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UNIVERSITY OF CALIFORNIA, LOS ANGELES

SCHOOL OF MEDICINE

Department of Biophysics and Nuclear Medicine
Laboratory of Nuclear Medicine and Radiation Biology
900 Veteran Avenue
Los Angeles 24, California
Contract No. AT(04-1)-GEN-12

MEETING OF THE BIOMEDICAL PROGRAM DIRECTORS OF THE UNITED STATES ATOMIC ENERGY COMMISSION

FEBRUARY 5-6, 1962

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BIOMEDICAL PROGRAM DIRECTORS MEETING

Laboratory of Nuclear Medicine and Radiation Biology

U.C.L.A.

February 5 - 6, 1962

PROGRAM

Monday, February 5, 1962

9:00 A.M. Welcome: Chancellor Franklin D. Murphy

Greeting: Dean Stafford L. Warren

Introduction: Dr. Joseph F. Ross

9:15 A.M. Scientific Program

Radiation Biochemistry and Radiation Biology:

Dr. James Mead - "A Tracer Study of the Biogenesis of the Brain Fatty Acids"

Dr. David Howton - "Gamma Irradiation of Dilute Aqueous Potassium Oleate: Mechanism of Formation of Products"

Dr. Judd Nevenzel - "Two New Techniques in Lipid Chemistry"

Dr. Andrew Benson - "Surfactant Lipids: Their Role in Cell Function"

Coffee

Dr. Lawrence Myers - "Effects of Ionizing Radiation on Pyrimidine Compounds"

Dr. Norman Simmons - "Serum - Basic Polypeptide Interaction"

Dr. Isaac Harary - "*In Vitro* Studies of Beating Rat Heart Cells"

Dr. James Cook - "Characteristics of Euglena Gracilis in Synchronized Cultures"

12:30 - 2:00 P.M. - Luncheon - Sproul Hall Dining Room

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2:00 P.M.

Environmental Sciences:

Dr. Norman French - "Ingestion of Radioisotopes by Kangaroo Rats Living in Contaminated Environments"

Dr. Janice Beatley - "Comparative Study of Certain Reproductive Characters in *Larrea divaricata* Cav. Populations near the Sites of, and on Sites Remote from Past Nuclear Detonations at the Nevada Test Site"

Dr. Hideo Nishita - "The Influence of Stable Cs and K on the Behavior of Cs-137 in Soils and Plants"

Dr. Evan Romney - "Beryllium in Soil and Beryllium Effects on Plants"

Dr. William Rhoads - "Utilization of C^{14} from Dark Assimilation by Roots of Iron Deficient Beans and Barley Plants"

Dr. Howard Hawthorne - "Strontium Uptake by Intact Plants Subjected to Moisture Stress"

Coffee

4:30 - 5:30 P.M. - Visit to Laboratories

6:30 P.M. - Cocktails and Dinner - Bel-Air Country Club

Tuesday, February 6, 1962

9:00 A.M. Scientific Program

Radiation Biology:

Dr. Arne Schjeide - "Effects of Radiations on Lipide Metabolisms of Intracellular Components"

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Dr. Lawrence Detrick - "Electronmicroscopic Changes Across Irradiated Rat Intestinal Villi"

Dr. James Leitch - "Total Dose and Rate Effects in AET-5HT Radiation Protection Studies"

Dr. Baldwin Lamson - "Impaired Sodium Chloride Metabolism - A Delayed Effect of Total Body Irradiation in Rats"

Dr. Thomas Haley - "Toxicity of Scandium Chloride"

Dr. Ralph Nusbaum - "Trace Elements in Biological Materials"

Coffee

Dr. Benedict Cassen - "Multicrystal Scintillation Counting"

Dr. Thomas Hennessy - "Radioiron Study of Erythropoiesis after X-Irradiation"

Nuclear Medicine:

Dr. George Taplin - "Recent Clinical Experience with Renocystograms and Studies of Reticuloendothelial Function"

Dr. Norman MacDonald - "Recent Studies with the Total Body Counter"

Dr. Esther Hays - "Nucleic Acid Induction of Parotid Gland and Other Neoplasms in Mice (A Demonstration of Infectivity of Polyoma Virus DNA)"

Dr. Joseph Ross - "The Influence of Inflammatory Processes on Erythropoiesis and Iron Metabolism"

12:30 - 2:00 P.M. - Luncheon - U.C.L.A. Medical Center Dining Room "C" and "D"

2:00 P.M. Division of Biology and Medicine Program - Dr. Charles Dunham

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INTRODUCTION

In February 1947, the U.C.L.A. Atomic Energy Project was established under the direction of Dr. Stafford L. Warren, as the first active operational unit of the new School of Medicine, with financial support provided by the U.S. Atomic Energy Commission on an annual contract basis. From 1947 to 1958 the Atomic Energy Project operated as a research laboratory with consultative scientific advice being provided by members of the faculty of the Medical School.

During this eleven year period the professional staff of the Laboratory made important scientific contributions to knowledge of the effects of ionizing radiation on organic compounds and on living organisms; of the distribution of radioactive products of nuclear detonations in the environment; of the assimilation of these radioactive substances by plants, animals and man; and developed new and valuable uses of radioactive isotopes for the study of human physiology and diagnosis of disease.

In 1958 the Atomic Energy Project was reorganized as the Department and Laboratory of Nuclear Medicine and Radiation Biology, and in 1960 was merged with the Department of Biophysics to constitute the Department of Biophysics and Nuclear Medicine, with administrative responsibility for the Departmental Laboratory of Nuclear Medicine and Radiation Biology. University funds provide financial support to the Department, and the Laboratory is supported with funds provided through contract AT(04-1)GEN-12 between the University and the Atomic Energy Commission.

During the first fourteen and one-half years of its existence the major portion of the Laboratory's endeavors were conducted in temporary buildings (formerly an Army hospital of approximately 25,000 gross square feet of space) located on the UCLA Campus. From 1958 to 1961, the Environmental Radiation Division of the Laboratory outgrew these quarters and was housed temporarily in a rented building, comprising almost 16,000 square feet of space, approximately 35 minutes drive from the main campus facility. The limited and split facilities which contained the Laboratory's research program during these 14-1/2 years were exchanged for the present building located on the West Medical Campus of the University of California at Los Angeles in July 1961.

The Atomic Energy Commission generously agreed to amortize the cost of the new laboratory building by means of a 25 year lease-occupancy

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contract with the University, and the Board of Regents advanced the necessary $2,900,000 to make possible construction of the building. Construction was commenced in October 1959 and was completed in July 1961. The new Laboratory of Nuclear Medicine and Radiation Biology facility provides approximately 90,000 gross square feet of laboratory and office space, and houses virtually all activities of the Laboratory in a setting which is well suited to a biomedical research endeavor.

ORGANIZATION AND MAJOR OBJECTIVES:

The Laboratory of Nuclear Medicine and Radiation Biology is administered through the Department of Biophysics and Nuclear Medicine of the School of Medicine, UCLA, but is wholly supported in its activities by the Atomic Energy Commission through Contract AT(04-1)GEN-12. The Laboratory is housed in separate facilities from the Department and is organized into nine divisions within these facilities (one administrative and eight research). Currently the Laboratory staff consists of approximately 36 academic staff, 14 graduate or post doctoral trainees, and 142 non-academic employees for a total staff of 192. The activities of the Laboratory are coordinated with those of the Department by means of a Council containing faculty members of the Department and academic professional research personnel of the Laboratory which is advisory to the Director.

The objectives of the Laboratory may be summarized in six major interrelated categories as follows:

1. Investigation of the effects of ionizing radiation on systems of biological significance and on living organisms, and studies of ways in which the detrimental effects of ionizing radiation may be minimized or prevented.

2. Investigation of the dynamic aspects of physiological and bio-chemical processes in man, animals and plants and how these processes are modified by radiation and related pathological states.

3. The development of beneficial uses of ionizing radiation and radioactive substances in medicine and biology.

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4. Assessment of the contamination of our environment by radioactive materials; study of the transport of these materials into living organisms; and the evaluation of the effects of the accumulation of these substances upon the health, function and structure of these organisms.

5. Additional programs in biology and medicine directed toward solution of special problems occasioned by mankind's use of ionizing radiation.

6. Provisions of graduate and post graduate education and training in Nuclear Medicine and Radiation Biology.

EDUCATIONAL PROGRAM:

The Department of Biophysics and Nuclear Medicine is authorized to provide graduate work leading to the M.S. and Ph.D. degrees. Specialized training in Nuclear Medicine and Radiation Biology will be provided to graduate students and to medical students. During Fiscal Year 1962, 14 graduate students and post doctoral trainees were enrolled in the Department. It is anticipated that enrollment will be increased to 25 in Fiscal Year 1963 and to 35 in Fiscal Year 1964.

RESEARCH PROGRAM:

Abstracts of the research programs in progress in the Laboratory are provided in the following pages.

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STAFF LIST

ADMINISTRATIVE DIVISION (1st floor)

Ross, Joseph F., M.D. (Director)
Hennessy, Thomas G., M.D. (Assistant Director)
Thompson, Harland B., B.S. (Laboratory Business Officer)

BIOCHEMISTRY DIVISION - Room 24-178 (2nd floor)

Mead, James F., Ph. D. (Division Chief)
Harary, Isaac M., Ph. D.
Howton, David R., Ph. D.
Kuramitsu, Howard, K., Ph. D.
Nevenzel, Judd C., Ph. D.
Simmons, Norman S., D.M.D., Ph. D.
Wu, Guey-Shuang, Ph. D.

BIOPHYSICS DIVISION - Room 14-193 (1st floor)

Nusbaum, Ralph E., Ph. D. (Division Chief)
Alexander, George V., M. S.
Cassen, Benedict, Ph. D.
Farmer, Ross W.
Silverman, Louis B., A. B.

ENVIRONMENTAL RADIATION DIVISION - Room 23-118 (2nd floor)

Larson, Kermit H., M. S. (Division Chief)
Beatley, Janice C., Ph. D.
French, Norman R., Ph. D.
Hawthorne, Howard A., Ph. D.
Martin, William E., Ph. D.
Nishita, Hideo Ph. D.
Olafson, Jon H., M. S.
Rhoads, William A., Ph. D.
Romney, Evan M., Ph. D.
Turner, Frederick, Ph. D.

MEDICINE DIVISION - Room 14-146 (1st floor)

Hays, Esther F., M. D. (Division Chief)
Ross, Joseph F., M. D.

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NUCLEAR RADIOLOGY DIVISION - Room 14-109 (1st floor)

Taplin, George V., M. D. (Division Chief)
Dore, Earl K., M. D.
Haddad, Jr., George N., M. D.
Leitch, James L., Ph. D.
MacDonald, Norman S., Ph. D.
Meredith, Orsell, M., Ph. D.

PATHOLOGY DIVISION - Room 12-141 (2nd floor)

Hennessy, Thomas G., M. D., Ph. D. (Acting Division Chief)
Lamson, Baldwin G., M. D.

PHARMACOLOGY & TOXICOLOGY DIVISION - Room 24-124 (2nd floor)

Haley, Thomas J., Ph. D. (Division Chief)
Detrick, Lawrence E., Ph. D.

RADIOBIOLOGY DIVISION - Room 11-114 (1st floor)

Myers, Jr., Lawrence S., Ph. D. (Division Chief)
Bennett, Leslie A., M. D.
Benson, Andrew A., Ph. D.
Billings, Marta S., M. D.
Cook, James R., Ph. D.
Hennessy, Thomas G., M. D., Ph. D.
Lamson, Baldwin G., M. D.
Schjeide, Ole A., Ph. D.

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A TRACER STUDY OF THE BIOGENESIS OF THE BRAIN FATTY ACIDS

J. F. Mead and A. J. Fulco

Several of the brain lipids contain fatty acids which are not typical in structure of the usual fatty acids found in the body. There is reason to believe that they may have interesting and unique functions and derivation. In order to investigate this possibility, the following experiments were performed:

Two-week-old rats were given intraperitoneal injections of acetate-1-C^{14} over a 4-day period and killed 3-1/2 hours after the last injection. The fatty acids obtained from the crude brain cerebrosides of these rats were then separated into four groups which included saturated unsubstituted, unsaturated unsubstituted, saturated 2-hydroxy, and unsaturated 2-hydroxy fatty acids. The individual unsubstituted acids were separated by reversed phase chromatography, and the C_{24} acids, lignoceric and nervonic, were isolated in a state of high purity. The 2-hydroxy acids were separated as the 2-acetoxy derivatives on the reversed phase column and the C_{24} acids, cerebronic and 2-hydroxynervonic, were obtained in the pure state. The C_{24} acids had high specific activities; the most highly active acid, lignoceric, had a specific activity 150 times greater than the average specific activity of the body fatty acids. Stepwise degradation of the C_{24} acids to determine the label distribution revealed that lignoceric acid is completely synthesized from acetate, with little dilution from acids of intermediate chain length during the chain elongation process. Cerebronic acid, in turn, is formed directly from lignoceric acid. Nervonic acid, on the other hand, is not derived from lignoceric acid by desaturation but rather appears to be formed by chain elongation of oleic acid.

A theoretical discussion and some speculation will be given.

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RECENT CLINICAL EXPERIENCES WITH RENOCYSTOGRAMS AND STUDIES OF RETICULOENDOTHELIAL FUNCTION

G. V. Taplin

Recent clinical experiences with renocystograms in chronic pyelonephritis and occlusive renal artery disease demonstrate the diagnostic value of current concepts of renocystogram interpretations. Original interpretations of radiorenograms are modified and the physiological basis of normal renocystogram dynamics is clarified. The heights of the renal vascular segments are no longer considered useful indices of renal vascular capacity. Analysis of the effects of fluid restriction and loading doses of para-aminohippurate (PAH) on renocystogram dynamics has led to new concepts and terminology for the tubular segments. These segments are now called tubular transport segments to imply a close relation between blood supply and tubular cell function and a time factor for movement of tracer from the blood into the cells and secretion into the collecting tubules. A new concept of minimum tubular transport time is developed and its relation to urine flow is described. Fluid restriction sufficient to reduce urine formation to 1 ml/minute/kidney may increase tubular transport time from the normal of about 2.5 minutes to 5 to 6 minutes. A difference in tubular transport time between kidneys of more than 1 minute suggests inequality of urine flow.

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RECENT STUDIES WITH THE TOTAL BODY COUNTER

N. S. MacDonald

Monitoring activities of the facility have included weekly determinations of body burden of Cs^{137} and K^{40} in a number of laboratory personnel. No significant change in burdens of Cs^{137} have been observed during the last 6 months. (The range has been 19-38 μμc Cs^{137} per gm of K). No nuclides other than Cs^{137} and K^{40} have been found in these subjects. Monitoring of two industrial workers over a period of a year following accidental exposures has indicated a biological "half time" for Cs^{137} retention of 85 days in one and 120 days in the other. The "biological half time" for Mn^{54} in the form of inhaled dust is about 175 days in one of these men. Body scanning indicates this burden is in the lung area.

Clinical studies have aimed at reducing the doses of radioactive nuclides required in established diagnostic tests involving radioisotopes and devising new medical applications. In conjunction with studies of Sr^{85} metabolism in humans, the TBC has proved of great value in providing data on body retention without the onerous task of excreta collection and assay. Body burdens from an injection of 5 μc of Sr^{85} have been measured over a period of more than a year. The time required to lose 50% of the dose following a single intravenous injection of Sr^{85} is very easily determined with the TBC. It may prove of value in assessing the metabolic activity of the skeleton in certain diseases. For example, the 50% time has ranged from 1-2 days for adults with severe, active osteoporosis, to 15 days for a 15 year old boy with osteogenesis imperfecta. These tests require less than 0.1 μc of Sr^{85}.

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THE INFLUENCE OF INFLAMMATORY PROCESSES ON ERYTHROPOIESIS AND IRON METABOLISM

J.F. Ross and M.R. Quastel

Rheumatoid arthritis, neoplasia, and other conditions associated with inflammatory processes frequently have an associated anemia, although body iron stores are adequate and the bone marrow appears morphologically capable of erythropoiesis. Studies with radioactive iron have shown that trace amounts of iron administered intravenously are utilized qualitatively and quantitatively in a normal fashion.

The possibility that inflammation might produce a disturbance in reutilization of iron released from senescent erythrocytes and thereby contribute to the anemia was investigated in dogs and in rats. In both species inflammation was induced by intramuscular injection of turpentine and the utilization for erythrocyte formation of radioiron given intravenously as transferrin bound iron and as hemoglobin iron in senescent erythrocytes was studied and compared with utilization of iron from these same sources by normal animals.

Both species utilized transferrin bound iron for erythrocyte formation in normal fashion, even in the presence of severe inflammation. However, animals with inflammatory reactions showed decreased rate and extent of utilization of iron administered in the form of senescent erythrocytes. The distribution of senescent erythrocyte iron in the tissues of rats with inflammatory reaction was different from the distribution of transferrin bound iron.

These observations suggest that inflammatory conditions disturb the processes of hemoglobin catabolism, and interfere with reutilization of iron released from destroyed erythrocytes.

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