. The magnitude and rate of increase in PS with CBF was highest in gray matter > mixed tissue > white matter. Tissue extraction of $^{13}\text{NH}_3$ vs CBF relationship was best described by a unidirectional transport model in which CBF increases by both recruitment of capillaries and by increases of blood velocity in open capillaries. This saturable-recruitment model provides a possible explanation for the mechanism of flow changes at the capillary level. Glutamine synthetase, which incorporates $^{13}\text{NH}_3$ into glutamine appears to be anatomically located in astrocytes in general and specifically in the astrocytic pericapillary end-feet that are in direct contact with gray and white matter capillaries. The net $^{13}\text{NH}_3$ extraction subsequent to an i.v. injection increases nonlinearly with CBF. Doubling or halving basal CBF produced from 40 to 50% changes in the ^{13}N tissue concentrations with further increases in CBF associated with progressively smaller changes in ^{13}N concentrations. $^{13}\text{NH}_3$ appears to be a good tracer for the detection of cerebral ischemia with positron tomography but exhibits a poor response at high values of CBF.

46. Phelps, M.E., Huang, S.C., Kuhl, D.E., Hoffman, E.J. and Selin, C.: Cerebral Extraction of (N-13) Ammonia (NH): Dependence on Cerebral Blood Flow and Capillary Permeability-Surface Area Product (PS). *J. Nuc. Med.* 21:69 (1980).

We have systematically examined the mechanisms of transport, metabolism and removal of $^{13}\text{NH}_3$ and its uses as a biological tracer in the brain. The cerebral extraction and clearance was measured by the single pass extraction fraction (E) technique in monkeys, and in dogs by the use of the μ sphere flow model. E for whole brain was determined at different PaCO_2 induced levels of cerebral blood flow (CBF). Net extraction of $^{13}\text{NH}_3$ was measured in gray and white matter, mixed tissue and cerebellum when CBF variations were produced by embolization, local brain compressions

and P_{aCO_2} in dogs. E for $^{13}NH_3$ varied from 70-20% over a CBF range of 12 to 140cc/min/100gms. Estimates of PS with a Renkin/Crone model showed it increasing with CBF: the magnitude and rate of increase was highest in gray matter > mixed tissue > white matter. From these data we have proposed a new unidirectional transport model in which CBF increases by recruitment of capillaries and increases of blood velocity. This saturable-recruitment (SR) model provides a possible explanation for the mechanism of flow changes at the capillary level. The local ^{13}N tissue concentration after an i.v. injection increases nonlinearly with CBF: doubling or halving basal CBF produced from 40 to 50% changes, and further increases in CBF were associated with smaller changes. $^{13}NH_3$ appears to be a good tracer for the detection of cerebral ischemia with positron tomography but exhibits a poor response at high CBF. Because $^{13}NH_3$ is specific to capillaries, PS dependent, rapidly incorporated into glutamine in astrocytic pericapillary end feet and has a long retention time, it has provided a new method to examine capillary mechanisms.

47. Phelps, M.E., Kuhl, D.E., Mazziotta, J.C.: Metabolic Mapping of the Brain's Response to Visual Stimulation: Studies in Man. Science, in press (1980).

These studies showed for the first time in man, increasing glucose metabolic rates in the primary (PVC) and associative (AVC) visual cortex as the complexity of visual scenes increases. The metabolic response of the AVC increased more rapidly with scene complexity than that of the PVC, indicating the greater involvement of the higher order AVC for complex visual interpretations. Increases in local metabolic activity up to a factor of 2, compared to controls with eyes closed, indicate the wide range and metabolic reserve of the visual cortex.

48. Phelps, M.E., Kuhl, D.E. and Mazziotta, J.: Tomographic Mapping of the Metabolic Changes in the Visual Cortex During Visual Stimulation of Volunteers and Patients with Visual Deficits. J. Nuc. Med. 21:21 (1980).

Positron computed tomography (PCT), F-18 fluorodeoxyglucose and an extension of Sokoloff et al's model provide an *in vivo* method that now allows the study of local metabolic function of the human brain. We have previously measured all of the rate constants and validated the precision ($\pm 4\%$ s.d.) for the measurement of the local (~ 1.5 cm²) cerebral metabolic rate for glucose (LCMRGlc) in man. In 9 volunteers, LCMRGlc was measured in the primary (area 17) and associative (areas 18 & 19) visual cortex during eyes closed and open to an oscillating checker board pattern. This visual evoked metabolic response (VEMR) generally showed good correlation to EEG visual evoked potential

(VEP). However, there were clearly instances when the two were not correlated, e.g., high VEP with low VEMR: equal VEP with one and two eye stimulation, whereas the VEMR from the two eye stimulations equaled 1.5 times the one eye value. Patients (5) with homonymous hemianopsia and structurally intact visual cortex by x-ray CT, clearly showed metabolic deficits (20-40% below normal) in the contralateral visual cortex consistent with their field cuts, exhibited high LCMRGlc in the functioning visual cortex, and generally the impaired visual cortex showed no or low metabolic responses to visual stimulation. Variable LCMRGlc patterns of the visual cortex were found in patients with acquired and congenital blindness or with visual aura. The ratio of LCMRGlc of left to right visual cortex was 1.03 ± 0.04 for one eye stimulation (normal two eye stimulation 1.02 ± 0.04), confirming that man has a 50% left-right crossing of the visual system. This technique provides an exciting new tool for investigation of local cerebral function in man.

49. Phelps, M.E., Mazziotta, J.C., Kuhl, D.E., Nuwer, M., Packwood, J. and Metter, J.: Tomographic Mapping of the Metabolic Response of the Visual Cortex to Stimulation: Studies in Man. Ann. Neurol., in press (1980).

These studies have shown for the first time in man, that metabolic activity of the visual cortex increases as the complexity of the visual scene increases. White light stimulation produced only modest increases in the metabolic activity of the PVC and even smaller increases in the AVC which is consistent with the fact that white light intensity discrimination primarily occurs at the level of the lateral geniculate and the superior colliculus. As the scene complexity increased to the moving edges and spatial frequency discrimination of the alternating black and white checkerboard pattern and finally to the complex visual scene of a park, there was a concomitant increase in the metabolic activity of both the PVC and AVC. A progressive metabolic response to the alternating checkerboard pattern was also observed as the input to the visual cortex increased from partial transmission from one eye (i.e. anterior PVC of blind subject), to complete transmission from one eye and to the largest increases with complete transmission from both eyes. This result, obtained with a constant stimulus, appears to demonstrate a progressive metabolic response of the visual cortex to graded increases in the number of input channels.

50. Phelps, M.E., Mazziotta, J., Miller, J. and Kuhl, D.E.: Comparison of Quantitative Transaxial and Coronal Position Tomography of the Brain. J. Nuc. Med. 21:15 (1980).

The compromises between in-plane resolution, axial resolution, statistical noise, radiation dose and imaging time in computed

tomography (CT) have resulted in ratios of plane thickness to in-plane resolution of 1 to 2 in emission CT and 4 to 10 in x-ray CT. The poorer resolution in slice thickness is accepted so that sufficient detection efficiency is provided to meet the high statistical requirements of CT. However, optimum orientation of resolution depends upon the orientations, shapes and sizes of the structures under study. We have developed a way to directly record and reconstruct coronal tomographic sections with our whole body positron tomography. The subject lays on his stomach with his chin resting in a foam rubber head holder such that the tomographic image plane is orthogonal to the orbital meatus and to the conventional transaxial image plane (i.e. orientation of coronal planes). Studies were carried out with (F-18) fluorodeoxyglucose (FDG) in normal volunteers in which tomographic images were taken at 1 cm intervals in both the transaxial and coronal direction throughout the entire intracranial compartment. The coronal images taken in this manner are of much higher quality than if they had been formed by reorganizing transaxial images using the method of Glenn et al. The coronal images show the best delineation of structures that have their smallest dimension primarily in the vertical direction while the transaxial approach is best for those structures where this is the case in transverse direction. The best approach therefore depends on the primary structures of interest.

51. Ricci, A.R., Hoffman, E.J., Phelps, M.E., Henze, E., Low, G.C., Carson, R.E., Meadors, A.K., Schelbert, H.R. and Kuhl, D.E.: Positron Emission Computed Tomography of the Heart: Quantitation with ECG Gated and Multiple Gated Images. J. Nuc. Med. 21:100 (1980).

Quantification and interpretation of Positron Emission Computed Tomography (PCT) images of the heart can be seriously impaired if the technique is applied with inadequate compensation for heart motion. Accordingly, an ECG gating system was designed and built which was suited to the requirements of our PCT system. This system is designed to dynamically track the length of the cardiac cycle, buffering the effect of irregular beats by averaging over a user-selectable number of cardiac cycles. To provide maximum temporal information in multiple gated studies from a limited number of image frames (8), the cardiac cycle is divided into 32 parts which the user can distribute appropriately among the 8 image frames.

Images of blood pool labelled with C-11 carbon monoxide obtained in a multiple gated data collection mode allow visualization of mechanical motion of heart with higher degree of regionality than conventional imaging. Valve plane between right ventricle and right atrium can be delineated because of the distinct motion of the two chambers, providing a method to increase accuracy in measurements of right

ventricular ejection fractions. Left ventricle ejection fractions were observed to vary from 40 to 80% from base to apex of heart in normals, suggesting a more sensitive index of heart function in distal portion of left ventricle.

The general problem of quantification of radioisotopes in myocardium in PCT will be reviewed and estimates of nature and magnitude of important sources of error will be presented.

52. Ricci, A.R., Hoffman, E.J., Phelps, M.E., Low, G.C. and Kuhl, D.E.: Emission Computed Tomography Simulator. IEEE Trans. Nuc. Sci. 27:479-484 (1980).

We have designed and built a system to simulate emission computed tomography (ECT) devices and measure physical parameters of the component parts in such systems. It consists of a heavy duty X, Y, Z, θ scanning table under computer control through CAMAC with modular NIM electronics for signal processing. The modular approach allows ready reconfigurations of detectors and lead shielding to test new design concepts. Direct computer control allows simulation of complex scanning motions and detector geometries by motion of the object rather than the detectors as well as ready capability in data analysis. A study is presented in which the simulator shows a significant increase in signal to noise ratio in a commercial tomograph by small changes in lead shield geometry.

53. Ricci, A.R., Hoffman, E.J., Phelps, M.E., Low, G.C. and Kuhl, D.E.: Emission Computed Tomography Simulator. 1979 Nuclear Science Symposium, October 1-19, San Francisco (1979).

A system has been designed to simulate emission computed tomography (ECT) devices and to measure physical parameters of the component parts in such systems. It consists of a heavy duty X, Y, Z, θ scanning table under computer control through CAMAC with modular NIM electronics for signal processing. The modular approach allows ready reconfigurations of detectors and lead shielding to test new design concepts. Direct computer control allows simulation of complex scanning motions and detector geometries by motion of object rather than detectors as well as ready capability in data analysis. A study is presented in which the simulator shows a significant increase in signal to noise ratio in a commercial tomograph by small changes in lead shield geometry.

54. Robinson, Jr., G.D.: In Vivo Tracer Studies of Myocardial Metabolism. In Biochemical and Chemical Studies with Short-Lived Radioisotopes, Washington, D.C.: American Chemical Society (1979).

Many different compounds can serve as substrates for myocardial metabolism. The complex biochemistry of myocardial metabolism results from a shifting between aerobic and anerobic metabolic modes, depending upon the composition of the available substrate pool.

Fatty acids have been labeled with a variety of short-lived radio-nuclides and evaluated as tracers of myocardial perfusion and metabolism. The success of these studies has been limited by the inability to distinguish between alternative metabolic pathways (triglyceride synthesis, β -oxidation, etc.). Labeled glucose analogs, such as F-18 labeled 2-deoxy-2-fluoro-D-glucose, have been used to assess myocardial glucose utilization. This is possible because the appropriately designed analogs compete with glucose for transport into and phosphorylation within myocardial cells. N-13 labeled ammonia is efficiently extracted by the heart and a substantial fraction of the label is rapidly incorporated into diverse chemical forms, primarily amino acids. Labeled amino acids, themselves, can be taken up by the myocardium.

55. Robinson, Jr., G.D.: Tracers for In Vivo Quantification of Myocardial Metabolism. National Meeting of the American Chemical Society, Washington, D.C., abstract (1979).

Many different compounds can serve as substrates for myocardial metabolism. The complex biochemistry of myocardial metabolism results from a shifting between aerobic and anerobic metabolic modes, depending upon the composition of the available substrate pool.

Fatty acids have been labeled with a variety of short lived radio-nuclides and evaluated as tracers of myocardial perfusion and metabolism. The success of these studies has been limited by the inability to distinguish between alternative metabolic pathways (triglyceride synthesis, β -oxidation, etc.). Labeled glucose analogs, such as F-18 labeled 2-deoxy-2-fluoro-D-glucose, have been used to assess myocardial glucose utilization. This is possible because the appropriately designed analogs compete with glucose for transport into and phosphorylation within myocardial cells. N-13 labeled ammonia is efficiently extracted by the heart and a substantial fraction of the label is rapidly incorporated into diverse chemical forms, primarily amino acids. Labeled amino acids, themselves, can be taken up by the myocardium.

56. Robinson, Jr., G.D. and Lee, A.W.: Reinvestigation of the Preparation of ^{131}I -4-iodoantipyrine from ^{131}I -iodine. Inter. J. Appl. Radiat. & Isot. 30:365-367 (1979).

Radioiodine labeled 4-iodoantipyrine (4-IAP) is rapidly formed from radioiodide and nonradioactive 4-IAP or 4-bromoantipyrine (4-BrAP)

at 100°C in acidic aqueous solution. Quantitative conversion to labeled 4-IAP is observed between pH 2 and 6 when 4-IAP is the non-radioactive starting material. This is in contrast to previous reports which found rapid incorporation only under limited conditions. When 4-BrAP is used, maximum yields of 80% are found between pH 1.5 and 2.5. Mechanistic implications of these differences are not clear. Labeled 4-IAP (> 98% radiochemically pure) is separated from radioiodide by TCL or anion-exchange chromatography.

57. Robinson, Jr., G.D., Lee, A.W. and Zielinski, F.W.: The Zinc-62/Copper-62 Generator: A Convenient Source of Copper-62 for Radiopharmaceuticals. Inter. J. Appl. Radiat. & Isot. 31:111-116 (1980).

^{62}Cu is a short-lived (9.8 min) positron emitter which results from the decay of ^{62}Zn (9.2 h). ^{62}Zn is easily produced in good yield (2.3 mCi/ μAh) by bombardment of a 0.4 mm thick target of natural copper with 22 MeV protons. A simple separation of zinc and copper as chloride complexes using anion exchange chromatography is described.

The performance of $^{62}\text{Zn}/^{62}\text{Cu}$ generator system based upon a similar anion exchange separation is evaluated. Using a 0.7 cm i.d. x 8.0 cm high column of "Dowex 1-X10" resin of 200-400 mesh, eluted with 0.1 N HCl containing 100 mg/ml NaCl and 1 $\mu\text{g}/\text{ml}$ CuCl_2 over 85% of the available ^{62}Cu is recovered in a 3.5 ml volume. The ^{62}Zn level is less than 0.001% at the time of elution. A variety of potentially useful radiopharmaceuticals using this generator system have been developed and are being evaluated in clinical trials.

58. Robinson, Jr., G.D., Phelps, M.E. and Huang, S.C.: 18F-2-Deoxy-2-Fluoro-D-Mannose: Biological Behavior Compared with 2-Deoxy-2-Fluoro-D-Glucose. J. Nuc. Med. 20:672, abstract (1979).

F-18 labeled 2-deoxy-2-fluoro-D-glucose (FDG) can be used to assess regional glucose utilization in humans *in vivo*. Steric considerations suggest that 2-deoxy-2-fluoro-D-mannose (FDM), which is produced during FDG syntheses, may have a biological behavior analogous to that of FDG. *In vitro* enzymatic studies verify that FDG is a substrate for phosphorylation by hexokinase.

F-18 labeled O-acetylated precursors of FDG and FDG were produced by reaction between F-18-fluorine and triacetyl glucal in "Freon 11" solution at -80°C. The compounds were separated using silica gel column chromatography and labeled FDG and FDM were obtained by subsequent acid hydrolysis. TLC analyses verified that FDG and FDM had radiochemical purities greater than 90%.

The biological behaviors of FDG and FDM were compared in rats by tissue sampling a 5, 15, 30 and 60 and 120 min post IV injection. Brain and heart uptakes, with renal excretion of the label, were noted for both compounds. Using 5 rats for each compound at each time interval, the tissue dynamics were indistinguishable. The behaviors of FDG and FDM were compared following IV injection in humans using the ECAT system with kinetic analysis of brain uptakes using a three compartment model. The tomographic brain images were similar for both compounds as were rates and amounts of brain uptake. Calculated rate constants for intercompartmental transport of FDM were approximately twice those for FDG. The results suggest that FDM may be a suitable tracer for glucose utilization studies.

59. Sattsangi, P.D., Barrio, J.R. and Leonard, N.J.: 1, N⁶-Etheno-Bridged Adenines and Adenosines. Alkyl Substitution, Fluorescence Properties, and Synthetic Applications. J. Amer. Chem. Soc. 102:770-774 (1980).

It has been shown that the reaction of chloroacetaldehyde with adenosine at pH 4.5 and 37°C that produces the fluorescent ϵ -adenosine species will not develop interfering fluorescence with N⁶-alkyladenosines. The preferred site of methylation and benzylation of ϵ -adenosine and ϵ -adenine was established as N(9) (a) by acidic ring opening of the products to substituted aminobimidazoles in which the two etheno protons were nonequivalent; (b) by reaction of N⁶-substituted adenines with chloroacetaldehyde followed by polyphosphoric acid to dehydrate the intermediate to an N(9)-substituted ϵ -adenine for an unequivocal synthesis. The fluorescence of the ϵ -adenosine and ϵ -adenine species at pH 7.0 has again been confirmed, and the fluorescence properties of their N(9)-alkylated derivatives under neutral and acidic conditions have been determined. It has been shown possible, earlier reports to the contrary, to prepare N⁶-substituted adenosines through Schiff-base formation on the 6-NH₂. The general method involves the use of sodium cyanohydrinborate to bring about reductive amination of aldehydes and ketones at acidic pH and is exemplified by the synthesis of N⁶-benzyladenosine- and N⁶-furfuryladenosine (kinetin riboside), using large excesses of aldehyde and reducing agent.

60. Schelbert, H.R. and Henning, H.: Imaging of Acutely Ischemic Myocardium, Myocardial Infarction and Its Complications. In Clinical Strategies in Ischemic Heart Disease - New Concepts and Current Controversies, Corday, E and Swan, H.J.C. eds. Baltimore-London: Williams and Wilkins, pp. 252-261 (1979).

This book chapter discusses a number of radionuclide techniques which can be useful in the diagnosis and management of patients

with acute myocardial infarction. Specifically, complications occurring during the early post-infarction period are described and their evaluation by radionuclide techniques discussed.

61. Schelbert, H.R., Henze, E. and Phelps, M.E.: Emission Tomography of the Heart. Seminars in Nuclear Medicine, in press (1980).

This invited review describes the state of the art in emission computed tomography of the heart. It discusses the current achievements with single photon emission tomography and emphasizes the value of positron emission tomography for the noninvasive measurement of regional myocardial blood flow, assessment of regional myocardial mechanical function and its value in studying myocardial carbohydrate, free fatty acid and amino acid metabolism.

62. Schelbert, H.R. and Phelps, M.E.: N-13 Ammonia for the Noninvasive Evaluation of Myocardial Blood Flow by Positron Emission Computed Tomography. Proceedings of the International Symposium on Microcirculation, January, Heidelberg (1980).

This invited paper describes the kinetics of N-13 ammonia in myocardium and provides an explanation for the uptake mechanism of N-13 ammonia in myocardium. The studies described in this paper are based on open chest dog experiments and the single pass extraction fraction of N-13 ammonia. It specifically deals with the aspects of metabolic trapping of N-13 ammonia in myocardium and concludes that metabolic trapping of this flow indicator is relatively constant over a wide range of hemodynamic and metabolic alterations.

63. Schelbert, H.R. and Phelps, M.E.: Noninvasive Measurement of Regional Myocardial Glucose Metabolism by Positron Emission Computed Tomography. Proceedings of the International Symposium on Microcirculation, January, Heidelberg (1980).

This invited paper describes the approach developed at UCLA for the assessment of regional myocardial glucose metabolism with positron emission computed tomography and F-18 2-deoxyglucose. The observations and conclusions presented in this paper are based on animal experiments with pacing induced acute myocardial ischemia.

64. Schelbert, H.R. and Phelps, M.E.: Physiologic Tomography: A New Means for the Non-invasive Measurement of Myocardial Metabolism, Blood Flow and Function. Eur. J. Nuc. Med. 5:209-215 (1980).

This invited review discusses positron emission tomography as a new means for studying myocardial physiology. It specifically describes the capabilities of positron emission tomography for the assessment of regional myocardial function, myocardial blood flow and metabolism

and discusses the future potential of this new imaging modality for studying cardiovascular physiology in health and disease and the possibility for establishing the metabolic link between substrate delivery and mechanical function.

65. Schelbert, H.R., Phelps, M.E., Hoffman, E.J. and Huang, S.C.: Regional Myocardial Perfusion Assessed by Nitrogen-13 Labeled Ammonia and Positron Emission Computerized Tomography. In Frontiers of Nuclear Medicine, Horst et al eds. Berlin, Heidelberg, New York: Springer, pp. 20-34, in press (1980).

This paper, which has been submitted for the Von Hevesy Prize, is to be published in a book entitled: Frontiers in Nuclear Medicine, edited by Horst et al. It describes the usefulness of N-13 ammonia as an indicator of regional myocardial blood flow that is suitable for positron emission tomography and compares in vitro results to those obtained with positron emission tomography in the experimental animal.

66. Scheibert, H.R., Phelps, M.E., Hoffman, E.J., Huang, S.C., Selin, C. and Kuhl, D.E.: Regional Myocardial Perfusion Assessed by N-13 Ammonia and Positron Emission Computerized Axial Tomography. Amer. J. Cardiol. 43:209-218 (1979).

This manuscript provides an overview of the state of the art in positron emission computed tomography of the heart. Specifically, it emphasizes the advantages of this new imaging modality over conventional imaging and focuses on the assessment of regional myocardial metabolism in ischemic heart disease.

67. Schelbert, H., Phelps, M., Huang, H., Hoffman, E., Selin, C., Hansen, H. and Kuhl, D.: N-13 Ammonia as an Indicator of Flow: Factors Influencing Its Uptake and Retention in Myocardium. J. Nuc. Med. 21(6):89-90, abstract (1980).

Previously we characterized N-13 ammonia (NA) as an indicator of myocardial blood flow (F) suitable for positron tomography. In this study we examined the effects of changes in F, the cardiac hemodynamic and metabolic state and in plasma pH on the extraction fraction (E) and clearance-time (T) of NA in myocardium. In 155 studies in 35 dogs NA was injected into the circumflex coronary artery. E and T were determined from the peak and slope of the residue function of the myocardial time-activity curve recorded with a scintillation probe. During its initial capillary transit NA was nearly 100% extracted followed by F related back diffusion that competed with metabolic trapping. E is the ratio of NA retained in myocardium to total injected NA. At F of 0.8 ml/min/gm, E averaged 0.87 ± 0.05 SD and T 4.8 ± 0.6 hrs. Both were

inversely related to F by $E = -0.607 \exp(-125/F)$ and $T = 358 \exp(-0.00027 \times F)$. Cardiac work, heart rate, propranolol, isoproterenol and changes in glucose uptake had no effect on E and T. High plasma pH (7.46 - 7.66) did not affect E and T but E fell by 16% ($p < 0.01$) at low plasma pH (7.03 to 7.12). Glutamine synthetase inhibition by methionine sulfoximine depressed E indicating that NA is fixed in myocardium by amination of glutamate to glutamine. Thus, metabolic trapping is important for fixation of NA in myocardium but over a wide range of conditions it is not affected by changes in cardiac metabolism and function. We conclude that T and E of NA are mainly related to F. The near linear relationship between $E \times F$ and F at physiologic F's confirms the suitability of NA as a flow indicator.

68. Schelbert, H.R., Phelps, M.E. and Kuhl, D.E.: Positron Emission Tomography of the Heart. A New Method for the Noninvasive Assessment of Regional Myocardial Blood Flow, Function and Metabolism. In Clinical Nuclear Cardiology, Berman, D.S. and Mason, D. eds., in press (1980).

This book chapter describes the use of positron emission tomography for the study of regional myocardial metabolism. Specifically, it discusses the potential value of this new imaging modality for the assessment of regional metabolic derangements in myocardium. It stresses the potential applicability in patients with acute myocardial infarcts for the detection of a metabolic border zone that can be detected with positron emission tomography. Moreover, it emphasizes the use of this new technique for evaluating currently proposed techniques for salvaging reversibly injured myocardium.

69. Schelbert, H.R., Phelps, M.E., Robinson, Jr., G.D., Hoffman, E., Hansen, H., Selin, C. and Kuhl, D.: Metabolic Changes in Acute Regional Myocardial Ischemia Determined by F-18 Deoxyglucose (FDG) and C-11 Palmitate (CPA) and Positron Emission Tomography. J. Nuc. Med. 21:90, abstract (1980).

In acute myocardial ischemia glycolysis is known to increase while β -oxidation of free fatty acids (FFA) declines. The potential of positron emission tomography (PCT) to noninvasively demonstrate these changes was studied in 9 dogs. Ischemia was induced by stenosing the anterior descending coronary (LAD) and atrial pacing. Oxygen (O_2), glucose (GLU) and FFA consumption and lactic extraction in LAD myocardium were determined from the A-V differences and blood flow (MBF) measured by microspheres. To compare MBF to metabolism by PCT, ischemia was induced twice: For PCT imaging of 1) MBF with N-13 ammonia; and 2) local GLU or FFA uptake with FDG or CPA. With pacing MBF in LAD myocardium fell by 20.3% (ns),

consumption of O by 30.2% (ns), and of FFA by 62.8% ($p < .01$). GLU uptake increased by 63.8% ($p < 0.05$). Lactic acid extraction fell by 88.3% ($p < 0.01$). On the PCT images, MBF and FDG or CPA concentrations fell in LAD myocardium; CPA concentrations matched MBF while FDG concentrations were in excess of MBF. Using *in vitro* tissue counting, FDG and CPA concentration were linearly related to MBF. However, at MBF < 3 to 6 ml/min/gm the linear relationship was maintained for CPA while FDG concentrations were in excess of MBF. Thus, FFA uptake in ischemia is proportional to MBF, while GLU uptake increases above MBF. PCT clearly delineated these regional changes in FFA and GLU metabolism. We conclude that PCT may permit noninvasive characterization of metabolic changes associated with acute myocardial ischemia.

70. Schelbert, H., Phelps, M., Selin, C., Hoffman, E. and Kuhl, D.: Glucose Metabolism of Regional Myocardial Ischemia Evaluated by ^{18} Fluoro-2-Deoxyglucose and Positron Emission Computed Tomography. Amer. J. Cardiol. 45(2):465, abstract (1980).

Glycolysis is known to increase in acute myocardial ischemia. The possibility of demonstrating this metabolic alteration noninvasively by positron emission computed axial tomography (PCT) and the glucose analog ^{18} fluoro-2-deoxyglucose (FDG) was examined in 5 dogs. Ischemia was induced by stenosing the anterior descending coronary artery (LAD) and atrial pacing. O_2 and glucose consumption and lactic acid production in the LAD distribution were determined by arterial and coronary venous blood sampling and myocardial blood flow (MBF) by microspheres. Ischemia was induced twice in each dog: for assessment of a) MBF by $N-^{13}$ ammonia and PCT and b) regional myocardial glucose uptake by PCT imaging of the myocardial FDG distribution. During pacing, MBF increased in normal myocardium by 27.5%, but fell in the LAD distribution from 83.2 to 62.7 ml/min/gm ($p < .03$). MVO_2 fell from 8.4 to 6.6 ml/min/100gm ($p < .01$). Glucose consumption increased from 1.97 to 7.64 mg/min/100gm ($p < .03$). Lactic acid production was variable but increased for the entire group (0.97 to 1.98 mg/min/100gm; NS). On the PCT images MBF in the LAD distribution decreased by 47.2% but FDG concentration by only 18.6% ($p < .01$) as compared to control segments. This "mismatch" was clearly visualized by PCT. Using *in vitro* tissue counting, FDG concentrations in normal myocardium were related linearly to MBF. In segments with MBF's < 60 ml/min/100gm the FDG:MBF ratio was 2.3 times above control ($p < .01$). Thus, a relative increase in glucose uptake occurs in acute myocardial ischemia that can be demonstrated noninvasively by PCT. We conclude that FDG and PCT may permit characterization of the changes in regional metabolism associated with acute myocardial ischemia.

71. Schelbert, H.R., Phelps, M.E., Selin, C., Marshall, R.C., Hoffman, E.J. and Kuhl, D.E.: Regional Myocardial Ischemia Assessed by ^{18}F -Fluoro-2-Deoxyglucose and Positron Emission Computed Tomography. In Advances in Clinical Cardiology Volume 1: Quantification of Myocardial Ischemia, Kreuzer, H., Parmley, W.W., Rentrop, P. and Weiss, H.W. eds. New York: Gerhard Witstrook Publishing House, pp. 437-449 (1980).

In acute myocardial ischemia an increase in glycolytic flux is known to occur. It was the purpose of this study to examine the possibility of demonstrating this metabolic alteration noninvasively by positron emission computed axial tomography (PCT) and ^{18}F -2-deoxyglucose (FDG) as an indicator of glucose metabolism. Acute regional myocardial ischemia was induced experimentally in open-chest dogs by partial constriction of the left anterior descending coronary artery and left atrial pacing at rates of up to 200 beats/min. In each animal ischemia was induced twice, first for assessment of regional myocardial perfusion with ^{13}N -ammonia and PCT imaging and second (1 h later) for assessment of regional myocardial distribution of FDG. In the ischemic segment myocardial blood flow (MBF) was reduced as indicated by ^{13}N -ammonia and radioactive microsphere concentrations. Similarly, FDG concentrations were lower in the ischemic segment yet to a much lesser degree than MBF. This "mismatch" was further demonstrated by subsequent in vitro measurements showing a close linear relationship between MBF and FDG concentrations in normal myocardium. In segments with low MBF (<30 ml/min/100g), however, FDG concentrations were considerably in excess of MBF, suggesting a relative increase in glycolytic flux probably due to both anerobic and aerobic metabolism. It is concluded that metabolic alterations associated with acute regional myocardial ischemia can be demonstrated noninvasively by PCT and that this technique may permit a more quantitative assessment of the extent and severity of acute regional myocardial ischemia.

72. Schelbert, H.R., Schuler, G., Ashburn, W.L. and Covell, J.W.: Time-Course of "Redistribution" of Thallium-201 Administered During Transient Ischemia. Eur. J. Nuc. Med. 4:351-358 (1979).

The "redistribution" of ^{201}Tl administered as a single dose during treadmill exercise and monitored by external imaging may permit differentiation between transient ischemia and old myocardial infarction. The time course of this "redistribution" of ^{201}Tl was examined in 20 closed chest dogs instrumented with indwelling left atrial catheters and occlusive cuffs placed around the proximal left circumflex coronary artery. In 15 of the dogs ^{201}Tl and ^{85}Sr microspheres (15 μ) were injected during transient coronary artery occlusion: Five of the dogs were sacrificed 2 min later

without releasing the occlusion; five dogs were sacrificed after 30 min and five dogs after 4 h of reperfusion. Five dogs with permanent occlusion of the left circumflex coronary artery were studied 4 h after Tl-201 administration. Compared to normal myocardium Tl-201 activity in regions with >95% flow reductions was decreased by 93.3% in the five dogs sacrificed 2 min after administration. After 30 min of reperfusion this difference was 59.7% and was only 16.5% after 4 h of reperfusion. During the initial 30 min of reperfusion this change in regional distribution was due to a 22% fall in activity in normal myocardium and a 4.4 fold increase in the transiently ischemic myocardium. Activity in normal myocardium declined further by 63% from 30 to 240 min of reperfusion while activity in the transiently ischemic myocardium decreased by 15.5%, although this change was statistically not significant. Thus, early "redistribution" of Tl-201 reflects active uptake of Tl-201 by transiently ischemic tissue and decrease in Tl-201 activity in normal myocardium. During late reperfusion redistribution is primarily due to a more rapid loss of Tl-201 from normal myocardium. We conclude that transient ischemia is visualized best early after stress. Imaging begun late after exercise, e.g., after 30 min, may not permit differentiation between transient ischemia and old myocardial infarction.

73. Schelbert, H., Wisenberg, G., Gould, L., Marshall, R., Phelps, M., Hoffman, E., Gomes, A. and Kuhl, D.: Detection of Coronary Artery Stenosis in Man by Positron Emission Computed Tomography and N-13 Ammonia. Circulation 60(4):60, abstract (1980).

The capability of positron emission computed axial tomography (PCT) and N-13 ammonia (NA) of detecting 47% diameter coronary stenosis has been demonstrated in animals. In this study the technique was evaluated in 5 normal volunteers (21-31 years) and 18 pts with coronary artery disease (CAD) (31 to 68 yrs). Ten pts had one-, 3 two-, and 5 three-vessel disease with a total of 31 coronary stenoses (40-100%). Cross-sectional myocardial images were obtained with PCT and NA at control (C) and during dipyridamol induced hyperemia (H). In the 5 normals, no perfusion defects were seen at C. or H. In 16 of 18 CAD pts the H images showed new or more extensive defects and of the 31 coronary stenoses, 24 were correctly identified. Six of 10 pts with single vessel disease had abnormal H images, two with 50-55% stenosis. In 7 pts with 3 vessel disease the least severe stenosis was not detected in 4 pts. The results indicate the usefulness of PCT and NA for detecting and localizing coronary stenoses. Quantification of myocardial blood flow with PCT may further enhance the sensitivity in identifying coronary stenosis and permit assessment of its severity.

74. Schelbert, H.R., Wisenberg, G. and Henze, E.: Imaging with Infarct Avid Agents. Critical Reviews in Diagnostic Imaging, in press (1980).

This invited review describes the current state of the art of infarct avid imaging. After discussing the development of radiopharmaceuticals that specifically localize in acutely infarcted myocardial tissue, it focuses on the mechanisms of uptake of Tc-99m Sn pyrophosphate, describes the normal and abnormal scintigraphs and the potential value of this new technique in the detection and sizing of acute myocardial infarcts in patients.

75. Schelbert, H.R., Wisenberg, G., Henze, E., Hansen, H., Selin, C., Marshall, R.C., Phelps, M.E., Hoffman, E., Huang, H. and Kuhl, D.E.: Positron ECT of the Heart: Work at UCLA. In Positron, Single-Photon, and Pinhole Emission Tomography, Kuhl, D.E. ed., in press (1980).

This book chapter describes the current research program and results of positron emission tomography of the heart. It specifically mentions our results with N-13 ammonia as an indicator of myocardial blood flow in the experimental animal and in patients with coronary artery disease, the noninvasive measurement of absolute myocardial indicator concentrations and the potential value of positron emission tomography for the assessment of regional metabolic derangements associated with acute myocardial ischemia.

76. Schelbert, H.R., Wisenberg, G. and Marshall, R.C.: Assessment of Ventricular Function by Radionuclide Techniques. In Progress in Nuclear Medicine - Cardiovascular Nuclear Medicine, Righetti, A., Donath, A. and Serafini, A. eds. Basel: S. Karger, in press (1980).

This book chapter describes the various radionuclide techniques that are currently in use for the noninvasive assessment of cardiac function. Specifically, it describes the technical aspects, potential sources of errors and indication of first pass radionuclide angiography and equilibrium blood pool imaging. In addition, potential applications and indications for the diagnosis and management of cardiac disease are discussed.

77. Schelbert, H.R., Wisenberg, G., Phelps, M.E., Gould, K.L., Marshall, R.C., Hoffman, E.J. and Kuhl, D.E.: ^{13}N -Ammonia and Positron Emission Computed Axial Tomography for the Noninvasive Assessment of Coronary Artery Disease in Humans. In Advances in Clinical Cardiology: Quantification of Myocardial Ischemia, Kreuzer, H., Parmley, W.W., Rentrop, P. and Weiss, H.W. eds. New York: Gerhard Witstroock Publishing House, Vol. 4, pp. 394-426 (1980).

^{13}N -Ammonia previously has been described as an indicator of myocardial blood flow suitable for positron emission computed tomography (PCT). Previously we demonstrated the capability of ^{13}N -ammonia and PCT for demonstrating mild, 47% diameter coronary stenosis in the experimental animal and evaluated in this study the feasibility of this technique in man. Five normal volunteers and nine patients with arteriographically documented coronary artery disease were studied at control and during dipyridamole-induced coronary vasodilatation. In the normals, left ventricular ^{13}N -ammonia activity was uniform on the cross-sectional images at control and was not altered by hyperemia. By contrast, eight of the nine patients with coronary artery disease (five with single-vessel disease) developed new or more extensive defects on the hyperemic images. Furthermore, on the images obtained during hyperemia the regional myocardial ^{13}N -ammonia concentrations were inversely related to the degree of coronary artery stenosis. We conclude that this new technique is highly suitable for the noninvasive detection of coronary artery disease and may permit quantification of myocardial blood flow and of the severity of coronary artery stenosis.

78. Schön, H.R., Marshall, R.C. and Schelbert, H.R.: Radionuclide Imaging of Patients with Acute Myocardial Infarction. Weekly Update in Cardiology, in press (1980).

This invited review critically discusses the use of radionuclide techniques for the noninvasive study of myocardial perfusion and function in patients with acute myocardial infarction.

79. Shine, K.I., Perloff, J.K., Child, J.S., Marshall, R.C. and Schelbert, H.R.: Noninvasive Assessment of Myocardial Function. Ann. Int. Med. 92:78-90 (1980).

Myocardial function can be assessed noninvasively by echocardiography and radionuclide techniques. M-mode echocardiography provides important clues to ventricular volumes, wall thickness, wall motion, ejection fraction, and shortening velocities. The relative movements of posterior wall and septum can be ascertained and several specific cardiomyopathies recognized. M-mode echocardiography gives a limited "ice-pick" view of the left ventricle. Two-dimensional techniques give additional information. Echocardiography is done during rest, while radionuclide procedures are done during rest and exercise. First-pass radionuclide angiography can estimate ventricular ejection fractions independently of geometric assumptions. Equilibrium gated blood pool imaging by multiple gated acquisition techniques allows repeated visual assessment of overall and regional ventricular function. Thallium-201 imaging provides insight into regional myocardial perfusion during rest and exercise but is limited by its resolution and isotope persistence. Newer techniques using $^{13}\text{NH}_3$ promise better approaches to perfusion with tomographic identification or regional changes.

80. Van Derlinjn, P., Barrio, J.R. and Leonard, H.S.: Inhibition of Adenylate Kinase by P^1 -(lin-Benzo-5'-adenosyl)- P^4 -(5'-adenosyl) Tetraphosphate and P^1 -(lin-Benzo-5'-adenosyl)- P^5 -(5'-adenosyl) Pentaphosphate. Biochemistry 18:5557-5561 (1979).

P^1 -(lin-benzo-5'-adenosyl)- P^5 -(5'-adenosyl)pentaphosphate and P^1 -(lin-benzo-5'-adenosyl)- P^4 -(5'-adenosyl)tetraphosphate have been synthesized from lin-benzoadenosine-5'-monophosphormorpholidate and adenosine 5'-tetraphosphate and adenosine 5'-triphosphate, respectively. These mixed dinucleoside polyphosphates are potent inhibitors of porcine muscle adenylate kinase with association constants of $2 \times 10^5 M^{-1}$ for the pentaphosphate and $2 \times 10^6 M^{-1}$ for the tetraphosphate, respectively, as determined by kinetics and fluorescence experiments. The increase in fluorescence intensities and fluorescence lifetimes of both inhibitors upon binding to adenylate kinase results from a breaking of the intramolecular stacking interaction observed when these ligands are free in solution and implicates their binding to the enzyme in an "open" or "extended" form. These results and the dimensional requirements of these inhibitors are discussed in relation to our current knowledge of the active site of adenylate kinase and to the known inhibitors of adenylate kinase, P^1 , P^5 -bis(5'-adenosyl) pentaphosphate and P^1 , P^4 -bis(5'-adenosyl)tetraphosphate.

81. Wisenberg, G., Kovick, R., Child, J., Marshall, R. and Schelbert, H.: Equilibrium Blood Pool Imaging for Studying Rate Dependent Hemodynamic Changes in Patients with Rate Programmable Pacemakers. Circulation 60(4):148, abstract (1980).

Rate programmable pacemakers (RPP) have been implanted in many patients recently. In this study, equilibrium blood pool imaging (EQ) was used to assess the relative changes in end diastolic volume (EDV), and systolic volume (ESV), stroke volume (SV), and cardiac output (CO) when heart rate (HR) alone is increased in patients with RPP. Seven patients were studied, supine, at rest, while heart rate was increased every 5 minutes. The table documents mean volume changes and mean values for ejection fraction and blood pressure (BP).

Rate	EDV	ESV	SV	CO	EF	BP
60	100%	100%	100%	100%	.54 $\pm$ .18	88
70	-6 $\pm$ 6	-5 $\pm$ 16	-9 $\pm$ 15	+7 $\pm$ 19	.51 $\pm$ .14	90
80	-17 $\pm$ 12	-12 $\pm$ 20	-19 $\pm$ 12	+9 $\pm$ 19	.51 $\pm$ .16	89
90	-23 $\pm$ 9	-19 $\pm$ 16	-27 $\pm$ 14	+9 $\pm$ 19	.51 $\pm$ .16	91
100	-29 $\pm$ 9	-18 $\pm$ 14	-37 $\pm$ 12	+4 $\pm$ 20	.48 $\pm$ .17	89

For the whole group, EDV, ESV, and SV decreased as HR increased, but the response varied considerably between patients. We conclude

that EQ permits evaluation of HR-induced hemodynamic changes and may be useful for selecting optimal pacemaker rates in individual patients.

82. Wisenberg, G., Schelbert, H., Hoffman, E., Huang, S.C., Phelps, M., Skorton, D. and Child, J.: Quantitation of Regional Myocardial Blood Flow by Positron Emission Tomography. Am. J. Cardiol. 45(2):465, abstract (1980).

This study was undertaken to demonstrate the ability of positron emission tomography (PCT) to accurately measure myocardial indicator concentrations and thus regional myocardial blood flow (RMBF). Gated PCT imaging was performed in 7 open chest dogs after left atrial injection of gamma-emitting and Ga-68 positron emitting microspheres. Two dogs were studied at control and 5 during circumflex ischemia or hyperemia (RMBF range .01 to 4.7ml/min/gm). RMBF determined in vivo from regions-of-interest on PCT images was compared to RMBF calculated in vitro after sacrifice by tissue counting and the arterial reference technique. According to phantom studies, count recovery with PCT is dependent on object size and thus on wall thickness (WT). Therefore, WT was measured a) postmortem and b) in vivo by echocardiography, 3 dogs having 2-D studies and 4 having M-mode. The echocardiographic diastolic measurements matched precisely the postmortem data. PCT measured RMBF corrected and uncorrected for WT effect correlated with in vitro measured RMBF by $y = .007 + .99x$ (SEE 0.12ml/min/gm), $r = .99$, and $y = .05 + .60x$ (SEE 0.14ml/min/gm), $r = .38$ ($n = 84$), respectively. Count recovery for a given region increased in proportion to the systolic increase in WT, as measured by echocardiogram. We conclude that a) RMBF can be quantitated in vivo by PCT when corrections are made for WT effect; b) these corrections can be made accurately using echocardiographic WT measurements; and c) systolic wall thickening, as an index of regional function, can be estimated from the change in regional count recovery from diastole to systole.

83. Wisenberg, G., Schelbert, H., Selin, C., Hoffman, E., Huang, S.C. and Phelps, M.: The Use of Positron Emission Tomography to Quantify Regional Myocardial Blood Flow. Circulation 60(4):268, abstract (1980).

This study was undertaken to establish the heretofore unproven ability of positron emission tomography (PCT) to accurately measure myocardial indicator concentrations, and thus regional myocardial blood flow (RMBF). Seven open chest dogs were studied with a total of 60 ungated imaging procedures, acquired after left atrial injection of gamma emitting and Cu-62 positron emitting microspheres. Control studies were followed by repeat studies hourly, while circumflex flow was altered from 0.1 to 4.6 ml/min/gm. After sacrifice, RMBF was determined in vitro by the arterial reference

techniques, and compared to RMBF calculated from *in vivo* PCT data. Cts/pixel were converted to cts/gm by a calibration factor and to ml/min/gm using the arterial reference sample. As count recovery by PCT is related to object size, the data was corrected for the effect of wall thickness (WT) using *in vivo* M-mode echocardiographic measurements. Uncorrected PCT data correlated poorly with *in vitro* data ($r=.38$ and $.61$) for anterior and posterior regions respectively while data corrected for WT effect correlated linearly and in a one to one relationship by $y=5.85 + 1.06x$ ($r=.85$) and $y=16.0 + .97x$ ($r=.95$) $n=60$. The results indicate that RMBF can be quantified *in vivo* by PCT if corrections are made for WT effect.

84. Wisenberg, G., Schön, H., Marshall, R., Henze, E. and Schelbert, H.: Value and Limitations of Left Ventricular Function Indices Derived by Exercise Equilibrium Blood Pool Imaging in the Diagnosis of Coronary Artery Disease. *J. Nuc. Med.* 21(6):63-64, abstract (1980).

An abnormal response in ejection fraction (EF) to exercise is considered as both highly sensitive and specific for coronary artery disease (CAD). In this study, we compared the sensitivity (SE) and specificity (SP) of exercise induced changes (Δ) in EF, end diastolic counts (EDC), heart rate corrected - ejection and filling rates (ER and FR), and regional EF (REF) during supine exercise for detection of (CAD) and cardiac disease (CD) in 10 normals (N), 36 CAD patients, and 9 patients with valvular regurgitation (VR). The mean changes in each patient group were:

	Δ EF	Δ EDC	Δ ER	Δ FR
H	$+6.5 \pm 8.4\%$	$-7 \pm 5\%$	$+0.64 \pm .71$	$+1.10 \pm 1.23$
CAD	$-3.7 \pm 9.0^*$	$+22 \pm 12^{**}$	$+0.21 \pm .58^*$	$+0.63 \pm 1.12$
VR	$-6.1 \pm 7.2^*$	-1 ± 17	$+0.16 \pm .46^*$	$+0.25 \pm 0.85^*$

* $p < .05$ ** $p < .001$ to N

Defining Δ EF $< 5\%$; asymmetric REF response with $< 5\%$ increase in at least one region; Δ EDC $> 5\%$; Δ ER $< .65$; and Δ FR 1.10 as abnormal responses, the SE and SP for CAD and CD in this patient population for each parameter were:

	Δ EF	Δ EDC	Δ ER	Δ FR	REF
SE-CAD	86%	100%	75%	75%	94%
SE-CD	87%	71%	76%	87%	75%
SP-CAD	42%	84%	53%	37%	100%
SP-CD	70%	100%	70%	50%	100%

We conclude that 1) ΔEF is sensitive but non-specific for CAD; 2) the variability of ΔER and ΔFR limit their diagnostic value; and 3) in this population, ΔEDC is most sensitive and REF most specific for diagnosing CAD by exercise equilibrium blood pool imaging.

STAFF RECOGNITION AND HONORS

Jean S. de Vellis

Associate Director for Education and Training

Mental Retardation Research Center

Member

American Society for Cell Biology

Chairman

Ad Hoc Promotion Review Committee of the Academic Senate

Review Committee for promotion of tenured faculty (Associate Professor level), Department of Anatomy

Research Training Advisory Committee
Mental Retardation Research Center

Editorial Board

Neurochemical Research

Associate Editor

Journal of Neuroscience Research

Reviewer

Journal of Neurochemistry

Brain Research

Developmental Neuroscience

Experimental Neurology

Journal of Cellular Physiology

Grant Reviewer

CICR

National Foundation, March of Dimes

Invited Speaker

The Bat-Sheva Seminar on Biochemical Development of Nervous Tissue in Culture, The Weizmann Institute of Science, Rehovot, Israel

Developmental Neuroendocrinology Workshop, Seventh Meeting of the International Society for Neurochemistry, Jerusalem, Israel

Molecular Biology Institute,
Pasteur Institute, Paris, France

University of Connecticut
Farmington, Connecticut

Jean S. de Vellis (continued)

Invited Speaker

**Eleventh Annual Meeting, American
Society for Neurochemistry, Houston**

**Paralysis Cure Foundation Workshop on
Nervous System Regeneration, Bermuda**

**Department of Physiological Chemistry
University of Wurzburg, Germany**

**Presenter at and Organizer of Workshop,
Winter Conference on Brain Research,
Keystone, Colorado**

Papers at Meetings

**Society for Neuroscience, Ninth
Annual Meeting, Atlanta (2)**

**Federation of American Societies
for Experimental Biology, Anaheim**

Govind A. Dhopeswarkar

Nominated as Member

**Committee on Nutrition, Brain
Development and Behavior, National
Research Council, Washington, D.C.**

Armand J. Fulco

**Invited Speaker and Session Chairman
Frontiers in Lipid Research International
Symposium, Falmouth, Massachusetts**

Invited Speaker

**Symposium on Membrane Fluidity
Toronto, Canada**

**Albert Einstein College of Medicine
New York**

**Hormal Institute, University of
Minnesota, Austin**

Reviewer

**National Science Foundation
National Institutes of Health**

Oliver Hankinson

Member

UCLA Jonsson Comprehensive Cancer Center

Invited Speaker

**University of Southern California
School of Medicine**

Oliver Hankinson (continued)	Invited Speaker Research Rounds in Mental Retardation and Developmental Disabilities, UCLA 25th Symposium of the California Department of Molecular Biology Department of Biological Chemistry, UCLA
Isaac M. Harary	Session Chairman Third International Meeting of the European Section of the International Society for Heart Research Dijon, France
Esther F. Hays	Session Chairman 71st Annual Meeting, American Association for Cancer Research, San Diego Invited Speaker Sidney Farber Cancer Institute, Harvard University, Boston Hematology Group, Oncology Center John Hopkins Hospital, Baltimore
Harvey R. Herschman	Director for Basic Research Resources UCLA Jonsson Comprehensive Cancer Center Chairman Cell Physiology Study Section National Institutes of Health National Institutes of Health Program Project ad hoc Site Visit Invited Speaker International Society for Neurochemistry Nerve Growth Factor Symposium, Jerusalem Bat-Sheva Symposium on Biochemical Development of Nervous Tissue in Culture Rehovot, Israel Paraplegia Foundation Workshop on Regeneration in the Nervous System, Bermuda National Institutes of Health Workshop on Maturation Factors and Cancer, Bethesda

Harvey R. Herschman (continued)   Invited Speaker

7th Conference on Epidermal Differentiation
and Proliferation, Boyne Mountain, Michigan

University of Colorado Eleanor Roosevelt
Institute for Cancer Research

University of California, San Diego
Department of Biology

Laboratory of Viral Carcinogenesis
National Cancer Institute

University of Cincinnati
Department of Biochemistry

Case-Western Reserve University
Department of Microbiology

David E. Kuhl

John Kerschman Memorial Lecturer
Eastern Association of Electro-
encephalographers

Herman L. Blumgart, M.D. Pioneer Award
New England Chapter of the Society of
Nuclear Medicine

James F. Mead

American Oil Chemists Society Award in
Lipid Chemistry

Invited Speaker

Clinical Correlation Lecture
University of California, Irvine

Wesleyan University Joint Chemistry-
Biology Seminar

Organizing Committee and Plenary Speaker
Golden Jubilee International Congress
on Essential Fatty Acids and Prostaglandins
Minneapolis

Editorial Board
Lipids

Journal of Neurochemistry
Physiological Chemistry and Physics
Progress in the Chemistry of Fats
and Other Lipids
AGE

Hideo Nishita

Invited Reviews
Thermoluminescence
The Encyclopedia of Soil Science

Park S. Nobel

Editorial Board
Plant Physiology
Co-Editor
Plant Physiological Ecology (3 vols.)
Invited Speaker
Desert Biology Symposium
Fullerton, California
Universidad de Chile
Santiago, Chile
Arid Zone Institute
Mendoza, Argentina
Louisiana State University
Baton Rouge
University of Toronto
Toronto, Canada
Charles Darwin Research Station
Galapagos Islands, Ecuador
North Carolina State University
Raleigh
Duke University, Durham, North Carolina
University of Washington, Seattle
Washington State University, Pullman

Michael E. Phelps

Award of Excellence for manuscript at
9th International Symposium on Cerebral
Blood Flow and Metabolism, Tokyo, Japan
Named Distinguished Alumnus
Western Washington University
Fellow and Member
Council on Circulation, American Heart
Association

Heinz Schelbert

Investigative Group Fellowship Award
American Heart Association
Fellow and Member
Council on Circulation, American Heart
Association

Frederic B. Turner

Invited Speaker

**Symposium on Wildlife in the California
Desert, Riverside**

**Annual Meeting of Institute of Environ-
mental Sciences, Philadelphia**

Invited Participant

**Workshop on Environmental Effects of
Photovoltaic Energy Technology, Brookhaven
National Laboratory**

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