

ACRH-103

**ARGONNE CANCER RESEARCH HOSPITAL**  
 950 EAST FIFTY-NINTH STREET • CHICAGO • ILLINOIS 60637

REPOSITORY Argonne / Chicago  
Federal Records Center

COLLECTION Laboratory Directors Files

BOX No. Argonne Job #1165, Box 3, Accession #  
434-91-0014

FOLDER \_\_\_\_\_

**Meeting of the Advisory Committee  
 to the  
 Argonne Cancer Research Hospital  
 Program**

**MARCH 4-5, 1965**

**LEON O. JACOBSON, M.D.**  
 Editor

**MARGOT DOYLE, Ph.D.**  
 Associate Editor

OPERATED BY THE UNIVERSITY OF CHICAGO  
 UNDER  
 CONTRACT AT-(11-1)-69

TABLE OF CONTENTS

	<u>Page</u>
FOREWORD . . . . .	ii
ADVISORY COMMITTEE TO THE ARGONNE CANCER RESEARCH HOSPITAL PROGRAM - FIRST MEETING: MARCH 4 - 5, 1965 . . . . .	iv
PROGRAM . . . . .	v
SCIENTIFIC STAFF LIST . . . . .	viii
COLLABORATING PERSONNEL AT THE UNIVERSITY OF CHICAGO . . . . .	xi
STUDENT RESEARCH ASSOCIATES . . . . .	xiii
ABSTRACTS . . . . .	1-142
RECENT PUBLICATIONS . . . . .	143-149

1167927

## F O R E W O R D

In 1948 the U. S. Atomic Energy Commission approved the establishment of a cancer research hospital with appropriate laboratory facilities at the University of Chicago. It was intended that this hospital be administered by the Medical School and Clinics of the University, and that its facilities be available to qualified investigators. After nearly three and one-half years of building, the first patient was admitted on January 10, 1953, and the formal opening date of the hospital was March 10, 1953.

The purpose and program of the hospital are directed toward the exploitation of high energy sources for the treatment of malignancies, the study of the biological effects of radiation, the use of radioisotopes as tracers in the study of normal and disease states, and in the diagnosis and therapy of disease. The scientific program is correlated in general with that of the Division of the Biological Sciences and the University of Chicago Hospital and Clinics, of which the Argonne Cancer Research Hospital is a part. Close relations are also maintained with the Argonne National Laboratory at Argonne, Illinois.

From the beginning the staff of the ACRH has encouraged participation in its research program by graduate and undergraduate medical students and advanced students in the biological sciences at the University of Chicago. It has also taken an active part in various research investigations of general interest with University faculty members in the Life and Physical Sciences. This interdisciplinary effort has proved of great value to the ACRH program. Student participation and faculty collaboration have also made possible the training of large numbers of undergraduate and graduate students (as well as faculty) in the use of radioisotopes in research, diagnosis and treatment of various disease states.

Argonne Cancer Research Hospital has eight floors, with a total area of 102,500 square feet. Two floors with 56 beds are devoted to clinical research. The remaining six floors house high energy radiation equipment, electronic and machine shops, an animal farm, and conventional research laboratories. The staff is composed of 55 scientists, 160 technicians, nurses, and non-technical laboratory personnel, many of whom are paid in part by the University. Since the University clinical departments assume care of the patients at the ACRH, any part of a staff member's time devoted to professional care as distinguished from research is paid for by the University and does not feature in the ACRH budget. This accounts

for the fact that the scientific staff totals 55, while the actual number of scientific man years devoted to the research program is 45.

H. Stanley Bennett, M.D.  
Dean  
Division of the Biological Sciences  
University of Chicago

ADVISORY COMMITTEE TO THE  
ARGONNE CANCER RESEARCH HOSPITAL PROGRAM

FIRST MEETING: MARCH 4 - 5, 1965

MEMBERS OF THE COMMITTEE

Dr. Robert H. Ebert  
Chief of Medical Staff Harvard Medical School  
Massachusetts General Hospital  
Boston, Massachusetts

Dr. Henry S. Kaplan  
Professor and Executive  
Department of Radiology  
Stanford University School of Medicine  
Palo Alto, California

Dr. Russell H. Morgan  
Radiologist-in-Chief  
The Johns Hopkins Hospital  
Baltimore, Maryland

Dr. Hans Neurath  
Professor of Biochemistry  
School of Medicine  
University of Washington  
Seattle, Washington

Dr. Joseph F. Ross  
Director  
Laboratory of Nuclear Medicine and Radiation Biology  
University of California School of Medicine  
Los Angeles, California

ctual  
n is 45.

Sciences

1167930

PROGRAM\*

Thursday, March 4, 1965 . . . CHAIRMAN, Dr. L. O. Jacobson

Morning Session

Immunology and Molecular Biology

9:00

Introductory Remarks

H. Stanley Bennett

Dean of Biological Sciences, University  
of Chicago

9:05

The Influence of Total-Body Irradiation  
and Other Factors on the Fate of Parti-  
culate Antigens and on the Migration of  
Antibody Forming Cells

R. W. Wissler (pp. 1 - 5)

Studies on the Destruction of Human Red  
Cells by the Complement System

S. Yachnin (pp. 23 - 27)

Some Biochemical Studies of Red Cell  
Differentiation

E. Goldwasser (pp. 28 -32)

10:35

INTERMISSION

10:50

Protein Synthesis in Heart Muscle

M. Rabinowitz (pp. 32 - 33)

An Effect of Polycyclic Aromatic Hydro-  
carbons on Bacteriophage Development

S. B. Weiss (pp. 34 - 36)

12:05

LUNCH

Afternoon Session

Experimental and Clinical Studies of Cell  
Differentiation

1:30

The Riddle of Polycythemia Vera

C. W. Gurney (pp. 37 - 40)

\* Page numbers locate abstracts and lists of senior authors and  
co-authors.

Afternoon Session (continued)

The Mechanism of the Testosterone Effect  
on Erythropoiesis

W. Fried (pp. 41 - 42)

A Lesson From an Anemic Mouse

A. Kales (pp. 43 - 44)

Chromosome Abnormalities in Patients with  
Hematological Abnormalities

J. Rowley (pp. 44 - 47)

3:00

INTERMISSION

3:15

General Metabolic Studies

Selected Aspects of Uric Acid Metabolism  
in Man

L. B. Sorensen (pp. 62 - 64)

Effects of Estrogens on Hepatic Excretory  
Activity

A. Kappas (pp. 65 - 67)

Intermediary Metabolism of Irradiated Rats

G. V. LeRoy (pp. 68 - 70)

6:00

DINNER for visitors and participants at  
the Quadrangle Club, 1155 East 57th  
Street

Friday, March 5, 1965 . . . . CHAIRMAN, Dr. P. V. Harper, Jr.

Morning Session

Problems in Scanning

9:00

Theoretical Considerations

R. N. Beck (pp. 76 - 79)

Instrumental Design and Construction

D. B. Charleston (pp. 79 - 101)

Chemical and Biological Aspects

P. V. Harper, Jr. (pp. 101 - 108)

1167932

Morning Session (continued)

ffect

10:30

INTERMISSION

10:45

Radiation Effects

s with

Neurological Studies in Monkeys Following  
Thalamic Lesions with <sup>90</sup>Y

S. Schulman (pp. 109 - 111)

Clinical Applications of Beta Sources in  
Neurosurgery

J. F. Mullan (pp. 112 - 114)

The Late Effects of the Deposition of  
Radium in Man

R. J. Hasterlik (pp. 116 - 119)

olism

12:00

LUNCH

retory

Afternoon Session

1:30

Tour of Argonne Cancer Research Hospital

ed Rats

2:00

Linear Electron Accelerator (demonstration  
in sub-basement)

L. S. Skaggs (pp. 126 - 129)

s at

2:30

Executive Session

on

)

ARGONNE CANCER RESEARCH HOSPITAL

H. Stanley Bennett	Dean, Division of Biological Sciences, and Professor of Anatomy, University of Chicago
Leon O. Jacobson	Director, Argonne Cancer Research Hospital, and Professor of Medicine, Chairman of the Department of Medi- cine, University of Chicago
Paul V. Harper	Associate Director, Argonne Cancer Re- search Hospital, and Professor of Surgery, University of Chicago
C. William Kupferberg	Assistant Director for Administration, Argonne Cancer Research Hospital, and Executive Assistant, Department of Medicine, University of Chicago

	<u>Scientific Staff</u>	<u>Departmental Affiliation</u> <u>University of Chicago</u>
Robert N. Beck	Research Associate (Asst. Prof.)	Medicine
Richard K. Blaisdell	Assistant Professor	Medicine
James C. Bland	Assistant	
James W. J. Carpender	Professor	Radiology
Donald B. Charleston	Research Associate (Assoc. Prof.)	Medicine
Donald Chow	Research Assistant	Medicine
Thomas Crane	Assistant	
Louis A. DeSalle	Associate Scientist	
Margot Doyle	Senior Scientist	
Peter P. Dukes	Research Associate (Asst. Prof.) Leave of absence - Germany, 1964-1965	Biochemistry

Scientific Staff (continued)

Frank W. Fitch	Associate Professor Markle Scholar	Pathology
Helmut W. Forsthoff	Chief Scientist (Germany)	
Agnes Gara	Associate Scientist	
Evelyn Gaston	Associate Scientist	
Eugene Goldwasser	Professor	Biochemistry
Alexander Gottschalk	Assistant Professor	Radiology
Melvin L. Griem	Associate Professor	Radiology
Clifford W. Gurney	Associate Professor Markle Scholar	Medicine Physiology
Paul V. Harper	Professor	Surgery
Robert J. Hasterlik	Professor	Medicine
Richard S. Hayward	Research Associate (Instructor) (Ireland)	Biochemistry
Gar Bo Ho	Research Associate (Japan)	Pharmacology
Wen-Tah Hsu	Research Associate (Formosa)	
Leon O. Jacobson	Professor and Chairman of the Department	Medicine
Feliciano Jiminez	Junior Scientist (Philippines)	
Attallah Kappas	Associate Professor	Medicine
Fred M. Katz	Assistant Professor	Medicine
Sanford B. Krantz	Assistant Professor Leave of absence - Glasgow, Scotland 1964-1965	Medicine

Scientific Staff (continued)

Charles Kuo-Hao King	Associate Scientist (China)	
Lawrence H. Lanzl	Associate Professor	Radiology
Katherine A. Lathrop	Research Associate (Asst. Prof.)	Surgery
Jean Legault-Demare	Research Assistant (France)	
George V. LeRoy	Professor	Medicine
Allan Lorincz	Associate Professor	Medicine
Edna K. Marks	Senior Scientist	
Edward W. Mason	Associate Scientist	
Paul Meier	Professor, Chairman of Department Director Biological Sciences Division Computation Center	Statistics
Gerald A. Mendel	Assistant Professor	Medicine
Robert D. Mosely	Professor, Chairman of Department Director, Radiation Protection Service	Radiology
Margaret Mulbrandon	Junior Scientist	
John F. Mullan	Professor	Neurosurgery
Carol M. Newton	Assistant Professor Research Associate (Asst. Prof.)	Medicine Committee on Mathematical Biology
Robert H. Palmer	Assistant Professor	Medicine
Murray Rabinowitz	Associate Professor Research Associate (Assoc. Prof.)	Medicine Biochemistry

Scientific Staff (continued)

William Robinson	Assistant Professor Leave of absence - U. of California at Berkeley, 1964-1965	Medicine
Melba J. Robson	Associate Scientist Technologist (Lab. Supervisor)	Medicine
Janet D. Rowley	Research Associate (Asst. Prof.)	Medicine
Martin L. Rozenfeld	Senior Scientist	
Eric L. Simmons	Research Associate (Assoc. Prof.)	Medicine
Lester S. Skaggs	Professor	Radiology
Leif B. Sorensen	Assistant Professor	Medicine
Alvin R. Tarlov	Assistant Professor	Medicine
Samuel B. Weiss	Professor	Biochemistry
Robert W. Wissler	Professor, Chairman of Department	Pathology
Stanley Yachnin	Assistant Professor Markle Scholar	Medicine
Lawrence T. Zimmer	Associate Scientist	

Collaborating Personnel at the University of Chicago

Donald Cannon	Instructor	Pathology
Paul E. Carson	Assistant Professor	Medicine
Jerry G. Chutkow	Instructor	Medicine
M. Edward Davis	Professor, Chairman of Department	Obstetrics and Gynecology; Chief of Service, Chicago Lying-In Hospital

Collaborating Personnel at the University of Chicago (continued)

Richard DeGowin	Assistant Professor	Medicine
Haratch Doumanian	Resident (3rd year)	Radiology
Katti Dzoga	Junior Scientist	Pathology
Cesar Fernandez	Research Associate (Assoc. Prof.)	Physiology and Surgery(Otolaryngology)
Asher J. Finkel	Research Associate (Asst. Prof.) Director, Health Division	Medicine Health Division, Argonne National Laboratory
Walter Fried	Post-Doctoral Fellow (Asst. Prof.)	Medicine
Thomas F. Gallagher	Resident (3rd year)	Medicine
Robert Goepf	Assistant Professor	Zoller Dental Clinic
Donald Homer	Resident (2nd year)	Radiology
Peter Lazarovitz	Resident (2nd year)	Radiology
Charles Miller	Associate Scientist	Argonne National Laboratory
John F. Mullan	Professor	Surgery
Daniel Paloyan	Intern	Surgery
Edward Paloyan	Instructor and Senior Resident	Surgery
Gary Pick	Resident (2nd year)	Dermatology
Jerome Petasnick	Resident (2nd year)	Radiology
Donald Rowley	Associate Professor	Pathology
John H. Rust	Professor	Pharmacology (Section of Nuclear Medicine)
Sidney Schulman	Associate Professor	Medicine

and  
y;  
Service,  
ying-In

Collaborating Personnel at the University of Chicago (continued)

Arnold I. Stern	Resident	Medicine
Nels M. Strandjord	Associate Professor	Radiology
Francis Straus	Instructor	Pathology
Radovan Zak	Assistant Instructor	Medicine Biochemistry

Student Research Associates

Carl Ahroon	Medical Student and M.S. Candidate	Pathology
Michael Axelrad	Post-Doctoral Trainee and Ph.D. Candidate	Pathology
Maurice Barcos	Graduate Student (1)	Biophysics
Howard Benensohn	Medical Student (3) and M.S. Candidate	Pathology
Donald Cantway	Medical Student (2) and M.S. Candidate	Pathology
Albert Dahlberg	Graduate Student (4)	Biochemistry and Medicine
Keith Dixon	Graduate Student (1)	Radiology
Martin Gross	Graduate Student (1)	Biochemistry and Medicine
Richard Gumpert	Graduate Student (2)	Biochemistry
Michael Hrinda	Graduate Student (2)	Biochemistry
Robert Hunter	Medical Student (4) and Ph.D. Candidate	Pathology
Arthur Kales	Medical Student Asst. (4)	Medicine
John Kurnick	Medical Student (3)	Medicine
Irving Lerch	Graduate Student (2)	Radiology

Student Research Associates (continued)

Bruce Merchant	Post M.D. Trainee and Ph.D. Candidate	Pathology
John W. Moohr	Medical Student (4)	Medicine (1 year Bio- chemistry)
Nehe Nwankwo	Medical Student (2) and M.S. Candidate	Pathology
Robert Okin	Medical Student (2) and M.S. Candidate	Pathology
Marius Panzarella	Predoctoral Trainee and M.S. Candidate	Pathology
Jack Pinnas	Medical Student (4) and M.S. Candidate	Pathology
Carl Pierce	Predoctoral Trainee and Ph.D. Candidate	Pathology
John Porter III	Graduate Student (1)	Radiology
Julian Rimpila	Medical Student (3) and M.S. Candidate	Pathology
David Ruschhaupt	Medical Student (3) and M.S. Candidate	Pathology
Edward Tarlov	Medical Student (4)	Medicine
Sarah Weinber	Graduate Student (2)	Biochemistry
Douglas White	Medical Student Asst. (2)	Medicine

and

and

ABSTRACTS

Page

STUDIES IN IMMUNOLOGY

<p>Studies in Host-Tumor Balance  R. W. Wissler, K. Dzoga, F. Straus, H. Benensohn  and K. Craft . . . . .</p>	1
<p>New Approaches to the Study of Tumor Immunity and  Tumor Specific Antigens  B. Merchant, F. Tweet, N. Nwankwo, and R. W. Wissler . .</p>	2
<p>The Influence of Total-Body Irradiation and Other  Factors on the Fate of Particulate Antigens and on the  Migration of Antibody Forming Cells  D. Cannon, R. Hunter, and R. W. Wissler . . . . .</p>	4
<p>Immune Mechanism in Tumor Rejection  E. L. Simmons . . . . .</p>	6
<p>Homeostasis of Antibody Formation in the Adult Rat  D. A. Rowley and F. W. Fitch . . . . .</p>	8
<p>The Mechanism of Tolerance Produced in Rats to Sheep  Erythrocytes. I. Plaque-Forming Cell and Antibody  Response to Single and Multiple Injections of Antigen  D. A. Rowley and F. W. Fitch . . . . .</p>	10
<p>The Mechanism of Tolerance Produced in Rats to Sheep  Erythrocytes. II. The Plaque-Forming Cell and Anti-  body Response to Multiple Injections of Antigen  Begun at Birth  D. A. Rowley and F. W. Fitch . . . . .</p>	12
<p>Antigen Metabolism in the Rat. I. Bovine Gamma  Globulin  C. W. Pierce and F. W. Fitch . . . . .</p>	15
<p>The Effect of Neonatal Thymectomy on the Immune Response  of the Rat  J. C. Pinna and F. W. Fitch . . . . .</p>	17
<p>Homeostasis of Antibody Formation. The Effects of  Passive and Minimal Adaptive Immunity on Homograft  Survival  M. Axelrad and F. W. Fitch . . . . .</p>	18

	<u>Page</u>
Antibody Response in the Rat. Immunoglobulin Types Produced after Immunization with Sheep Erythrocytes F. W. Fitch . . . . .	20
The Histology of Antibody Formation F. W. Fitch and C. R. Ahroon . . . . .	21
Studies on the Inhibition of Complement by Polyinosinic Acid S. Yachnin and D. Rosenblum . . . . .	23
pH Optima in Immune Hemolysis: A Comparison Between Guinea Pig and Human Complement S. Yachnin . . . . .	24
The Initiation and Enhancement of Human Red Cell Lysis by an Activator of the First Component of Complement S. Yachnin . . . . .	25
The Hemolysis of Red Cells from Patients with Paroxysmal Nocturnal Hemoglobinuria by Isolated Subcomponents of the Third Complement Component S. Yachnin . . . . .	27

STUDIES IN MOLECULAR BIOLOGY

Studies of Erythropoietin-Induced Differentiation: I. The Effects of Inhibitors on Hemoglobin Synthesis O. Gallien-Lartigue and E. Goldwasser . . . . .	28
Studies of Erythropoietin-Induced Differentiation: II. The Effect on RNA Synthesis S. B. Krantz and E. Goldwasser . . . . .	28
Studies of Erythropoietin-Induced Differentiation: III. Some Aspects of Induced Hemoglobin Synthesis S. B. Krantz and E. Goldwasser . . . . .	29
Studies of Erythropoietin-Induced Differentiation: IV. The Stimulation of Stroma Synthesis P. P. Dukes, S. Shin and E. Goldwasser . . . . .	30
Studies of Erythropoietin-Induced Differentiation: V. The Partial Purification of Erythropoietin E. Goldwasser and C. Kung . . . . .	31
Protein Synthesis in Heart Muscle M. Rabinowitz, R. Zak, K. G. Nair and L. DeSalle . . . . .	32

<u>Page</u>		<u>Page</u>
	Studies on RNA Biosynthesis	
20	S. B. Weiss . . . . .	34
	Studies with Polycyclic Aromatic Hydrocarbons	
21	S. B. Weiss, W.-T. Hsu and J. W. Moohr . . . . .	35
	EXPERIMENTAL AND CLINICAL STUDIES OF CELL DIFFERENTIATION	
	Physiological Studies of Primitive Hemopoietic Cells	
23	C. W. Gurney, D. Hofstra and A. Mangalik . . . . .	37
	Relationship Between Duration and Intensity of Hypoxia and Erythropoietic Response	
24	C. W. Gurney . . . . .	38
	Quantitation of Erythroid Hypoplasia in Mice Following Irradiation	
25	C. W. Gurney, D. Hofstra, E. Simmons and C. Newton . . . . .	39
	The Erythropoietic Effect of Testosterone in the Plethoric Mouse	
27	C. W. Gurney and W. Fried . . . . .	41
	An Erythropoietic Defect in a Congenitally Anemic Mouse	
	A. Kales, W. Fried and C. W. Gurney . . . . .	43
28	Autoradiographic Studies of Human Chromosomes	
	J. Rowley . . . . .	44
	Results of Chromosome Analysis in Patients with Primary Refractory Anemia	
28	J. Rowley and R. K. Blaisdell . . . . .	45
	STUDIES ON THE BLOOD	
29	The Kidney and Erythropoietin Production	
	L. O. Jacobson, E. K. Marks and E. O. Gaston . . . . .	48
30	Effects of Long-Term High Pressure Oxygen in Animals	
	E. L. Simmons, J. Doull, L. O. Jacobson and E. K. Marks . . . . .	50
31	The Regulation of Iron Absorption: Hepatic Regeneration as a Stimulus to Increased Iron Absorption	
32	G. A. Mendel . . . . .	52

	<u>Page</u>
Biochemistry of Biological Membranes: Studies on Red Blood Cells	
A. Tarlov . . . . .	54
<u>In Vitro</u> Studies of Human Blood Lymphocytes in Lymphoproliferative Disorders	
R. K. Blaisdell . . . . .	56
Studies of Mouse Leukemia Viruses	
G. B. Humphrey and E. Goldwasser . . . . .	57
Effect of 5', 5', 5'-Trifluoroleucine on Transplanted Mouse Leukemias	
E. L. Simmons, N. Larkin, C. Pierce, H. S. Anker and O. M. Rennert . . . . .	58
 GENERAL METABOLIC STUDIES	
Uric Acid Metabolism in Wilson's Disease	
L. B. Sorensen, R. Reilly and A. Kappas . . . . .	62
Molybdenum-99, A New Isotope for Scintillation Scanning of the Liver	
L. B. Sorensen . . . . .	63
Steroid Studies	
A. Kappas, F. Katz and R. H. Palmer . . . . .	65
Radiation Injury	
G. V. LeRoy, J. H. Rust and G. B. Ho . . . . .	68
Respiration Pattern Analysis	
G. V. LeRoy . . . . .	69
The Argonne Cancer Research Hospital' Total-Body Counter	
R. J. Hasterlik, G. V. LeRoy and C. M. Newton . . . . .	70
Studies of Real and Simulated Fallout	
G. V. LeRoy, J. H. Rust and R. J. Hasterlik . . . . .	72
Studies on the Metabolism of Magnesium in the Rat	
J. G. Chutkow . . . . .	73
Specific Metabolic Processes in Skin	
A. L. Lorincz . . . . .	75

	<u>Page</u>
<b>PROBLEMS IN SCANNING</b>	
A Theory of Radioisotope Scanning Systems R. N. Beck . . . . .	76
Collimators for Radioisotope Scanning Systems R. N. Beck . . . . .	77
Techniques Which Aid in Quantitative Interpretation of Scan Data D. B. Charleston, R. N. Beck, P. Eidelberg and M. W. Schuh . . . . .	79
Collimators for Gamma Ray Cameras R. N. Beck, P. V. Harper, E. Schmidt and L. T. Zimmer . . . . .	81
Response of Scintillation Detectors to Scattered Radiation R. N. Beck and M. W. Schuh . . . . .	82
A Precision Scanning System Employing Digital Drive and Digital Control Techniques D. B. Charleston, R. N. Beck and J. C. Wood . . . . .	83
Resolution Versus Sensitivity in Scanning P. V. Harper and R. N. Beck . . . . .	85
A $^{47}\text{Ca}$ Animal Counter Using Plastic Scintillators D. B. Charleston and N. J. Yasillo . . . . .	87
Modification of the ACRH Brain Scanner R. N. Beck, D. B. Charleston, P. Eidelberg and P. V. Harper . . . . .	89
Modification of the Picker Magnascanner R. N. Beck, D. B. Charleston and P. V. Harper . . . . .	91
Modification of a Laminated Iron Room by the Addition of a "Drawbridge" Type Patient Transfer Assembly for Whole-Body Scanning D. B. Charleston, E. Mason and J. J. Stupka . . . . .	92
Behavioral Indicators of Small or Transient Lesions in the Nervous System L. T. Zimmer . . . . .	94
Technetium- $^{99\text{m}}$ as a Scanning Agent P. V. Harper and K. Lathrop . . . . .	96

	<u>Page</u>
The Pharmacodynamics of Technetium Pertechnetate ( $^{99m}\text{TcO}_4^-$ )	
P. V. Harper and K. Lathrop . . . . .	97
$^{131}\text{I}$ -Antifibrinogen	
P. V. Harper and I. Spar . . . . .	98
Short-Lived Isotopes	
P. V. Harper, K. Lathrop and E. Schmidt . . . . .	100
The Mapping and Display of 3-Dimensional Isotope Distributions	
P. V. Harper, R. N. Beck and A. Gottschalk . . . . .	102
CLINICAL AND EXPERIMENTAL STUDIES ON THE EFFECTS OF RADIATION	
Impairment in Delayed Response Following Bilateral Destruction of the Dorsomedial Nucleus of the Thalamus in Rhesus Monkeys	
S. Schulman . . . . .	104
The Destruction of Small Volumes of Tissue with Beta Sources	
P. V. Harper and K. Lathrop . . . . .	106
Strontium Cordotomy Report 1964	
J. F. Mullan . . . . .	107
The Use of Low Energy Photon Emitters for Interstitial Therapy	
P. V. Harper and K. Lathrop . . . . .	109
A General Method for Internal Dosimetry of Objects of Arbitrary Shape	
P. V. Harper and E. Schmidt . . . . .	110
The Late Effects of the Deposition of Radium in Man	
R. J. Hasterlik . . . . .	111
The Effect of Bone Marrow Protection on Response to Irradiation	
L. O. Jacobson, E. L. Simmons, E. K. Marks and E. O. Gaston . . . . .	115
Control of Infection in Radiation Death	
E. L. Simmons, C. Pierce and N. Larkin . . . . .	119

	<u>Page</u>
<b>STUDIES WITH HIGH ENERGY RADIATIONS</b>	
High Energy Radiation Sources, Their Development and Maintenance L. S. Skaggs . . . . .	121
The Analog Computer L. S. Skaggs . . . . .	123
The Therapeutic Application of High Energy Sources J. W. J. Carpender . . . . .	125
Effects on Mouse Hair Roots Produced by X Ray Irradiation Combined with Radiopotentiating or Radioprotective Compounds F. D. Malkinson and M. L. Griem . . . . .	126
Modification of Radiation Response of Tissue by Actinomycin -- Preliminary Clinical Evaluation M. L. Griem and K. Ranniger . . . . .	128
Modification of Radiation Response of Tissue by Colchicine -- Clinical Evaluation of Tumor Response M. L. Griem and F. D. Malkinson . . . . .	129
Chemical Modification of Radiation Effect in Mice E. L. Simmons . . . . .	130
Physical and Biological Investigations with High Energy Radiations L. H. Lanzl . . . . .	133
Automatic Patient Contour Plotting Device L. H. Lanzl, L. Bess and M. L. Rozenfeld . . . . .	137
Analog Computer Calculation of Rotation Isodose Distribution M. L. Rozenfeld . . . . .	138
A Semi-Automatic Isodose Curve Plotter M. L. Rozenfeld, H. Vetter and L. H. Lanzl . . . . .	139
Radium Leak Detector M. L. Rozenfeld and E. W. Mason . . . . .	140
Measurement of Bone Mineral Content Using a Radio-isotopic Device L. H. Lanzl and N. M. Strandjord . . . . .	141

## GENERAL METABOLIC STUDIES

Uric Acid Metabolism in Wilson's Disease

L. B. Sorensen, R. Reilly and A. Kappas

Hypouricemia represents one of the biochemical manifestations of Wilson's disease. In this study uric acid-2-<sup>14</sup>C was intravenously administered to 2 patients with this metabolic disorder in order to study pool size and turnover of this purine and cumulative urinary recovery of injected material before and after therapy with penicillamine. Pretreatment values in 1 patient were: pool, 217 mg; plasma uric acid, 0.9 mg per cent; turnover, 477 mg/day; uric acid clearance, average 32.6 ml/minute; and cumulative recovery 95.9 per cent (recovery of injected dose in normals is about 2/3). After 5 months therapy with clinical improvement values were: pool, 300 mg; plasma uric acid, 2.7 mg per cent; turnover, 426 mg/day; clearance, average 9.5 ml/minute; and cumulative recovery, 89.9 per cent. In the second patient, pretreatment values were: pool, 370 mg; plasma uric acid, 2.0 mg per cent; turnover, 720 mg/day; uric acid clearance, 24.0 ml/minute; and cumulative recovery, 86.8 per cent. After 19 months treatment with marked clinical improvement values were: pool, 486 mg; plasma uric acid, 3.0 mg per cent; turnover, 734 mg/day; clearance, average 14.1 ml/minute; and cumulative recovery 72.6 per cent. Pool size, renal clearance, cumulative

recovery of injected dose, and plasma uric acid were markedly abnormal in both patients before therapy; following treatment and subsequent clinical improvement, these chemical and physiological indices reverted towards normal. These parameters of uric acid metabolism provide useful objective measures of the beneficial effects of penicillamine therapy in Wilson's disease associated with renal-tubular dysfunction; they may also serve as important adjuncts to direct estimation of liver copper in evaluating clinical status in general in this disorder.

#### Molybdenum-99, A New Isotope for Scintillation

##### Scanning of the Liver

L. B. Sorensen

Recent studies have shown that molybdenum-99 injected in a single tracer dose as ammonium molybdate disappears rapidly from the circulation of man. Six hours after injection of carrier-free material into normal subjects, the blood level of  $^{99}\text{Mo}$  falls to less than 1/300 of the initial concentration. By use of collimated probes, as well as by postmortem radioassay of tissues, this rapid clearance has been shown to be due to a selective concentration of molybdenum in the liver.

From excretion data it is estimated that the uptake of  $^{99}\text{Mo}$  by the normal liver is about 80 per cent when carrier-free material is injected. The biological half-life of  $^{99}\text{Mo}$  determined from

whole-body counts is about 20 days. Studies in rats have shown that labeled molybdenum is incorporated as a non-dialyzable component of the xanthine oxidase molecule. In man, this enzyme is chiefly -- perhaps exclusively -- located in the liver.

The specificity of the liver for molybdate permits scanning of the organ for which purpose the 0.140 MeV  $\gamma$  radiation of the daughter technetium-99m is particularly suitable. Good visualization of the liver is obtained when scans are done 24 hours after injection of 40  $\mu\text{c}$  of  $^{99}\text{Mo}$ . At this time, maximum build-up of technetium-99m has taken place in the liver. Space-occupying lesions are readily visualized. In diffuse hepatocellular diseases, the liver accumulates less of the administered dose of  $^{99}\text{Mo}$ , leaving more of the isotope available for urinary excretion.

Molybdenum-99 has several advantages over colloidal gold and  $^{131}\text{I}$ -labeled rose bengal: 1) it accumulates in the hepatic parenchymal cells and its uptake portrays effectively disease states of parenchymal cells; 2) the concentration of the tracer does not change during the interval of the scan since the isotope has a long biological half-life; and 3) there is superior scanning resolution due to the softer  $\gamma$ -radiation of technetium-99m.

Steroid Studies

A. Kappas, F. Katz and R. H. Palmer

The major research interests of this program center on steroid metabolism and pharmacology, with particular emphasis on study of the biological properties of metabolites derived from the in vivo degradation of adrenal and gonadal hormones -- a line of investigation which has demonstrated that the extensive chemical transformations which steroid hormones undergo in vivo (including conjugation) do not necessarily "inactivate" them but may lead to the formation of new compounds having novel and potent biological activities, certain of which have relevance to clinical medicine. A new class of fever-producing agents has been described. These pyrogens are steroid metabolites of the  $5\beta$ -H (A:B cis) class and are derived from the endogenous transformations of precursor hormones, none of which display this biological effect. Extensive studies of these  $5\beta$ -H compounds (previously considered "inert") have dealt with the characteristics of the febrile reaction which they induce in man; the species specificity of this action; and its structural determinants. The mechanism by which  $5\beta$ -H steroids produce fever is not yet clear; no evidence has been adduced to implicate the "leukocyte pyrogen" in the process of thermogenesis. Participation of steroid pyrogen in the mechanism of clinical fever has been demonstrated in studies by others (Bondy, Yale University) in periodic fever;

steroid pyrogen action has been related to the mechanism of fever in certain patients with the adreno-genital syndrome and liver disease. In addition, further studies on steroid fever are being conducted in leukopenic patients, and the species specificity and characteristics of the inflammatory reaction induced by these compounds are being examined in experimental animals; the hemolytic properties of these neutral  $5\beta$ -H steroids have also been studied. Among structurally related derivatives of cholesterol, certain C<sub>24</sub> steroid (bile) acids also have fever-producing and hemolytic properties. Lithocholic acid, the most potent of these breakdown products of cholesterol, has been of particular interest to us and studies are being conducted on its metabolic degradation; its cirrhosis-producing activity; and its newly discovered role in the experimental production of gallstones in animals.

Estriol, a major metabolite of natural estrogen, is a prototype of another class of substances (C<sub>18</sub> phenolic steroids) which has previously unsuspected biological properties which we have found in the course of our studies. These include potent suppressive action on certain delayed-type immunologic responses such as those represented by the skin reaction to tuberculin and thyroglobulin; as well as those organ responses in which delayed-type sensitivity is considered to play a prominent role, such as auto-immune thyroiditis and adjuvant-induced immune polyarthritis. The close morphologic and histologic resemblance of immune

(adjuvant) polyarthrititis in rats to human rheumatoid disease, and the marked suppressive action of estriol on the former, have prompted its use in large amounts in therapy of rheumatoid patients and the results are clearly beneficial; an extensive clinical trial appears desirable. Estriol and its natural and synthetic congeners have also been shown to markedly impair the capacity of the liver to excrete sulfobromophthalein (BSP) into the bile. The mechanism of this steroid action has been examined in detail in man and experimental animals; its structural basis has also been established. This estrogen effect applies equally to hepatic disposal of bilirubin and probably also to drugs such as tetracycline, for which the liver represents a major excretory pathway. An estrogen action of this type undoubtedly accounts in large part for certain hepatic excretory impairments which characterize pregnant women, neonatal infants, and of particular interest, women who use the new contraceptive pills containing synthetic hormones.

A variety of other studies, principally metabolic in type, is also in progress. These include investigations on the capacity of estrogens to counteract the chemical derangements accompanying hyperparathyroidism in man; the effects of estradiol and estriol on hydroxyproline metabolism in humans; the effects of these steroids on secretory rates of cortisol and aldosterone and on production of cortisol and thyroxine-binding globulin (with

particular emphasis on the principal basis of these actions) and the nature, source and role of hormonal substances in parotid gland secretions.

#### Radiation Injury

G. V. LeRoy, J. H. Rust and G. B. Ho

It is known that radiation injury is associated with alterations in a number of biochemical processes, such as biosynthesis of nucleic acids, metabolism of sulfhydryl-containing compounds, biosynthesis of cholesterol, increased glycogenesis, et cetera. None of these changes, however, seems drastic enough to be lethal either individually or in concert. Seeking a biochemical lesion caused by a lethal dose of radiation, we investigated some aspects of the intermediary metabolism of simple carbon compounds that are oxidized for energy production. When we looked for evidence of inactivation of enzymes in intact animals we studied the time-course of  $^{14}\text{CO}_2$  in expired air after administration of certain substrates (bicarbonate, formate, acetate, pentose and hexoses) labeled with radiocarbon. In addition, we examined in a preliminary fashion the fixation of  $\text{CO}_2$  in liver glycogen, and the transfer of carbon from various sources into urea.

The results of the first series of experiments -- using nearly 1,000 rats -- can be summarized:

(1) There is a significant decrease in the output of  $\text{CO}_2$  in expired air: the respiratory quotient becomes less than 0.7.

(2) The apparent rate of oxidation of pentose, hexose, and acetate, as measured by the appearance of  $^{14}\text{CO}_2$  in expired air, decreases to about 3/4 of the value in controls: this cannot be attributed to injury to intracellular oxidative enzyme systems.

(3) The metabolic pathway for the transfer of carbon from alanine (pyruvate) to urea was not sensitive to radiation, whereas that for glucose carbon was seriously impaired.

(4) Glycogenesis by the liver was significantly increased.

(5) Fixation of  $\text{CO}_2$  in liver glycogen was more than 70 times greater in the irradiated rats than in the controls.

It seems that radiation may have a greater effect on anabolic processes -- which it appears to enhance -- than on catabolic or oxidative reactions. Further studies of the enhanced glycogenesis are in progress.

#### Respiration Pattern Analysis

G. W. LeRoy

Respiration pattern analysis is a relatively new technique for the in vivo study of biological systems. Analysis of the rate of expiration of  $^{14}\text{CO}_2$  following administration of an appropriately labeled substrate provides a powerful tool for the study

of metabolic pathways and for examination of individual variations in different metabolic states and disorders with little or no disturbance of the subject. The early work in this field began independently about 12 years ago at the Donner Laboratory (University of California) and here at the Argonne Cancer Research Hospital. We use a GM detector in our instrument, while most other workers use an ionization chamber system. Our instrument was the first to incorporate a complete information-logging and processing system, thus permitting machine analysis of data.

We have devoted a great deal of effort to studies of the  $\text{CO}_2$  pool in man since it is the final common pathway through which  $^{14}\text{CO}_2$  of metabolic origin must pass. Although dimensions can be assigned to the pool there are good reasons to question their validity. Doubt arises because of the need to assume the existence of a steady-state during an isotope dilution experiment. It is debatable if this is a valid assumption for short-term periods of observation in man.

It appears that it may not be necessary to know the dimensions of the  $\text{CO}_2$  pool for many applications of respiration pattern analysis.

The Argonne Cancer Research Hospital' Total-Body Counter

R. J. Hasterlik, G. V. LeRoy and C. M. Newton

Metabolic studies using calcium-47 as a tracer of calcium metabolism have been completed on 16 hospitalized patients. In

addition, studies of the metabolism of real and simulated fission products have been carried out on 102 healthy volunteers.

In order to quantitate changes in body content of a radioisotope with the greatest precision, it is necessary to design the facility with maximum flexibility for crystal arrangement and then to arrange the crystals in their optimally determined positions. Studies carried out in the past 2 years have been concerned specifically with 2 factors contributing to the insensitivity of the counters to redistribution of an isotope in the body.

(1) The crystal array may count an isolated source with an efficiency sensitive to source position. (2) Distortion of the observed  $\gamma$  spectrum by Compton and other absorptive effects is sensitive to body build and isotope distribution.

We have written a computer program for the University's IBM 7094 which expedites determination of the optimal 2-, 3-, and 4-crystal linear arrays for any specified linear source locus parallel to the array axis. Degree of optimization for any crystal array is estimated by an error function, and the calculated error is printed for crystal positions near the optimal.

A method has been developed for approximate correction for counting efficiency shifts resulting from distortion of the  $\gamma$  spectrum within bodies of varying size and shape. A standard radioactive source was taped to selected points on the surface of a subject's body and the subject counted prone and supine.

Averaged prone and supine spectra provided data for a regression calculation of constant coefficients. Using these coefficients, the formula's ability to correct for shifts in photopeak counts was then tested by counting the same patient at certain times after ingestion of a nonabsorbable capsule containing a known quantity of the same isotope.

Inspection of data derived by these methods leads to the conclusion that the described methods do indeed provide a desired correction. These studies are preliminary to the development of methods for the derivation of corrections for accurate quantitation of two  $\gamma$ -emitting radioisotopes counted simultaneously in individuals of differing size and shape and which may translocate during the course of the studies.

#### Studies of Real and Simulated Fallout

G. V. LeRoy, J. H. Rust and R. J. Hasterlik

Real and simulated particulate fallout and solutions of strontium-85 chloride and cesium-134 chloride were fed to 102 healthy volunteers. Absorption and retention of ingested radioactivity were measured by whole-body counting using the gamma-ray spectrometer that was constructed for the Argonne Cancer Research Hospital. An average of 3 per cent of the  $\gamma$ -radioactivity of week-old local fallout was absorbed. The doses fed were too small to permit estimates of rate of elimination or identification of

particular nuclides. Using simulants and solutions of  $^{85}\text{Sr}$  and  $^{134}\text{Cs}$ , useful information was obtained on the distribution of values for absorption and retention.

The average absorption of strontium was 16 per cent, and the range was 8 to 34 per cent. Excretion of strontium varied considerably: the median value for retention at one year was estimated as about 16 per cent, and the range was from none detectable to about 25 per cent. The metabolism of strontium was the same when it was given as a solution of chloride, or leached slowly from simulated fallout.

The biological half-time for excretion of cesium was  $91 \pm 18$  days. About 90 per cent of the material was absorbed when it was fed as a solution of cesium-134 chloride.

Absorption and retention of barium was as variable as that of strontium. When  $^{133}\text{BaO}$  was fed, absorption ranged from 1 to 15 per cent.

#### Studies on the Metabolism of Magnesium in the Rat

J. G. Chutkow

Previous work on the absorption, excretion and tissue distribution of magnesium in normal animals using  $^{28}\text{Mg}$  has been extended to young rats fed a diet low in magnesium. Symptomatic magnesium deficiency was accompanied by hypomagnesemia; hypophosphatemia that could be corrected by realimentation with magnesium; continued

fecal and negligible urinary excretion of  $^{28}\text{Mg}$ ; and an increased absorption which was not due either to hypomagnesemia per se or to a selective increase in uptake of magnesium in any one segment of bowel. These absorptive changes could be reversed initially but not later by large amounts of magnesium administered by gavage.

In normal bone, kidney, heart, and liver, exchangeable magnesium appeared to be in at least 2 forms, one of which turned over more rapidly than the other. Brain, muscle, and testicle took up  $^{28}\text{Mg}$  slowly and lacked the more labile phase. The radioisotope was diverted from bone to the soft tissues in hypomagnesemic rats.

Experiments on the central nervous system, renal and cutaneous effects of magnesium deficiency are under design at present. These will include tissue electrolyte and light microscopy studies. The kidneys will be examined by electron microscopy. In addition to the electroencephalographic changes accompanying the development of the audiogenic seizures in magnesium deficiency, possible alterations in the content and distribution of serotonin and norepinephrine in the brain will be studied. Similar chemical determinations will be made on the skin during the phase of intense vasodilatation.

Specific Metabolic Processes in Skin

A. L. Lorincz

It was recently demonstrated in this laboratory that normal appearing skin surfaces in psoriatic patients have only one-tenth the cholesterol esterifying ability shown by skin surfaces of non-psoriatic persons. There is reason to believe that this epidermal biochemical deficiency related to disturbed keratinization may represent the basic, genetically determined, defect underlying susceptibility to psoriasis. Experiments are currently underway using  $^{14}\text{C}$  acetate incubated with epidermal sheets to show by means of thin layer chromatographic techniques the precise ways in which cholesterol producing metabolic pathways differ in normal-appearing skin of psoriatic subjects from such pathways in skin of normal subjects. Further studies on skin surface cholesterol esterifying ability in the kindred of psoriatic patients are also being initiated to determine the mode of inheritance of the deficiency shown by psoriatics, and to see whether latent susceptibility to psoriasis can be detected.

Additional studies to develop a means for quantitatively measuring the rate of physiological desquamation under normal and various disease conditions using radiosulfur-labeled cysteine tracer techniques are being pursued. The rate of physiological desquamation is believed to have critical bearing on susceptibility to a number of skin diseases and infections.

**REFERENCE REQUEST—FEDERAL RECORDS CENTERS**

**NOTE: Use a separate form for each request.**

**SECTION I—TO BE COMPLETED BY REQUESTING AGENCY**

ACCESSION NO. <b>434-91-0014</b>	AGENCY BOX NUMBER <b>3 OF 29</b>	RECORDS CENTER LOCATION NUMBER <b>532349</b>
-------------------------------------	-------------------------------------	---

DESCRIPTION OF RECORD(S) OR INFORMATION REQUESTED

BOX

FOLDER (include file number and title) **1 Book Job # 1165**

REMARKS

**Meeting of Advisory Committee  
Argonne Cancer Research Hosp,  
March 4-5, 1965**

**NATURE OF SERVICE**

FURNISH COPY OF RECORD(S) ONLY     PERMANENT WITHDRAWAL     TEMPORARY LOAN OF RECORD(S)     REVIEW     OTHER (Specify)

**SECTION II—FOR USE BY RECORDS CENTER**

- RECORDS NOT IN CENTER CUSTODY     RECORDS DESTROYED
- WRONG ACCESSION NUMBER—PLEASE RECHECK
- WRONG BOX NUMBER—PLEASE RECHECK
- WRONG CENTER LOCATION—PLEASE RECHECK
- ADDITIONAL INFORMATION REQUIRED TO IDENTIFY RECORDS REQUESTED
- MISSING (Neither record(s), information nor charge card found in container(s) specified)
- RECORDS PREVIOUSLY CHARGED OUT TO (Name, agency and date):

REMARKS

**Viewing Room**

DATE

SERVICE

TIME REQUIRED

SEARCHER'S INITIALS

**3/28/95**

**SECTION III—TO BE COMPLETED BY REQUESTING AGENCY**

NAME OF REQUESTER **JANET ANDERSON**    TELEPHONE NO. **708 252 8699**     FTS    DATE **3/28/95**

**RECEIPT OF RECORDS**

NAME AND ADDRESS OF AGENCY

(Include street address, building, room no. and ZIP Code)



Requester please sign, date and return this form, for file item(s) listed above, ONLY if the block to right has been checked by the Records Center.

SIGNATURE

**J. Anderson**

DATE

**3/28/95**

NSN 7540-00-682-6423  
5011-108

**1167962**

PREVIOUS EDITION USABLE

OPTIONAL FORM 11 (Rev. 7-87)  
NATIONAL ARCHIVES AND  
RECORDS ADMINISTRATION  
36 CFR 1228.162