1196R

717255

OFFICE OF CHIEF COUNSEL
FILE
No papers will be removed herefrom
without special authority

BEST COPY AVAILABLE

REPOSITORY Oak Ridge Operations Records Holding Area
COLLECTION Documentary 244-94 PERSONNEL - 1
BOX No. A-12-9 Bldg. 2714-H FOIA
FOLDER Personnel-1 FOIA Howard Rosenberg

Howard Rosenberg
Washington Merry-Go-Round
Jack Anderson Enterprises
1979- July '81
Book I

1113675

JUL 28 1981

Mr. Howard L. Rosenberg
c/o Jack Anderson Enterprises
1401 16th Street, NW
Washington, D. C. 20036

Dear Mr. Rosenberg:

Please accept this letter in complete response to your Freedom of Information Act request dated July 10, 1981, which was accepted for response on July 15, 1981.

The following information has been determined to be responsive to your request and is transmitted herewith:

1. The following proposals/protocols concerning radiation therapies and treatments submitted to the Committee on Human Studies:

   - Study of Granulocyte Kinetics in Myeloproliferative Diseases
   - Studies of TBI in Patients with Hematologic Disorders
   - Therapeutic Allogeneic Transplantation of Human Bone Marrow
   - Changes in Blood Enzyme Levels Following Exercise and/or TBI in Man
   - Effect of Splenectomy and TBI on Onset of Blast Crisis and Survival in Chronic Granulocytic Leukemia

   In addition to the above proposals and protocols, which are all the radiation therapy proposals submitted to the Committee for review, you will find included all related Committee notes, minutes, recommendations and actions, and any interim progress or final reports submitted to the Committee concerning the therapy or course of treatment under the study. We have been unable to identify any other particular repository of, or source for, unpublished reports that may have resulted from therapy approved or reviewed by the Committee.

CONCURRENCE
RTG. SYMBOL CC-10
INITIALS/SIG. DEL
DATE 7/21/8
RTG. SYMBOL CC-10
INITIALS/SIG. JL
DATE 7/21/81
RTG. SYMBOL ER-13
INITIALS/SIG. REB
DATE 7/27/81
G. SYMBOL R-13
RB
E
/27/8
SYMBOL
-40
ALS/SIG.
W
28/81
YMBOL
S/SIG.
MBOL
SIG.
OL
3.

PERSONNEL
FOIA

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

DOE F 1325.10 OFFICIAL FILE COPY

1113676

100 R PROTRACTED @ 0.0 R/MIN. ☒ DURING IRRADIATION ☐ AFTER IRRADIATION

L.T.B.I.-II

Name [redacted] number [redacted]

Day of treatment	F		0	1	2	3	4	→	→	7	—	9	→	11	→	14	→	16	→	18	→	→	21		25			28		32			35		37
			M	T	W	Th	F			M		W		F		M		W		F			M		F			M		F			M		F
			OCTOBER																						NOVEMBER										
Date month / day	5		8	9	10	11	12			15		17		19		22		24		26			29		2			5		9			12		16
Hematology																																			
CBC	•		•																																
Platelets	•		•																																
Diff	•																																		
Retics	•																																		
MARROW Morphology Cytogenetics	•																						CYTOGEN.												
Serum total, direct bilirubin	•																																		
Uric Acid	•																																		
LDH	•																																		
Chemistry																																			
Serum B_{12}			•																																
Serum Unsat. Fe-Bind. Capacity			•																																
Serum Iron			•																																
Serum TIBC			•																																
Leukocyte Alk. PO4	•																																		
2 tubes heparinized blood-pts. Colyer			•																																
Bacteriology																																			
Rec Serum-Ricks			•																																
Rec Sahra Ginsberg			•																																
Liver Spleen Scan	•																																		
Marrow Scan	•																																		
SPLENECTOMY -																																			

1113677

OAK RIDGE ASSOCIATED UNIVERSITIES
Oak Ridge, Tennessee

Consent to Operation

PATIENT _____ AGE _____

DATE _____ TIME _____ A.M. P.M. PLACE _____

1. I hereby authorize the medical staff of the ORAU Medical Division, or such physician as they may designate, to perform upon _____ (state name of patient or myself) the following operation: _____

_____.

If in the course of the operation any unforeseen condition arises calling for procedures in addition to or different from those now authorized, I further request and authorize him to do whatever he deems advisable.

2. The nature and purpose of the operation, possible alternative methods of treatment, the risks involved, and the possibility of complications have been fully explained to me, I acknowledge that no guarantee or assurance has been made as to the results that may be obtained.

3. I consent to the administration of anesthesia by or under the direction of a staff member of the ORAU Medical Division or such other qualified person as he may designate. I further consent to the use of such anesthetics as he may deem advisable with the exception of _____. (if none, so state)

4. I consent to the disposal by authorities of the ORAU Medical Division of any tissues or parts which may be removed.

5. I consent to the taking and publication of any photographs in the course of this operation for the purpose of advancing medical education and science.

6. For the purpose of advancing medical education and science, I also consent to the admittance of observers to the operating room.

I CERTIFY THAT I HAVE READ AND FULLY UNDERSTAND THE FOREGOING CONSENT TO OPERATION, THAT THE EXPLANATIONS THEREIN REFERRED TO WERE MADE, AND THAT ALL BLANKS OR STATEMENTS REQUIRING INSERTION OR COMPLETION WERE FILLED IN AND INAPPLICABLE PARAGRAPHS, IF ANY, WERE STRICKEN BEFORE I SIGNED.

Signature of Patient _____

Signature of Patient's Spouse _____

When the patient is a minor or incompetent to give consent:

Signature of person authorized to give consent _____

Relationship to Patient _____

WITNESS: _____

1113678

OAK RIDGE ASSOCIATED UNIVERSITIES

OAK RIDGE, TENNESSEE

Authorization for the Administration of Radioactive Substance

I hereby authorize the staff of the ORAU Medical Division to administer to _____ the following radioactive substance _____ _____

Nuclide Chemical

The purpose of this procedure has been explained to me as being:

_____

_____

_____

Its relevance to my condition, the risks and any possible alternatives have been explained to me.

_____

Signature of Patient or Guardian

_____

Date

AUTHORIZATION FOR THE ADMINISTRATION OF RADIOACTIVE SUBSTANCE MED-148 (11-72)

1113679

VIII. Analysis of Results:

A. The study will focus on:

1. Length of survival.

2. Relative effects on morbidity including duration of time patient is in complete or partial remission.

3. Effect of splenectomy on eradication of the Ph^1 chromosome.

4. Duration of time from onset of disease and from date of splenectomy to onset of the blast crisis.

IX. Consent Forms:

A. Protocol Laboratory Data Sheet

B. Consent for Administration of Radioactive Material.

C. Consent for Operation.

D. Consent for Experimental Protocol.

X. References:

A. Williams, W. J. et al, Hematology p. 689, 1972. McGraw-Hill, Inc.

B. Kahn, S. B. and Brodsky, I.: Therapy of Myeloproliferative Disorders. In Cancer Chemotherapy II. 22nd Hahnemann Symposium. I. Brodsky and S. B. Kahn (Eds.). Grune and Stratton, New York, 1972.

C. Medical Research Council's Working Party for Therapeutic Trial in Leukemia. Chronic Granulocytic Leukemia; Comparison of Radiotherapy and Busulfan Therapy. Brit. Med. J. 1:201, 1968.

D. Brodsky, I., Ross, E., Petkov, G., and Kahn, S. B.: Platelet and Fibrinogen Kinetics with (^{75}Se) Selenomethionine in Patients with Myeloproliferative Disorders. British J. Haemat. 22: 179, 1972.

E. Frei, E.: Therapy of Acute Leukemia. In Cancer Chemotherapy II. 22nd Hahnemann Symposium. I. Brodsky and S. B. Kahn (Eds.) Grune and Stratton, New York, 1972.

XI. Isotopes and New Drugs:

No new radioisotopes or new drugs would be involved in this study.

1113680

5. Maintenance: After obtaining a remission, those patients who are splenectomized will not receive additional treatments until the wound is completely healed. Patients will be followed and treated with either fractionated doses of total-body irradiation or protracted doses of total-body irradiation to maintain their remission state. Patients who are treated with 30 R fractionated doses will be easier to follow and maintain their blood cell counts at normal levels. It will be more difficult to maintain in remission patients who are to be treated with protracted doses of total-body irradiation. These patients for the most part would be given 100 or 150 R. This group of patients should not have white counts ever exceeding 50,000 cu/mm or platelet counts exceeding 1,000,000 cu/mm.

6. Splenic infarct: There will be no change in treatment for this condition.

7. Blast crisis: Development of blast crisis will result in discontinuation of total-body irradiation.

8. Measurement of effect, of course, will be determined by whether or not the patients achieve a complete remission, partial remission, or are just improved following treatment.

III. Dose Modification and Toxicity:

Radiation doses will be modified in accordance with toxicity during maintenance or as present at time of beginning the next course of radiation treatment.

A. Hematologic: No total-body irradiation will be given if the platelets fall below 100,000 during maintenance phase or if the white count falls below 3,000.

B. Associated myelofibrosis: The dose of total-body irradiation will not be changed for the presence of associated myelofibrosis unless these patients have blood counts which prevent treatment.

C. Splenic infarct: There will be no change in treatment of this condition.

D. Blast crisis: The development of blast crisis will result in discontinuation of total-body irradiation.

IV. Measurement of Effect:

A. Complete remission: Complete remission will be defined as a white count between 4,000 cu/mm and 12,000 cu/mm in the absence of splenomegaly and in the presence of a stable weight. The hemoglobin should be above 12 g % and hematocrit above 36%. Systemic complaints such as excessive fatigue, sweating, fever, night sweats, and anorexia should be absent. If the total-body irradiation therapy would lead to normal platelet count or thrombocytopenia without a change in the white count to 4,000 to 12,000 cu/mm or should the patient maintain thrombocytosis ($>450,000/mm^3$) but change to a normal white blood cell count, then a complete remission will not have occurred. The bone marrow cellularity should return to normal and the GE ratio must not exceed 5:1. Serum vitamin B-12, unsaturated vitamin B-12 binding capacity and leukocyte alkaline phosphatase should be normal. Spleen size should be evaluated by means of the radiocolloid scan.

1113681

100 R TRUNCATED @ 0.0 R/MIN.

X DURING IRRADIATION
● AFTER IRRADIATION

L.E.T.B.I.-II

Name [redacted] number [redacted]

Day of treatment	F		0	1	2	3	4	→	→	7	–	9	→	11	→	14	→	16	→	18	→	→	21		25			28		32			35		37
			M	T	W	Th	F			M		W		F		M		W		F			M		F			M		F			M		F
Date month			OCTOBER																																NOVEMBER
day	5		8	9	10	11	12			15		17		19		22		24		26			29		2			5		9			12		16
Hematology																																			
CBC	•		•																																
Platelets	•		•																																
Diff	•																																		
Retics	•																																		
MARROW Morphology Cytogenetics	•																						Cytogen.												
Serum total, direct bilirubin	•																																		
Uric Acid	•																																		
LDH	•																																		
Chemistry																																			
Serum B_{12}			•																																
Serum Unsat. B_{12}-Bind. Capacity			•																																
Serum Iron			•																																
Serum TIBC			•																																
Leukocyte Alk. PO4	•																																		
Bacteriology																																			
2 tubes heparinized blood - Mrs. Colyer			•																																
2cc Serum - RICKS			•																																
12cc Saliva EVANS KAS			•																																
Liver, Spleen Scan	•																																		
Marrow Scan	•																																		

1113682

Lindbaugh Edwards. Vodoviche. Nemile

Cytogenetics

PS Form 3811, Jan. 1979

RETURN RECEIPT, REGISTERED, INSURED AND CERTIFIED MAIL

SENDER: Complete items 1, 2, and 3.
Add your address in the "RETURN TO" space on reverse.

1. The following service is requested (check one.)
- ☐ Show to whom and date delivered..... ___¢
- ☐ Show to whom, date and address of delivery.... ___¢
- ☐ RESTRICTED DELIVERY
  Show to whom and date delivered..... ___¢
- ☐ RESTRICTED DELIVERY.
  Show to whom, date, and address of delivery.$___

(CONSULT POSTMASTER FOR FEES)

2. ARTICLE ADDRESSED TO:
Howard L. Rosenberg
1401 16th St., NW
Washington, DC 20036

3. ARTICLE DESCRIPTION:

REGISTERED NO.	CERTIFIED NO.	INSURED NO.
	811764	

(Always obtain signature of addressee or agent)

I have received the article described above.
SIGNATURE ☐ Addressee ☐ Authorized agent

4. DATE OF DELIVERY | POSTMARK

5. ADDRESS (Complete only if requested)

6. UNABLE TO DELIVER BECAUSE: | CLERK'S INITIALS

GPO : 1979-300-488

No. 811764

RECEIPT FOR CERTIFIED MAIL

NO INSURANCE COVERAGE PROVIDED—
NOT FOR INTERNATIONAL MAIL
(See Reverse)

SENT TO
Howard Rosenberg

STREET AND NO.
1401 16th St. NW

P.O., STATE AND ZIP CODE
Washington, DC 20036

POSTAGE			$
CONSULT POSTMASTER FOR FEES	CERTIFIED FEE		¢
OPTIONAL SERVICES	SPECIAL DELIVERY		¢
	RESTRICTED DELIVERY		¢
	RETURN RECEIPT SERVICE	SHOW TO WHOM AND DATE DELIVERED	¢
		SHOW TO WHOM, DATE AND ADDRESS OF DELIVERY	¢
		SHOW TO WHOM AND DATE DELIVERED WITH RESTRICTED DELIVERY	¢
		SHOW TO WHOM, DATE AND ADDRESS OF DELIVERY WITH RESTRICTED DELIVERY	¢
TOTAL POSTAGE AND FEES			$

POSTMARK OR DATE

PS Form 3800, Apr. 1976

1113683

HOWARD LAWRENCE ROSENBERG
8709 Sundale Drive, Silver Spring, Maryland 20910
(301) 585-6408

July 10, 1981

MR. Wayne Range
Department of Energy
Oak Ridge Operations
P.O. Box E
Oak Ridge, TN 37830

RE: FOIA Request
and your response of
March 5, 1981

Dear Mr. Range:

Please consider this request as a continuation of my request of Feb. 13, 1981 and Jan. 27, 1981. I am still hoping for more elaborative documentation regarding protocols for certain medical therapies tried at ORAU and ORNL and submitted for review to the Human Use Committee there.

Under the provisions of the Freedom of Information Act, 5 U.S.C 522, I am requesting access to detailed information relating to experimental therapies tried at ORAU and ORNL over the past 14 years. In your prior response to me of March 5, 1981, you included a listing of proposals submitted for review to the "ORAU/ORNL Committee on Human Studies." Specifically, I am requesting verbatim copies of the protocols submitted, any progress reports written concerning those protocols and all final reports of the experiments.

As you know, the act permits you to reduce and waive fees when the release of the information is considered as "primarily benefitting the public." Since I am requesting this information as part of an on-going inquiry into the effects of radiation on man, and into the U.S. government' efforts to quantify those effects, and since these questions are still open to wide debate, I believe that this request fits that category and I therefore ask you to waive any fees. My request for a fee waiver was granted on Feb. 20, 1981, and since this request is a continuation of the same inquiry, I assume fees will continue to be waived.

If all or any part of this request is denied, please cite the specific exemption(s) which you think justifies your refusal to release the information, and inform me of the appeal procedures available to me under the law. I would appreciate your handling this request as expeditiously as possible. I look forward to hearing from you within 10 days, as the law stipulates.

Please respond to the address listed below:

1401 16th St. NW
Washington, D.C. 20036

Sincerely,

Howard L. Rosenberg

1113684

PERSONNEL
FOIA

I have talked with _____ about the
Name

proposed course of treatment to be given _____
Name

including the following:* _____

1. The planned treatment consists of total-body irradiation and possibly splenic radiation to achieve a remission in the disease; white blood cell count below 15,000/mm^3, platelet count below 600,000/mm^3, and spleen smaller than 10 cm below rib margin.
2. When the patient is in remission, a splenectomy will be done at the Oak Ridge Hospital of the Methodist Church or another hospital that he (she) selects and by a surgeon of his (her) choice.
3. Throughout the treatment and observation periods, frequent tests and examinations will be done to check on the progress of the disease and its response to therapy. These tests include:
   A. Blood samples of 5-25 ml up to 3 times a week.
   B. Bone marrow aspirate or biopsy as required to note the course of the disease.
   C. Scans of bone marrow, liver and spleen.
4. The risks involved in this treatment plan are A) the early and late risk of irradiation; B) the early and late risks of splenectomy.
   A. The early risk of TBI is limited to the slight risk of the patient getting a greater exposure than planned, plus the risk that the prescribed dose is too great or that the patient is unusually susceptible to radiation. The degree and duration of the resulting pancytopenia and the risk of infection or bleeding would depend on the magnitude of the over-dosage. We believe that the total risk is minimal because of our built-in controls, our frequent monitoring of the radiation and its effect, and our experience at selecting and predicing the response to single exposures of TBI.
   The late risks of TBI include theoretical or possible risk of acceleration of the onset of the blast cell crisis or cataract formation.
   B. The early risk of splenectomy is that attending any major abdominal surgery with general anesthesia plus the risks of thrombosis or abnormal clotting associated with the post splenectomy thrombocytosis.
   The late risks of splenectomy is a possible decreased resistence to infection or other yet unknown or unanticipated risks of splenectomy specifically in this disease.
5. The benefits anticipated from the splenectomy at this stage in CGL include: 1) Elimination of the enlarged spleen which often causes discomfort and other symptoms, 2) Eliminating risks of serious complications, specifically related to the large spleen, viz., splenic infarctions, splenic rupture and hypersplenism, 3) possible subsequent easier management of the CGL and 4) possible longer survival or prolonged remissions.
6. The patient has the right to withdraw at anytime from the study.
7. The patient assumes responsibility to cover the costs of the surgery and hospitalization.

Physician _____

WITNESS _____ (Patient)

_____

Date _____

1113685

Ident. No. 24

APPLICATION FOR THE USE OF HUMANS AS EXPERIMENTAL SUBJECTS

TO: COMMITTEE ON HUMAN STUDIES
Oak Ridge Associated Universities and
Oak Ridge National Laboratory

Date: December 11, 1973

Principal Investigator: Francis A. Goswitz, M.D.

Co-Investigators: C. Lowell Edwards, M.D.
Helen Vodopick, M.D.
Gayle Littlefield, Ph.D.

Title of Project: EFFECT OF SPLENECTOMY AND TOTAL-BODY IRRADIATION ON ONSET OF BLAST CRISIS AND SURVIVAL IN CHRONIC GRANULOCYTIC LEUKEMIA

I. Objectives of Experiment:

A. Background and introduction: Prior studies at NIH and at the Hahnemann Hospital in Philadelphia have revealed that patients who have been splenectomized are easier to manage when the blast crisis ensues than those who are not splenectomized. One explanation for this fact is that the spleen becomes extremely large and often undergoes infarction in the blast crisis. This can cause severe pain and incapacitate the patient. At the same time, the patient's metabolic rate increases, and there is increased weight loss due to the hypermetabolism engendered by this enlarged organ and by its pressure on adjacent gastrointestinal organs. For this reason, some clinicians have considered splenectomy to be in order prior to the onset of the blast crisis merely to make the remaining time for the patient more tolerable and to allow the patient to remain ambulatory for a longer period of time after onset of the blast crisis (Brodski et al, British Journal Haematology, Volume 22:179, 1972). However it has become apparent that with the use of drugs effective in the therapy of acute myelocytic leukemia remissions in the blast crisis can occur. Presently a large scale study is being done in the Eastern Cooperative Oncology Group to determine whether or not splenectomy, with or without intensive combination chemotherapy, utilizing newly acquired drugs might delay the occurrence of the blast crisis and thus prolong the life of the patient.

Recently Bayard Clarkson performed splenectomy in 20 patients with chronic granulocytic leukemia who were in remission and had conversion of the Ph^{+1} chromosome to Ph^{-1} in 4 cases. All 4 patients have normal marrows with the longest state of remission being 2 1/2 years (unpublished data).

At the Medical Division of Oak Ridge Associated Universities we have treated patients with chronic granulocytic with total-body irradiation to control their disease. Since the majority of our patients also die from the blast crisis, we would like to determine whether or not splenectomy, with or without total-body irradiation, might also postpone the occurrence of blast crisis.

1113688

5. CLINICAL IMMUNOLOGY: The patient will be carefully watched for reactions to ALG and for signs and symptoms of a GVH reaction. Before immunosuppression and after we will determine immunoglobulins and determine the degree of immunosuppression by skin tests.

6. SCIENTIFIC OBSERVATIONS: The success of the graft will be measured by the following observations in addition to the clinical observations of the patient:

   1) Hematology - CBC and platelets, reticulocyte counts, differential counts on the circulating leukocytes and bone marrow aspirate.

   2) Cytogenetic - Karyotypes of the patients' circulating lymphocytes and bone marrow cells will be compared with donor cells.

   3) Immunologic - HLA profile of leukocytes, RBC subgroups, and genetic varients of immunoglobulins will be determined for comparison with donor and recipient.

B. Patient Selection: Patients with acute leukemia (children and adults) and patients with chronic granulocytic leukemia in blast cell crisis are prospective candidates for bone marrow transplants. Later in the program, which is tentatively planned for at least three years, we might include patients with aplastic anemias, hemoglobinopathies and immune deficiency diseases. Approximately 3 to 5 bone marrow transplants per year are planned at this time, although it is difficult to anticipate how many patients will eventually be treated this way.

A patient with leukemia is considered a candidate for a marrow graft attempt only if:

   a) he has at least one living healthy sibling who could be a donor.

   b) patient, parent, or other involved family members agree in principle and are willing to participate in the effort after a thorough explanation.

1113687

Draft 12-26-69/vrs

APPLICATION FOR USE OF HUMANS AS EXPERIMENTAL SUBJECTS

I. Senior Investigator: Nazareth Gengozian, Ph. D.

Co-Investigators: C. L. Edwards, M. D.

H. A. Vodopick, M. D.

Karl Hübner, M. D.

TITLE: Therapeutic allogeneic transplantation of human bone marrow.

II. Objectives of Experiment:

A. Therapeutic: Develop techniques for achieving allogeneic bone marrow grafts in humans as treatment of:

1) patients with incurable hematological disorders and immunological deficiency diseases, and

2) persons accidentally exposed to total-body irradiation potentially lethal due to hematologic depression.

B. Scientific: Demonstration that total body irradiation at a high dose rate in combination with anti-lymphocyte-globulin (ALG) is useful immunosuppressive regimen to induce tolerance to a foreign bone marrow graft in man.

The therapeutic goals are replacement of an abnormal or damaged hematopoietic systems with normal bone marrow or the transplantation of a functioning immune-system.

As an adjunct to chemotherapy of leukemia, the transfer of lymphoid cells with the bone marrow might interfere with the growth of any malignant cells that had not been eliminated by the preceding chemotherapy or total-body irradiation.

Radiation accident victims might not require additional immunosuppression, depending on the time elapsed between the accidental irradiation and the planning of a bone marrow transplant for such a patient.

1113688

OAK RIDGE ASSOCIATED UNIVERSITIES
INCORPORATED
P. O. BOX 117
OAK RIDGE, TENNESSEE 37830

AREA CODE 615
TELEPHONE 483-5811

August 1, 1972

To: Committee on Human Studies

A. B. Brill
C. L. Edwards
M. E. Koons
R. D. Lange
T. A. Lincoln
B. M. Nelson
J. B. Storer

The Medical Division has been carrying out a research project entitled "Therapeutic Allogeneic Transplantation of Human Bone Marrow." This is based on a very extensive write-up that was presented to the Committee in December 1969 and approved in January 1970. The purpose of the present communication is to call your attention to our desire to extend this kind of treatment to patients with aplastic anemia and to provide an opportunity for comments from the Committee.

You will recall that the protocol involves one week of treatment with antilymphocyte globulin, then total-body irradiation to an air dose of 500 R and the infusion of bone marrow from a selected sibling.

So far this has been undertaken in three patients, all adults with acute leukemia. The first man had a distinct graft and remission but died about four months later of complications of cardiac and pulmonary disease without clearly demonstrable graft-vs-host reaction, and with no evidence of persistent leukemia detectable at autopsy. The second patient also had a clear-cut graft and a brief clinical remission, but within a few weeks after the treatment she developed a recurrence of her leukemia which proved fatal. The third patient is only two weeks from the time of marrow infusion. He is doing reasonably well. His bone marrow shows erythroid regeneration but the blood values do not yet demonstrate evidence of graft.

Dr. Edwards, Dr. Gengozian, and our clinical staff wish to undertake this same treatment in a patient with aplastic anemia who is seriously ill and who has been deemed by his physicians as unresponsive to therapy. His outlook at present is considered extremely poor. It is proposed to use exactly the same protocol including total-body irradiation. The reasons for this are that the protocol has proved effective in achieving a graft in the first two patients, and it appears that this program of treatment would allow a reasonable chance for maintaining the patient through the postirradiation period, even if no graft were achieved.

The original proposal stated that the patients initially selected would have acute leukemia and later the program might be extended to include patients with aplastic anemia, hemoglobinopathies, and immune deficiency diseases.

1113689

-more

With regard to the stage of leukemia we observed that in the first patient there was no recurrence of leukemia. He died from causes unrelated to his leukemia, and on autopsy there was no evidence of leukemia. The second patient (female) showed initial absence of leukemia cells from the blood or bone marrow. However, approximately 10 1/2 weeks after the transplant she developed a sudden blast cell crisis, subsequently to which she died from septicemia. In the third patient we never saw evidence for a successful take of the graft and we never observed a complete disappearance of leukemic cells from the peripheral blood and/or bone marrow.

1113690

A. The donor must be old enough and large enough to assure a sufficient amount of bone marrow for the transplant.

B. Each patient should have a satisfactory trial with combined corticosteroid-androgen therapy with no evidence of spontaneous recovery before a bone marrow graft is attempted.

AMENDMENT #2 TO THE PROTOCOL ON THERAPEUTIC TRANSPLANTATION OF HUMAN BONE MARROW

The indication for bone marrow transplantation shall be extended for patients with aplastic anemia (idiopathic and secondary). For those patients whose prognosis is potentially better than that of patients with acute leukemia we would use the previously approved radiation dose of 500 R (370 rads). But we would like to have the option to use a higher dose, since principally the same arguments with regard to HL-A and MLC matching apply to these patients. However, with approval we would like to gradually increase the radiation dose for these patients and evaluate the feasibility of higher radiation doses (up to 800 rads) for these patients with regard to tolerance and side effects as we go along.

A patient with aplastic anemia is considered to be a candidate for a marrow graft only if;

A. He has at least one living, healthy sibling, or parent, who could be a donor.

B. The patient, parent, or other involved family members agree in principle and are willing to participate in the effort after a thorough explanation of the procedure.

The pre-selection laboratory studies shall be the same as indicated on page 2 and 3 of the original proposal for bone marrow grafting in man.

Conditions to be met in patients with aplastic anemia and potential recipients of allogenic bone marrow grafts:

1113692

to accept an allogenic bone marrow graft with the antigenic differences in the HL-A system. In retrospect it may have been wise to have used a higher radiation dose before the transplant.

With these observations in mind, we should like to increase the radiation dose, especially in cases where more immunosuppression seems to be indicated. Of course, an alternative would be to increase the dosage of anti-thymocyte globulin and extend the immunosuppressive therapy before the transplant and into the immediate post transplant period. This, however, would not be desirable, since the biological activity of anti-thymocyte globulin might interfere with the successful engraftment of the bone marrow transplant. We therefore would prefer to increase the irradiation dose, since the immunosuppressive and tissue toxic effects of the irradiation are limited in time and should not interfere with the graft. Investigators in other centers report the use of up to 1,000 rads in preparation of patients for bone marrow grafting. In these centers the dose rates at which these irradiations are performed are much lower than the dose rate we use. Comparing dose rates, our dose would have to be raised to approximately 800 rads at 40 R per minute to be comparable to 1,000 rads at 5R per minute. We would like to increase our irradiation dose up to a level of 800 rads. The advantage of using a higher irradiation dose would be greater immunosuppression which appears to be needed for patients who have a donor who is less than HL-A identical (B, C or possible D matches). But even for leukemic patients with an HL-A identical donor greater immunosuppression would be desirable since HL-A typing and MLC does not seem to detect all histocompatibility differences. Since the

1113693

Ident. No. 13 (Amendment 1 & 2)

APPLICATION FOR THE USE OF HUMANS AS EXPERIMENTAL SUBJECTS

To: COMMITTEE ON HUMAN STUDIES
Oak Ridge Associated Universities and
Oak Ridge National Laboratory

Date 19 Dec. 72

Principal Investigator: N. Gengozian

Co-Investigators: C. Lowell Edwards

Helen Vodopick

Karl Hubner

Title of Project: Therapeutic Allogeneic Transplantation of Human Bone Marrow: (1) Request to increase radiation dose (2) Request to include patients with aplastic anemia.

Use Following Format (Submit Original and 8 Copies)

I. Objectives of Experiment:

(Include statement why experiment must be done in humans, and expected benefits from the knowledge.)

II. Methods of Procedure:

Brief description of methods, all medications including name and dose range, number and types of subjects anticipated, time for single session, total number of sessions, total duration of study, methods used to screen subjects, etc.

III. Possible Hazards and their Evaluation:

IV. Radioisotopes and New Drugs

If the study involves radioisotopes, indicate action of the Isotopes Committee. If new drugs are involved, indicate that appropriate application to FDA has been made.

See page 2

1113694

L. T.B.I.

Name _____ number _____

Day of treatment	-6	-5	-4	-3	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18		24		31		38		45		52
	Tu	W	Th	F	S	S	M	Tu	W	Th	F	S	S	M	Tu	W	Th	F	S	S	M	Tu	W	Th	F		Th		Th		Th		Th		Th
Date month	JUNE																										JULY								
day	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27		3		10		17		24		31
Hematology																																			
CBC		■		■			■		■		■			■		■		■			■		■		■		■		■		■		■		■
Differential		■		■			■		■		■			■		■		■			■		■		■		■		■		■		■		■
Retics		■		■			■		■		■			■		■		■			■		■		■		■		■		■		■		■
Platelets		■		■			■		■		■			■		■		■			■		■		■		■		■		■		■		■
Bone Marrow				■																					■										
Chemistry																																			
Irosorb test'	■			■			■		■		■			■		■		■			■		■		■		■		■		■		■		■
Plasma Fe	■			■			■		■		■			■		■		■			■		■		■		■		■		■		■		■
Muramidase	■			■			■		■		■			■		■		■			■		■		■		■		■		■		■		■
Serum																																			
Cholesterol				■							■										■						■								■
Triglycerides				■							■										■						■								■
Total Lipids				■							■										■						■								■
Glyceryl glycerol				■							■										■						■								■
Free glycerol				■							■										■						■								■
Bacteriology																																			
Swabs	■		■				■			■				■			■				■			■			■		■		■		■		■
Urine	■		■				■			■				■			■				■			■			■		■		■		■		■
Blood	■			■			■				■			■				■			■				■		■		■		■		■		■
Serum	■			■			■				■			■				■			■				■		■		■		■		■		■
Stool	■		■				■			■				■			■				■			■			■		■		■		■		■
Gastric	■		■				■			■				■			■				■			■			■		■		■		■		■
Catecholamines (Van Woert)		■		■		■		■		■		■		■		■		■		■		■		■											
Chromatography of Metabolism (Scott)					■										■																				

1113695

In chronic granulocytic leukemia the report of D.A.G. Galton, et al, indicates that patients given splenic irradiation and a variety of other types of external radiation develop earlier blast cell transformations than patients treated with busulfan. E. E. Osgood, on the basis of a very careful long-term study, finds that carefully titrated doses of ^{32}P give results better than any other form of reported treatment. Our past use of total-body irradiation may not be as good since it is not as well titrated as Osgood's ^{32}P. We are conscious also of the problems of busulfan including a significant incidence of early over-treatment and certain peculiar late metabolic complications.

In chronic lymphocytic leukemia there is a good deal of difference of opinion about the value of suppressive therapy, with many hematologists tending to believe that in patients who are tolerating the disease well, the less therapy the better. We recognize the possible validity of this viewpoint and adopt it with some patients, excluding them from the total-body radiation ~~times.~~ series.

V. Radioisotopes and New Drugs:

If the study involves radioisotopes, indicate action of the ORAU Medical Division Isotope Committee. If new drugs are involved, indicate that appropriate application to FDA has been made.

B. Radiation Protocols.

1. Single dose
   a. METBI - 50 R, 100 R at 1.5 R/min. Approximately 80 treatments have been given to about 75 patients. Only a few additional patients are planned for this series.

   b. LETBI - 50 - 250 R at 1.5 R/hr (up to about 9 days in the unit). Twenty patients treated. We hope to add about one patient a month for the next 3 years.

   c. UT-AEC High-Rate Irradiator - 50 - 100 R at 50 R/min. None treated till now. Objective: to determine dose-rate effect on the degree of response (compared to group A, B) in 6 cases of chronic granulocytic leukemia. Similar comparison may be possible in the other disease categories (3-10 patients/disease).

2. Fractionated Doses.
   a. METBI up to 250 R at 1.5 R/min with daily doses of approximately 30 R. Five patients treated. Objective: to add enough patients to make a valid comparison with the same total dose in LETBI protracted to the same time span.

   b. Repeated low-dose maintenance exposures in METBI or LETBI (weekly or monthly doses in the 10 - 30 R range). None treated. Numbers to be included in the series depends on availability of patients and results of early studies. Five to ten patients in each disease category would be desirable.

III.

C. Laboratory Studies (see copy attached protocol).

1113697

II. Objectives of Experiment:

medium-exposure-rate total-body facility (METBI) comprised of eight 500-curie ^{137}Cs sources providing a homogeneous irradiation field with a dose rate between 1 and 4 R/min. The low-exposure total-body irradiator (LETBI) is also in operation and at present provides exposures of 1 to 5 R/hr in a homogeneous field of gamma radiation provided by 10 cobalt-60 sources.

The experimental high-dose-rate unit at UT-AEC provides 50-75 R/min exposures from ^{60}Co sources.

The study will emphasize:

1. Precise measurements of irradiation dose and dose rate.
2. Frequent blood counts and bone-marrow examinations at specified days to permit comparison between patients and groups of patients.
3. Careful monitoring of symptoms and biochemical changes which may indicate physiologic effects of irradiation.
4. A comparison of different doses, dose rates, and protracted versus fractionated doses as to therapeutic effect, symptoms produced, hematologic and biochemical responses.

III. Methods of Procedure:

Brief description of methods, all medications including name and dose range, number and types of subjects anticipated, time for single session, total number of sessions, total duration of study, methods used to screen subjects, etc. (Use additional blank pages if needed.)

A. Selection of Patients.

Patients will be selected from among the patient population as referred to the Medical Division. The selection will not be randomized but only patients meeting the following criteria as to diagnosis and manifestations of their disease will be selected.

Diagnoses:

1. Polycythemia vera
2. Chronic granulocytic leukemia
3. Chronic lymphocytic leukemia
4. Lymphosarcoma

Manifestations:

1. Thrombocytosis
2. Leukocytosis
3. Symptomatic lymphadenopathy, non-hemolytic anemia without thrombocytopenia
4. Bone-marrow invasion plus those in #3 above.

No. 10 Studies of TBI in Patients with Hematologic Disorders

With the closing of the clinical facility, the therapeutic total-body irradiation project was discontinued after a total of 194 patients received exposures of 50 R to 250 R in METBI or LETBI. See 1973 Research Report ORAU-123, page 5, and an updated Table 1. These patients are no longer being followed at ORAU. The data are being compiled for publication.

1113699

REFERENCES

(1) Grob, D., Lilienthal, J. L., Jr., Harvey, A. M. and Jones, B. F. The administration of diisopropylfluorophosphate (DFP) to man. Bull. Johns Hopkins Hosp., *81*, 217 (1947).

(2) Cohen, J. A. and Warringa, M. G. P. J. The fate of P^{32} labeled diisopropylfluorophosphate in the human body and its use as a labelling agent in the study of the turnover of blood plasma and red cells. J. Clin. Invest., *33*, 459 (1954).

(3) Leeksma, C. H. W. and Cohen, J. A. Determination of the life span of human blood platelets using labeled diisopropylfluorophosphate. J. Clin. Invest., *35*, 964 (1956).

(4) Athens, J. W., Mauer, A. M., Ashenbrucker, H., Cartwright, G. E. and Wintrobe, M. M. Leukokinetic Studies I. A method for labeling leukocytes with diisopropylfluorophosphate (DFP^{32}). Blood *14*, 303 (1959).

(5) Mauer, A. M., Athens, J. W., Ashenbrucker, H., Cartwright, G. E. and Wintrobe, M. M. Leukokinetic Studies II. A method for labeling granulocytes *in vitro* with radioactive diisopropylfluorophosphate (DFP^{32}). J. Clin. Invest., *39*, 1481 (1960).

(6) Kurth, D., Athens, J. W., Cronkite, E. P., Cartwright, G. E. and Wintrobe, M. M. Leukokinetic Studies V. Uptake of tritiated diisopropylfluorophosphate by leukocytes. Proc. Soc. Exper. Biol. & Med., *107*, 422 (1961).

(7) Athens, J. W., Raab, S. O., Haab, O. P., Mauer, A. M., Ashenbrucker, H., Cartwright, G. E. and Wintrobe, M. M. Leukokinetic Studies III. The distribution of granulocytes in the blood of normal subjects. J. Clin. Invest., *40*, 159 (1961).

(8) Vejlens, G. The distribution of leucocytes in the vascular system. Acta Path. Microbiol. Scand. Suppl., *33* (1938).

(9) Athens, J. W., Haab, O. P., Raab, S. O., Mauer, A. M., Ashenbrucker, H., Cartwright, G. E. and Wintrobe, M. M. Leukokinetic Studies IV. The total blood, circulating and marginal granulocyte pools and the granulocyte turnover rate in normal subjects. J. Clin. Invest., *40*, 989 (1961).

Editor's Note: Other references which may be of interest to labeled DFP users are:

(10) Oosterbaan, R. A., Jausz, H. S. and Cohen, J. A. The chemical structure of the reactive group of esterases. Biochem et Biophys. Acta, *20*, 402 (1956).

(11) Schaffer, N. K., Simet, L., Harshman, S., Engle, R. R. and Drisko, R. W. Phosphopeptides from acid-hydrolyzed P^{32}-labeled diisopropylphosphoryl chymotrypsin. J. Biol. Chem., *225*, 197 (1957).

(12) Mazur, A. and Bodansky, O. The mechanism of *in vitro* and *in vivo* inhibition of cholinesterase activity by diisoproplyfluorophosphate. J. Biol. Chem., *163*, 261 (1946).

(13) Jandorf, B. J. and McNamara, P. D. Distribution of radiophosphorus in rabbit tissues after injection of phosphorus-labeled diisopropylfluorophosphate. J. Pharmacol. & Exper. Therap., *98*, 77 (1950).

(14) Eadie, G. S., Smith, W. W. and Brown, I. W., Jr. The use of DFP^{32} as a red cell tag with and without simultaneous tagging with $Chromium^{51}$ in certain animals in the presence or absence of random destruction. J. Gen. Physiol., *43*, 825 (1960).

(15) Hjort, P. F., Paputchis, H. and Cheney, B. Labeling of red blood cells with radioactive diisopropylfluorophosphate (DFP^{32}). Evidence for an initial release of label. J. Lab. & Clin. Med., *55*, 416 (1960).

(16) Mayer, K. and Ley, A. B. The measurement of erythrocyte survival with P^{32}-tagged diisoproplyfluorophosphate (DFP^{32}). Clin. Res. Proc., *4*, 80 (1956).

(17) Bove, J. R. and Ebaugh, F. G., Jr. The use of $diisopropylfluorophosphate^{32}$ for the determination of *in vivo* red cell survival and plasma cholinesterase turnover rates. J. Lab. & Clin. Med., *51*, 916 (1958).

(18) Pollycove, M., Dal Santo, G. and Lawrence, J. H. Simultaneous measurement of erythrocyte, leukocyte and platelet survival in normal subjects with diisopropylfluorophosphate^{32} (DFP^{32}). Clin. Res. Proc., 6, 45 (1958).

(19) Eernisse, J. G. and van Rood, J. J. Erythrocyte survival time determinations with the aid of DFP^{32}. Brit. J. Haemat., 7, 382 (1961).

1113700

III. Methods of Procedure:

Brief description of methods, all medications including name and dose range, number and types of subjects anticipated, time for single session, total number of sessions, total duration of study, methods used to screen subjects, etc. (Use additional blank pages if needed.)

Radioisotope:

^{32}P-DFP (diisopropyl fluorophosphate) will be used to label the granulocytes according to the procedure described by Athens and co-workers (Blood 14:303, 1959). Both in vitro and in vivo labeling of granulocytes will be performed. With the in vitro method, 30-40 microcuries of ^{32}P and 120-150 micrograms of DFP are added to a transfusion pack containing 300-400 ml of blood which is then given intravenously to the patient. In vivo labeling of granulocytes is accomplished by the intravenous injection of 400 microcuries of ^{32}P and 2 mg of DFP. Both of these methods have been used extensively and reported in the literature.

(continued)

IV. Possible hazards and their evaluation:

Radiation Dose:

Radiation dosage after the in vitro type of study in normal subjects has been reported by Mauer and co-workers (J. Cl. Invest. 39:1481, 1960). It was found that the ^{32}P-DFP was bound firmly to erythrocytes, leukocytes, platelets and plasma proteins, and therefore 30 microcuries of isotope were distributed predominantly in the blood estimated to be 5 kg with little radioactivity reaching the bone marrow or other tissue. In three subjects, urinary excretion of radioactivity was studied and 40% of the administered dose appeared in the urine within the first 3 hours after infusion of the labeled blood. They stated that the biologic half-life of ^{32}P was approximately 6 days and effective half-life was 4.4 days. The infinite dose of radioactivity administered to blood was calculated to be about 560 millirads. This dose did not take into consideration the excretion of ^{32}P-DFP by routes other than the kidneys.

Athens and co-workers (Blood 14:303, 1959) calculated radiation dose after in vivo administration of a maximum of 400 microcuries of ^{32}P-DFP and reported that "a 70 kg man would receive 0.24 equivalent roentgens on the first day and 9.04 equivalent roentgens total dose."

1113101

II. Objectives of Experiment (continued):

Application of this information for treatment of hematopoietic disorders with irradiation would be the ultimate aim. In addition, mechanism of WBC injury by irradiation may be better defined.

1113702

Each patient selected for possible bone marrow transplantation shall have:

1) RBC typing prior to any transfusion of whole blood or separated blood constituents (but previous blood transfusions should not exclude the patient eo ipso).
2) typing for leukocyte antigens (HL-A) of patient and all possible donors.
3) the histocompatibility test as provided by the mixed lymphocyte culture (MLC), which should be performed bidirectionally between him and all possible donors.
4) the best available chemotherapy.

Bone marrow transplantation will be performed only if histocompatibility tests, MLC, and HL-A typing indicate a match.

Conditions to be met in children with acute leukemia:

a) The donor must be old and large enough (approximately 10 to 12 years old or 70 to 90 pounds) so an adequate number of marrow cells can be obtained for transplantation.
b) The recipient should be at the end of the second remission of his disease before transplant will be attempted. Transplant is also considered if two drugs or drug combinations failed to produce an initial remission.

It is difficult to define "end of the second remission" clinically, but the following guidelines shall be used:

A relapse is strongly suspected when:

the physical examination shows a re-occurrence of splenomegaly and palpable enlargement of the lymph nodes.

the patient has symptoms severe enough to reduce the physical activity.

the hemogram shows < 9.0 g% Hgb, < 1000 neutrophils/mm^3, $> 5\%$ blast cells and $< 75,000$ thrombocytes.

1113703

During the one week course of immunosuppression with ALG, the patient may receive some antileukemia therapy, but no corticosteroids.

On day 0 the patient will be irradiated with 500 R to his whole body at a rate of 40 R/min. The total body irradiation will be given at the UT AEC farm High Dose Rate ^{60}Co Irradiator. The patient will be kept under sedation during the day of irradiation.

Special precautions will be taken to avoid microbiobial contamination of the patient during the transport to and from the irradiation facility as well as during the irradiation. The patient will be covered with sterile sheets and wear a surgical face mask at all times that he is outside the Laminar Flow Unit. Immediately after return to the Laminar Flow Unit, specimens for bacterial cultures will be taken from the patient's face (skin), nares, and throat.

Bone marrow transplant.

Donor: The marrow aspiration will be done under general anesthesia (or spinal anesthesia if general anesthesia is contraindicated). Volumes of 2-3 ml each will be taken from multiple (30-40) sites from his pelvic bones and collected in TC-199 culture medium containing phenol-free heparin (5000 units per 200 ml TC-199) as anticoagulant. The final cell suspension will be passed through a 200 μ mesh stainless steel or nylon filter before transfusion.

Recipient: Twenty-four hours after total-body irradiation and forty-eight hours after the last ALG injection, the patient will receive the transplant, approximately 20 x 10^9 nucleated bone marrow cells, corrected for contamination with peripheral blood nucleated cells. The infusion will be given intravenously during a period of 30 to 45 minutes.

1113704

Contract No. W-7405 eng-36

Modification No. 1

Dated: 1 December 1943

SECRET

SUPPLEMENTAL AGREEMENT

This supplemental agreement entered into this 1st day of December, 1943, by and between the UNITED STATES OF AMERICA, hereinafter called the Government, represented by the Contracting Officer executing this agreement, and THE REGENTS OF THE UNIVERSITY OF CALIFORNIA, a California Corporation, hereinafter called the Contractor, WITNESSETH THAT:

WHEREAS, on the 20th day of April, 1943, and effective as of the 1st day of January 1943, the parties hereto entered into Contract No. W-7405 eng-36 for the procuring and furnishing of the necessary personnel, supplies, materials, equipment, and performing such other services as shall be directed by the Contracting Officer, or his duly authorized representative, and conducting certain studies and experimental investigations; and

WHEREAS, It is found advantageous and in the best interests of the United States to modify the said contract for the following reasons:

To provide for the accounting of monies which may be received by the Contractor as a result of any operation of certain facilities etc., which funds shall be applied to the reduction of the cost of the work to be performed under the above-described contract;

To increase the authorized limit of expenditures under the contract from 5,000,000 to 8,000,000;

To authorize the Contractor to make payments in advance out of the funds advanced to him pursuant to Article I of the contract to an insurance carrier or carriers for the purpose of establishing and replenishing a collateral or guarantee fund or funds to secure the payment of premiums for such insurance coverage as may be required or approved by the Contracting Officer;

To provide for the payment by the Government in compensation cases of all medical, surgical, and other attendants or hospital nurses and hospital service, medicine, crutches and appliances with respect to injuries to employees at the site.

To authorize the Contractor to use monies collected as advanced payments in connection with the prosecution of the work hereunder.

NOW, THEREFORE, the said contract is hereby modified in the following particulars, but in no others:

DECLASSIFICATION AUTHORIZED
ROY ANDERSON, ANALYSAS
Name (ADD) - Organization
8-23-94
Date

DECLASSIFICATION RECOMMENDED
Rich Blandell Analysas
Name (ADC) - Organization
8/23/94
Date

CERTIFIED A TRUE COPY
C. A. Cornell
C. A. CORNELL, LT. COL. C. E.

SECRET

1113705

(b) At the discretion of the insurance carrier or carriers the funds advanced hereunder may from time to time be invested in all or any part in United States Government securities. The insurance carrier or carriers shall have the right to sell all or any part of such securities as they see fit and to determine how much of the fund advanced shall be invested and how much retained in cash on deposit. All securities purchased with such funds shall be deposited in a safety deposit box in such bank. Suitable provisions shall be made in the contract of insurance between the Contractor and the insurance carrier or carriers that all purchases and sales of such securities shall be upon the recommendation and approval of the Finance Committee or other similar executive body of the carrier or carriers approved by the Contracting Officer.

(c) The interest earnings, if any, actually earned from the investment of the whole or any part of the funds advanced to the insurance carrier or carriers hereunder, less expenses incurred in the investment, management, custody and safekeeping of said funds shall be paid to the Contractor for the account of the Government.

(d) The insurance carrier or carriers shall have the right to draw on the special account with any such bank, subject only to the provisions of the contract of insurance between the Contractor and the insurance carrier or carriers.

(e) Whenever the face amount of securities purchased with cash advanced funds and deposited at any bank is either increased or decreased the bank shall report the amount of such increase or decrease to the Contractor and in addition to such reports the bank shall also furnish periodic reports to the Contractor as to such advanced funds showing the amount of cash on hand in its special account and the face amount of the securities deposited with it.

9. Notwithstanding any other provision of this Article I, the Government, upon the request of the Contractor from time to time throughout the effective period of this contract, shall advance to the Contractor, without interest, sums not to exceed the amounts necessary to replenish in full the collateral or guarantee funds provided for by Section 8 of this Article I of this contract. Upon the making by the Contractor of payments to insurance carriers pursuant to Section 8 of this Article X, the advance payments made to the Contractor by the Government under this Article X shall be deemed to be liquidated to the extent of the payments and withdrawls so made by the Contractor.

10. The Contractor shall use any funds collected as advanced payments with the prosecution of the work hereunder.

The following article is hereby included in the Contract:

ARTICLE XXVI - MEDICAL EXPENSES

The Government shall in compensation cases provide medical, surgical, and other attendants or treatment, nurses and hospital service, medicine, crutches and apparatus with respect to injuries to employees at the site. In the event any payments for the above services shall be made by the Contractor, the same shall be reimbursable by the Government."

SECRET

1113706

IN WITNESS WHEREOF, The parties hereto have executed this agreement as of the day and year first above written.

THE UNITED STATES OF AMERICA,

By /s/ K. D. Nichols
K. D. NICHOLS,
Colonel, Corps of Engineers,
Contracting Officer.

Witnesses:

THE REGENTS OF
THE UNIVERSITY OF CALIFORNIA

/s/ Anne M. Pollaczek

BY /s/ Robert Underhill

Title Secretary

/s/ B. M. Miller

Berkeley, California
(Address)

Approved as to form
/s/ A. H. Conant
Attorney for The
Regents of the University
of California

SECRET 35

1113707

This document consists of 25 page(s)
Number 1 of 4 copies, Series A

SECRET

Contract No. W-7405 eng-36

THIS CONTRACT entered into this 20th day of April, 1943, effective as of the 1st day of January, 1943, by THE UNITED STATES OF AMERICA, (hereinafter called the "Government"), represented by the Contracting Officer executing this contract, and THE REGENTS OF THE UNIVERSITY OF CALIFORNIA, a California Corporation, (hereinafter called the "Contractor");

WITNESSETH THAT:

WHEREAS, the Government believes that the performance of certain work, hereinafter described, is necessary in facilitating the prosecution of the War; and

WHEREAS, the prompt and successful performance of certain contracts entered into by the Government requires the furnishing of certain supplies, materials, equipment and personnel; and

WHEREAS, the accomplishment of such work by the Contractor under a cost contract, entered into after negotiations approved by the Secretary of War, and without advertising for proposals, is authorized by law and will facilitate the prosecution of the War; and

WHEREAS, as a result of such negotiation, the Secretary of War has directed the Government to enter into such a contract with the Contractor for the accomplishment of the work hereinafter described;

NOW, THEREFORE, the parties hereto do mutually agree as follows:

SECRET

DECLASSIFICATION RECOMMENDED
Robert B. Bundy Analysas
Name (ADC) - Organization
8/23/94
Date
DECLASSIFICATION AUTHORIZED
ROY ANDERSON, ANALYSAS
Name (ADD) - Organization
8-23-94
Date
True Copy
By R. G. Cornell
R. G. CORNELL, Major, C.E.

1113708

ARTICLE I - GENERAL STATEMENT OF WORK AND SERVICES

The Contractor shall, with the utmost dispatch, and to the best of its ability, procure and furnish the necessary personnel, supplies, materials, equipment and perform such other services as shall be directed by the Contracting Officer or his authorized representative, for the conduct of certain studies and experimental investigations at a laboratory located at a site which has or will be informally made known to the Contractor.

ARTICLE II - TERM OF CONTRACT

The Contractor shall continue the work to be performed hereunder for the period beginning January 1, 1943, and continuing until June 30, 1944. At the option of the Government and upon written notice to the Contractor from the Contracting Officer not less than ninety (90) days prior to the expiration of said initial period of operation, the Contractor shall continue such work for a further period or periods not exceeding the duration of hostilities with the Axis Powers, plus six (6) months. At the termination or expiration of the contract, the Contractor shall be free to discontinue all work of every nature under this contract, and settlement thereof shall be made promptly thereafter in accordance with the terms hereinafter set forth in Article III hereof.

ARTICLE III - TERMINATION OF CONTRACT BY GOVERNMENT

1. The Government may terminate this contract at any time by a notice in writing from the Contracting Officer to the Contractor. Such termination shall be effective in the manner and upon the date specified in said notice and shall be without prejudice to any claims which the Government may have against the Contractor or the Contractor may have against the Government. Upon receipt of such notice, the Contractor shall, unless the notice directs otherwise, immediately discontinue all work and the placing of all orders for materials, facilities and supplies in connection with performance of this contract, and shall proceed to cancel promptly all existing orders and terminate all subcontracts insofar as such orders and/or subcontracts are chargeable to this contract. The Contractor shall further make full and complete settlement of all obligations, commitments and claims existing or arising as a result of such termination, subject to approval of the Contracting Officer.

1113709

2. Upon the termination of this contract, full and complete settlement of all claims of the Contractor arising out of this contract shall be made as follows:

a. The Government shall assume and become liable for all obligations, commitments, and claims that the Contractor may have therefore in good faith undertaken or incurred in connection with said work and the cost of which would be reimbursable in accordance with the provisions of this contract; and the Contractor shall, as a condition of receiving the payments mentioned in this Article, execute and deliver all such papers and take all such steps as the Contracting Officer may require for the purpose of fully vesting in the Government the rights and benefits of the Contractor under such obligations or commitments.

b. The Government shall reimburse the Contractor for all expenditures not previously reimbursed.

c. The Government shall reimburse the Contractor for such further expenditures, made after the date of termination, for transportation of Government property and for services in connection with the settlement of this contract as are required or approved by the Contracting Officer.

d. The obligation of the Government to make any of the payments required by this Article shall be subject to any unsettled claims in connection with this contract which the Government may have against the Contractor.

e. No settlement hereunder shall prejudice the Contractor's rights to reimbursement with respect to claims subsequently found or determined to have been incurred in the performance of this contract and not known or determined at the time of such settlement.

ARTICLE IV - TITLE TO WORK

Title to all materials, tools, machinery, equipment and supplies for which the Contractor shall be entitled to reimbursement under Article V shall vest in the Government at the site or at such point or points as the Contracting Officer may designate in writing; provided, that the right of final inspection and acceptance or rejection of such materials, equipment and supplies at such place or places

1113710

as he may designate in writing is reserved to the Contracting Officer; Provided, further, that upon such final inspection the Contractor shall be given written notice of acceptance or rejection as the case may be. In the event of rejection, the Contractor shall be given written notice of acceptance or rejection as the case may be. In the event or rejection, the Contractor shall be responsible for the removal of the rejected property within a reasonable time.

ARTICLE V - COST OF THE WORK

1. Reimbursement for Contractor's Expenditures In approving reimbursement for all costs and expenses of the Contractor under this contract, the Contracting Officer shall be governed by the provisions of Article XII. The Contractor shall be reimbursed in the manner hereinafter described for such of its actual costs and expenses in the performance of the work under this Article, as may be approved or ratified by the Contracting Officer, and as are included in but not limited to the following items:

a. All labor, materials, tools, machinery, equipment, facilities, supplies, utilities and services necessary for either temporary or permanent use for the benefit of the work.

b, All subcontracts made in accordance with the provisions of this contract.

c. Transportation, loading, unloading and storage charges on materials, supplies and equipment.

d. Transportation and traveling expenses to the work of the necessary field forces for the economical and successful prosecution of the work, and return therefrom when such services are no longer required. All costs and expenses reimbursed to regular employees of the Contractor transferred to or from the site of the work in connection with such transfers, including transportation of employees' immediate families, household goods and effects and living expenses of such employees while obtaining new residences. Allowances for living expenses while obtaining new residences shall be limited to a period of fifteen (15)

1113711

days unless otherwise specifically authorized or approved by the Contracting Officer. The amounts of expenditures reimbursable to the Contractor under this paragraph d shall be equal to, but shall not exceed, the amounts determined in accordance with the policy followed, and supported by such receipts as are required by the Contractor in the regular conduct of its business, and reimbursed to its employees. Expenditures under these items shall be either authorized or approved in writing by the Contracting Officer.

e. Expenses of procuring or endeavoring to procure personnel and expediting the production and transportation of materials, supplies and equipment, including transportation and traveling expenses incident thereto. Subject to the prior approval and at the direction of the Contracting Officer, expenses of feeding and housing employees at the site, including feeding and housing without cost to such individuals.

f. (1) If the Contractor or any representative thereof shall be required to travel in the performance of its work hereunder, the Government will reimburse the Contractor for the transportation of persons directly engaged therein, plus actual subsistence expenses (not exceeding the sum of Ten Dollars ($10.00) per day, however) of such persons incurred during the periods of travel, or, at the Contractor's option, an allowance not exceeding Six Dollars ($6.00) per person for each calendar day or major fraction thereof during a period of travel, in lieu of actual subsistence expenses of such persons; provided, that expenses for transportation hereunder by motor vehicle other than common carrier shall be reimbursed on a mileage basis at a rate not exceeding five (5¢) cents per mile per vehicle, in lieu of the actual expenses of such transportation.

(2) All travel shall be either authorized or approved in writing by the Contracting Officer.

g. Salaries of employees of the Contractor engaged in full time directly on the work provided hereunder whether at the site or elsewhere. In case the full time of any such employee of the Contractor at the site

1113712

or elsewhere (except at the Contractor's home offices covered by paragraph 1 of this Section 1) is not applied to the work, his salary shall be included in this item only in proportion to the actual time applied thereto. No person shall be assigned to service by the Contractor as superintendent of operation, chief engineer, chief purchasing agent, chief accountant, or similar position in the Contractor's organization at the site or elsewhere, or as principal assistant to any such person until there has been submitted to and approved by the Contracting Officer a statement of the previous salary, proposed salary, qualifications, and experience of the person selected for such assignment. It is recognized that in transferring men from their regular positions to this work at the site or elsewhere, it may be necessary to make some increase in their remuneration, which shall be subject to the approval of the Contracting Officer.

h. Premiums on such bonds and insurance policies as the Contracting Officer may approve or require as reasonably necessary for the protection of the Government or the Contractor. In every instance where this contract requires or permits the United States to pay the premium on a bond or insurance policy, either directly or ultimately as a reimbursable item, the bond or insurance policy shall contain an indorsement or other recital excluding by appropriate language any claim on the part of the insurer or obliger to be subrogated, on payment of a loss or otherwise, to any claim against the United States. It is recognized that complete insurance coverage may not be readily obtainable for this project at acceptable rates. The Contracting Officer will make every effort, therefore, to enable the Contractor to effect an arrangement with a reputable insurance carrier or carriers to the end that mutually satisfactory insurance coverage of the following types may be obtained by the Contractor: Workmen's Compensation, Occupational Disease, Employer's Liability and Comprehensive Public Liability for bodily injury and property damage.

i. Payments made by the Contractor under the Social Security Act (employer's contribution) and any disbursements required by law which the Contractor may be required to pay on account of this contract on or for any plant, equipment, process, organization, materials, supplies, or personnel or on moneys received as reimbursement thereof;

1113713

and, if approved in writing by the Contracting Officer in advance, permit and license fees and royalties on patents used, including those owned by the Contractor.

j. (1) Extra compensation to employees, discontinuance wages and charges under welfare and other employee relations policies maintained by the Contractor, insofar as the same are applicable to the work performed under this contract; provided that the Government shall be chargeable therefor only insofar as the same are consistent with the general employee relations policies existing throughout the Contractor's organization or as they may be modified due to the extraordinary circumstances and hazards surrounding the project or are incurred pursuant to agreement made as a result of collective bargaining with the representatives of employes or are expressly authorized in writing by the Contracting Officer.

(2) It is recognized that the work to be performed under this contract involves unusual and unpredictable hazards. In view of this fact, the Contractor will be reimbursed for premiums on such insurance as may be required or approved by the Contracting Officer because of the extra-hazardous nature of the work, as follows:

(a) In case of death as a result of injury or disease arising in the course or as a result of work at the site, payment not exceeding a maximum of Ten Thousand Dollars ($10,000.00) will be made to the administrator, executor, widow or dependents of the deceased employee. Said payment shall be in addition to any amount paid on account of said death pursuant to any workmen's compensation law or other statutory requirement.

(b) In case of disability, including occupational disease, arising in the course or as a result of work at the site or elsewhere, payment will be made to the employee during the period of such disability in an amount equal to the difference between his regular basic salary rate and any payments made on account of such disability pursuant to statutory requirements or the Contractor's welfare plans, not exceeding an aggregate of Ten Thousand Dollars ($10,000.00).

k. Accounting (including salaries and other expenses) in connection with special audits of accounts for the Government and special audits approved by the Government in connection with work hereunder.

l. Disbursements incident to payment of payrolls, including but not limited to, the cost of disbursing cash, necessary guards, cashiers and pay meters. If payments to employees are made by check, facilities for cashing checks must be provided without expense to employees, and the Contractor shall be reimbursed therefor.

m. An allowance for overhead costs not otherwise reimbursable hereunder in an amount equal to fifteen percent (15%) of the total wages and salaries (but not taxes) reimbursable under paragraphs a and g above.

n. Borrowed Personnel - Expenditures by the Contractor to reimburse other employers for salaries and wages paid by them to their employees released for and engaged in performance of the Contractor's undertakings hereunder; the pro rata share of welfare and other employee relations benefits accruing to the employee during the period for which he is loaned; Federal and State Social Security taxes paid on such borrowed personnel by such employers.

o. Such other items not expressly excluded by other provisions of this contract as should, in the opinion of the Contracting Officer, be included in the cost of the work. When such an item is allowed by the Contracting Officer, it shall be specifically certified as being allowed under this paragraph.

43

1113715

SECRET

ARTICLE VI - EIGHT HOUR LAW

The Contractor shall compensate laborers and mechanics for all hours worked by them hereunder in excess of eight (8) hours in any one calendar day at a rate of not less than one and one-half (1½) times the basic rate of pay of such laborers and mechanics, and shall include such provision in each subcontract. For each violation of the requirements of the Article, a penalty of Five Dollars ($5.00) shall be imposed upon the Contractor or Subcontractor for each laborer or mechanic for each calendar day in which such employee is required or permitted to work hereunder more than eight (8) hours without receiving such additional compensation, and all penalties thus imposed shall be withheld for the use and benefit of the Government.

ARTICLE VII - RESERVATIONS BY GOVERNMENT

1. The Government reserves the right to furnish any materials, machinery, tools, or services (except personal services), including communication services necessary for the completion of the work; provided that in the judgment of the Contractor and the Contracting Officer such items are of suitable type and in satisfactory condition. The Contractor shall use reasonable care with respect to such property. The Contractor shall, as required by the Contracting Officer, cause all equipment, machinery and tools, to which title is vested in the Government to be suitably marked with an identifying mark or symbol indicating that such items are the property of the United States. Upon the completion of this contract or upon demand, the Contractor shall return such equipment, machinery, tools and unused materials to the place designated by the Contracting Officer.

2. The Government reserves the right to pay directly to common carriers any or all freight charges on materials and supplies.

3. The Government reserves the right to pay directly to the person concerned all sums due from the Contractor for labor, materials or other charges.

SECRET

44

1113716

4. Telephone messages (including teletype and facsimile, when authorized by the Contracting Officer to be installed) sent by the Contractor or its representatives, in connection with this contract, shall be charged to the Government tax free to the extent that the Government supplies the Contractor with tax exemption certificates.

ARTICLE VIII - DISCOUNTS

The Contractor shall, to the extent of its ability, take all cash and trade discounts, rebates, allowances, credits, salvage, commissions, and benifications, and when unable to take advantage of such benefits, it shall promptly notify the Contracting Officer of the reason therefor.

ARTICLE IX - PAYMENTS

1. The Government shall currently reimburse the Contractor, upon the submission of public vouchers supplied by the Government and approved by the Contracting Officer, for all items reimbursable under this contract, in an amount not exceeding Five Million Dollars ($5,000,000.00) Generally, reimbursement will be made monthly but may be made at more frequent intervals if conditions so warrant. The Contracting Officer may withhold all or any part of the final reimbursement payment until receipt of the final report, the property accounting and the patent disclosure and designation required hereunder.

2. Monthly Payments Under Article V. The monthly payments called for by paragraph [illegible] of Section 1 of Article V shall be made promptly after the submission to the Contracting Officer by the Contractor of an invoice for each such amount.

3. Payments by Contractor. If bills for purchase of material, machinery or equipment, or payrolls covering employment of laborers or mechanics incurred by the Contractor or by any subcontractor hereunder are not paid promptly by the Contractor or by any subcontractor hereunder, the Government shall have the right to pay such bills or payrolls directly.

4. Failure of the Government to make Payments.

In the event of failure of the Government to make any payments or advances as provided in this contract (other than by reason of normal delay in the payment of current expenditures incident to the checking by the disbursing officer of statements of such expenditures), the Contractor may suspend its performance hereunder until the full amount of any deficiency shall have been paid. The exercise of this right shall be without prejudice to any other rights or remedies of the Contractor on account of such failure by the Government; and failure of the Contractor to exercise such right shall not constitute a waiver thereof with respect to any continuing or subsequent failure on the part of the Government.

5. Availability of Funds. Notwithstanding any other provision hereof, when and if the allowable costs of and agreed compensation for the work performed hereunder, including expenses incurred and obligated hereunder, shall equal the amount set forth in Article IX, Section 1, the Contractor shall not be expected or required to incur or obligate further expenses hereunder unless and until the Government shall first agree in writing to reimburse the Contractor for such further work. The Contractor will promptly advise the Contracting Officer when it is discovered that additional funds will be needed and shall estimate the amount of such additional funds and the time when they will be needed.

6. Final Payment. Upon completion of the work and its final acceptance in writing by the Contracting Officer, the Government shall reimburse the Contractor for all items not previously reimbursed in connection with this contract. The Contracting Officer shall accept the completed work with reasonable promptness. The Contractor shall, if required, furnish the Government with a release of all claims against the Government arising under and by virtue of this contract other than such claims, if any, as may be specifically excepted by the Contractor from the operation of the release in stated amounts to be set forth herein, and other than any claims subsequently found or determined to have been incurred in the performance of this contract and not known to the Contractor at the time of furnishing the foregoing release.

40

1113718

ARTICLE X - ADVANCES

1. At any time and from time to time after the execution of this contract, the Government at the request of the Contractor and subject to the approval of the Chief of Engineers, or his duly authorized representative, or the person to whom authority to make advance payments has been delegated, as to the present need therefor shall advance to the Contractor, without payment of interest thereon by the Contractor, sums not to exceed thirty percent (30%) of the estimated cost of this contract (exclusive of the Contractor's fixed-fee), as it may be amended from time to time.

2. As a condition precedent to the making of any advance payment or payments as hereinbefore provided, the Contractor shall furnish the Government with such adequate security as the Under Secretary of War or the person to whom authority has been delegated to make advance payments shall prescribe; provided that if other security is not prescribed, the terms of this contract shall be considered adequate security for such advance payments; and provided, further, that if at any time the Under Secretary of War deems the security furnished by the Contractor inadequate - the Contractor shall furnish such additional security, in the form of a surety bond or surety bonds, as shall be satisfactory to the Under Secretary of War.

3. Until all advance payments hereunder are liquidated, all funds received as advance payments under this contract, together with all funds received as reimbursements for the cost of the work under Article V, exclusive of the Contractor's fixed-fee, shall be deposited in a special bank account or accounts at a member bank or banks of the Federal Reserve System or any "insured" bank within the meaning of the Act creating the Federal Deposit Insurance Corporation (Act of August 23, 1935; 49 Stat. 684) as amended (12 U. S. C. 264) separate from the Contractor's general or other funds. Such special bank account or accounts shall be designated as to indicate clearly to the bank their special character and purpose, and the balance in such account or accounts shall be used by the Contractor exclusively as a revolving fund for carrying out the purposes of the principal contract and any amendments thereto and not for

47

1113719

other business of the Contractor. Any balances from time to time in such special account or accounts shall at all times secure the repayment of the advances in connection with which the special account or accounts are opened, and the Government shall have a lien upon such balances to secure the repayment of such advances, which lien shall be superior to any lien of the bank or any other person upon such account or accounts by virtue of assignment to it of such contract or otherwise; provided, that the bank shall be under no liability to any party hereto for the withdrawal of any funds from said special account upon checks, properly indorsed and signed by the Contractor, except that after the receipt by the bank of written directions from the Chief of Engineers or his duly authorized representative, the bank shall act thereon and be under no liability to any party hereto for any action taken in accordance with the said written directions. Any instructions or written directions received by the bank through the Contracting Officer upon War Department stationery and purporting to be signed by, or by the direction of, the Chief of Engineers or his duly authorized representative, shall, insofar as the rights, duties and liabilities of the bank are concerned, be conclusively deemed to have been properly issued and filed with the bank by the Chief of Engineers or his duly authorized representative.

4. It is agreed that the aggregate of the advance payments outstanding under this contract, together with funds received as reimbursement for the cost of the work by the Contractor under Article V, shall at no time exceed the total estimated cost of the work under this contract as it may be revised from time to time and any such excess shall be immediately repaid by the Contractor to the Government, or, if any reimbursement is due from the Government to the Contractor, shall be deducted therefrom; provided, however, that if the total cost of the work shall be in excess of the amount so paid to the Contractor, including said advance payments, the Government upon presentation of satisfactory evidence shall currently and promptly reimburse the Contractor to the extent of such excess cost (subject to any delay in the availability of appropriated funds).

5. If, upon completion of the contract, or upon termination thereof for other than the fault of the Contractor, the advance payments made to the Contractor in

respect of such contract have not been fully liquidated in the manner herein provided, the unliquidated balance of such advance payments shall be deducted from any payments otherwise due the Contractor in respect of this contract; and if the sum or sums due the Contractor be insufficient to cover such balance, the deficiency shall be paid by the Contractor in cash forthwith after demand and final audit by the Government of all accounts hereunder in respect of such contract; provided, however, that in the event of such termination of the contract for other than the fault of the Contractor, such deduction shall not be made prior to final audit unless, and only to the extent that, the Contracting Officer or his duly authorized representative shall determine that such action is reasonably required in order to secure the eventual repayment in full to the Government of such unliquidated advance payments. In the event of cancellation or termination of this contract because of the fault of the Contractor, the Contractor, notwithstanding any ultimate rights to be reimbursed, agrees to return to the Government, upon demand, without set-off of any sums alleged to be due the Contractor, the unliquidated balance of any advance payment. Furthermore, if, in the opinion of the Chief of Engineers or his duly authorized representative, the unobligated balance of the advance payments made by the Government under Section 1 hereof exceeds the amount necessary for the current needs of the Contractor, as determined by the Chief of Engineers or his duly authorized representative, the amount of such excess shall, upon demand by the Chief of Engineers or his duly authorized representative, be promptly returned to the Government and will be credited against the balance due the Government on advances previously made. If the demand made in any event set forth in this Section is not met upon receipt of such demand by the Contractor, the amount demanded will bear interest at the rate of six percent (6%) per annum from the date of the receipt of the demand until payment is made; provided, however, that such payment of interest is hereby waived as to any sum paid by the Contractor within 15 days after the amount becomes due hereunder. If and when the Contractor has, by means of deductions or otherwise reimbursed the Government in full for payments made, any money remaining in the special bank account or accounts shall be free and clear of any lien hereunder and the bank or banks concerned shall have authority to pay same to the Contractor and shall thereupon be relieved of any further obligation to the Government on account thereof.

ARTICLE XXIII - ANTI DISCRIMINATION

1. The Contractor, in performing the work required by this contract, shall not discriminate against any worker because of race, creed, color or national origin.

2. The Contractor agrees that the provisions of paragraph (1) above will also be inserted in all of its subcontracts. For the purpose of this Article, a subcontract is defined as any contract entered into by the Contractor with any individual, partnership, association, corporation, estate, or trust, or other business enterprise or other legal entity, for a specific part of the work to be performed in connection with the supplies or services furnished under this contract; provided, however, that a contract for the furnishing of standard or commercial articles or raw material shall not be considered as a subcontract.

ARTICLE XXIV - DEFINITIONS

1. The term "Contracting Officer" as used herein shall mean the Contracting Officer who executed this contract and shall include his duly appointed representative.

2. The terms "Secretary of War" and "Chief of Engineers" shall include their duly authorized representatives, as the case may be, other than the Contracting Officer.

3. The term "his duly authorized representative" shall mean any person or board authorized by the Secretary of War or the Chief of Engineers, as the case may be, to act for him, other than the Contracting Officer.

ARTICLE XXV - ALTERATIONS

The following changes were made in this contract before it was signed by the parties hereto:

1113722

SECRET

I, _____, certify that I am the Secretary of the Corporation named as Contractor herein; that _____ who signed this contract on behalf of the Contractor was then _____ of said corporation; that said contract was duly signed for and on behalf of said corporation by authority, of its governing body and is within the scope of its corporate powers.

IN WITNESS WHEREOF, I have hereunto affixed my hand and the seal of said Corporation this ____ day of _____, 1943.

_____

(Corporate Seal)

I hereby certify that, to the best of my knowledge and belief, based upon observation and inquiry, _____ _____ who signed this contract for the _____ _____ had authority to execute the same, and is the individual who signs similar contracts on behalf of this corporation with the public generally.

_____

SECRET

1113723

SECRET

THIS DOCUMENT CONSISTS OF 1 PAGES
NO. 3 OF 7 SERIES A

STATEMENT OF APPROVAL

Contract No. W-7405 eng-36 entered into between the United States of America and University of California on the 20th day of April, 1943 is hereby approved.

Dated: June 16, 1944

/s/ L. R. Groves

L. R. GROVES
Major General, Corps of Engineers

DECLASSIFICATION RECOMMENDED
Robin G. Burrell Analysas
Name (ADC) - Organization
8/23/94
Date

DECLASSIFICATION AUTHORIZED
ROY ANDERSON, ANALYSAS
Name (ADD) - Organization
8-23-94
Date

SECRET

1113724

6. The Contractor shall, at all times, afford to the Contracting Officer, or his duly authorized representative, proper facilities for the inspection and audit of the Contractor's accounts, and the Contractor hereby agrees that the Contracting Officer, or his duly authorized representative shall have the right so far as the Contractor's rights are concerned, during business hours to inspect and make copies of any entrees in the books and records of the bank or banks relating to the said special account or accounts.

7. Subject to the approval of the Contracting Officer or his duly authorized representative, the Contractor may make payments to subcontractors and materialmen in advance out of the special account, for labor or services, or to pay for materials in advance of delivery at the site of the work or at an approved storage site. Such subadvances shall not exceed thirty percent (30%) of the subcontract price or estimated cost, as the case may be, and the subcontractor or materialmen to whom such advances are made shall furnish adequate security therefor. Unless other security is furnished, covenants in subcontracts, expressly made for the benefit of the Government, providing for a subspecial account with Government lien thereon and for a Government lien on or title to property, tangible or intangible, purchased from the special account, and imposing upon the subcontractor substantially the same duties and giving the Government substantially the same rights as are provided herein between the Government and the Contractor, have been prescribed by the Under Secretary of War as minimum adequate security for such subadvances.

ARTICLE XI - RECORDS AND ACCOUNTS, INSPECTION AND AUDIT

1. Records and Books of Account. The Contractor agrees to keep records and books of account, showing the actual cost to it of all items of labor, materials, equipment, supplies, services, and other expenditures of whatever nature for which reimbursement is authorized under the provisions of this contract. The system of accounting to be employed by the Contractor shall be that customarily utilized by the Contractor in the regular conduct of its business.

2. Access to Records by Contracting Officer and Contractor. The Contracting Officer shall at all times be afforded proper facilities for inspection of the work and shall at all times have access to the premises, work and materials, to all books, records, correspondence, instructions, plans, drawings, receipts, vouchers and memoranda of every description of the Contractor pertaining to said work except such documents as are submitted in support of reimbursement vouchers, and the Contractor shall preserve such papers, without additional compensation therefor other than the actual costs thereof, for a period of three (3) years after completion or termination of this contract. Likewise, any duly authorized representative of the Contractor shall be accorded the privilege of examining the books, records, and papers of the Contracting Officer relating to the actual cost of the work for the purpose of checking up and verifying such cost.

ARTICLE XII - SPECIAL REQUIREMENTS

The Contractor hereby agrees that it will

(a) Procure and maintain bonds (other than performance bonds) and insurance if obtainable in such forms and in such amounts and for such periods of time as the Contracting Officer may approve or require. Insurance, if obtainable, shall cover all work required by this contract, regardless of whether it is performed by the Contractor's own forces or its subcontractors at the site of the laboratory.

(b) Reduce to writing, unless this provision is waived in writing by the Contracting Officer, every contract in excess of Two Thousand Dollars ($2,000.00) made by it for the purpose of the work hereunder for services (except contracts for employment), materials, supplies, machinery, equipment, or for the use thereof; make all such contracts in its own name, and not bind or purport to bind the Government or the Contracting Officer thereunder. No purchase in excess of Fifteen Thousand Dollars ($15,000.00) shall be made or placed without the prior approval of the Contracting Officer.

(c) Enter into no subcontracts for any portion of the work except in the form approved by the Contracting Officer. Subcontracts are defined as contracts entered into by the Contractor with others which involve the performance in whole or in part at the site of the work, of some part of the work described in this contract.

(d) The Contracting Officer may require the Contractor to dismiss from the work such employee or employees as the Contracting Officer deems incompetent, careless or insubordinate or whose continued employment is deemed by the Contracting Officer to be inimical to the public interest. The Contractor shall make every reasonable effort in the selection of its employees and in the prosecution of the work under this contract to safeguard drawings and specifications furnished it and to prevent the theft or unauthorized use of the same.

(e) When, in the opinion of the Contracting Officer, the Contractor's personnel at the site is excessive for the proper performance of this contract, reductions thereof shall be made as required by the Contracting Officer.

ARTICLE XIII - DISPUTES

Except as otherwise specifically provided in this contract, all disputes concerning questions of fact which may arise under this contract, and which are not disposed of by mutual agreement, shall be decided by the Contracting Officer, who shall reduce his decision to writing and mail a copy thereof to the Contractor at his address shown herein. Within 30 days from said mailing the Contractor may appeal in writing to the Secretary of War, whose written decision or that of his designated representative or representatives thereon shall be final and conclusive upon the parties hereto. The Secretary of War, may, in his discretion, designate an individual or individuals, other than the Contracting Officer, or a board as his authorized representative to determine appeals under this Article. The Contractor shall be afforded an opportunity to be heard and offer evidence in support of his appeal. The president of the board, from time to time, may divide the board into divisions of one or more members and assign members thereto. A majority of the members of the board or of a division thereof shall constitute a quorum for the transaction of the business of the board or of a division, respectively, and the decision of a majority of the members of the board or of a division shall be deemed to be the decision of the board or of a division, as the case may be. If a majority of the members of a division

are unable to agree on a decision or if within 30 days after a decision by a division, the board or the president thereof directs that the decision of the division be reviewed by the board, the decision will be so reviewed, otherwise, the decision of a majority of the members of a division shall become the decision of the board. If a majority of the members of the board is unable to agree upon a decision, the president will promptly submit the appeal to the Under Secretary of War for his decision upon the record. A vacancy in the board or in any division thereof shall not impair the powers, nor affect the duties of the board or division, respectively. Any member of the board, or any examiner designated by the president of the board, for that purpose, may hold hearings, examine witnesses, receive evidence and report the evidence to the board or to the appropriate division, if the case is pending before a division. Pending decision of a dispute hereunder the Contractor shall diligently proceed with the performance of this contract. Any sum or sums allowed to the Contractor under the provisions of this Article shall be paid by the United States as part of the cost of the articles or work herein contracted for and shall be deemed to be within the contemplation of this contract.

ARTICLE XIV - CONVICT LABOR.

The Contractor shall not employ any person undergoing sentence of imprisonment at hard labor. This provision shallnot be construed to prevent the Contractor or any subcontractor hereunder from obtaining any of the supplies, or any component parts or ingredients thereof, to be furnished under this contract or any of the materials or supplies to be used in connection with the performance of this contract, directly or indirectly from any Federal, State or territorial prison or prison industry, provided, that such articles, materials, or supplies are not produced pursuant to any contract or other arrangement under which prison labor is hired or employed or used by any private person, firm, or corporation.

ARTICLE XV - MINIMUM OF WAGES

The Contractor shall comply with the regulations of the Secretary of Labor pursuant to the Act of June 13, 1934, 48 Stat. 948(U. S. Code, title 40, secs. 276a and 276b)

and any amendments or modifications thereof, shall cause appropriate provisions to be inserted in subcontracts to insure compliance therewith by all subcontractors subject thereto, and shall be responsible for the submission of affidavits required of subcontractors thereunder, except as the Secretary of Labor may specifically provide for reasonable limitations, variations, tolerances and exemptions from the requirements thereof.

ARTICLE XVI - OFFICIALS NOT TO BENEFIT.

No member of or delegate to Congress or Resident Commissioner shall be admitted to any share or part of this contract or to any benefit that may arise therefrom, but this provision shall not be construed to extend to this contract, if made with a corporation for its general benefit.

ARTICLE XVII - COVENANT AGAINST CONTINGENT FEES.

The Contractor warrants that he has not employed any person to s licit or secure this contract upon any agreement for a commission, percentage, brokerage or contingent fee. Breach of this warranty shall give the Government the right to terminate the contract, or in its discretion, to deduct from payments due the Contractor the amount of such commission, percentage, brokerage or contingent fee. This warranty shall not apply to commissions payable by the Contractor upon contracts or sales secured or made through bona fide established commercial or selling agencies maintained by the Contractor for the purpose of securing business.

ARTICLE XVIII - ASSIGNMENT OF CLAIMS

Neither this contract nor any in'erest therein or claim thereunder shall be assigned or transferred by the Contractor to any party or parties.

ARTICLE XIX - DISCLOSURE OF INFORMATION

1. It is understood that disclosure of information relating to the work contracted for hereunder to any per son not entitled to receive it, or failure to safeguard all secret, confidential and restricted matter that may come

to the Contractor or any person under his control in connection with the work under this contract, may subject the Contractor, his agents, employees and subcontractors to criminal liability under the laws of the United States, (See Title 1 of an Act approved June 15, 1917, 40 Stat. 217; 50 U.S.C. 30-42), as amended by an Act approved March 25, 1940 (54 Stat. Chap. 72); and the provisions of an Act approved January 12, 1938 (52 Stat. 3; 50 U.S.C. Supp. V 45-454), as supplemented by Executive Order No. 8381, dated March 22, 1940, 5 F. R. 1147, M. I.

2. The Contractor shall cause a like provision to be inserted in all subcontracts under this contract where classified information will be disclosed to the subcontractor.

ARTICLE XX - EMPLOYMENT OF ALIENS

1. The Contractor will not permit any alien employed or to be employed by it to have access to the drawings, specifications and accompanying enclosures relating to the performance of this contract, or to the models or material referred to therein, or to engineering principles, composition, subassemblies, or assemblies which are vital to the functioning or use of the article or articles forming the subject matter of this contract, without the written consent beforehand of the secretary of War.

2. The Contractor shall cause a like provision to be inserted in all subcontracts under this contract where classified information will be disclosed to the subcontractor.

ARTICLE XXI - RESPONSIBILITY OF CONTRACTOR-CONTINGENCIES

(a) Responsibility of Contractor - The Contractor shall be responsible to the Government for loss of or damage to materials, supplies, apparatus, equipment and any other property, real or personal, the disposition of which is governed hereby, only if and so far as attributable to the wilful misconduct or lack of good faith of an officer of the Contractor or of any other person having complete or substantially complete charge of the establishment where any undertaking hereunder by the Contractor is performed.

55

1113730

(b) The Government deems the work to be performed under this contract to be in the interest of the prosecution of the War and has urgently requested the Contractor to undertake such work. In view of the fact that the Contractor is undertaking the work without fee or profit, and in view of the unusual and unpredictable hazards involved in carrying out the work under this contract, as well as the abnormal conditions now existing, it is agreed that all work under this contract is to be performed at the expense of the Government, and that the Contractor shall not be liable for, and the Government shall indemnify and hold the Contractor harmless against any delay, failure, loss, expense (including expense of litigation) or damage (including personal injuries and deaths of persons and damage to property) of any kind and for any cause whatsoever, arising out of or connected with the work, including any loss, expense or damage arising out of or connected with the unauthorized doing of business by the Contractor within the jurisdiction where this contract is being performed, and whether or not any employee or employees of the Contractor is or are responsible therefor, unless such delay, failure, loss, expense or damage should be established by the Government to have been caused directly by bad faith or wilful misconduct on the part of some officer or officers of the Contractor acting within the scope of his or their authority and employment; that the Government shall assume and carry on, at its own expense, the defense of all claims, suits or legal proceedings which may be asserted or instituted against the Contractor on account of acts or omissions in the performance of the work; and that the Government shall pay directly and discharge completely all final judgment, including assessed costs, entered against the Contractor in such litigation and all claims which may be settled by agreement approved by the Contracting Officer. The assumption of these obligations on the part of the Government has been approved and authorized by the President of the United States acting in exercise of the powers conferred upon him by the First War Power Act of 1941.

ARTICLE XXII - PATENTS

(a) It is understood and agreed that whenever any patentable discovery or invention is made by the Contractor or its employees in the course of the work called for in this contract, the Contractor shall furnish the Contracting Officer

with complete information thereof, and the Contracting Officer shall have the sole power to determine whether or not and where a patent application shall be filed, and to determine the disposition of the title to and the rights under any application or patent that may result. It is further understood and agreed that the judgment of the Contracting Officer on such matters shall be accepted as final, and the Contractor, for itself and for its employees agrees that the inventor or inventors will execute all documents and do all things necessary or proper to carry out the judgment of the Contracting Officer. The Contractor agrees that it will include the provisions of this paragraph in all contracts of employment with persons who do any part of the work called for in this contract.

(b) In view of the fact that the Contractor has not made an investigation as to the possibility of patent infringement, and both parties desire to avoid the delay incident to a patent investigation, and further in view of the fact that the Contractor has not included in its price any provisions for the settlement of possible patent claims, it is agreed that the Government shall hold and save the Contractor harmless from liability of any nature or kind, including costs and expenses for infringement of patent rights arising in the performance of this contract.

(c) The Contractor shall promptly notify the Contracting Officer, in writing, of any and all claims of infringement that may from time to time be brought to the attention of the Contractor, and in the event of litigation on account thereof, the Contractor shall assist the Government at the Government's expense, including the service of employees of the Contractor, in furnishing such evidence as to the use of the patents and other matters of fact as may be required by the Government in such litigation.

(d) The Patent Adviser attached to the Office of Scientific Research and Development, Washington, D. C., will act as the representative of the Contracting Officer for the purpose of administering the provisions of this Article, unless another representative is appointed in writing by the Contracting Officer. It is understood, however, that such Patent Adviser shall not be considered a representative of the Contracting Officer for the purpose of making any financial commitments or incurring any financial obligations hereunder.

SECRET

IN WITNESS WHEREOF, the parties hereto have executed this contract as of the day and year first above written.

THE UNITED STATES OF AMERICA

BY /s/ J. C. Marshall

J. C. MARSHALL
Colonel, Corps of Engineers
Contracting Officer

THE REGENTS OF THE
UNIVERSITY OF CALIFORNIA

BY /s/ Robert M. Underhill, Secy.

ROBERT M. UNDERHILL
Berkeley, California

Witnesses:

/s/ Arthur A/ Levin

[redacted], N. Y. C.
(Address)

/s/ Ruth R. Hauser

[redacted], N. Y. C.
(Address)

SECRET

53

1113733

VANDERBILT UNIVERSITY

NASHVILLE, TENNESSEE 37232 TELEPHONE 322-7311 AREA 615

Division of Nuclear Medicine & Biophysics • School of Medicine • Direct phone 322-2394

February 6, 1973

Dr. G. A. Andrews
Oak Ridge Associated Universities, Inc.
P.O. Box 117
Oak Ridge, Tennessee 37830

Dear Andy:

Thank you very much for your letter supporting the appointment of Gene Johnston.

I'm sorry that I've been slow in responding to your request for a review of the minutes of the meeting of the Committee on Human Studies. I have gone over the proposals and the comments raised in the meeting. I concur with the judgment of those present in all cases and would like to go on record as approving the decisions reached on each case. I do have the same reservations concerning proposal #13 as were expressed in the meeting concerning the use of hazardous therapy in patients with aplastic anemia. I think it will be important to review the results of the first six to twelve cases in comparison to what might have been expected for other currently accepted means of therapy of this disease.

I'm sorry I wasn't able to be at the meeting and apologize for the lateness of my response. With best personal regards.

Sincerely yours,

A. B. Brill, M.D.
Director, Division of Nuclear Medicine & Biophysics

ABB:ce

1113734

OA. RIDGE ASSOCIATED UNIVE ITIES
INCORPORATED
P. O. BOX 117
OAK RIDGE, TENNESSEE 37830

14 December 72

AREA CODE 5
TELEPHONE 483-

To: Committee on Human Studies

A. B. Brill
C. L. Edwards
Melvin Koons
R. D. Lange
T. A. Lincoln
John B. Storer

Subject: Agenda
Meeting of Committee on Tuesday, 19 December 72
9:00 a.m.
Second Floor Conference Room, ORAU Medical Division

Proposals to be considered:

Proposal No.	Title
13.	Amendments No. 1 and No. 2 to proposal: Therapeutic allogeneic transplantation of human bone marrow.
20.	Use of a radioprotective drug in radiation therapy: Metabolism of ^{35}S labeled WR 2721.
21.	Mechanism of immunotherapy of human and animal cancers by intralesional injection of Mycobacterium Bovis (BCG).
22.	Comparison of ^{111}In, ^{67}Ga, and ^{206}Bi as tumor scanning agents.
23.	Evaluation of heart and lung by the use of an external radioisotope.
24.	Human performance testing of cancer patients as controls for a study of uremia.
25.	Clinical testing of ^{85m}Sr as a bone scanning agent.
26.	Tracer studies on ^{47}Sc.
27.	Application of a computer-interfaced gamma-ray spectrometer for dynamic function tests.

Hold over

. . .

Review of ongoing projects.

G. A. Andrews

1113735

Minutes of the Meeting of the Committee on Human Studies
2nd Floor Conference Room, Medical Division

19 December 1972

The meeting convened at 9:00 a.m. and adjourned at 12:30 p.m. Those present were:

Committee
G. A. Andrews
C. L. Edwards
Melvin Koons
Robert D. Lange
T. A. Lincoln
John B. Storer

Absent: A. B. Brill
(Bill Nelson)

Visiting Investigators
R. L. Hayes
Lee Washburn
John Yuhas

Dr. Andrews stated that proposals involving new isotopes had not been passed on by the ORAU Isotopes Committee, but that this would be done before any research is activated on these projects.

Proposals considered were:

Proposal No. 27 - "Preclinical Studies of the Application of a Computer - Interfaced Gamma-ray Spectrometer for Dynamic Function Tests," - Kim Goswitz, Shafroth, Morris.

The committee discussed the proposal, saw no problems, and it was approved.

Proposal No. 13 - "Therapeutic Allogeneic Transplantation of Human Bone Marrow," - Gengozian, Edwards, Vodopick, Hubner.

Two Amendments to this proposal were presented. Amendment No. 1 dealt with a request to increase the radiation dose; Amendment No. 2 proposed to include patients with aplastic anemia.

This proposal was first approved by the committee in 1967; it was reviewed again in January 1970, and was reported upon at subsequent meetings of the committee. The two amendments presented at this meeting were widely discussed. It was recognized that the radiation dose used here is less than the doses used at other places. Dr. Edwards reviewed the three cases treated with this protocol and said that the lack of difficulties attributable to radiation injury was impressive and no problems were encountered in keeping the patients alive. He would like

1113736

to increase the radiation dose, as outlined in Amendment 1, especially in cases where more immunosuppression seems to be indicated. He proposes to increase it up to approximately 800 rads at 40 R/min, to be comparable to 1,000 rads at 5 R/min. In discussion there was hesitance to go directly to the highest level and it was agreed to advance by increments — for example, to 500 R, 600 R, and 800 R.

Amendment No. 2, to include patients with aplastic anemia, was discussed at length. Dr. Lange pointed out results of E. D. Thomas, et al., which suggest that Cytoxan might be a better immunosuppressive agent than radiation. Edwards responded that these results were based on a comparison with low dose-rate irradiation, believed less valuable than what ORAU uses. Consideration was given to the potential spontaneous recovery in some cases of aplastic anemia which makes hazardous treatments need even more careful consideration than in leukemia. The committee approved the proposal, with the stipulation that if results in the first six cases or so should appear poorer than those obtainable with Cytoxan, reevaluation should be made.

A long discussion was held on donor selection and tissue typing.

Proposal No. 20 - "Use of Radioprotective Drugs in Radiation Therapy: Phase I Studies -- The metabolism of ^{35}S labeled S-2-(3-aminopropylamino) ethyl phosphorothioic acid in humans," - Edwards, Yuhas, Washburn, Comas.

This proposal was discussed especially from the point of view that the initial patients would be volunteers who would have nothing to gain from the procedure and would need to be fully informed of this. It was pointed out that no enzyme measurement or tests of kidney or liver function were planned according to the proposal; Dr. Edwards agreed that the latter, at least, should be included. There was a question about whether a patient might be used more than once, perhaps at different dose levels, and would this be appropriate? Edwards said that because of our small number of available patients, we would like to do this in some cases. The committee's view was that repeated studies in the same patient should not be prohibited, but that due care should be given to the implications of this in each patient, both for the scientific study and for the stress or inconvenience to the patient.

The committee expressed general approval of the project in the proposal but at Dr. Edwards' suggestion, withheld specific approval pending submission by mail of new version of the proposal including the above points and also samples of consent forms and statements of the information to be given to patients, including the specific number of blood samples, etc., required.

Proposal No. 21 - "Mechanism of Immunotherapy of Human and Animal Cancers by Injection of Mycobacterium Bovis (BCG)," — Hanna, Hubner, Gengozian, Solomon, Krauss.

This proposal was approved without reservation. It was suggested that for clarification, it might be stated that Paragraph D on Page 9 refers to the possibility of clinical infection with the organism (BCG) used for immune stimulation. If such infections do occur they are said to be easily treatable.

Review of Ongoing Research Projects:

Proposal No.

1. Clinical Trials of $^{113}In^{m}$ as a Kidney and Bone-scanning Agent. Not activated.

5. Use of Radioiodine in Surgical Removal of Thyroid Cancers. We are still seeing an average of one new thyroid cancer patient a month. Standard protocol is followed, using radioiodine for identification of tumor, and treatment is carried out when feasible. It has been a successful protocol; not a death in years.

8. Study of Granulocyte Kinetics in Myeloproliferative Disorders.

A report was published on cycling of white cells on chronic granulocytic leukemia. No further work on this has been done during the last twelve months.

9. Tumor Scanning with ^{67}Ga.

Since the Committee last met, we activated 2 protocols with the Cooperative Group to Study Localization of Radiopharmaceuticals. Over 1,000 cases have been reviewed; large bulk of these were Hodgkin's disease, lymphoma, and cancer of the lung. The group is now divided into subcommittees to work at different tumor types. (Dr. Edwards works with the Hodgkin's group.) The data is now being looked at and a report will be written early next year.

10. Studies of Total-Body Irradiation in Patients with Hematologic Disorders.

We have treated probably 20 patients with total-body irradiation. Most had CLL, CGL, or polycythemia vera. One had hemorrhagic thrombocytosis and one disseminated lymphosarcoma. Work is being done on fractionation procedures aimed at giving continuous control. Results this past year have been relatively gratifying.

12. Scanning Tumors of Retroperitoneal Lymph Nodes after Intralymphatic Injection of Radioactive Gallium.

Six or seven patients were originally studied with disappointing resulrs; nothing has been done since last report to Committee.

13. Therapeutic Transplantation of Allogeneic Human Bone Marrow.

Three patients were subjected to this protocol. Quite a number of cases were tested and not used. Report was sent out.

1113738

Review of ongoing projects cont'd.

Proposal No.

15. Histologic Changes in the Skin Related to the Graft-Versus-Host Reaction after Marrow Transplantation.

With Dr. Nelson away, nothing has been done on this since the last report.

16. Changes in Blood Enzyme Levels Following Exercise and/or Total-Body Irradiation in Man.

This project is continuing on selected patients; summary of results will be sent to Committee.

17 Chromosomal Breakages in Fibroblasts from Women Taking Oral Contraceptives.

Completed. Did get a few skin biopsies without complication. Report is being written. Summary of results to be sent to Committee.

18. Scandium-Augmented Gallium Localization in Tumors. Phase I and Phase II Studies.

This study is in abeyance because a brief transient hemolytic anemia was produced in one patient at a dose of 0.125 mgm/kilo. Prolonged in vitro studies with red cells tend to confirm that this is a scandium effect and that human red cells behave differently from those of other species. This is an interesting basic point that is being explored. The Committee will be consulted before any further scandium is given to patients.

19. Regulation of Granulopoiesis.

Dr. Vodopick is now ready to commence her studies on normal volunteers as initially proposed. (As yet no human samples have been used.) After finishing studies on normal volunteers, patients with myeloproliferative disorders will be studied. Initially, 50 ml or less samples of whole blood will be needed, but this will vary according to the individual's blood count. Prior approval from the Committee will be sought before we proceed to other experiments in which larger volumes of blood or plasma are needed.

1113739

We had not sent in, until very recently, the request to be given a "general" assurance from NIH, but we do plan to attempt to arrange this type of assurance. Presumably this will lessen the paperwork on individual NIH-supported proposals.

Item 5. Ongoing Research Projects

The following list of ongoing research projects and comments was distributed:

Ident. No.

1. Clinical Trials of $^{113}In^{m}$ as a Kidney and Bone-Scanning Agent. In abeyance — no recent work.

5. Use of Radioiodine in Surgical Removal of Thyroid Cancers. Few patients being added.

8. Study of Granulocyte Kinetics in Myeloproliferative Disorders. Continuing.

9. Tumor Scanning with Gallium-67. Very active. Many patients being added. No untoward reactions of any sort are being encountered.

10. Studies of Total-Body Irradiation in Patients with Hematologic Disorders. Continuing. More patients being given small intermittent doses at intervals of a few weeks to achieve smoother suppression of hematologic disorders.

12. Scanning Tumors of Retroperitoneal Lymph Nodes after Intralymphatic Injection of Radioactive Gallium. In abeyance. Early results not promising.

13. Therapeutic Transplantation of Allogeneic Human Bone Marrow. Recent graft given December 2 with successful take. Possibility of treating aplastic anemia has been considered. Also the possibility of using for a leukemic patient a donor younger than prescribed. If either of these becomes a likely eventuality, we will communicate with the committee in advance.

15. Histologic Changes in the Skin Related to the Graft-Versus-Host Reaction after Marrow Transplantation. No recent data collected but project considered active.

16. Changes in Blood Enzyme Levels Following Exercise and/or Total-Body Irradiation in Man. Active. Special resuscitation equipment has been obtained according to recommendations of committee.

17. Chromosomal Breakages in Fibroblasts from Women Taking Oral Contraceptives. Active. Drs. Edwards and Hubner are supervising skin biopsies.

There were brief comments about the possibility that the marrow graft procedure (No.13) might be extended to other types of patients, or might involve younger donors than had been envisaged. We indicated that we would communicate with the committee if we felt at any point that such a change should be undertaken for a specific case.

1113740

Status of Ongoing Approved Projects

31 January 1972

1. Clinical Trials of $^{113}In^{m}$ as a Kidney and Bone-Scanning Agent. In abeyance — no recent work.

2. Use of Radioiodine in Surgical Removal of Thyroid Cancers. Few patients being added.

3. Study of Granulocyte Kinetics in Myeloproliferative Disorders. Continuing.

4. Tumor Scanning with Gallium-67. Very active. Many patients being added. No untoward reactions of any sort are being encountered.

5. Studies of Total-Body Irradiation in Patients with Hematologic Disorders. Continuing. More patients being given small intermittent doses at intervals of a few weeks to achieve smoother suppression of hematologic disorders.

6. Scanning Tumors of Retroperitoneal Lymph Nodes after Intralymphatic Injection of Radioactive Gallium. In abeyance. Early results not promising.

7. Therapeutic Transplantation of Allogeneic Human Bone Marrow. Recent graft given December 2 with successful take. Possibility of treating aplastic anemia has been considered. Also the possibility of using for a leukemic patient a donor younger than prescribed. If either of these becomes a likely eventuality, we will communicate with the committee in advance.

8. Histologic Changes in the Skin Related to the Graft-Versus-Host Reaction after Marrow Transplantation. No recent data collected but project considered active.

9. Changes in Blood Enzyme Levels Following Exercise and/or Total-Body Irradiation in Man. Active. Special resuscitation equipment has been obtained according to recommendations of committee.

10. Chromosomal Breakages in Fibroblasts from Women Taking Oral Contraceptives. Active. Drs. Edwards and Hubner are supervising skin biopsies.

1113741

From Minutes 8/13/71

4. Marrow Grafting Following Total-Body Irradiation, superseded by No. 13.

7. A Study of Infections in Cancer Patients, not activated.

11. Blood Lymphocyte Survival and Distribution in Patients with Lymphoproliferative Disorders, not activated.

14. Proposal to Visualize Lymph Node Drainage After Scanning Doses of ^{67}Ga, concluded.

6. Use of Small Tracer Doses of Rare Elements in Human Volunteers: The Committee withdrew its approval of this proposal and requested a detailed application of any specific proposal.

. . .

9. Review of Ongoing Research Projects

Each of the projects that have been discussed and presented to the Committee since its formation in April, 1967, was reviewed. Status was described, and plans for continuation were noted. The Committee approved continuation of the following proposals:

1. Clinical Trials of $^{113}In^{m}$ as a Kidney and Bone Scanning Agent. (Status Report: Inactive, no work under way at present.)

5. Use of Radioiodine in Surgical Removal of Thyroid Cancers. (Status Report: Study is under way at present to examine the 20-yr experience and determine whether and how to continue this project.)

8. Study of Granulocyte Kinetics in Myeloproliferative Diseases. (Status Report: Continuing in patients receiving total-body irradiation.)

9. Tumor Scanning with Gallium-67. (Status Report: Continuing.)

10. Studies of Total-Body Irradiation in Patients with Hematologic Disorders. (Status Report: Continuing.)

12. Scanning Tumors of the Retroperitoneal Lymph Nodes After Intralymphatic Injection of Radioactive Gallium. (Status Report: Results in 7 patients have been discouraging. Permission was given to continue the project in order to gain conclusive answers. At present the value of this procedure is dubious.)

1113742

✓ Sam

Ongoing Projects - Cont'd.

13. Therapeutic Allogeneic Transplantation of Human Bone Marrow. (Status Report: A detailed report was given of the one patient who has entered this protocol. Summarized results: A successful graft was obtained, there was no recurrence of leukemia, there was no rejection of the graft, or graft-versus-host disease. Patient had preexisting cardiovascular disease and showed evidence of immunologic inadequacy. His death, about 4 months after the procedure, was attributed to cardiovascular complications, infection, and the treatment thereof.)

15. Histologic Changes in the Skin Related to the Graft-Versus-Host (GVH) Reaction After Marrow Transplantation. Bill Nelson, Senior Investigator. Approved this meeting (8/13/71)

16. Changes in Blood Enzyme Levels Following Exercise and/or Total-Body Irradiation in Man. C. C. Lushbaugh Senior Investigator. Approved this meeting (8/13/71).

17. Chromosomal Breakages in Fibroblasts from Women Taking Oral Contraceptives. Gayle Littlefield, Senior Investigator. Approved this meeting (8/13/71).

For the sake of committee efficiency, a list of currently active projects should be provided for each meeting obtained from the minutes of the previous meeting. Those projects completed or discontinued should be placed in a separate file. Deferred projects which have approval should be so labeled in the listing.

Meeting adjourned at 3:00 p.m.

Submitted,

R. M. Kniseley, M.D.
for Dr. Andrews

pe

1113743

MEETING OF COMMITTEE ON HUMAN STUDIES OF

Oak Ridge Associated Universities

Held 19 January, 1970 at Medical Division.

Members of Committee Present	Staff Members Present
G. A. Andrews	N. Gengozian
A. B. Brill	C. L. Edwards
Melvin Koons	Helen Vodopick
R. D. Lange	Karl Hubner
Wm. Nelson	
John Storer	
Tom Lincoln	

The Meeting was held to discuss the initiation of a project entitled:

Therapeutic Allogenic Transplantation of Human Bone Marrow.

Gould Andrews introduced the proposal and gave a brief historical background of the use of bonemarrow transplantation.

There was a great deal of discussion of the proposed project and many questions were raised. Among the questions were the advisability of using anti-lymphocyte-serum before additional animal studies were performed and also regarding consideration of the use of extracorporeal irradiation. There were questions regarding the method to be used for producing and obtaining the anti-lymphocyte-serum as well as a discussion of the selection of participants and dangers of fat embolism.

It was brought out that the AEC was very interested in the "informed consent" procedure and would need to be satisfied regarding the form to be signed.

There was a discussion of the safety factors involved in the use of the high dose facilities at U.T.A.E.C. and the possibility of purchasing an auxilliary power source was suggested.

1113744

There followed a discussion of the graft versus host reaction and it was pointed out that this was a real hazard.

Each of these foregoing questions were answered to the satisfact on of the committee.

At this point Drs. Andrews, Gengozian, Edwards, Vodopick and Hubner retired and the following motion was proposed by Dr. Storer, seconded by Dr. Brill and was passed unanimously by the remaining members of the committee:

> The committee approves the project as submitted contingent on the preparation of a release which meets all legal requirements. The committee further recommends that an independent evaluation of the extent of understanding of the release on the part of the patient or parent be made if feasible. It is suggested that a member of the clergy might make such an evaluation. The committee also expressed a wish that they be kept informed on the progress of this project.

Submitted by

R D Lange

Robert D. Lange, M.D.
Committee on Human Studies

Minutes of Jan. 19, 1970 Meeting sent to:

Brill	Cloutier	Pollard
Edwards	Lushbaugh	Kniseley
Koons	Gengozian	Harmon
Lange	Hubner	
Lincoln	Vodopick	
Nelson		
Storer		

1113745

pe
1-30-70

COPY

Committee on Human Studies

Minutes of Meeting - July 10, 1969

The following members were present: Mr. Melvin A. Koons and Drs. A. Bertrand Brill, Gould Andrews, Kong-oo Goh, Edward Balish, and Robert D. Lange.

The following new proposals were discussed and approved:

1. A Study of Infections in Cancer Patients. Investigators: Drs. Edward Balish and C. Lowell Edwards.

#7 moved activated

It was noted that not all patients would have small intestinal specimens obtained three times weekly and that only adults would have bowel sterilization procedures. The committee expressed concern that all patients should be informed that it was possible for them to withdraw without prejudice. A new consent form is to be prepared. The committee urged that the senior investigators keep a continued surveillance for possible drug reactions and emergence of any drug resistant organisms. It was also emphasized that the committee be informed at each meeting about the results of this project.

2. Tumor Scanning with Gallium-67. Senior Investigator: C. L. Edwards.

The committee noted with favor that cooperative studies were being carried out with established investigators. It was noted that ORAU was legally responsible for material sent out for human use.

3. Study of Granulocytic Kinetics in Myeloproliferative Diseases. Senior Investigator: Helen Vodopick.

#8

Dr. Vodopick was present for this discussion.

The project was approved. The only question was in regard to which "consent form" would be used.

The next meeting of the committee was tentatively scheduled for September 18, 1969.

Submitted by

R D Lange

Robert D. Lange, M.D.

1113746

MEDICAL 1950

Bruner, H. D., and Andrews, G. A. "Cancer resarch program of Oak Ridge Institute of Nuclear Studies." Southern Surgeon 16:577-83 (1950).

King, E. R., and Perkinson, J. D. "Preliminary distribution studies of $_{31}GA^{72}$ in the wistar rat." Texas Reports on Biology and Medicine 8:491-97 (1950).

1113747

MEDICAL 1951

Berg, H. F. "Localization of radioactivity of colloidal gold^{198}" AMA Archives of Surgery 545-53 (1951).

Brucer, M. "Distribution of gallium in man: autopsy evidence." Journal of Pharmacology and Experimental Therapeutics 101:4-5 (1951). (Abstract.)

-----. "Radioisotope hazards and protection in a hospital." Journal of the American Medical Association 147:1745-51 (1951).

Brucer, M.; King, E. R.; and Bruner, H. D. A method for standardization of gallium^{72}. Washington, D.C.: U.S. Atomic Energy Commission, 1951. (ORO-44.)

Bruner, H. D. An expendable cage to separate the urine and feces of rats in tracer experiments. Washington, D.C.: U.S. Atomic Energy Commission, 1951. (ORO-5.)

-----. "Renal extraction ratio of radioactive diodrast in anesthetized dogs." Journal of Pharmacology and Experimental Therapeutics 101:5 (1951). (Abstract.)

Bruner, H. D.; King, E. R.; and Smyser, M. P. Tables to correct for physical decay of some frequently used isotopes. Washington, D.C.: U.S. Atomic Energy Commission, 1951. (ORO-26.)

Bruner, H. D.; Perkinson, J. D., Jr.; Hayes, R. L.; and Wilson, C. "Distribution of intravenously injected Ga^{67} citrate compared with Ga^{72} citrate." Journal of Pharmacology and Experimental Therapeutics 103:338 (1951). (Abstract).

1113748

Furth, J.; Andrews, G. A.; Storey, R. H.; and Wish, L. "The effect of x-irradiation on erythrogenesis, plasma and cell volumes." Southern Medical Journal 44:85-92 (1951).

King, E. R.; Perkinson, J. D., Jr.; Bruner, H. D.; and Gray, J. "Excretion of gallium by the rat and by man." Science 113:555-57 (1951).

Kittle, C. F.; King, E. R.; Bahner, C. T.; and Brucer, M. "Distribution and excretion of radioactive hafnium^{181} sodium mandelate in the rat." Proceedings of the Society for Experimental Biology and Medicine 76:278-82 (1951).

Skipper, H. E.; Chapman, J. B.; Boyd, G. A.; Riser, W. H., Jr.; and Bell, M. "Preferential incorporation of formate carbon into leukemic blood cells as indicated by autoradiography." Proceedings of the Society for Experimental Biology and Medicine 77:849-54 (1951).

1113749

MEDICAL 1952

Andrews, G. A. "The possibilities and limitations of isotope therapy of cancer." Journal of the Kansas Medical Society 53:561-64 (1952).

-----. "Status of radiogold therapy." Nucleonics 10:48-49 (1952).

Archdeacon, J. W., and Brucer, M. "Application of perfused rat liver preparation to isotope study." Proceedings of the Society for Experimental Biology and Medicine 81:325-27 (1952).

Archdeacon, J. W.; Nash, J. B.; and Wilson, G. C. "The biliary excretion of gallium^{72}, gold^{198}, hafnium^{181} in the rat." Texas Reports on Biology and Medicine 10:281-85 (1952).

Bahner, C. T.; Zilversmit, D. E.; and McDonald, E. "The preparation of wet ashed tissues for liquid counting." Science 115:597-98 (1952).

Brucer, M. "Evaluation of teletherapy sources." Nucleonics 19:9 (1952).

-----. "Internally administered isotopes for cancer therapy and new developments in teletherapy." Nucleonics 10:40-51 (1952).

-----. "Symposium report: cancer therapy with radioisotopes." Science 115:183 (1952).

-----. Teletherapy design problems: I. Cs^{137}. Washington, D.C.: U.S. Atomic Energy Commission, 1952. (TID-5086.)

1113750

-----. "Therapeutic potentialities of radioisotopes." Merck Reports 61:9-15 (1952).

-----. "The use of external radiation sources, beta and gamma." In Proceedings of the Second National Cancer Conference, vol. 2, pp. 1647-51. New York: American Cancer Society, 1952.

Bruner, H. D. "Problems with newer isotopes being investigated." Nucleonics 10:49-59 (1952).

Bruner, H. D., and Perkinson, J. D., Jr. "A comparison of iodine-131 counting methods." Nucleonics 10:57-61 (1952).

Bruner, H. D.; Perkinson, J. D., Jr.; and Hayes, R. L. "Effect of quantity of carrier gallium on distribution of metal in rats." Federation of American Societies for Experimental Biology. Federation Proceedings 11:328 (1952). (Abstract.)

Ferguson, J. H.; Andrews, G. A; and Brucer, M. "Blood-clotting studies in dogs internally irradiated with radiogold." Proceedings of the Society for Experimental Biology and Medicine 80:541-45 (1952).

Grimmett, L. G.; Kerman, H. D.; Brucer, M.; Fletcher, G. H.; and Richardson, J. E. "Design and construction of a multicurie cobalt teletherapy unit." Radiology 59:19-29 (1952).

Kerman, H. D. "Medical uses of cobalt 60." Southern Medical Journal 45:495-503 (1952).

1113751

MEDICAL 1953

Andrews, G. A. "Treatment of thyroid carcinoma with radioactive iodine." Journal of the Kansas Medical Society 54:7-10 (1953).

Andrews, G. A.; Root, S. W.; and Kerman, H. D. "A study of gallium^{72}: VI. Clinical studies with gallium^{72}." Radiology 61:570-88 (1953).

Andrews, G. A.; Root, S. W.; Kerman, H. D.; and Bigelow, R. R. "Intracavitary collodial radiogold in the treatment of effusions caused by malignant neoplasms." Annals of Surgery 137:375-81 (1953).

Andrews, G. A.; Root, S. W.; and Kniseley, R. M. "Metabolism and distribution of colloidal Au^{198} injected into serous cavities for treatment of effusions associated with malignant neoplasms." Cancer 6:294-302 (1953).

Andrews, G. A.; Root, S. W.; Kniseley, R. M.; and Kerman, H. D. "Intracavitary use of colloidal radioactive gold." Radiology 61:922-29 (1953).

Andrews, G. A., and Tyor, M. P. "Early results of the treatment of chronic granulocytic leukemia with intravenous colloidal gold^{198}." Journal of Laboratory and Clinicl Medicine 42:777-78 (1953).

Berg, H. F.; Christopherson, A. M.; Isaacs, A. M.; and Bryant, J. R. "Localization of radioactivity in regional lymph nodes." AMA Archives of Surgery 67:228-43 (1953).

1113752

Kniseley, R. M.; Andrews, G. A.; and Brucer, M. "Radiation problems in the pathology laboratory of a hospital using radioisotopes." Laboratory Investigation 1:447-55 (1952).

Lotz, W. E.; Gallimore, J. C.; and Boyd, G. A. "How to get good gross autoradiographs of large un-decalcified bones." Nucleonics 10:28-31 (1952).

Perkinson, J. D., Jr., and Bruner, H. D. "Preparation of tissues for iodine-131 counting." Nucleonics 10:66-67 (1952).

Stevens, K. M. "Content of, and incorporation of P^{32} into the nucleic acids of the liver, spleen, and lymphosarcomatous tissue of man." Cancer 5:122-25 (1952).

Wood, J. L., and Perkinson, J. D., Jr. "Yeast biosynthesis of radioactive sulfur compounds." Journal of the American Chemical Society 74:2445 (1952).

Yates, W. K. "Experimental location of myocardial infarction using radioisotopes." U.S. Armed Forces Medical Journal 3:1597-602 (1952).

Zilversmit, D. B.; Boyd, G. A.; and Brucer, M. "The effect of particle size on blood clearance and tissue distribution of radioactive gold colloids." Journal of Laboratory and Clinical Medicine 40:255-60 (1952).

-----. "The preparation and particle size measurement of monodisperse radioactive gold colloids." Journal of Laboratory and Clinical Medicine 40:261-66 (1952).

1113753

Brucer, M. "Encouraging and discouraging research with therapeutic radioisotopes." Journal of the Kentucky State Medical Association 51:243-47 (1953).

-----. "Gli isotopi radioattivi nella terapia clinica." Problemi del Servizio Sociale 8, January-February 1953.

-----. "Teletherapy evaluation board." Radiology 60:738-39 (1953). (Editorial.)

Brucer, M.; Andrews, G. A.; and Bruner, H. D. "A study of gallium^{72}: Summary and conclusions." Radiology 61:534-36 (1953).

Brucer, M.; Andrews, G. A.; Rehbock, D. J.; Root, S. W.; and Gray, J. "A study of gallium^{72}: VIII. Autopsy studies of distribution of gallium^{72}." Radiology 61:590-95 (1953).

Brucer, M., and Bruner, H. D. "A study of gallium^{72}: I. Physics and radiation characteristics of gallium^{72}." Radiology 61:537-43 (1953).

Brucer, M.; Pollard, W. G.; Leiter, H.; and Scarf, H. "Shaped sources for teletherapy units." Nucleonics 11:38-41 (1953).

Bruner, H. D.; Cooper, Betty M.; and Rehbock, D. J. "A study of gallium^{72}: IV. Toxicity of gallium citrate in dogs and rats." Radiology 61:550-55 (1953).

Bruner, H. D.; Gray, J.; Root, S. W.; and Brucer, M. "A study of gallium^{72}: VII. Studies of the urinary excretion of gallium^{72} in man." Radiology 61:588-90 (1953).

1113754

Bruner, H. D.; Hayes, R. L.; and Perkinson, J. D., Jr. "A study of gallium^{72}: X. Preliminary data on gallium^{67}." Radiology 61:602-12 (1953).

Bruner, H. D.; Perkinson, J. D., Jr.; and Hayes, R. L. "Deposition of Mn in the thyroid using Mn$^{52-54}$." Federation of American Societies for Experimental Biology. Federation Proceedings 12:305-06 (1953).

Bruner, H. D.; Perkinson, J. D., Jr.; King, E. R.; Andrews, G. A.; Nash, J. B.; and Brucer, M. "A study of gallium^{72}: V. Distribution studies on gallium^{72} in rats." Radiology 61:555-70 (1953).

Bryant, J. R.; Berg, H. F.; and Christophersen, W. M. "Localization of radioactivity in the lung and the lymph nodes." Journal of Thoracic Surgery 26:221-32 (1953).

Buher, W. R. "Direct exposure enlargement using a fractional focal spot x-ray tube." The X-ray Technician 24:321-23 (1953).

Gallimore, J. C., Jr.; Boyd, G. A.; Andrews, G. A.; and Brucer, M. "A study of gallium^{72}: IX. Autoradiographic studies." Radiology 61:595-602 (1953).

Hutchinson, L. A.; Andrews, G. A.; and Kniseley, R. M. "Influence of cortisone on the toxicity of nitrogen mustard in rats." Proceedings of the Society for Experimental Biology and Medicine 83:376-77 (1953).

Kniseley, R. M., and Andrews, G. A. "Pathological changes following intracavitary therapy with colloidal Au^{198}." Cancer 6:303-12 (1953).

1113755

Little, R. C., and Kelly, H. B. "Removal of radioactive gold colloid by the perfused mammalian liver." American Journal of Physiology 173:265-69 (1953).

MacDonald, E., and Bahner, C. T. "Hafnium complexes for biological investigation." Proceedings of the Society for Experimental Biology and Medicine 83:801-04 (1953).

Mayr, G.; Bruner, H. D.; and Brucer, M. "Boron detection in tissues using the (n, alpha) reaction." Nucleonics 11:21-25 (1953).

Perkinson, J. D., Jr.; Eldridge, J. S.; and Cooper, Betty M. "A study of gallium ^{72}: II. Gallium chemistry of biological interest." Radiology 61:543-45 (1953).

Perkinson, J. D., Jr., and Ingols, R. S. "A study of gallium^{72}: III. Effect of internal irradiation on respiration of rat liver slices." Radiology 61:545-50 (1953).

Root, S. W., and Andrews, G. A. "Effect of ACTH on the eosinophil count in peripheral blood and bone marrow." American Journal of Medical Sciences 226:304-9 (1953).

Stembridge, V. A.; Kniseley, R. M.; and Andrews, G. A. "Cellular changes in effusions following intracavitary administration of colloidal Au^{198} in human beings." Journal of Laboratory and Clinical Medicine 41:760-66 (1953).

Stembridge, V. A.; Kniseley, R. M.; and Gibbs, W. "Autoradiographic distribution of intravenous colloidal gold (Au^{198}) in the rat." Laboratory Investigation 2:349-56 (1953).

1113756

MEDICAL 1954

Andrews, G. A. "The clinical use of bone marrow study." Journal of the Tennessee State Medical Association 47:361-66 (1954).

Andrews, G. A.; Kniseley, R. M.; Bigelow, R. R.; Root, S. W.; and Brucer, M. "Pathological changes in normal human thyroid tissue following large doses of I-131." American Journal of Medicine 16:372-81 (1954).

Bahner, C. T. "Localization of antimony in blood." Proceedings of the Society for Experimental Biology and Medicine 86:371-73 (1954).

Berg, H. F.; Christopherson, W. M.; and Bryant, J. R. "Time and site study for optimum lymph node concentration of radiogold following intrabronchial injection." Cancer Research 14:775-79 (1954).

Berg, H. F.; Isaacs, A. M.; and Christophersen, W. M. "Localization of radioactivity in the urinary bladder and the regional lymph nodes." Journal of Urology 72:382-88 (1954).

Brucer, M. "An available Co^{60} source for teletherapy." Nucleonics 12:45-46 (1954).

-----. Marble Used as a Radiation Shield. Mt. Vernon, New York: Marble Institute of America, 1954.

-----. "A standard cobalt 60 teletherapy source capsule." British Journal of Radiology 27:410-12 (1954).

1113757

-----. "Standardized Co^{60} source capsule for teletherapy." Nucleonics 12:58-59 (1954).

-----. "Statement in hearings before the Subcommittee on Research and Development of the Joint Committee on Atomic Energy, Eighty-third Congress of the United States." Second Session: The Contribution of Atomic Energy to Medicine, pp. 26-76. Washington, D.C.: U.S. Government Printing Office, 1954.

-----. "Teletherapy design problems." Radiology 62:91-98 (1954).

Gallimore, J. C.; Bauer, E. C.; and Boyd, G. A. "A non-leaching technique for autoradiography." Stain Technology 29:95-98 (1954).

Gallimore, J. C.; Boyd, G. A.; and Stannard, J. N. "An autoradiographic study of the distribution of polonium in the rat during 24 hours after intravenous injection." The Anatomical Record 118:253-74 (1954).

Kyker, G. C. "Biochemical consideration of distribution." American Journal of the Medical Sciences 227:572-89 (1954).

-----. "The distribution of interstitial and intracavitary injections of certain radiochemical preparations of medical interest." Bulletin of the Medical Association of Puerto Rico 46:362-74 (1954)

Kyker, G. C.; Cress, E. A.; and Gleason, G. I. "Distribution of yttrium administered by various routes." Federation of American Societies for Experimental Biology. Federation Proceedings 13:245 (1954). (Abstract.)

1113758

Richardson, J. E. "Effect of chamber voltage on electron build-up measurements." Radiology 62:584-88 (1954)

Richardson, J. E.; Kerman, H. D.; and Brucer, M. "Skin dose from a cobalt 60 teletherapy unit." Radiology 63:25-36 (1954).

Root, S. W.; Andrews, G. A.; Kniseley, R. M.; and Tyor, M. P. "The distribution and radiation effects of intravenously administered colloidal Au^{198} in man." Cancer 7:856-66 (1954).

Root, S. W.; Tyor, M. P.; Andrews, G. A.; and Kniseley, R. M. "Distribution of colloidal radioactive chromic phosphate after intracavitary administration." Radiology 63:251-57 (1954).

Tyor, M. P. "Human serum albumin tagged with I^{131} in patients with ascites caused by abdominal carcinomatosis and portal cirrhosis: the rates of interchange between the vascular compartment and peritoneal cavity." Journal of Laboratory and Clinical Medicine 44:110-17 (1954).

1113759

MEDICAL 1955

Andrews, G. A. "Intracavitary use of radioisotopes." In Radioisotopes in Medicine, pp. 552-63. Washington, D.C.: U.S. Atomic Energy Commission, 1955. (ORO-125.)

Andrews, G. A.; Brucer, M.; and Anderson, E. B.; eds. Radioisotopes in Medicine. Washington, D.C.: U.S. Atomic Energy Commission, 1955. (ORO-125.)

Andrews, G. A.; Kyker, G. C.; Kniseley, R. M.; and Palmer, E. L. "Preliminary studies of yttrium-90 in man." Proceedings of the American Association for Cancer Research 2:1 (1955). (Abstract.)

Bahner, C. T. "Colorimetric study of absorption and excretion of 4-(p-dimethylaminostyrl) quinoline methiodide and related compounds." Proceedings of the Society for Experimental Biology and Medicine 90:133-35 (1955).

-----. "Effect of compounds related to 4-(p-dimethylaminostyrl) quinoline methiodide on lymphoma 8." Cancer Research 15:588-92 (1955).

Brucer, M. "Gamma ray absorption and radiation dosimetry." In Radioisotopes in Medicine, pp. 103-53. Washington, D.C.: U.S. Atomic Energy Commission, 1955. (ORO-125.)

-----. "Marble as a radiation shield." Nucleonics 13:65-66 (1955). (Abstract.)

-----. Special report of the Medical Division on teletherapy design problems: I. Cs^{137}. Washington, D.C.: U.S. Atomic Energy Commission, 1955. (TID-5086, second revision.)

1113760

-----. Teletherapy design problems: IV. Isodose charts for the Co^{60} hectocurie teletherapy machine. Washington, D.C.: U.S. Atomic Energy Commission, 1955. (ORINS-10.)

Brucer, M., et al. Teletherapy design problems III. Washington, D.C.: U.S. Atomic Energy Commission, 1955. (ORO-127.)

-----. Teletherapy design problems III. Supplement. Washington, D.C.: Atomic Energy Commission, 1955. (ORO-127.)

Brucer, M.; Kerman, H. D.; and Richardson, J. E. Teletherapy design problems--cobalt 60 teletherapy unit. Washington, D.C.: U.S. Atomic Energy Commission, 1955. (ORO-109.)

Comar, C. L. "Some aspects of radioassay and interpretation." In Radioisotopes in Medicine, pp. 63-72. Washington, D.C.: U.S. Atomic Energy Commission, 1955. (ORO-125.)

Harris, N. O., and Hayes, R. L. "A tracer study of the effect of acute and chronic exposure to sodium fluoride on the thyroid iodine metabolism of rats." Journal of Dental Research 34:470-77 (1955).

Hayes, R. L.; Brucer, M.; and Arakawa, E. "Some integral dose relationships in Co^{60} teletherapy." Radiation Research 3:64 (1955).

Kniseley, R. M. "Some aspects of the biology of radiation." In Radioisotopes in Medicine, pp. 35-44. Washington, D.C.: U.S. Atomic Energy Commission, 1955. (ORO-125.)

1113761

Kniseley, R. M., and Andrews, G. A. "Pathologic changes produced in the thyroid by I-131." In Radioisotopes in Medicine, pp. 400-411. Washington, D.C.: U.S. Atomic Energy Commission, 1955. (ORO-125.)

Kyker, G. C. "Biochemical considerations of distribution." In Radioisotopes in Medicine, pp. 50-62. Washington, D.C.: U.S. Atomic Energy Commission, 1955. (ORO-125.)

Kyker, G. C.; Toriello, J.; and Kniseley, R. M. "Interstitial yttrium in prostrate and parametrium." Federation of American Societies for Experimental Biology. Federation Proceedings 14:240-41 (1955). (Abstract.)

Levene, M.; Andrews, G. A.; and Kniseley, R. M. "Large doses of I^{131} in dogs: radiation dosage correlated with histologic and autoradiographic changes." American Journal of Roentgenology 73:88-97 (1955).

MacDonald, L. D.; Hayes, R. L.; and Brucer, M. "Integral dose measurements: preliminary report on a Co^{60} teletherapy beam." Radiology 64:115-16 (1955).

Medical Division, Oak Ridge Institute of Nuclear Studies. Semi-annual progress report for the period ending December 31, 1954. Oak Ridge, Tennessee: ORINS, 1955.

Richardson, J. E., and Brucer, M. "Modification of electron filter to improve light localization of a cobalt 60 beam." Radiology 64:398-403 (1955).

1113762

MEDICAL 1956

Anderson, E. B. Ten years with the peaceful atom. Oak Ridge, Tennessee: ORINS, 1956. (ORINS-15.)

Andrews, G. A. "The effect of dose on the mobilization of rare-earth radioisotopes: II. Preliminary clinical studies." In Rare Earths in Biochemical and Medical Research: A Conference Sponsored by the Medical Division, Oak Ridge Institute of Nuclear Studies, October 1955, pp. 241-58. Washington, D.C.: U.S. Atomic Energy Commission 1956. (ORINS-12.)

-----. "The intrapleural use of radioactive colloidal materials." In Therapeutic Use of Artificial Radioisotopes, Paul F. Hahn, ed.; pp. 295-315. New York: John Wiley & Sons, 1956.

Andrews, G. A.; Kniseley, R. M.; Palmer, E. L.; and Kretchmar, A. L. "Therapeutic usefulness of radioactive colloids: comparative value of gold 198, chromic phosphate (P32), yttrium 90, and lutecium 177." In Peaceful Uses of Atomic Energy: Proceedings of the International Conference in Geneva, August 1955, pp. 122-37. New York: United Nations, 1956.

Brucer, M. "An automatic controlled pattern cesium 137 teletherapy machine." American Journal of Roentgenology 75:49-55, (1956).

1113763

-----. "Dosimetry calculations and conference summary." In Rare Earths in Biochemical and Medical Research: A Conference Sponsored by the Medical Division, Oak Ridge Institute of Nuclear Studies, October 1955, pp. 336-41. Washington, D.C.: U.S. Atomic Energy Commission, 1956. (ORINS-12.)

-----. The industrial atom: teletherapy devices with radioactive isotopes. Washington, D.C.: U.S. Atomic Energy Commission, 1956. (TID-8007.)

-----. "Statement in hearings before the Subcommittee on Research and Development of the Joint Committee on Atomic Energy, Eighty-fourth Congress of the United States." Atomic Energy Research in Medicine, Biology, Agriculture, and Food Preservation, pp. 210-41. Washington, D.C.: U.S. Government Printing Office, 1956.

-----. "Teletherapy devices with radioactive isotopes." In Peaceful Uses of Atomic Energy: Proceedings of the International Conference in Geneva, August 1955, pp. 68-74. New York: United Nations, 1956.

Brucer, M.; Eldridge, J.; and Trombka, J. "Thyroid radioiodine uptake calibration." In Peaceful Uses of Atomic Energy: Proceedings of the International Conference in Geneva, August 1955, pp. 359-64. New York: United Nations, 1956.

Brucer, M.; Oddie, T. H.; and Eldridge, J. S. Thyroid uptake calibration: I. Mock-iodine, a radioactive iodine gamma-ray standard. Washington, D.C.: U.S. Atomic Energy Commission, 1956. (ORINS-14.)

1113764

Christopherson, W. M.; Berg, H. F.; Kyker, G. C.; and Brucer, M. "Studies of interstitial radiolutetium (Lu^{177}) in the dog." AMA Archives of Pathology 62:441-44 (1956).

-----. "Studies of radiolutetium in the mammary gland." In Rare Earths in Biochemical and Medical Research: A Conference Sponsored by the Medical Division, Oak Ridge Institute of Nuclear Studies, October 1955, pp. 332-39. Washington, D.C.: U.S. Atomic Energy Commission, 1956. (ORINS-12.)

Comar, C. L. "Applications of high energy radiation in agriculture." In Proceedings of the Conference of Collaborators from Southern Regional Research Experiment Stations, March 19-21, 1956, pp. 64-76. New Orleans, Louisiana: Southern Regional Research Laboratory, 1956.

-----. "Radiocalcium studies in pregnancy." Annals of the New York Academy of Sciences 64:281-98 (1956).

-----. "Radioisotopes in agriculture." In Atoms in Business, pp. 33-40. San Antonio, Texas: Southwest Research Institute, 1956.

-----. "Radioisotopes in agriculture." In Prospects for Atomic Energy in the South, pp. 84-95. Washington, D.C.: Atomic Industrial Forum, 1956.

-----. "Radioisotopes in animal physiology and nutrition-mineral metabolism." In Peaceful Uses of Atomic Energy: Proceedings of the International Conference in Geneva, August 1955, pp. 245-51. New York: United Nations, 1956.

1113765

Comar, C. L., and Wasserman, R. H. "Radioisotopes in the study of mineral metabolism." In Progress in Nuclear Energy, series VI, vol. 1, pp. 153-96. London: Pergamon, 1956.

Comar, C. L.; Wasserman, R. H.; and Nold, M. M. "Strontium-calcium discrimination factors in the rat." Proceedings of the Society for Experimental Biology and Medicine 92:859-63 (1956).

Gabrielsen, Z., and Kretchmar, A. L. "Studies on salivary secretion of iodide." Journal of Clinical Endocrinology 16:1347-53 (1956).

Harris, C. C.; Bigelow, R. R.; Francis, J. E.; Kelley, G. G.; and Bell, P. R. "CsI (Tl)-crystal surgical scintillation probe." Nucleonics 14(11):102-8 (1956).

Hood, S. L., and Comar, C. L. "Behavior of radioactive yttrium in the blood of ruminants." In Rare Earths in Biochemical and Medical Research: A Conference Sponsored by the Medical Division, Oak Ridge Institute of Nuclear Studies, October 1955, pp. 301-10. Washington, D.C.: U.S. Atomic Energy Commission, 1956. (ORINS-12.)

-----. "Tissue distribution and placental transfer of yttrium 91 in rats and cattle." In Rare Earths in Biochemical and Medical Research: A Conference Sponsored by the Medical Division, Oak Ridge Institute of Nuclear Studies, October 1955, pp. 280-300. Washington, D.C.: U.S. Atomic Energy Commission, 1956. (ORINS-12.)

Kniseley, R. M., and Andrews, G. A. "Transformation of thyroidal carcinoma to clear-cell type." American Journal of Clinical Pathology 26:1427-38 (1956).

1113766

Kyker, G. C. "The effect of dose on the mobilization of rare earth radioisotopes: I. Animal studies." In Rare Earths in Biochemical and Medical Research: A Conference Sponsored by the Medical Division, Oak Ridge Institute of Nuclear Studies, October 1955, pp. 222-40 Washington, D.C.: U.S. Atomic Energy Commission, 1956. (ORINS-12.)

Kyker, G. C.; Christopherson, W. M.; Berg, H. F.; and Brucer, M. "Selective irradiation of lymph nodes by radiolutetium (Lu^{177})." Cancer 9:489-98 (1956).

Kyker, G. C.; Rafter, J.; Cress, E. A.; and Stevens, N. "Radioyttrium with complex heterogeneous carrier." Federation of American Societies for Experimental Biology. Federation Proceedings 15:295 (1956). (Abstract.)

Kyker, G. C., and Stewart, M. "Rare-earth radioisotopes of biochemical interest." Southern Chemist 16:146-47 (1956). (Abstract.)

Kyker, G. C., and Anderson, E. B., eds. Rare earths in biochemical and medical research. Washington, D.C.: U.S. Atomic Energy Commission, 1956. (ORINS-12.)

Loos, R. "Investigation of the complexing action of amino acids by means of paper electrophoresis." In Rare Earths in Biochemical and Medical Research: A Conference Sponsored by the Medical Division, Oak Ridge Institute of Nuclear Studies, October 1955, pp. 163-68. Washington, D.C.: U.S. Atomic Energy Commission, 1956. (ORINS-12.)

Medical Division, Oak Ridge Institute of Nuclear Studies. Midyear report for the period ending December 31, 1955. Oak Ridge, Tennessee: ORINS, 1956. (ORINS-13.)

1113767

Meschan, I.; Oddie, T. H.; and Brucer, M. "The utilization of europium 152-154 in a cervical carcinoma applicator." Radiology 67:422-23 (1956).

Okawa, C., and Trombka, J. I. "The technic of making microangiograms of rabbit bone marrow." American Journal of Clinical Pathology 26:758-64 (1956).

Schachinger, L. "Aus dem krebskrankhaus in Oak Ridge." Atomkernenergie 1:321-23 (1956).

Stewart, M., and Kyker, G. C. "Standardization of beta emitting radioisotopes." Southern Chemist 16:126 (1956).

Totter, J. R., and Comar, C. L. "Function of molybdenum in xanthine oxidase." In A Symposium on Inorganic Nitrogen Metabolism, pp. 513-20. Baltimore, Maryland: The Johns Hopkins Press, 1956.

Tyor, M. P., and Eldridge, J. S. "A comparison of the metabolism of rubidium 86 and potassium 42 following simultaneous injection into man." American Journal of the Medical Sciences 232:186-93 (1956).

Wasserman, R. H.; Comar, C. L.; and Nold, N. M. "The influence of amino acids and other organic compounds on the gastrointestinal absorption of calcium^{45} and strontium^{89} in the rat." Journal of Nutrition 59:371-83 (1956).

-----. "Influence of amino acids and other organic compounds on gastrointestinal absorption of radiocalcium and radiostrontium." Federation of American Societies for Experimental Biology. Federation Proceedings 15:576 (1956). (Abstract.)

1113768

Anderson, E. B. "Ten years with the peaceful atom." Translated into Japanese by Junichi Fujita. Journal of Nursing (Tokyo) 21(11):41-46 (1957).

Andrews, G. A. "A few notions involved in the clinical use of radioisotopes." Annals of Internal Medicine 47:922-38 (1957).

-----. "Clinical uses of radioactive colloids." In U.S. Atomic Energy Commission Report TID-7554, pp. 433-47, Washington, D.C.: U.S. Atomic Energy Commission, 1957.

Belanger, L. F.; Visek, W. J.; Lotz, W. E.; and Comar, C. L. "The effects of fluoride feeding on the organic matrix of bones and teeth of pigs as observed by autoradiography after in vitro uptake of Ca^{45} and S^{35}." Journal of Biophysical Cytology 3:559-66 (1957).

Brucer, M. Isotopes in medicine--are they worth the trouble? Washington, D.C.: U.S. Atomic Energy Commission, 1957. (ORINS-17.)

-----. "Progress and potentialities in teletherapy." Mississippi Valley Medical Journal 79:260-70 (1957).

-----. "Radioiodine uptake measurement." Acta Radiologica Interamer 7:129-43 (1957).

-----. "Teletherapy." In U.S. Atomic Energy Commission Report TID-7554, pp. 418-29. Washington, D.C.: U.S. Atomic Energy Commission, 1957.

1113769

Christopherson, W. M.; Kyker, G. C.; Berg, H. F.; and Brucer, M. "Effect of specific activity on distribution of radiolutecium (Lu^{177})." Proceedings of the Society for Experimental Biology and Medicine 95:750-54 (1957).

Comar, C. L. "Experience in animal experimentation from the standpoint of salvage and waste disposal." In U.S. Atomic Energy Commission Report TID-7512, pp. 105-9. Washington, D.C.: U.S. Atomic Energy Commission, 1957.

Comar, C. L.; Russell, R. S.; and Wasserman, R. H. "Strontium-calcium movement from soil to man." Science 126:485-92 (1957).

Comar, C. L.; Trum, B. F.; Kuhn, U. S. G., III; Wasserman, R. H.; Nold, N. M.; and Schooley, J. C. "Thyroid radioactivity after nuclear weapons tests." Science 126:16-18 (1957).

Comar, C. L., and Wasserman, R. H. "Macronutrient metabolism." In Atomic Energy and Agriculture. AAAS Symposium, vol. 49, pp. 249-304. Washington, D.C.: American Association for the Advancement of Science, 1957.

Comar, C. L.; Wasserman, R. H.; Ullberg, S.; and Andrews, G. A. "Strontium metabolism and strontium-calcium discrimination in man." Proceedings of the Society for Experimental Biology and Medicine 95:386-91 (1957).

Comas, F., and Brucer, M. "First impressions of therapy with cesium 137." Radiology 69:231-35 (1957).

Cooper, B. M. "Contribution of radioactive isotopes to the study of electrolyte balance in surgery." Annals of the New York Academy of Sciences 66:976-82 (1957).

1113770

Cress, E. A., and Kyker, G. C. Problems in the establishment of a colony of specific-pathogen-free rats. Washington, D.C.: U.S. Atomic Energy Commission, 1957. (ORINS-22.)

Johnson, G. T. "Fatty acids as carbon sources for the growth of Spicaria violacea." Mycologia 49:172-77 (1957).

Johnston, P. M., and Comar, C. L. "Autoradiographic studies of the utilization of S^{35}-sulfate by the chick embryo." Journal of Biophysical Biochemical Cytology 3:231-38 (1957).

Kretchmar, A. L.; Andrews, G. A.; Brucer, M.; and Glaser, W. "Measurement of thyroid clearance of plasma iodide: the effect of expansion of the iodide space." International Journal of Applied Radiation and Isotopes 2:140-44 (1957).

Kretchmar, A. L., and Kyker, G. C. "A modified reaction vessel for ninhydrin determination of a-amino acids." Archives of Biochemistry and Biophysics 70:454-56 (1957).

Kyker, G. C., and Cress, E. A. "Acute toxicity of yttrium, lanthanum, and other rare earths." AMA Archives of Industrial Health 16:475-79 (1957).

Kyker, G. C.; Cress, E. A.; Sivarama-Krishnan, V. M.; Steffee, C. H.; and Stewart, M. "Fatty infiltration due to rare earths." Federation of American Societies for Experimental Biology. Federation Proceedings 16:207 (1957). (Abstract.)

Lengemann, F. W., and Comar, C. L. "The secretion of the minerals of milk as studied with radioisotopes." In U.S. Atomic Energy Commission Report TID-7512, pp. 387-94. Washington, D.C.: U.S. Atomic Energy Commission, 1957.

1113771

Lengemann, F. W.; Comar, C. L.; and Wasserman, R. H. "Absorption of calcium and strontium from milk and nonmilk diets." Journal of Nutrition 61:571-83 (1957).

Medical Division, Oak Ridge Institute of Nuclear Studies. Midyear report for the period ending December 31, 1956. Oak Ridge, Tennessee: ORINS, 1957. (ORINS-16)

Mewissen, D. J. "Action de la cystamine per os sur la survie des souris irradiees par le radiocobalt 60." Acta Radiologica 48:141-50 (1957).

-----. "The effect of mercaptoethylamine on survival of mice irradiated with cobalt 60." Radiation Research 6:85-97 (1957).

Mewissen, D. J., and Brucer, M. "Late effects of gamma radiation on mice protected with cysteamine or cystamine." Nature (London) 179:201-2 (1957).

Mewissen, D. J.; Comar, C. L.; Trum, B. R.; and Rust, J. H. "A formula for chronic dosage versus shortening of life span: application to a large mammal." Radiation Research 6:450-59 (1957).

St. Aubin, P. M.; Kniseley, R. M.; and Andrews, G. A. "External irradiation of the thyroid gland in dogs: effects of large doses of roentgen rays upon histologic structure and I^{131} metabolism." American Journal of Roentgenology 78:864-75 (1957).

Schweitzer, G. K., and Eldridge, J. S. "Reproducibility of radioactive sample preparation techniques." Analytica Chimica Acta 16:189-93 (1957).

1113772

Singer, L.; Maqsood, M.; Medlen, A. B.; and Comar, C. L. "Endogenous and biliary excretion of calcium-45 and strontium-89." Archives of Biochemistry and Biophysics 66:404-10 (1957).

Talmage, R. V.; Schooley, J. C.; and Comar, C. L. "Differential removal of strontium 85 and calcium 45 from rat skeleton by peritoneal lavage." Proceedings of the Society for Experimental Biology and Medicine 95:413-17 (1957).

Trombka, J. I., and O'Foghludha, F. "The effects of degraded radiation in thyroid uptake measurements." Physics in Medicine and Biology 1:340-51 (1957).

Wasserman, R. H. "Radiation processing of foods." Journal of the American Dietetic Association 33:33-36 (1957).

Wasserman, R. H.; Comar, C. L.; Nold, M. M.; and Lengemann, F. W. "Placental transfer of calcium and strontium in the rat and rabbit." American Journal of Physiology 189:91-97 (1957). Also in Federation of American Societies for Experimental Biology. Federation Proceedings 16:267 (1957). (Abstract.)

Wasserman, R. H.; Comar, C. L.; and Papadopoulou, D. "Dietary calcium levels and retention of radiostrontium in the growing rat." Science 126:1180-82 (1957).

Wasserman, R. H.; Comar, C. L.; Schooley, J. C.; and Lengemann, F. W. "Interrelated effects of L-lysine and other dietary factors on the gastrointestinal absorption of calcium 45 in the rat and chick." Journal of Nutrition 62:367-76 (1957).

1113773

MEDICAL 1958

Andrews, G. A. "Acute effects of irradiation in man." In Proceedings of the Sixth International Congress of the International Society of Hematology, pp. 371-82. 1958.

-----. "Operations revealing incurable cancer." Surgery, Gynecology, and Obstetrics 107:787-88 (1958). (Editorial.)

Bahner, C. T. "Response of Walker 256 tumors to 4M2M and 4M20." Cancer Research 18:537-42 (1958).

Belanger, L. F.; Visek, W. J.; Lotz, W. E.; and Comar, C. L. "The effects of fluoride ingestion on the organic matrix of the teeth of growing pigs." Journal of Dental Research 37:264-75 (1958)

-----. "Rachitomimetic effect of fluoride feeding on the skeletal tissues of growing pigs." American Journal of Pathology 34:25-35 (1958).

Bellenghi, G. "Sul metodo standard per la determinazione della captazione tiroidea di radioiodio." Minerva Medica 49:2920-23 (1958).

Brucer, M. "Brachytherapy." American Journal of Roentgenology 79:1080-90 (1958).

-----. "Die grundlagen der therapie mit radioaktiven isotopen." Atomkernenergie 3:217-21 (1958).

-----. "Medical instrumentation." In Radiation Biology and Medicine, pp. 864-81. Reading, Massachusetts: Addison-Wesley, 1958.

1113774

-----. "Progress in teletherapy." In Radiation Biology and Medicine, pp. 589-603. Reading, Massachusetts: Addison-Wesley, 1958.

-----. "Radiation-its hopes and hazards." In Courtroom Medicine. Springfield, Illinois: Charles C. Thomas, 1958.

-----. "Radioactive drugs." Mississippi Valley Medical Journal 80:221-24 (1958).

-----. "Radioisotope laboratory facilities and health safety practices." In Proceedings of the Conference on Peaceful Uses of Atomic Energy, May 1957, pp. 204-9. Washington, D.C.: U.S. Atomic Industrial Forum, 1958.

-----. Radioisotope scanning. Washington, D.C.: U.S. Atomic Energy Commission, 1958. (ORINS-20.)

-----. "Radioisotopes and the clinical pathologist." American Journal of Clinical Pathology 29:266-68 (1958). (Editorial.)

-----. "The therapeutic limitations of radioisotopes in urology." Lederle Bulletin Symposium Report 1(2):1-14 (1958).

Brucer, M.; Harmon, J. H.; and Gude, W. D. Radioisotopes in the United States hospitals. Washington, D.C.: U.S. Atomic Energy Commission, 1958. (ORINS-21.)

Brucer, M., and Simon, N. "Teletherapy: progress since 1955: technological and clinical evaluation." In Peaceful Uses of Atomic Energy, Proceedings of Second International Congress, September 1958, pp. 291-92. New York: United Nations, 1958.

1113775

Ganz, A., and Brucer, M. "Blood clearance and tissue distribution studies in the dog following intravenous administration of radioactive colloidal gold (Aurocolloid)." Journal of Laboratory and Clinical Medicine 52:20-26 (1958).

Johnson, G. T. "Oxidation of fatty acids by cell suspensions of Spicaria violacea." Mycologia 50:677-80 (1958).

Kretchmar, A. L. "On the mode of action of the adrenal cortical hormones in protein metabolism." Dissertation Abstracts 19:1195 (1958). (Abstract.)

Medical Division, Oak Ridge Institute of Nuclear Studies. Midyear report for the period ending December 31, 1957. Oak Ridge, Tennessee: ORINS, 1958. (ORINS-23.)

Nold, M. M.; Hayes, R. L.; and Comar, C. L. "Tissue dose from internally administered Y-90." Radiation Research 9:160 (1958). (Abstract.)

Rust, J. H., and Ullberg, S. G. F. Urea formation from one carbon fragment. New York: UNESCO, 1958.

Tsuya, A., and Brucer, M. The TsuyaTscan. Washington, D.C.: U.S. Atomic Energy Commission, 1958. (ORINS-24.)

Wasserman, R. H.; Lengemann, F. W.; and Comar, C. L. "Comparative metabolism of calcium and strontium in lactation." Journal of Dairy Science 41:812-21 (1958).

1113776

MEDICAL 1959

Andrews, G. A. "Medical problems encountered in the handling of radioisotopes." In Symposium on Health Physics in Biology and Medicine, pp. 72-91. Washington, D.C.: U.S. Atomic Energy Commission, 1959. (TID-7572.)

Andrews, G. A.; Sitterson, B. W.; Kretchmar, A. L.; and Brucer, M. "Accidental radiation excursion in the Oak Ridge Y-12 plant: Part IV. Preliminary report on clinical and laboratory effects in the irradiated employees." Health Physics 2:134-38 (1959).

Bigelow, R. R. "The treatment of thyroid carcinoma." Journal of the Tennessee State Medical Association 52:78-79 (1959).

Black, R. Neck scanning with iodine-131. Oak Ridge, Tennessee: ORINS, 1959. (ORINS-28.)

Brucer, M. "The acute radiation syndrome." In The Acute Radiation Syndrome: A Medical Report on the Y-12 Accident, June 16, 1958, pp. 13.1-13.13. Washington, D.C.: U.S. Atomic Energy Commission, 1959. (ORINS-25.)

-----. "An exhibition of the installation of Co^{60} teletherapy machines." In Roentgens, Rads, and Riddles, pp. 132-39. Washington, D.C.: U.S. Atomic Energy Commission, 1959.

-----. The medical schools in nuclear medicine. Paper presented to the Association of American Medical Schools and colleges, Chicago, Illinois, November 3, 1959.

1113777

-----. "Radioisotope hazards and protection in a hospital." In Protection in Diagnostic Radiology; E. P. Sonnenblick, ed.; pp. 204-12. New Jersey: Rutgers University Press, 1959.

-----. "A survey of brachytherapy." In Roentgens, Rads, and Riddles, pp. 449-56. Washington, D.C.: U.S. Atomic Energy Commission, 1959.

-----. Thyroid radioiodine uptake measurement: A standard system for universal Intercalibration. Washington, D.C.: U.S. Atomic Energy Commission, 1959. (ORINS-19.)

-----. "World production estimates." In Roentgens, Rads, and Riddles, pp. 155-61. Washington, D.C.: U.S. Atomic Energy Commission, 1959.

Brucer, M., and Simon, N. "Teletherapy: progress since 1955." In Progress in Nuclear Energy; J. C. Bugher, J. Coursaget, and J. F. Loutit, eds.; Medical Science Series VII, vol. 2, pp. 290-315. London: Pergamon Press, 1959.

Brucer, M., and Umegaki, Y. Radiation measurements and the spectrum. Washington, D.C.: U.S. Atomic Energy Commission, 1959. (ORINS-32.)

Brucer, M., comp. The acute radiation syndrome: A medical report on the Y-12 accident, June 16, 1958. Washington, D.C.: U.S. Atomic Energy Commission, 1959. (ORINS-25.)

Comas, F., and Brucer, M. "First impressions of therapy with cesium-137." Yearbook of Radiology, pp. 420-21. Chicago: Year Book Publishers, 1959. (Abstract.)

1113778

Cress, E. A., and Kyker, G. C. Effect of rare earths on oxygen consumption of rat liver slices. Oak Ridge, Tennessee: ORINS, 1959. (ORINS-29.)

Cronkite, E. P.; Fliedner, R. M.; Bond, V. P.; Andrews, G. A.; and Johnson, A. M. "Special hematologic studies on radiation casualities in the Y-12 accident." In The Acute Radiation Syndrome: A Medical Report on the Y-12 Accident, June 16, 1958, pp. 3.1-3.9. Washington, D.C.: U.S. Atomic Energy Commission, 1959. (ORINS-25.)

Darling, D. "The practicality of cesium as a teletherapy source." In Roentgens, Rads, and Riddles, pp. 485-89. Washington, D.C.: U.S. Atomic Energy Commission, 1959.

Fliedner, T. M; Cronkite, E. P.; Bond, V. P.; Rubini, J. R.; and Andrews, G. "The mitotic index of human bone marrow in healthy individuals and irradiated human beings." Acta Haematologica 22:65-78 (1959).

Friedman, M.; Brucer, M.; and Anderson, E.; ed. Roentgens, rads, and riddles. Washington, D.C.: U.S. Atomic Energy Commission, 1959.

Glaser, W.; Gibbs, W. D.; and Andrews, G. A. "The mechanism of removal of rose bengal from the plasma of the rat determined by autoradiography and radioassay." Journal of Laboratory and Clinical Medicine 54:556-61 (1959).

Harris, C. C.; Hamblen, D. P.; and Francis, J. E. Basic principles of scintillation counting for medical investigators. Washington, D.C.: U.S. Atomic Energy Commission, 1959. (ORNL-2802/ORINS-30.)

1113779

Hayes, R. L. "Chemical measurements of integral dose." In Roentgens, Rads, and Riddles, pp. 61-68. Washington, D.C.: U.S. Atomic Energy Commission, 1959.

Kniseley, R. M. "Important non-biological contributions to radioisotopic diagnosis." Journal of the Iowa State Medical Society 49:619-24 (1959).

-----. "Panel on radioisotopes." Journal of the Iowa State Medical Society 49:741 (1959).

Kretchmar, A. L. "An alteration in the excretion of free serine in urine from irradiated humans." Nature (London) 183:1809-10 (1959).

Kyker, G. C. "Serum protein studies." In The Acute Radiation Syndrome: A Medical Report on the Y-12 Accident, June 16, 1958, pp. 7.1-7.2. Washington, D.C.: U.S. Atomic Energy Commission, 1959. (ORINS-25.)

Medical Division, Oak Ridge Institute of Nuclear Studies. Midyear report for the period ending December 31, 1958. Oak Ridge, Tennessee: ORINS, 1959. (ORINS-27.)

Morris, A. C., Jr. A physician's introduction to electronics. Oak Ridge, Tennessee: ORINS, 1959. (ORINS-31.)

Papavasiliou, C. G. "Calcification in secondary tumors of the spleen." Acta Radiologica 51:278-82 (1959).

Papavasiliou, C. G., and Speas, C. J. "Fracture of the hyoid bone." Radiology 72:272-74 (1959).

1113780

Ross, D. A. "Linear scans." In The Acute Radiation Syndrome: A Medical Report on the Y-12 Accident, June 16, 1958, pp. 9.1-9.3. Washington, D.C.: U.S. Atomic Energy Commission, 1959. (ORINS-25.)

-----. The medical spectrometer. Oak Ridge, Tennessee: ORINS, 1959. (ORINS-30.)

Sitterson, B. W. "Clinical report." In The Acute Radiation Syndrome: A Medical Report on the Y-12 Accident, June 16, 1958, pp. 1.1-1.32. Washington, D.C.: U.S. Atomic Energy Commission, 1959. (ORINS-25.)

Snyder, F.; Cress, E. A.; and Kyker, G. C. "Liver lipid response to intravenous injection of rare earths in rats." Journal of Lipid Research 1:125-31 (1959).

Snyder, F.; Cress, E. A.; Stephens, N.; and Kyker, G. C. "Characterization of liver lipid response to intravenous rare earths in rats." Federation of American Societies for Experimental Biology. Federation Proceedings 18:327 (1959). (Abstract.)

Snyder, F., and Stephens, N. "A simplified spectrophotometric determination of ester groups in lipids." Biochimica et Biophysica Acta 34:244-45 (1959).

Steffee, C. H. "Histopathologic effects of rare earths administered intraperitoneally to rats--a preliminary report." Archives of Industrial Health 10:414-19 (1959.)

1113781

MEDICAL 1960

Andrews, G. A. "Medical students and radioisotopes." New Physician 9(12):23-27 (1960).

-----. "Radiation accidents." In Fallout; J. M. Fowler, ed.; pp. 106-14. New York: Basic Books, 1960.

-----. "Some general concepts of the clinical use of radioisotopes." In Medical Physics; Otto Glasser, ed.; vol. 3, pp. 302-6. Chicago: Year Book Publishers, 1960.

Brucer, M. "External gamma-ray measurements with sodium-iodide crystals." In Medical Physics; Otto Glasser, ed.; vol. 3, pp. 484-88. Chicago: Year Book Publishers, 1960.

-----. "High-energy sources for teletherapy." In Medical Physics; Otto Glasser, ed.; vol. 3, pp. 320-22. Chicago: Year Book Publishers, 1960.

-----. "Intercalibration technics for thyroid uptake." In Medical Physics; Otto Glasser, ed.; vol. 3, pp. 322-28. Chicago: Year Book Publishers, 1960.

-----. The ORINS human radiation counters: A preliminary report. Washington, D.C.: U.S. Atomic Energy Commission, 1960. (ORINS-38.)

-----. "The search for the hole." In A Symposium on Scintillation Counting, pp. 1-24. Bethesda, Maryland: National Naval Medical Center, 1960.

1113782

-----. Thyroid Radioiodine Uptake Measurement: A Standard System for Universal Intercalibration. Translated into Japanese by Hirotake Kakehi and Teruo Nagai. Tokyo: Bunkodo Company, 1960.

Brucer, M., and Cloutier, R. J. "Radiation warning signs for medical installations." International Journal of Applied Radiation 8:143-45 (1960).

Brucer, M., and Anderson, E. B., eds. Radiation protection at the medical division. Oak Ridge, Tennessee: ORINS, 1960.

Comas, F., and Brucer, M. "Irradiation of the ovaries from the urinary excretion of iodine 131." American Journal of Roentgenology 83:501-6 (1960).

Fliedner, T. M.; Cronkite, E. P.; Bond, V. P.; and Andrews, G. A. "Mitotic activity and cytology of human bone marrow after accidental exposure to ionizing radiation." In Proceedings of the 7th Congress of the European Society of Haematologists, part II, pp. 458-67. 1960.

Hayes, R. L. Standard-man phantoms. Washington, D.C.: U.S. Atomic Energy Commission, 1960. (ORINS-35.)

Hayes, R. L., and Brucer, M. "Compartmentalized phantoms for the standard man, adolescent, and child." International Journal of Applied Radiation 9:113-18 (1960).

Hayes, R. L., and Butler, W. R., Jr. "Growth and decay of radionuclides: a demonstration." Journal of Chemical Education 37-590-92 (1960).

1113783

Hayes, R. L; Nold, M. M; Comar, C. L.; and Kakehi, H. "Internal radiation dose measurements in live experimental animals. Part I." Health Physics 4:79-85 (1960).

Kniseley, R. M. "Training for clinical use of radioisotopes: qualification courses." Journal of Nuclear Medicine 1:239-50 (1960).

Kretchmar, A. L. "Quantitative urinary amino acid excretion of normal men on controlled diets." Clinical Research 8:84 (1960). (Abstract.)

Medical Division, Oak Ridge Institute of Nuclear Studies. Report for 1959. Oak Ridge, Tennessee: ORINS, 1960. (ORINS-34.)

Morris, A. C., Jr. "A linear scanner for human radioisotope research." Radioisotopes 9:216-24 (1960). Washington, D.C.: U.S. Atomic Energy Commission, 1960. (ORINS-33.)

Nold, M. M.; Hayes, R. L.; and Comar, C. L. "Internal radiation dose measurements in live experimental animals. Part II." Health Physics 4:86-100 (1960).

Pircher, F.; Andrews, G. A.; Brucer, M; and Ross, D. A. The linear scanner in clinical studies. Washington, D.C.: U.S. Atomic Energy Commission 1960. (ORINS-36.)

Pircher, F.; Sitterson, B. W.; and Andrews, G. A. "The ORINS linear scanner in diagnosis and treatment of thyroid carcinoma with iodine 131." Journal of Nuclear Medicine 1:251-61 (1960).

Ross, D. A. "Medical spectrometer." In Medical Physics; Otto Glasser, ed.; vol. 3, pp. 341-45. Chicago: Year Book Publishers, 1960.

1113784

Simon, N.; Brucer, M.; and Hayes, R. L. "Radiation and leukemia in carcinoma of the cervix." Radiology 74:905-11 (1960).

Snyder, F.; Baker, F.; Rafter, J.; and Kyker, G. C. "Octanoate oxidation in the cerium-induced fatty liver." Biochimica et Biophysica Acta 43:554-55 (1960).

Snyder, F.; Cress, E. A.; and Kyker, G. C. "Rare-earth fatty liver." Nature (London) 185:480-81 (1960).

Snyder, F.; Stephens, N.; Gerst, L.; and Kyker, G. C. "The rare-earth fatty liver: plasma free fatty acids." Federation of American Societies for Experimental Biology. Federation Proceedings 19:299 (1960). (Abstract.)

Tsuya, A., and Hayakawa, I. "Linear scanner (ORINS): possibility of its clinical applications." Acta Radiologica Japonica 20:2001-11 (1960).

1113785

MEDICAL 1961

Andrews, G. A.; Sitterson, B. W.; Kretchmar, A. L.; and Brucer, M. "Criticality accident at the Y-12 plant." In Diagnosis and Treatment of Acute Radiation Injury, pp. 27-48. Geneva: World Health Organization, 1961.

Andrews, G. A.; Sitterson, B. W.; Kretchmar, A. L.; and Tanida, R. "Studies of total-body irradiation and attempted marrow transplantation in acute leukemia." Acta Haemat (Basel) 26:129-53 (1961).

Bond, V. P.; Fliedner, T. M.; Cronkite, R. P.; and Andrews, G. A. "Deoxyribonucleic acid synthesizing cells in the blood of man and dog exposed to total body radiation." Journal of Laboratory and Clinical Medicine 57:711-17 (1961).

Brucer, M. "The development of radioisotope scanning." In Applications of Radioisotopes and Radiation in the Life Sciences, pp. 402-26. Washington, D.C.: U.S. Government Printing Office, 1961.

-----. "The film badge and the cricket: an exercise in political medicine." Journal Mississippi State Medical Association, September 1961, pp. 453-56.

-----. "Human radiation exposure." In Radioactivity in Man; G. R. Meneely, ed.; pp. 373-91. Springfield, Illinois: Charles C. Thomas, 1961.

-----. "Levels of radiation." Journal of the American Medical Association 175:36-39 (1961).

1113786

-----. "Radiation hysteria." Journal of the American Medical Association 176:680 (1961). (Editorial.)

-----. "Radioisotopes in medicine." In Science and the New Nations; Ruth Gruber, ed.; pp. 113-17. New York: Basic Books, 1961.

-----. "A total-body irradiator." International Journal of applied Radiation 10:99-105 (1961).

Cloutier, R. J., and Brucer, M. "Leaks in standard sealed teletherapy sources." Health Physics 6:32-35 (1961).

Comas, F. "Exploratory laparotomies to minimize 'geographical misses' in radiotherapy." American Surgeon 27:513-17 (1961).

Henry, H. F. "Is all nuclear radiation harmful?" Journal of the American Medical Association 176:671-75 (1961).

Johnson, G. T., and Kyker, G. C. "Fission-product and cerium uptake by bacteria, yeasts, and molds." Journal of Bacteriology 81:733-40 (1961).

Kretchmar, A. L., and Congdon, C. C. "Amino acid changes in mice with grafted homologous bone marrow." Federation of American Societies for Experimental Biology. Federation Proceedings 20:402b (1961). (Abstract.)

-----. "Biochemical changes and increased liver weight in bone barrow chimeras." American Journal of Physiology 200:102-6 (1961).

Medical Division, Oak Ridge Institute of Nuclear Studies. A high magnetic field bubble chamber report. Oak Ridge, Tennessee: ORINS, 1961.

1113787

-----. Report for 1960. Oak Ridge, Tennessee: ORINS, 1961. (ORINS-39.)

Morris, A. C., Jr. "Measurements in a total-body irradiation facility." International Journal of Applied Radiation 11:108-13 (1961).

Snyder, F., and Cress, E. "Choline oxidase in fatty livers induced by cerium." Experientia 17:303-5 (1961).

Snyder, F., and Godfrey, P. "Collecting $C^{14}O_2$ in a Warburg Flask for subsequent scintillation counting." Journal of Lipid Research 2:195 (1961).

Snyder, F., and Stephens, N. "Plasma free fatty acids and the rare-earth fatty liver." Proceedings of the Society for Experimental Biology and Medicine 106:202-4 (1961).

Snyder, F.; Stephens, N.; and Kyker, G. C. "Fatty acids of liver and adipose lipids during cerium-induced fatty liver infiltration." Federation of American Societies for Experimental Biology. Federation Proceedings 20:275f (1961). (Abstract.)

1113788

MEDICAL 1962

Andrews, G. A. "The acute radiation syndrome." Nuclear Safety 3:69-76 (1962).

-----. "Criticality accidents in Vinca, Yugoslavia, and Oak Ridge, Tennessee: Comparison of radiation injuries and results of therapy." Journal of the American Medical Association 179:191-97 (1962).

-----. "High dose irradiation injury." Journal of the American Medical Association 179:220 (1962). (Editorial).

Brucer, M. "The great fallout controversy." Journal of the American Medical Association 179:164-65 (1962). (Editorial.)

-----. "Medical high-energy radiation." Radiazioni di Alta Energia 1:5-13 (1962).

-----. "When do you leave a fallout shelter?" Journal of the American Medical Association 180:144-46 (1962).

Gengozian, N. "Radiation immunology: effects of hematopoietic tissue transplantation." In Ionizing Radiations and Immune Processes; Charles A. Leone, ed,; pp. 403-54. New York: Gordon and Breach, 1962.

Gengozian, N.; Batson, J. S.; and Smith, T. A. "Tamarinus nigricollis as a laboratory primate." In Bone Marrow Therapy and Protection in Irradiated Primates, pp. 245-69. The Netherlands: Krips, Rijswijk, 1962.

1113789

Glaser, W., and Gibbs, W. D. "Localization of radiomagnesium in puppies: radioautographic study of heart and bone." American Journal of Physiology 202:585-88 (1962).

Godfrey, P., and Snyder, F. "A procedure for in vivo $C^{14}O_2$ collection and subsequent scintillation counting." Analytical Biochemistry 4:310-15 (1962).

Kniseley, R. M.; White, D. A.; Sitterson, B. W.; and Andrews, G. A. "Effects of total-body irradiation on platelet values in human beings." In Symposium on Recent Developments in Studies of Blood Platelets, June 22-23. Oak Ridge, Tennessee: Oak Ridge National Laboratories, Biology Division, 1962. (Abstract.)

Kretchmar, A. L., and Congdon, C. C. "Increased free aspartic acid in liver of mice with grafted homologous bone marrow." Federation of American Societies for Experimental Biology. Federation Proceedings 21:424a (1962). (Abstract.)

Kyker, G. C. "Rare earths." In Mineral Metabolism, vol. 2B, pp. 499-541. New York: Academic Press, 1962.

Medical Division, Oak Ridge Institute of Nuclear Studies. Research report, 1961, for the year ending December 31, 1961. Oak Ridge, Tennessee: ORINS, 1962. (ORINS-41.)

Nagai, T., and Kniseley, R. M. "The fate of H^3 thymidine labelled cells injected as a potential human-marrow graft: a preliminary report." In Proceedings of the VIIIth International Congress of Hematology, Tokyo, September 4-10, 1960, vol. 1, pp. 275-80. Tokyo: Pan Pacific Press, 1962.

1113790

Odell, T. T., Jr., and Kniseley, R. M. "The origin, life span, regulation and fate of blood platelets." In Progress in Hematology, vol. 3, pp. 203-17. New York: Grune and Stratton, 1962.

Pircher, F.; Brucer, M.; Morris, A. C., Jr.; and Black, R. "The ORINS linear scanner in clinical diagnosis." Journal of Nuclear Medicine 3:26-40 (1962).

Snyder, F.; Cress, E. A.; and Stephens, N. "Bone marrow lipids after total-body irradiation." Federation of American Societies for Experimental Biology. Federation Proceedings 21:424f (1962). (Abstract.)

Snyder, F., and Stephens, N. "Quantitative carbon-14 and tritium assay of thin-layer chromatography plates." Analytical Biochemistry 4:128-31 (1962).

1113791

MEDICAL 1963

Andrews, G. A.; Sitterson, B. W.; and Ross, D. A. "The use of scanning in thyroid cancer." In Progress in Medical Radioisotope Scanning, pp. 312-325. Atomic Energy Commission Symposium Series no. 1. Washington, D.C.: Atomic Energy Commission, 1963.

Arnold, Patricia "Total-body irradiation and marrow transplantation." American Journal of Nursing 63:83-88 (1963).

Brown, D. W., and Kretchmar, A. L. "Analog computer simulation of radioiodine tracer studies in thyroid disease." Journal of Nuclear Medicine 4:197 (1963). (Abstract.)

Cloutier, R. J. "Fast neutron generators: radiation levels and shielding requirements." American Industrial Hygiene Association Journal 24:497-501 (1963).

-----. "Radiation safety." Science Teacher 30:35-39 (1963).

Congdon, C. C., and Kretchmar, A. L. "Increased liver weight in bone-marrow chimeras." Journal of Molecular Pathology 2:277-90 (1963).

Cosgrove, G. E.; Nelson, W. M.; and Jones, A. W. "Spirura tamarini sp. n. (Nematoda: Spiruridae) from an Amazonian primate, Tamarinus nigricollis (Spix, 1823)." Journal of Parasitology 49:1010-13 (1963).

1113792

Edwards, C. L.; Andrews, G. A.; Sitterson, B. W.; and Kniseley, R. M. "Clinical radioisotope bone marrow scanning." Clinical Research 11(2): 193 (1963). (Abstract.)

Gengozian, N., and Batson, J. "Effects of radiation on a small South American primate, Tamarinus nigricollis." Radiation Research 19:223-24 (1963). (Abstract.)

Goswitz, F. A.; Andrews, G. A.; and Kniseley, R. M. "Effects of local irradiation (Co^{60} teletherapy) on the peripheral blood and marrow." Blood 21:605-19 (1963).

Hayes, R. L. "A method for collection and radioassay of specimens of human stools." American Journal of Clinical Pathology 39:203-5 (1963).

Hayes, R. L.; Carlton, J. E.; and Butler, W. R., Jr. "Radiation dose to the human intestinal tract from internal emitters." Health Physics 9:915-20 (1963).

Hayes, R. L.; Nelson, W. M.; and Carlton, J. E. "Lanthanum-140 as a measure of the completeness of stool collections for the oral iron-59 absorption test." Journal of Nuclear Medicine 4:208 (1963). (Abstract.)

Honda, T.; Rafter, J. J.; and Kyker, G. C. "Intralymphatic administration of radioisotope to lymph nodes." Journal of Nuclear Medicine 4:188 (1963). (Abstract.)

Kniseley, R. M.; Andrews, G. A.; and Harris, C. C.; eds. Progress in Medical Radioisotope Scanning. Atomic Energy Commission Symposium Series no. 1. Washington, D.C.: Atomic Energy Commission, 1963.

1113793

Kretchmar, A. L.; Andrews, G. A.; and Sitterson, B. W. "Attempted bone marrow autografts after large doses of nitrogen mustard." New England Journal of Medicine 268:427-28 (1963).

Kretchmar, A. L., and Congdon, C. C. "The levels of free aspartic acid, glycine, and serine in tissues of bone marrow chimeras." Transplantation 1: 298-305 (1963).

-----. "RNA and DNA in liver of irradiation chimeras." Blood 22:503 (1963). (Abstract.)

-----. "Serine metabolism in mice carrying homologous bone-marrow grafts." Federation of American Societies for Experimental Biology. Federation Proceedings 22:392 (1963). (Abstract.)

McArthur, W. H.; Kretchmar, A. L.; and Congdon, C. C. "Study of nitrogen balance in irradiated mice given foreign bone marrow." Blood 22:502-3 (1963). (Abstract.)

Medical Division, Oak Ridge Institute of Nuclear Studies. Research report, 1962, for the year ending December 31, 1962. Oak Ridge, Tennessee: ORINS, 1963. (ORINS-42.)

Oda, F. T.; Andrews, G. A.; Bigelow, R. R.; Sitterson, B. W.; and Buxton, R. W. "Surgery in patients with leukemia and lymphoma." American Surgeon 29:33-47 (1963).

Oda, F. T.; Gibbs, W. D.; and Andrews, G. A. "Distribution of radioisotopes in tumors of the rat liver." Journal of Nuclear Medicine 4:18-28 (1963).

1113794

Ross, D. A. "Linear scanning." In Progress in Medical Radioisotope Scanning, pp. 190-204. Atomic Energy Commission Symposium Series no. 1. Washington, D.C.: Atomic Energy Commission, 1963.

Sitterson, B. W., and Andrews, G. A. "Introduction to thyroid scanning." In Progress in Medical Radioisotope Scanning, pp. 279-95. Atomic Energy Commission Symposium Series no. 1. Washington, D.C.: Atomic Energy Commission, 1963.

Snyder, F. "Aluminum plates for thin-layer chromatography." Analytical Chemistry 35:599 (1963).

Snyder, F., and Cress, E. A. "Bone marrow lipids in rats exposed to total-body irradiation." Radiation Research 19:129-41 (1963).

Suu, Vu-Thi; Congdon, C. C.; and Kretchmar, A. L. "Increases in lysozyme activity in the kidney of irradiated chimeras." Proceedings of the Society for Experimental Biology and Medicine 113:481-85 (1963).

Vodopick, H. A., and Kniseley, R. M. "Sulfur-35 studies in man: platelet survival and urinary radioactivity assayed by beta liquid scintillation spectrometry." Journal of Laboratory and Clinical Medicine 62:109-20 (1963).

White, D. A. "Useful chemotherapeutic agents." Journal of the Tennessee State Medical Association 56:42-45 (1963).

1113795

MEDICAL 1964

Andrews, G. A. "Book review: Silver, Solomon. Radioactive Isotopes in Medicine and Biology: Medicine." Archives of Internal Medicine 113:310-11 (1964).

-----. "Discussion of E. P. Cronkite's The Diagnosis, Treatment, and Prognosis of Human Radiation Injury from Whole-body Exposure." Annals of the New York Academy of Sciences 144:349-54 (1964).

-----. "Mexican Co^{60} radiation accident." Isotopes and Radiation Technology 1:200-201 (1964).

Burger, C. L.; Harris, W. W.; Anderson, N. G.; Bartlett, T. W.; and Kniseley, R. M. "Virus-like particles in human leukemic plasma." Proceedings of the Society for Experimental Biology and Medicine 115:151-56 (1964).

Comas, F. V. "Comparative changes in radiosensitivity between bone marrow and a rat tumor irradiated under anoxia." Radiology 83:528-33 (1964).

Edwards, C. L.; Andrews, G. A.; Sitterson, B. W.; and Kniseley, R. M. "Clinical bone marrow scanning with radioisotopes." Blood 23:741-56 (1964).

Fliedner, T. M.; Andrews, G. A.; Cronkite, E. P.; and Bond, V. P. "Early and late cytologic effects of whole body irradiation on human marrow." Blood 23:471-87 (1964).

Gengozian, N. "Heterotransplantation of human antibody-forming cells in diffusion chambers." Annals of the New York Academy of Sciences 120:91-118 (1964).

1113796

-----. "Human A- and B-like antigens on red cells of marmosets." Proceedings of the Society for Experimental Biology and Medicine 117:858-61 (1964).

-----. "Transplantation of rat bone marrow in irradiated mice: effect of exposure rate." Science 146:663-64 (1964).

Gengozian, N.; Batson, J. S.; and Eide, P. "Hematologic and cytogenetic evidence for hematopoietic chimerism in the marmoset, Tamarinus nigricollis." Cytogenetics 3:384-93 (1964).

Gengozian, N., and Doria, G. "Allotypic specificities in four strains of inbred mice as revealed by reciprocal immunizations." Journal of Immunology 93:426-32 (1964).

Gibbs, W. D., and Lushbaugh, C. C. "A new counter for radioactive samples." Journal of Nuclear Medicine 5:726 (1964). (Abstract.)

Gibbs, W.; Wilson, E.; Hodges, H.; and Lushbaugh C. C. "Comparative study of thyroid and whole-body retention of iodine in box turtles." In U.S. Atomic Energy Commission Report TID-7689, pp. 20-21. Washington, D.C.: U.S. Atomic Energy Commission, 1964. (Abstract.)

Hayes, R. L., and Carlton, J. E. "In vivo mobilization of barium-137m." Journal of Nuclear Medicine 5:378 (1964). (Abstract.)

Hayes, R. L.; Carlton, J. E.; and Nelson, W. M. "Lanthanum-140 as a measure of the completeness of stool collections: demonstration of delayed excretion of iron-59." Journal of Nuclear Medicine 5:200-208 (1964).

1113797

Hayes, R. L.; Oddie, T. H.; and Brucer, M. "Dose comparison of two total-body irradiation facilities." International Journal of Applied Radiation 15:313-18 (1964).

Kakehi, H., and Hayes, R. L. "Counting characteristics of a medium-level whole-body counter." Journal of Nuclear Medicine 5:372 (1964).

Kniseley, R. M. "Radioisotope scanning." Science 145:416-18 (1964).

Kniseley, R. M.; Andrews, G. A.; Edwards, C. L.; and Tanida, R. "Scanning of bone marrow in hematopoietic disorders." In Medical Radioisotope Scanning, vol. 2, pp. 207-25. Vienna: International Atomic Energy Agency, 1964.

Kniseley, R. M., and Tauxe, W. N., eds. Dynamic Clinical Studies with Radioisotopes. Atomic Energy Commission Symposium Series no. 3. Washington, D.C.: Atomic Energy Commission, 1964.

Kretchmar, A. L., and Comas, F. V. "Correlation between kidney muramidase activity and plasma iron removal in rats with Walker-256 carcinosarcoma." Proceedings of the Society for Experimental Biology and Medicine 116:275-77 (1964).

Kyker, G. C., and Rafter, J. "Rare earth fatty liver induced by lanthanum chelates." Federation of American Societies for Experimental Biology. Federation Proceedings 23:375 (1964). (Abstract.)

-----. "Scanning of bone marrow in animals." Journal of Nuclear Medicine 5:726-27 (1964). (Abstract.)

1113798

Lushbaugh, C. C., and Gibbs, W. "A rapid screening method for detecting abnormal plasma vitamin B_{12} bonding sites in chronic myelogenous leukemia using arm counting." In U.S. Atomic Energy Commission Report TID-7689, pp. 11-14. Washington, D.C.: U.S. Atomic Energy Commission, 1964. (Abstract.)

Lushbaugh, C. C.; Kretchmar, A.; and Gibbs, W. "Liver function measured by the blood clearance of rose bengal-I^{131}: A review and a model based on compartmental analysis of changes in arm, blood, and liver radioactivity." In Dynamic Clinical Studies with Radioisotopes, pp. 319-57. Atomic Energy Commission Symposium Series no. 3. Washington, D.C.: Atomic Energy Commission, 1964.

McArthur, W. H.; Congdon, C. C.; and Kretchmar, A. L. "Nitrogen balance in radiation chimeras." Proceedings of the Society for Experimental Biology and Medicine 117:171-75 (1964).

MacLeod, J.; Hotchkiss, R. S.; and Sitterson, B. W. "Recovery of male fertility after sterilization by nuclear radiation." Journal of the American Medical Association 187:637-41 (1964).

Medical Division, Oak Ridge Institute of Nuclear Studies. Research Report, 1963, for the year ending December 31, 1963. Oak Ridge, Tennessee: ORINS, 1964. (ORINS-43.)

Morris, A. C., Jr. "A diagnostic-level whole-body counter." Journal of Nuclear Medicine 5:364 (1964). (Abstract.)

Morris, A. C., Jr.; Ross, D. A.; and Travis, J. C. "A high-level whole-body counter." International Journal of Applied Radiation 15:391-96 (1964).

1113799

Nelson, W. M., and Andrews, G. A. "Breast cancer and cytologic dysplasia in many organs after busulfan (myleran)." American Journal of Clinical Pathology 42:37-44 (1964).

Nelson, W. M.; Vichai Poshyachinda; and Makumkrong Wasanasomsithi. "A method for comparing collimator systems applied to external counting of Cr^{51} in the spleen." Journal of Nuclear Medicine 5:725-26 (1964). (Abstract.)

Pfannenstiel, P., and Sitterson, B. W. "Clinical usefulness of iodine-130 in serial tracer-studies in patients with functioning thyroid cancer." Journal of Nuclear Medicine 5:727 (1964). (Abstract.)

Saito, H., and Nagai, T. Labeling of myeloma cells and leukemic leukocytes in short-term cultures with tagged precursors of nucleic acid and protein. Washington, D.C.: U.S. Atomic Energy Commission, 1964. (ORINS-45.)

Snyder, F. "Radioassay of thin-layer chromatograms: a high-resolution zonal scraper for quantitative C^{14} and H^3 scanning of thin-layer chromatograms." Analytical Biochemistry 9:183-96 (1964).

-----. "Zonal scanning of thin-layer chromatograms." Atomlight 38:7-12 (1964).

Snyder, F.; Alford, T. S.; and Kimble, H. Radioassay of thin-layer chromatograms: blueprints for zonal scraper. Washington, D.C.: U.S. Atomic Energy Commission, 1964. (ORINS-44.)

1113800

Snyder, F., and Kimble, H. Blueprints of an automatic zonal scraper and sample collector for radioassay of thin-layer chromatograms. Washington, D.C.: U.S. Atomic Energy Commission, 1964. (ORINS-47.)

Snyder, F., and Kyker, G. C. "Triglyceride accumulation and release in the rare-earth fatty liver." Proceedings of the Society for Experimental Biology and Medicine 116:890-93 (1964).

Snyder, F., and Lewis, W. "Phospholipid patterns in livers accumulating fat." Proceedings of the Society for Experimental Biology and Medicine 116:459-62 (1964).

Suu, Vu-Thi; Congdon, C. C.; and Kretchmar, A. L. "Lysozyme activity in radiation chimeras." Proceedings of the Society for Experimental Biology and Medicine 115:825-29 (1964).

Urso, P., and Gengozian, N. "Immunofluorescent detection of proliferating human antibody-forming cells." Nature 203:1391-92 (1964).

Wilson, E. D.; Gibbs, W. D.; and Lushbaugh, C. C. "Thyroid uptake and whole-body retention of I^{131} in box turtles." Texas Reports of Biology and Medicine 22:211-12 (1964).

1113801

MEDICAL 1965

Andrews, G. A. "Radiation accidents." Journal of the American Medical Association 191:151-52 (1965). (Editorial).

Andrews, G. A.; Auxier, J. A.; and Lushbaugh, C. C. "The importance of dosimetry to the medical management of persons accidentally exposed to high levels of ionizing radiation." In Personnel Dosimetry for Radiation Accidents, pp. 3-16. Vienna: International Atomic Energy Agency, 1965.

Andrews, G. A., and Cloutier, R. J. "Accidental acute radiation injury: the need for recognition." Archives of Environmental Health 10:498-507 (1965).

Bergner, P.-E. E. "Exchangeable mass: determination without assumption of isotopic equilibrium." Science 150:1048-50 (1965).

-----. "On stationary and non-stationary red cell survival curves." Journal of Theoretical Biology 9:366-88 (1965).

-----. "Stochastic concepts in clinical red cell survival studies." Nature (London) 205:975-77 (1965).

Bergner, P.-E. E., and Lawson, J. D. "Red cell survival: on the analysis of DF^{32} P-data." Clinical Research 13:66 (1965). (Abstract.)

Edwards, C. L., and Gengozian, N. "Autoimmune hemolytic anemia treated with d-penicillamine." Annals of Internal Medicine 62:576-79 (1965).

1113802

Gengozian, N.; Edwards, L.; and Hübner, K. "Clinical and experimental studies on the effect of penicillamine on antibody formation." Clinical Research 13:68 (1965). (Abstract.)

Gengozian, N.; Rabette, B.; and Congdon, C. C. "Abnormal immune mechanism in allogeneic radiation chimeras." Science 149:645-47 (1965).

Gibbs, W. D.; Lushbaugh, C. C.; and Morris, A. C., Jr. "Preliminary efficiency and calibration studies with a new whole-body counter with an ultralow background shield." Journal of Nuclear Medicine 6:337 (1965). (Abstract.)

Goh, K. O. "Book review: Human Chromosome Methodology." Annals of Internal Medicine 63:925-26 (1965).

-----. "Cytogenetic interrelation of the myeloproliferative disorders." Clinical Research 13:273 (1965). (Abstract.)

Harris, C. C.; Satterfield, M. M.; Kimble, H. E.; and Uchiyama, G. "A 'rescanner' with photographic readout." Journal of Nuclear Medicine 6:332 (1965). (Abstract.)

Hayes, R. L.; Carlton, J. E.; and Byrd, B. L. "Bone scanning with gallium-68: a carrier effect." Journal of Nuclear Medicine 6:605-10 (1965).

-----. "^{68}Gallium as a bone scanning agent." Journal of Nuclear Medicine 6:358 (1965). (Abstract.)

Hübner, K., and Brown, D. W. "Scanning of the spinal subarachnoid space after intrathecal injection of ^{131}I labeled human serum albumin." Journal of Nuclear Medicine 6:465-72 (1965).

1113803

Hubner, K., and Gengozian, N. "Depression of the primary immune response by dl-penicillamine." Proceedings of the Society for Experimental Biology and Medicine 118:561-65 (1965).

Kniseley, R. M.; Andrews, G. A.; Tanida, R.; Edwards, C. L.; and Kyker, G. C. "Whole-body scanning of the bone marrow organ." Journal of Nuclear Medicine 6:361 (1965). (Abstract.)

Kretchmar, A. L. "Stability and response characteristics of the red blood cell system: a computer study." Clinical Research 13:67 (1965). (Abstract.)

Kretchmar, A. L., and Congdon, C. C. "The metabolic problem in secondary disease." In La Greffe des Cellules Hematopoietiques, pp. 347-52. Paris: Centre National de la Recherche Scientifique, 1965.

Kretchmar, A. L.; McArthur, W. H.; and Congdon, C. C. "Shift in the relative distribution of body nitrogen between skin and carcass in mouse radiation chimeras." Journal of Nutrition 87:261-66 (1965).

Kyker, G. C., and Rafter, J. J. "Scanning of bone marrow in animals." Journal of Nuclear Medicine 6:361 (1965). (Abstract.)

Lushbaugh, C. C.; Hofstra, R.; Roth, R. E.; and Andrews, G. A. "ED_{50} for gastrointestinal responses in man." Radiation Research 25:213-14 (1965). (Abstract.)

Lushbaugh, C. C., and Lushbaugh, D. B. "Rapid electronic cell sizing as an aid in clinical diagnosis." Southern Medical Journal 58:1208-12 (1965).

1113804

Medical Division, Oak Ridge Institute of Nuclear Studies. Research report, 1964, for the year ending December 31, 1964. Oak Ridge, Tennessee: ORINS, 1965. (ORINS-49.)

Meyer, L. M.; Schiffer, L. M.; White, D. A.; and Cronkite, E. P. "The plasma disappearance of radioactive cobalamin: effect of prior administration of vitamin B_{12} analogues." British Journal of Haematology 11:370-79 (1965).

Miller, B.; Anderson, C. E.; Kyker, G. C.; Yarbro, C. L.; and Cress, E. A. "Plasmalogen in rare earth-induced fatty infiltration in rat liver." Journal of the Elisha Mitchell Scientific Society 81(1):12-18 (1965).

Miller, I. H., Jr., and Kyker, G. C. "Nutritional protection against fatty liver due to cerium." Federation of American Societies for Experimental Biology. Federation Proceedings 24:564 (1965). (Abstract.)

Miller, L., and Goh, K. O. "Prevention of in vitro cultured leukocyte clumping." The Human Chromosome Newsletter, December 1965, pp. 17-18. (Abstract.)

Morris, A. C., Jr. "A diagnostic-level whole-body counter." Journal of Nuclear Medicine 6:481-88 (1965).

Nelson, B.; Rush, E. A.; Takasugi, M.; and Wittenberg, J. "Lipid embolism to the brain after lymphography." New England Journal of Medicine 273:1132-34 (1965).

Pfannenstiel, P.; Andrews, G. A.; and Brown, D. W. "Congenital hypothyroidism from intrauterine ^{131}I damage." In Current Topic in Thyroid Research, pp. 749-58. New York: Academic Press, 1965.

1113805

Snyder, F. "Fatty acid oxidation in irradiated bone marrow cells." Nature (London) 206:733 (1965).

-----. "Quantitative radioassay of methods for thin-layer chromatography: zonal and autoradiographic scans." In Radioisotope Sample Measurement Techniques in Medicine and Biology, pp. 521-33. Vienna: International Atomic Energy Agency, 1965.

-----. "Zonal scanning of thin-layer chromatograms." In Advances in Tracer Methodology, vol. 2, pp. 107-13. New York: Plenum Press, 1965.

Snyder, F., and Kimble, H. "An automatic zonal scraper and sample collector for radioassay of thin-layer chromatograms." Analytical Biochemistry 11:510-18 (1965).

Snyder, F.; Piantadosi, C.; and Oswald, E. "The deposition and metabolism of α-batyl alchohol-1-^{14}C in the rat." Journal of the American Oil Chemists' Society 42:461A (1965). (Abstract.)

Snyder, F., and Wright, R. "Effect of localized irradiation on the metabolism of bone marrow lipids." Radiation Research 25:417-22 (1965).

Steckel, R. J.; Hendrix, E. L.; and Bigelow, R. R. "Malignant solid teratoma of the ovary in an 8-year-old child." Obstetrics and Gynecology 25:249-52 (1965).

Uchiyama, G.; Harris, C. C.; Kimble, H.; and Morris, A. C., Jr. "Color recording for a rescanning device." Clinical Research 13:82 (1965). (Abstract.)

1113806

Urso, P., and Gengozian, N. "Host-graft agglutinin activity by spleen cells of heterologus radiation chimeras cultivated in diffusion chambers." Transplantation 3:762-64 (1965).

1113807

MEDICAL 1966

Andrews, G. A. "Book review: Progress in Medical Radioisotope Scanning." Health Physics 12:1511 (1966).

-----. "Treatment of radiation injury." Journal of the Mississippi State Medical Association 7:534-38 (1966).

Andrews, G. A.; Kniseley, R. M.; and Wagner, H. N., Jr. Radioactive Pharmaceuticals. Washington, D.C.: U.S. Atomic Energy Commission, 1966.

Bergner, P.-E. E. "Tracer theory: a review." Isotope and Radiation Technology 3:245-62 (1966).

Bollinger, J. N. "Incorporation of dietary lineoleic acid into triglycerides of irradiated bone marrow." Radiation Research 28:121-31 (1966).

Cloutier, R. J., and Dalton, C. P. "Radiation safety problems connected with the medical use of radioisotopes." Health Physics 12:1835 (1966). (Abstract.)

Cloutier, R. J., and Watson, E. E. "Measurement of plutonium in wounds: self-absorption by plutonium." Health Physics 12:1203 (1966). (Abstract.)

Edwards, C. L.; Congdon, C. C.; Gengozian, N.; Vodopick, H.; and Andrews, G. A. "Treatment of acute leukemia: an experimental immunologic approach." Experimental Hematology 9:23-24 (1966). (Abstract.)

1113808

Edwards, C. L.; Hayes, R.; Ahumada, J.; and Kniseley, R. M. "Gallium-68 citrate: a clinically useful skeletal scanning agent." Journal of Nuclear Medicine 7:363-64 (1966). (Abstract.)

Gengozian, N. "Formation of isohaemagglutinins in the marmoset, Tamarinus nigricollis." Nature (London) 209:722-23 (1966).

-----. "Isohemagglutinin formation in the marmoset, T. nigricollis." Federation of American Societies for Experimental Biology. Federation Proceedings 25:435 (1966). (Abstract.)

Gengozian, N., and Batson, J. S. "Effects of whole-body irradiation on a small South American primate, Saguinus fuscicollis." International Journal of Radiation Biology and Related Studies in Physics, Chemistry, and Medicine 11(6):539-51 (1966).

Gengozian, N.; Batson, J. S.; and Nelson, B. M. "Bone marrow grafting attempts in marmosets after whole-body irradiation." International Journal of Radiation Biology and Related Studies in Physics, Chemistry, and Medicine 11(6):553-61 (1966).

Gengozian, N., and Carlson, D. "Consideration of radiation exposure rates in transplantation of xenogeneic and allogeneic bone marrow in irradiated mice." Third International Congress of Radiation Research, p. 90. (1966). (Abstract.)

Gengozian, N.; Lushbaugh, C. C.; Humason, G. L.; and Kniseley, R. M. "'Erythroblastosis foetalis' in the primate, Tamarinus nigricollis." Nature (London) 209:731-32 (1966).

1113809

Goh, K. O. "Inner chromosomal structure of the somatic metaphase of mammals: a light microscopic observation." Clinical Research 14:310 (1966). (Abstract.)

-----. "Smaller G chromosome in irradiated man." Lancet 1:659-60 (1966).

Harris, W. W.; Anderson, N. G.; Bartlett, T. W.; Rutenberg, E. L.; McCauley, L. L.; and Kniseley, R. M. "Unusual particles in human plasma from leukemia and lymphosarcoma." National Cancer Institute Monographs 21:389-94 (1966).

Hayes, R. L. "Radioisotopes of gallium." In Radioactive Pharmaceuticals, pp. 603-18. Washington, D.C.: U.S. Atomic Energy Commission, 1966.

Hayes, R. L.; Carlton, J. E.; and Rafter, J. J. "Scanning with hydrous ferric oxide colloid labeled with gallium-68." Journal of Nuclear Medicine 7:335-36 (1966). (Abstract.)

Hayes, R. L., and Rafter, J. J. "Rhenium-188 as a possible diagnostic agent." Journal of Nuclear Medicine 7:797 (1966). (Abstract.)

Holten, V. Z.; Kyker, G. C.; and Pulliam, M. "Effects of lanthanide chlorides on selected enzymes." Proceedings of the Society for Experimental Biology and Medicine 123:913-19 (1966).

Johnson, G. T., and Kyker, G. C. "The mechanism of cerium uptake by Saccharomyces cerevisiae." Mycologia 58:91-99 (1966).

1113810

Kniseley, R. M. "Book review: Progress in Atomic Medicine." American Journal of Clinical Pathology 45:487 (1966).

Kniseley, R. M.; Andrews, G. A.; Tanida, R.; Edwards, C. L.; and Kyker, G. C. "Delineation of active marrow by whole-body scanning with radioactive colloids." Journal of Nuclear Medicine 7:575-82 (1966).

Kretchmar, A. L. "Erythropoietin: hypothesis of action tested by analog computer." Science 152:367-70 (1966).

-----. "A model of hemopoiesis for mammalian recovery experiments." Experimental Hematology 9:42-44 (1966). (Abstract.)

Kretchmar, A. L., and Conover, W. R. "Secondary mortality and body-weight loss in lethally irradiated mice given small doses of isologous bone marrow cells." Experimental Hematology 10:11-12 (1966). (Abstract.)

Kyker, G. C., and Rafter, J. J. "Colloidal properties of the lanthanides." In Radioactive Pharmaceuticals, pp. 503-24. U.S. Atomic Energy Commission Symposium Series no. 6. Washington, D.C.: U.S. Atomic Energy Commission, 1966.

Lushbaugh, C. C.; Comas, F.; Saenger, E. L.; Jacobs, M.; Hofstra, R.; and Andrews, G. A. "Radiosensitivity of man by extrapolation from studies of total-body irradiation of patients." Radiation Research 27:487-88 (1966). (Abstract.)

Medical Division, Oak Ridge Institute of Nuclear Studies. Research report, 1965, for the year ending December 31, 1965. Oak Ridge, Tennessee: ORINS, 1966. (ORINS-53.)

1113811

Merrit, C.; Gengozian, N.; and Hampton, J. "Human A- and B-like antigens and antibodies in marmoset serum." Federation of American Societies for Experimental Biology. Federation Proceedings 25:435 (1966). (Abstract.)

Morris, A. C., Jr., and Ross, D. A. The design of a low-background whole-body counting facility. Washington, D.C.: U.S. Atomic Energy Commission, 1966. (ORINS-51.)

Nelson, B.; Cosgrove, G. E.; and Gengozian, N. "Diseases of an imported primate Tamarinus nigricollis." Laboratory Animal Care 16:255-75 (1966).

Nelson, B., and Takasugi, M. "Caution in lymphography." New England Journal of Medicine 274:110 (1966.) (Editorial.)

Oswald, E. O; Piantadosi, C.; Anderson, C. E.; and Snyder, F. "The synthesis of ^{14}C- and ^{3}H-labeled glycerol ethers." Lipids 1:241-46 (1966).

Pfleger, R. C.; Piantadosi, C.; and Snyder, F. "The metabolism of α-alkoxy glyceryl monoethers in rat liver." Journal of the American Oil Chemists' Society 43:140A (1966). (Abstract.)

Rogers, W. A., Jr., and Nelson, B. "Strongyloidiasis and malignant lymphoma: 'opportunistic infection' by a nematode." Journal of the American Medical Association 195:685-87 (1966).

Snyder, F. "A comparison of zonal scans and strip scans of thin-layer chromatograms." Separation Science 1:655-57 (1966).

1113812

-----. "Triglyceride and phospholipid biosynthesis in irradiated bone marrow." Radiation Research 27:523 (1966). (Abstract.)

-----. "Triglyceride biosynthesis in irradiated bone marrow." Radiation Research 27:375-83 (1966).

Snyder, F.; Cheng, S.-S.; and Piantadosi, C. "An unusual lipid present in Ehrlich ascites cells and other tumors." Journal of the American Oil Chemists' Society 43:140A (1966). (Abstract.)

Snyder, F.; Cress, E. A.; and Stephens, N. "An unidentified lipid prevalent in tumors." Lipids 1:381-86 (1966).

Snyder, F., and Pfleger, R. C. "Metabolism of alpha-alkoxy glyceryl monoethers in rat liver, in vivo and in vitro." Lipids 1:328-34 (1966).

Snyder, F., and Piantadosi, C. "Labeling and radiopurity of lipids." Advances in Lipid Research 4:257-83 (1966).

-----. "The synthesis and purity of labeled lipids." In Radioactive Pharmaceuticals, pp. 553-65. Washington, D.C.: U.S. Atomic Energy Commission, 1966.

Snyder, F., and Smith, D. "An automated system for sample collection and computer analysis of thin-layer radiochromatograms." Separation Science 1:709-22 (1966).

Snyder, F., and Wood, R. "The incorporation of labeled lipids into a glyceryl ether component of Ehrlich ascites cells." ACS Abstracts, p. C-258. New York: American Chemical Society, 1966. (Abstract.)

1113813

Webb, A. M., and Lushbaugh, C. C. "Automated measurements of erythrocyte fragility using a linearly decreasing salt gradient." Clinical Chemistry 12:538 (1966). (Abstract.)

Wood, R.; Bever, E. L.; and Snyder, F. "The GLC and TLC resolution of diastereoisomeric polyhydroxystearates and assignment of configurations." Lipids 1:399-408 (1966).

-----. "The resolution of long-chain isomeric polyhydroxy acids by gas-liquid chromatography." Journal of the American Oil Chemists' Society 43:139A (1966). (Abstract.)

Wood, R., and Snyder, F. "Characterization and tentative identification of lipid ether present in Ehrlich ascites cells and other tumors." ACS Abstracts, p. C-257. New York: American Chemical Society, 1966. (Abstract.)

-----. "Gas-liquid chromatographic analysis of long chain isomeric glyceryl monoethers." Lipids 1:62-72 (1966).

-----. "A modified applicator for the uniform coating of thin-layer plates." Journal of Chromatography 21:318-19 (1966).

-----. "Modified silver ion thin-layer chromatography." Journal of the American Oil Chemists' Society 43:53-54 (1966).

1113814

MEDICAL 1967

Andrews, G. A. "Ethical considerations in human experimentation." In U.S. Atomic Energy Commission Report CONF-661018. Washington, D.C.: U.S. Atomic Energy Commission, 1967.

-----. "Radiation accidents and their management." Radiation Research Supplement 7:390-97 (1967).

-----. "Total-body irradiation in the human being." In Proceedings of the XIth International Congress of Rome, September 1965, pp. 1583-89. Excerpta Medica Foundation, 1967.

Andrews, G. A.; Congdon, C. C.; Edwards, C. L.; Gengozian, N.; Nelson, B.; and Vodopick, H. "Preliminary trials of clinical immunotherapy." Cancer Research 27:2535-41 (1967).

Andrews, G. A., and Lushbaugh, C. C. Radiobiological Factors in Manned Space Flight. Washington, D.C.: National Academy of Sciences--National Research Council, 1967.

Andrews, G. A.; Lushbaugh, C. C.; Kniseley, R. M.; White, D. A.; and Friedman, B. I. "Haematological effects of whole-body radiation in the human being." In IAEA Panel: Effects of Ionizing Radiations on the Haematopoietic Tissue, pp. 75-83. Vienna: International Atomic Energy Agency, 1967.

Arimizu, N., and Morris, A. C., Jr. "Area scanning for quantitative measurement of radioactivity in internal organs." Journal of Nuclear Medicine 8:312 (1967). (Abstract.)

1113815

Bergner, P.-E. E. "The concepts of mass, volume, and concentration." In Atomic Energy Commission Symposium Series no. 11, CONF-661010, pp. 21-37. Washington, D.C.: U.S. Atomic Energy Commission, 1967.

-----. Ergodic properties of the tracer system. Washington, D.C.: U.S. Atomic Energy Commission, 1967. (ORAU-103.)

-----. Turnover compartmentalization: a statistical tracer theory for analysis of whole-system retention data. Washington, D.C.: U.S. Atomic Energy Commission, 1967. (ORAU-104.)

-----. "Turnover compartmentalization theory." Journal of Nuclear Medicine 8:327 (1967). (Abstract.)

Bergner, P.-E. E., and Lushbaugh, C. C., eds. Compartments, pools, and spaces in medical physiology. U.S. Atomic Energy Commission Symposium Series no. 11, CONF-661010. Washington, D.C.: U.S. Atomic Energy Commission, 1967.

Bergner, P.-E. E.; Lushbaugh, C. C.; Gibbs, W. D.; and Franz, W. "Analogue computer analysis of human chromium-51 RBC survival and whole-body retention data." Journal of Nuclear Medicine 8:292-93 (1967). (Abstract.)

Cheng, S.-S.; Piantadosi, C.; and Snyder, F. "Lipid droplets and glyceryl ether diesters in Ehrlich ascites cells grown in tissue culture." Lipids 2:193-94 (1967).

Cloutier, R. J.; O'Foghludha, F.; and Comas, F. V. Conference on dosimetry of total-body irradiation by external photon beams. U.S. Atomic Energy Commission Report CONF-670219. Washington, D.C.: U.S. Atomic Energy Commission, 1967.

1113816

Cloutier, R. J., and Watson, E. E. "Measuring plutonium in wounds: advantages of using the americium gamma ray." Health Physics 13:811-13 (1967).

Comas, F. V., and Byrd, B. L. "Hemopoietic spleen colonies in the rat." Radiation Research 32:355-65 (1967).

Dalton, C. P., and Cloutier, R. J. "An arrangement of radioactive sources for a low exposure rate total-body irradiation facility." Physics in Medicine and Biology 12:116 (1967). (Abstract.)

-----. Source arrangement for a low-exposure rate total-body irradiation facility for man. Washington, D.C.: U.S. Atomic Energy Commission, 1967. (ORINS-52.)

Fanger, H., and Lushbaugh, C. C. "Radiation death from cardiovascular shock following a criticality accident." Archives of Pathology 83:446-60 (1967).

Gengozian, N.; Gottlieb, C. F.; and Allen, E. M. "Demonstration of an early host-graft incompatibility reaction in radiation chimeras with the Jerne plaque technique." Proceedings of the Society for Experimental Biology and Medicine 126:135-40 (1967).

Gengozian, N., and Hübner, K. F. "Effect of phytohemagglutinin (PHA) on an antibody-forming system." Journal of Immunology 99:184-90 (1967).

Gibbs, W. D.; Hodges, H. D.; and Lushbaugh, C. C. "Another method for correcting the initial whole-body count in iron-59 absorption studies in anemia." Blood 29:934-36 (1967). (Editorial).

1113817

Goh, K. O. "Cytogenetic studies in blastic crisis of chronic myelocytic leukemia." Archives of Internal Medicine 120:315-20 (1967).

-----. "The in vitro autoradiographic studies of the Ph^1 chromosome cells." Clinical Research 15:278 (1967). (Abstract.)

-----. "Inner chromosomal structures in the somatic metaphase of rat kangaroo (Potorous tridactylis): A light microscopic observation." Cytologia 32:416-19 (1967).

-----. "Pseudodiploid chromosomal pattern in chronic lymphocytic leukemia." Journal of Laboratory and Clinical Medicine 69:938-49 (1967).

Goh, K. O.; Swisher, S. N.; and Herman, E. C. "Chronic myelocytic leukemia and identical twins: additional evidence of the Philadelphia chromosome as postzygotic abnormality." Archives of Internal Medicine 120:214-19 (1967).

Hartman, R. E., and Hayes, R. L. "Gallium binding by blood serum." Federation of American Societies for Experimental Biology. Federation Proceedings 26:780 (1967). (Abstract.)

Hayes, R. L.; Carlton, J. E.; Byrd, B. L.; and Rafter, J. J. "Factors influencing the distribution of labeled hydrous ferric oxide colloid." Journal of Nuclear Medicine 8:302 (1967). (Abstract.)

Kimble, H. Interface scanner. Oak Ridge, Tennessee: ORAU, 1967. (ORAU-105.)

1113018

Kniseley, R. M. "The bone marrow." In Principles of Nuclear Medicine; Henry N. Wagner, Jr., ed.; pp. 404-12. Philadelphia: W. B. Saunders, 1967.

-----. "Book review: Clinical Capillary Microscopy." American Journal of Clinical Pathology 48:199 (1967).

Likuski, H. J.; Debons, A. F.; and Cloutier, R. J. "Inhibition of gold thioglucose-induced hypothalamic obesity by glucose analogues." American Journal of Physiology 212:669-76 (1967).

Lim, J.; Piantadosi, C.; and Snyder, F. "A comparison of phospholipid biosynthesis in irradiated bone marrow and liver." Proceedings of the Society for Experimental Biology and Medicine 124:1158-61 (1967).

Lushbaugh, C. C. "Radiation and shock." Journal of the American Medical Association 200:181 (1967). (Editorial.)

-----. "Some biological end points of dosimetric value derived from clinical data." In U.S. Atomic Energy Commission Report CONF-670305, pp. 94-113. Washington, D.C.: U.S. Atomic Energy Commission, 1967.

Lushbaugh, C. C.; Cloutier, R. J.; Humason, G.; Langham, J.; and Guzak, S. "Histopathologic study of intradermal plutonium metal deposits: their conjectured fate." Annals of the New York Academy of Sciences 145:791-97 (1967).

Lushbaugh, C. C.; Comas, F.; and Hofstra, R. "Clinical studies of radiation effects in man. A preliminary report of a retrospective search for dose-relationships in the prodomal syndrome." Radiation Research Supplement 7:398-412 (1967).

1113819

Lushbaugh, C. C., and Gibbs, W. D. "Decreased ^{24}Na excretion in rat GI syndrome after 1200-rad fission neutron exposures." Radiation Research 31:593-94 (1967). (Abstract.)

Medical Division, Oak Ridge Associated Universities. Research report, 1966, for the year ending December 31, 1966. Oak Ridge, Tennessee: ORAU, 1967. (ORAU-101.)

Oswald, E. O.; Piantadosi, C.; Anderson, C. E.; and Snyder, F. "Infrared spectra and polymorphism of glycerol ether derivaties." Chemistry and Physics of Lipids 1:270-81 (1967).

Pfleger, R. C.; Piantadosi, C.; and Snyder, F. "The biocleavage of isomeric glyceryl ethers by soluble liver enzymes in a variety of species." Biochimica et Biophysica Acta 144:633-48 (1967).

Pfleger, R. C., and Snyder, F. "Lipid turnover in an isolated population of irradiated bone marrow cells." Radiation Research 30:325-28 (1967).

Snyder, F. "Book review: Advances in Chromatography, Vol. 2." Journal of the American Oil Chemists' Society 44:464 (1967).

-----. "Book review: Advances in Chromatography, Vol. 3." Journal of the American Oil Chemists' Society 44:464-65 (1967).

-----. "Thin-layer chromatography radioassay: a review." Atomlight 58:1-16 (1967).

1113820

Snyder, F.; Pfleger, R. C.; and Piantadosi, C. "Cleavage of the 1- and 2-isomers of ^{14}C-labeled glyceryl ethers by a soluble multienzyme system of rat liver." In Abstracts IV, p. 734. Tokyo: Seventh International Congress of Biochemistry, 1967.

Snyder, F., and Smith, D. "An automated system for sample collection and computer analysis of thin-layer radiochromatograms." In Separation Techniques in Chemistry and Biochemistry; Roy A. Keller, ed.; pp. 331-44. New York: Marcel Dekker, 1967.

Snyder, F., and Wood, R. "The subcellular distribution and metabolism of glyceryl ether diesters in Ehrlich ascites cells." Journal of the American Oil Chemists' Society 44:381 (1967). (Abstract.)

Uchiyama, G.; Hitchcock, A. A. C.; and Morris, A. C., Jr. "Clinical results with a color-recording rescanner." Journal of Nuclear Medicine 8:437-43 (1967).

Van Woert, M. H. "Oxidation of reduced nicotinamide adenine dinucleotide by melanin." Life Sciences 6:2605-12 (1967).

Wood, R. "GLC and TLC analysis of isopropylidene derivatives of isomeric polyhydroxy acids derived from positional and geometrical isomers of unsaturated fatty acids." Lipids 2:199-203 (1967).

Wood, R., and Snyder, F. "Characterization and identification of glyceryl ether diesters present in tumor cells." Journal of Lipid Research 8:494-500 (1967).

-----. "Chemical and physical properties of isomeric glyceryl monoethers." Lipids 2:161-71 (1967).

1113821

-----. "Quantitative determination of glyceryl alk-1-enyl and alkyl-alkenyl ethers in neutral and phospholipids." Journal of the American Oil Chemists' Society 44:380-81 (1967). (Abstract.)

1113022

MEDICAL 1968

Anderson, R. E.; Cumming, R. B.; and Snyder, F. "The lipid composition of L-M cells grown in suspension culture." Journal of the American Oil Chemists' Society 45:129 (1968). (Abstract.)

Andrews, G. A. "The therapeutic use of bone-marrow transplantation." In Proceedings of the International Conference on Leukemia - Lymphoma; Chris J. D. Zarafonetis, ed.; pp. 423-432. Philadelphia: Lea and Febiger, 1968.

Beck, W. L.; Callis, E. L.; and Cloutier, R. J. "Phantom depth-dose measurement with extruded LiF in a low-exposure-rate total-body irradiator." In U.S. Atomic Energy Commission Report CONF-680920, pp. 976-89. Washington, D.C.: U.S. Atomic Energy Commission, 1968.

Berger, J. D.; Watson, E. E.; and Cloutier, R. J. "Health physics aspects of low-energy accelerators." In U.S. Atomic Energy Commission Report CONF-680411, pp. 112-37. Washington, D.C.: U.S. Atomic Energy Commission, 1968.

Blank, M., and Snyder, F. "Determination of the position of double bonds in naturally occurring alkyl glyceryl ethers." Journal of the American Oil Chemists' Society 45:121 (1968). (Abstract.)

Carlson, D., and Gengozian, N. "The radiation exposure-rate effect: action upon the primary immune response in mice." Radiation Research 35:572 (1968). (Abstract.)

1113823

Cloutier, R. J., and Dalton, C. P. "Radiation safety problems connected with the medical use of radioisotopes." In Proceedings of the First International Congress of Radiation Protection, Rome, September 5-10, 1966, pp. 1603-13. London: Pergamon Press, 1968.

Comas, F. V. "The time factor in fractionated irradiation of mouse skin." In U.S. Atomic Energy Commission Report CONF-680410, pp. 18.1-18.12. Washington, D.C.: U.S. Atomic Energy Commission, 1968.

Comas, F. V.; Andrews, G. A.; and Nelson, B. "Spleen irradiation in secondary hypersplenism." American Journal of Roentgenology 104:668-73 (1968).

Cosgrove, G. E.; Lushbaugh, D. B.; Humason, G.; and Anderson, M. G. "Synhimantus (Nematoda) associated with gastric squamous tumors in muskrats." Bulletin of the Wildlife Diseases Association 4:54-57 (1968).

Cosgrove, G. E.; Nelson, B.; and Gengozian, N. "Helminth parasites of the tamarin, Saguinus fuscicollis." Laboratory Animal Care 18:654-56 (1968).

Debons, A. F.; Krimsky, I.; Likuski, H. J.; From, A.; and Cloutier, R. J. "Gold thioglucose damage to the satiety center: inhibition in diabetes." American Journal of Physiology 214:652-58 (1968).

Edwards, C. L.; Tanida, R.; and Gibbs, W. D. "Tracer and treatment discrepancy as a complication of radioiodine therapy." Journal of Nuclear Medicine 9:367-68 (1968). (Abstract.)

1113824

Edwards, C. L.; Tanida, R.; and Mora, R. "Laminar scintiscans for determining depth of small metastases of thyroid carcinoma." Journal of Nuclear Medicine 9:313-14 (1968). (Abstract.)

Frome, E. L., and Beauchamp, J. J. "Maximum likelihood estimation of survival curve parameters." Biometrics 24:595-605 (1968).

Gengozian, N.; Carlson, D. E.; and Gottlieb, C. F. "Radiation exposure rates: effects on the immune system." In U.S. Atomic Energy Commission Report CONF-680410, pp. 16.1-16.23. Washington, D.C.: U.S. Atomic Energy Commission, 1968.

Gibbs, W. D.; Hodges, H. D.; and Lushbaugh, C. C. "Precise geometry-independent radioassay of large biological samples." Journal of Nuclear Medicine 9:264-66 (1968).

Goh, K. O. "Autoradiographic studies in chronic myelocytic leukemia." In Atomic Energy Commission Symposium Series no. 13, CONF-671111, pp. 695-715. Washington, D.C.: U.S. Atomic Energy Commission, 1968.

-----. "Chromosomes in chronic lymphocytic leukemia." The Lancet 2:104 (1968.) (Editorial.)

-----. "Cytogenetic studies of bone-marrow lymphocytes after total-body irradiation." Clinical Research 16:42 (1968). (Abstract.)

-----. "The effect of deoxyribonucleotide triphosphates on pulverized human chromosomes at G_2." Clinical Research 16:452 (1968).

1113825

-----. "Large abnormal acrocentric chromosome associated with human malignancies. Possible mechanism of establishing clone of cells." Archives of Internal Medicine 122:241-48 (1968).

-----. "Smaller G (Gp-) and t (Gp-; Dpt) chromosomes. a familial study with one member having acute leukemia." American Journal of Diseases in Children 115:732-38 (1968).

-----. "Total-body irradiation and human chromosomes: cytogenetic studies of the peripheral blood and bone marrow leukocytes seven years after total-body irradiation." Radiation Research 35:155-70 (1968).

Goh, K. O., and Sumner, H. "Breaks in normal human chromosomes: are they induced by a transferable substance in the plasma of persons exposed to total-body irradiation?" Radiation Research 35:171-81 (1968).

Goswitz, F. A.; Edwards, C. L.; and Vodopick, H. "Assessment of erythropoiesis by ferrokinetics and radiocolloid bone-marrow scanning." Journal of Nuclear Medicine 9:319 (1968). (Abstract.)

Hartman, R. E., and Hayes, R. L. "Indium and gallium binding by blood serum." Federation of American Societies for Experimental Biology. Federation Proceedings 27:838 (1968). (Abstract.)

Hayes, R. L.; Byrd, B. L.; and Carlton, J. E. "^{131}mIn as a possible bone scanning agent." Journal of Nuclear Medicine 9:323 (1968). (Abstract.)

1113826

Hayes, R. L.; Goswitz, F. A.; and Murphy, B. E. P.; eds. Radioisotopes in medicine: in vitro studies. U.S. Atomic Energy Commission Symposium Series no. 13, CONF-671111. Washington, D.C.: U.S. Atomic Energy Commission, 1968.

Hodges, H. D.; Lushbaugh, C. C.; and Gibbs, W. D. "Calibration of a whole-body counter for quantitating total potassium in human subjects." Journal of the Tennessee Academy of Science 43:49 (1968). (Abstract.)

Lambremont, E. N., and Wood, R. "Glyceryl ethers in insects: identification of alkyl- and alk-1-enyl glyceryl ether phospholipids." Lipids 6:503-10 (1968).

-----. "Glyceryl ethers in insects: identification of the alk-1-enyl and alkyl alkenyl ethers in the phospholipid fraction of three insect species." Journal of the American Oil Chemists' Society 45:157 (1968). (Abstract.)

Lushbaugh, C. C. "Absence of electrolyte loss in the gastrointestinal syndrome." In Round Table Discussion on Mechanism of Intestinal Radiation Death, pp. 356-62. Washington, D.C.: Excerpta Medica Foundation, 1968.

-----. "Recent progress in assessment of human resistance to total-body irradiation." In Postattack Recovery from Nuclear War, pp. 193-98. Washington, D.C.: National Academy of Sciences, 1968.

Lushbaugh, C. C.; Comas, F.; Edwards, C. L.; and Andrews, G. A. "Clinical evidence of dose-rate effects in total-body irradiation in man." In U.S. Atomic Energy Commission Report CONF-680410, pp. 17.1-17.23. Washington, D.C.: U.S. Atomic Energy Commission, 1968.

1113827

Lushbaugh, C. C.; Comas, F. V.; and Andrews, G. A. "Radiation dose-response relations derived from clinical data." Health Physics 15:165-66 (1968). (Abstract.)

Lushbaugh, C. C., and Lushbaugh, D. B. "Evaluation of therapeutic response using change in electronically determined red blood cell size distribution." American Journal of Clinical Pathology 50:627 (1968). (Abstract.)

Medical Division, Oak Ridge Associated Universities. Research report, 1967, for the year ending December 31, 1967. Oak Ridge, Tennessee: ORAU, 1968. (ORAU-106.)

Pfannenstiel, P.; Sitterson, B. W.; and Anderson, G. A. "^{130}I for studying the effects of thyroid-stimulating hormone in patients with thyroid cancer." Journal of Nuclear Medicine 9:90-95 (1968).

Pfleger, R. C.; Anderson, N. G.; and Snyder, F. "Lipid class and fatty acid composition of rat liver plasma membranes isolated by zonal centrifugation." Biochemistry 7:2826-33 (1968).

Porter, R. P. "Chimerism and immunologic tolerance: a consequence of fraternal twinning in the marmoset." Dissertation Abstracts 29:479-B (1968). (Abstract.)

Porter, R. P., and Gengozian, N. "Immunologic tolerance of grafted skin exchanged between marmoset dizygotic cotwins." Federation of American Societies for Experimental Biology. Federation Proceedings 27:505 (1968). (Abstract.)

-----. "Transplantation in the marmoset (Callithricidae): a technique for orthotopic, fitted skin grafts." Proceedings of the Society for Experimental Biology and Medicine 127: 860-67 (1968).

1113828

Ross, D. A., and Morris, A. C., Jr. "A stable, low-background whole-body counter designed for uniform detector geometry." International Journal of Applied Radiation and Isotopes 19:731-39 (1968).

Snyder, F. "Automated thin-layer chromatography." Journal of the American Oil Chemists' Society 45:143 (1968). (Abstract.)

-----. "Thin-layer chromatography radioassay: a review." Advance Tracer Method 4:81-104 (1968).

Snyder, F., and Cress, E. A. "Application of thin-layer chromatographic zonal ^{14}C-profile scans to the analysis of urinary constituents derived from lipids." Clinical Chemistry 14:529-34 (1968).

Snyder, F., and Piantadosi, C. "Acylation and degradation of alkoxyglycerols in vitro." Federation of American Societies for Experimental Biology 27:458 (1968). (Abstract.)

-----. "Deacylation of isomeric diacyl (1-^{14}C) alkoxyglycerols by pancreatic lipase." Biochimica et Biophysica Acta 152:794-97 (1968).

Snyder, F.; Piantadosi, C.; and Wood, R. "The metabolism of glyceryl thioethers." Journal of the American Oil Chemists' Society 45:84 (1968). (Abstract.)

Snyder, F., and Wood, R. "Deposition of triglycerides of increased carbon number in irradiated rat marrow." Radiation Research 33:142-29 (1968).

1113829

-----. "The occurrence and metabolism of alkyl and alk-1-enyl ethers of glycerol in transplantable rat and mouse tumors." Cancer Research 28:972-78 (1968).

Ur, A., and Lushbaugh, C. C. "Some effects of electrical fields on red blood cells with remarks on electronic red cell sizing." British Journal of Haematology 15:527-38 (1968).

Van Woert, M. H. "Reduced nicotinamide-adenine dinucleotide oxidation by melanin: inhibition by phenothiazines." Proceedings of the Society for Experimental Biology and Medicine 129:165-71 (1968).

Webb, A. M.; Edwards, C. L.; and Wright, M. F. "Automated determination of muramidase activity." Clinical Chemistry 14:820 (1968). (Abstract.)

Wood, R. "Gas-liquid chromatographic analysis of long-chain fatty alcohols." Journal of Gas Chromatography 6:94-96 (1968).

Wood, R., and Bauman, W. J. "Gas-liquid chromatographic analyses of 1,2-ethanediol monoethers and monoesters." Journal of Lipid Research 9:733-38 (1968).

Wood, R., and Snyder, F. "Analysis of glyceryl-alkyl and alk-1-enyl ethers by gas-liquid chromatography and thin-layer chromatography." Journal of the American Oil Chemists' Society 45:175 (1968). (Abstract.)

-----. "Quantitative determination of alk-1-enyl- and alkyl-glyceryl ethers in neutral lipids and phospholipids." Lipids 3:129-35 (1968).

1113830

MEDICAL 1969

Anderson, R. E.; Cumming, R. B.; Walton, M.; and Snyder, F. "Lipid metabolism in cells grown in tissue culture: O-alkyl, O-alk-1-enyl, and acyl moieties of L-M cells." Biochimica et Biophysica Acta 176:491-501 (1969).

Anderson, R. E.; Garrett, R. D.; Blank, M. L.; and Snyder, F. "The quantitative production of aldehydes from O-alk-1-enyl glycerols." Lipids 4:327-30 (1969).

Anderson, R. E., and Snyder, F. "Quantitative collection of $^{14}CO_2$ in the presence of labeled short-chain acids." Analytical Biochemistry 27:311-14 (1969).

Andrews, G. A.; Balish, E.; Edwards, C. L.; Kniseley, R. M.; and Lushbaugh, C. C. "Possibilities for improved treatment of persons exposed in radiation accidents." In Handling of Radiation Accidents, pp. 119-35. Vienna: International Atomic Energy Agency, 1969.

Andrews, G. A.; Congdon, C. C.; Edwards, C. L.; Gengozian, N.; Nelson, B.; and Vodopick, H. "Preliminary trials of clinical immunotherapy." In Year Book of Cancer, pp. 232-84. Chicago: Year Book Medical Publishers, 1969. (Abstract.)

Arimizu, N.; Kakehi, H.; and Morris, A. C., Jr. "Area scanning for quantitative measurement of radioactivity in internal organs." In Medical Radioisotope Scintigraphy, vol. 1, pp. 653-63. Vienna: International Atomic Energy Agency, 1969.

1113831

Arimizu, N., and Morris, A. C., Jr. "Quantitative measurement of radioactivity in internal organs by area scanning." Journal of Nuclear Medicine 10:265-69 (1969).

Balish, E., and Pearson, T. A. "Studies on the bacterial flora of three men accidentally exposed to total-body irradiation." Radiation Research 39:525-26 (1969). (Abstract.)

Balish, E., and Shapiro, S. K. "S-adenoxylmethionine: homocysteine methyl-transferase activity in Candida albicans." Bacteriological Proceedings 69:145 (1969). (Abstract.)

Barclay, T. R., and Morris, A. C., Jr. "On-line computer interfacing of an analytrol film reader for measuring size of radioactive colloid particles." Journal of Nuclear Medicine 10:387 (1969). (Abstract.)

Berger, J. D. "Book review: Code of Practice for the Protection of Persons Exposed to Ionizing Radiations in Research and Teaching." Nuclear Safety 10:521 (1969).

Bergner, P.-E. E. Theory of quantitative radiation--response time-data. Washington, D.C.: U.S. Atomic Energy Commission, 1969. (ORAU-109.)

Blank, M. L., and Snyder, F. "The occurrence of fatty alcohols in normal tissues and neoplasms." Journal of the American Oil Chemists' Society 46:139 (1969). (Abstract.)

-----. "The preparation of alkyl-1, 2 diols and their chromatographic behavior in relation to O-alkyl-glycerols." Biochimica et Biophysica Acta 187:154-56 (1969).

1113832

Carlson, D. E. "The radiation exposure-rate effect: actions upon the immune response in mice." Dissertation Abstracts 29:4040B (1969). (Abstract.)

Cloutier, R. J. "Book review: Atlas of Radiation Dose Distribution, Vol. III." Health Physics 16:815 (1969).

Cloutier, R. J.; Smith, S. A.; Snyder, W. S.; and Warner, G. G. "Dose to the fetus from gamma emitters present in the bladder." Health Physics 17:362 (1969). (Abstract.)

Comas, F. V.; Andrews, G. A.; and Edwards, C. L. "Changes in leukocyte values in patients with chronic granulocytic leukemia receiving spleen irradiation." Radiation Research 39:491 (1969). (Abstract.)

Cotman, C.; Blank, M. L.; Moehl, A.; and Snyder, F. "Lipid composition of synaptic plasma membranes isolated from rat brain by zonal centrifugation." Biochemistry 8:4606-12 (1969).

Debons, A. F.; Krimsky, I.; From, A.; and Cloutier, R. J. "Rapid effects of insulin on the hypothalmic satiety center." American Journal of Physiology 217:1114-18 (1969).

Edwards, C. L., and Hayes, R. L. "Gallium-67 for tumor scanning." In Book of Abstracts, pp. 92-93. Tokyo: International Congress of Radiology, 1969.

-----. "Scanning tumors of soft tissue and bone with ^{67}Ga-citrate." Journal of Nuclear Medicine 10:332 (1969). (Abstract.)

-----. "Tumor scanning with ^{67}Ga-citrate." Journal of Nuclear Medicine 10:103-5 (1969).

1113833

Gengozian, N. "Marmosets: their potential in experimental medicine." Annals of the New York Academy of Sciences 162:336-62 (1969).

Gengozian, N.; Batson, J. S.; Greene, C. T.; and Goslee, D. G. "Hemopoietic chimerism in imported and laboratory-bred marmosets." Transplantation 8:633-52 (1969).

Gengozian, N.; Carlson, D. E.; and Allen, E. M. "Transplantation of allogeneic and xenogeneic (rat) marrow in irradiated mice as affected by radiation exposure rates." Transplantation 7:259-73 (1969).

Gengozian, N., and Congdon, C. C. "Effect of syngeneic antilymphocyte serum on rat-mouse radiation chimeras." Transplantation Proceedings 1:34-38 (1969).

Gibbs, W. D.; Hodges, H. D.; Queener, R. F.; and Lushbaugh, C. C. "Improvement in accuracy of whole-body radioisotope quantitation by the scatter-window method." Journal of Nuclear Medicine 10:332 (1969). (Abstract.)

Gibbs, W. D., and Lushbaugh, C. C. "Whole-body counter systems." In Handbook of Radioactive Nuclides; Yen Wang, ed.; pp. 134-40. Cleveland, Ohio: Chemical Rubber Company, 1969.

Goh, K. "Chromosomal vacuolization, dissociation, and breakage associated with chloramphenicol." Clinical Research 17:326 (1969). (Abstract.)

-----. "Exogenous deoxyribonucleoside triphosphates: their effect on pulverized human chromosomes at the G_2 phase." Proceedings of the Society for Experimental Biology and Medicine 131:942-46 (1969).

1113834

Goswitz, F. A.; Edwards, C. L.; Wright, M. F.; and Clevenger, M. "Value of radioisotopic tests in primary myelfibrosis." Southern Medical Journal 62:1431 (1969). (Abstract.)

Goswitz, F. A.; Vodopick, H.; and Clevenger, M. "Blood lymphocyte kinetics in patients with chronic lymphocytic leukemia (CLL)." Journal of Nuclear Medicine 10:404 (1969). (Abstract.)

-----. "The need to measure red-cell mass and plasma volume independently in patients with hematologic disorders." Southern Medical Journal 62:1431-32 (1969). (Abstract.)

Harlow, R. D.; Lumb, R. H.; and Wood, R. "Insect lipids: carbon number distribution of triglycerides in five species." Comparative Biochemistry and Physiology 30:761-69 (1969).

Hartman, R. E., and Hayes, R. L. "The binding of gallium by blood serum." Journal of Pharmacology and Experimental Therapeutics 168:193-98 (1969).

Hayes, R. L.; Byrd, B. L.; Carlton, J. E.; Nelson, B.; and Swartzendruber, D. C. "Studies of the concentration of gallium in soft-tissue tumors." Southern Medical Journal 62:1432 (1969). (Abstract.)

Hayes, R. L.; Carlton, J. E.; and Byrd, B. L. "Localization of ^{67}Ga in soft-tissue tumors in experimental animals." Journal of Nuclear Medicine 10:406 (1969). (Abstract.)

Hodges, H. D.; Edwards, C. L.; Lushbaugh, C. C.; and Gibbs, W. D. "Whole-body ^{131}I retention as a quantitative measure of thyroid function." Journal of Nuclear Medicine 10:459 (1969). (Abstract.)

1113835

Hübner, K. F., and Gengozian, N. "Critical variables of the Jerne plaque technique as applied to rodent antibody-forming systems responding to heterologous red cell antigens." Immunology 102:155-67 (1969).

Humason, G. L., and Lushbaugh, C. C. "Sirius supra blue FGL-CF; superior to analine blue in the combined elastin, reticulum, and collagen stain." Stain Technology 44:105-6 (1969).

Hurst, S. K.; Mardon, D. N.; and Balish, E. "Germ-tube formation by Candida albicans in a defined liquid culture medium." Bacteriological Proceedings 69:33-34 (1969). (Abstract.)

Kakehi, H.; Gibbs, W. D.; and Hayes, R. L. Counting characteristics of a medium-level whole-body counter. Washington, D.C.: U.S. Atomic Energy Commission, 1969. (ORAU-108.)

Kniseley, R. M. "Book review: Progress in Atomic Medicine." American Journal of Clinical Pathology 52:484 (1969).

Kniseley, R. M.; Andrews, G. A.; Edwards, C. L.; and Hayes, R. L. "Bone-marrow and skeletal scanning." Radiological Clinics of North America 7:265-80 (1969).

Lee, T.-C.; Swartzendruber, D. C.; and Snyder, F. "Zonal centrifugation of microsomes from rat liver: resolution of rough- and smooth-surfaced membranes." Biochemical and Biophysical Research Communications 36:748-55 (1969).

1113836

Lozzio, B. B., and Comas, F. V. "Biological effects of poke weed mitogen." International Archives of Allergy and Applied Immunology 36:266-81 (1969).

Lushbaugh, C. C. "Reflections on some recent progress in radiation biology." In Advances in Radiation Biology, vol. 3, pp. 277-313. New York: Academic Press, 1969.

-----. "Theoretical and practical aspects of models explaining 'gastrointestinal death' and other lethal radiation syndromes." In Comparative Cellular and Species Radiosensitivity; V. P. Bond and T. Sugaharo, eds.; pp. 288-97. Tokyo: Igaku Shoin, 1969.

Lushbaugh, C. C., and Auxier, J. "Reestimation of human LD_{50} radiation levels at Hiroshima and Nagasaki." Radiation Research 39:526 (1969). (Abstract.)

Lushbaugh, C. C.; Frome, E. L.; Davis, H. T.; and Bibler, D. S. "Power spectrum of the impedance pneumograph: a data reduction system producing analytical parameter of potential clinical usefulness." Aerospace Medicine 40:425-29 (1969).

Lushbaugh, C. C.; Humason, G.; and Gengozian, N. "Intrauterine death from congential chagas disease in laboratory-bred marmosets (Saguinus fuscicollis lagonatus)." American Journal of Tropical Medicine and Hygiene 18:662-65 (1969).

Mardon, D. N., and Balish, E. "Modifications in a French pressure cell-laboratory press system." Applied Microbiology 17:777 (1969).

1113837

Medical Division, Oak Ridge Associated Universities. Research report, 1968, for the year ending December 31, 1968. Oak Ridge, Tennessee: Oak Ridge Associated Universities, 1969. (ORAU-107.)

Pearson, T. A., and Balish, E. "Isolation and characterization of a Sphaerophorus-type microorganism from the large intestines of man." Bacteriological Proceedings 69:103-4 (1969). (Abstract.)

Piantadosi, C.; Snyder, F.; and Wood, R. "Synthesis of ^{35}S- and ^{14}C-labeled glyceryl thioethers." Journal of Pharmaceutical Sciences 58:1028-29 (1969).

Porter, R. P., and Gengozian, N. "Immunological tolerance and rejection of skin allografts in the marmoset." Transplantation 8:653-65 (1969).

Regan, J. D.; Vodopick, H.; Takeda, S.; Lee, W. H.; and Faulcon, F. M. "Serine requirement in leukemic and normal blood cells." Science 163:1452-53 (1969).

Savage, N., and Balish, E. "Induction of auxotrophs of Candida albicans." Bacteriological Proceedings 69:33 (1969).

Snyder, F. "The biochemistry of lipids containing ether bonds." In Progress in the Chemistry of Fats and Other Lipids, vol. 10, part 3, pp. 287-335. New York: Pergamon Press, 1969.

-----. "Enzymic pathways for the biosynthesis and bioclevage of alkyl glyceryl ethers." Journal of the American Oil Chemists' Society 46:115 (1969). (Abstract.)

1113838

-----. "Ether-linked lipids in neoplasms of man and animals: methods of measurement and the occurrence and nature of alkyl and alk-1-enyl moieties." In Advances in Experimental Medicine and Biology, vol. 4, pp. 609-21. New York: Plenum Press, 1969.

-----. "A review of instrumentation and procedures for ^{14}C and ^{3}H radioassay by thin-layer and gas-liquid chromatography." Isotope and Radiation Technology 6:381-400 (1969).

Snyder, F., and Blank, M. L. "Relationships of chain lengths and double bond locations in O-alkyl, O-alk-1-enyl, acyl, and fatty alcohol moieties in preputial glands of mice." Archives of Biochemistry and Biophysics 130:101-10 (1969).

Snyder, F.; Blank, M. L.; and Morris, H. P. "Occurrence and nature of O-alkyl and O-alk-1-enyl moieties of glycerol in lipids of Morris transplanted hepatomas and normal rat liver." Biochimica et Biophysica Acta 176:502-10 (1969).

Snyder, F.; Blank, M. L.; Sodsma, J.; and Morris, H. P. "Occurrence and enzymatic clevage of glyceryl ethers in Morris transplanted hepatomas and normal rat liver." Proceedings of the American Association for Cancer Research 10:84 (1969). (Abstract.)

Snyder, F.; Malone, B.; and Blank, M. L. "The biosynthesis of alkyl glyceryl ether by microsomal enzymes of digestive glands and gonads of the starfish, Asterias forbesi." Biochimica et Biophysica Acta 187:302-6 (1969).

1113839

Snyder, F.; Malone, B.; and Soodsma, J. "Metabolism of long-chain fatty alcohols: formation of waxes and glyceryl ethers." Journal of the American Oil Chemists' Society 46:9 (1969). (Abstract.)

Snyder, F.; Malone, B.; and Wykle, R. L. "The biosynthesis of alkyl ether bonds in lipids by a cell-free system." Biochemical and Biophysical Research Communications 34:40-47 (1969).

Snyder, F., and Moehl, A. "Use of liquid scintillation quenching to quantitate lipid mass." Analytical Biochemistry 28:503-9 (1969).

Snyder, F.; Piantadosi, C.; and Wood, R. "The metabolism of glyceryl thioethers." Proceedings of the Society for Experimental Biology and Medicine 130:1170-74 (1969).

Snyder, F., and Wood, R. "Alkyl and alk-1-enyl ethers of glycerol in lipids from normal and neoplastic tumor tissues." Cancer Research 29:251-57 (1969).

Snyder, F.; Wykle, R. L.; and Malone, B. "The biosynthesis of alkyl ether bonds in lipids from glyceraldehyde-3-phosphate and fatty alcohols by microsomal enzymes." Federation of American Societies for Experimental Biology. Federation Proceedings 28:595 (1969). (Abstract.)

-----. "A new metabolic pathway: biosynthesis of alkyl ethers bonds from glyceraldehyde-3-phosphate and fatty alcohols by microsomal enzymes." Biochemical and Biophysical Research Communications 34:315-21 (1969).

1113840

Swartzendruber, D. C. "Localization of C-type viruses in preleukemic AKR mouse spleen." In Proceedings, 27th Annual Meeting, Electron Microscopy Society of America; Claude J. Arceneaux, ed.; pp. 386-87. Baton Rouge, Louisiana: Claitor's Publishing Division, 1969.

Upton, A. C.; Cosgrove, G. E.; and Lushbaugh, C. C. "Induction of carcinoma of the glandular stomach in mice by whole-body irradiation." In Experimental Carcinoma of the Glandular Stomach, pp. 63-74. Tokyo: Maruzen Company, 1969.

Upton, A. C., and Lushbaugh, C. C. "Pathological anatomy of total-body irradiation." In Atomic Medicine, 5th edition, pp. 154-88. Baltimore: Williams and Wilkins, 1969.

Vodopick, H.; Rupp, E. M.; Comas, F. V.; Goswitz, F. A.; and Edwards, C. L. "^{32}P-DFP leukokinetic study of the mechanisms of splenic irradiation in CGL." Journal of Nuclear Medicine 10:449 (1969). (Abstract.)

Vodopick, H. A.; Rupp, E. M.; and Gengozian, N. "The bidirectional in vitro mixed leukocyte reaction: a mutual inhibitory phenomenon?" Transplantation 7:155-64 (1969).

Watson, E. E.; Cloutier, R. J.; and Berger, J. D. "Tritium concentrations in neutron generator pump oil." Health Physics 17:739-40 (1969).

Webb, A. M. "A new semiautomated thyroxine determination by iodine displacement." Clinical Chemistry 15:764 (1969). (Abstract.)

1113841

Wood, R.; Baumann, W. J.; Snyder, F.; and Mangold, H. K. "Gas-liquid chromatography of dialkyl, alkyl acyl, and diacyl derivatives of glycerol." Journal of Lipid Research 10:128-31 (1969).

Wood, R., and Harlow, R. D. "Gas-liquid chromatographic analysis of free long-chain aldehydes." Journal of Lipid Research 10:463-65 (1969).

-----. "Metabolic relations derived from structural analyses of neutral glycerides and phosphoglycerides." Journal of the American Oil Chemists' Society 46:116 (1969). (Abstract.)

-----. "Rat liver lipids: metabolic relationships derived from structural analyses of neutral glycerides and phosphoglycerides." Journal of the American Oil Chemists' Society 46:7 (1969). (Abstract.)

-----. "Structural analyses of rat liver phosphoglycerides." Archives of Biochemistry and Biophysics 135:272-81 (1969).

-----. "Structural Studies of neutral glycerides and phosphoglycerides of rat liver." Archives of Biochemistry and Biophysics 131:495-501 (1969).

Wood, R.; Harlow, R. D.; and Lambremont, E. N. "GLC analysis of Heliothis virescens triglycerides at various metamorphic stages." Lipids 4:159-62 (1969).

Wood, R.; Harlow, R. D.; and Snyder, F. "Alkyl and alk-1-enyl glyceryl ethers derived from various rat tissue phospholipids." Biochimica et Biophysica Acta 176:641-43 (1969).

1113842

Wood, R.; Piantadosi, C.; and Snyder, F. "Quantitative analysis and comparison of the physical properties of O-alkyl and S-alkyl ethers of glycerol." Journal of Lipid Research 10:370-73 (1969).

Wood, R., and Snyder, F. "Tumor lipids: metabolic relationships derived from structural analyses of acyl, alkyl, and alk-1-enyl moieties of neutral glycerides and phosphoglycerides." Archives of Biochemistry and Biophysics 131:478-94 (1969).

Wykle, R. L., and Snyder, F. "The glycerol source for the biosynthesis of alkyl glyceryl ethers." Biochemical and Biophysical Research Communications 37:658-62 (1969).

1113843

MEDICAL 1970

Andrews, G. A.; Comas, F. V.; Edwards, C. L.; Kniseley, R. M.; Lushbaugh, C. C.; and Vodopick. H. Hematologic and therapeutic effects of total-body irradiation (50 R-100 R) in patients with malignant lymphoma, chronic lymphocytic and granulocytic leukemias, and polycythemia vera. Washington, D.C.: U.S. Atomic Energy Commission, 1970. (ORAU-112.)

Andrews, G. A.; Kniseley, R. M.; Vodopick, H.; Bergner, P.-E.; and Lushbaugh, C. C. "Hematologic responses to total-body irradiation." In Radioisotope in Pharamakokinetick und Klinischer Biochemie; G. Hoffmann and H. A. Ladner, eds.; pp. 517-27. Stuttgart: Nuklear Medizin, 1970.

Arimizu, N.; Kakehi, H.; and Saequsa, K. "New accessories of the scintillation camera for producing the simultaneous section scintigrams of multiple layers." Journal of Nuclear Medicine 11:618 (1970). (Abstract.)

Arimizu, N., and Morris, A. C., Jr. "Quantitative measurements of radioactivity deposited in internal organs using computer analysis of scintigraphy." In Proceedings of the 9th Japan Conference on Radioisotopes, pp. 378-81. 1970.

Balish, E.; Pearson, T. A.; and Chaskes, S. "Irradiated humans: microbial flora, immunglobulins, complement (C'3), transferrin, agglutins, and bacteriocidins." Radiation Research 43:729-56 (1970).

1113844

Barclay, T. R.; Morris, A. C., Jr.; Hayes, R. L.; Carlton, J. E.; and McDow, A. E., Jr. "On-line computer interfacing of a densitometer film reader for measuring the size of radioactive colloid particles." Analytical Chemistry 42:685-86 (1970).

Beck, W. L.; Cloutier, R. J.; Comas, F. V.; and Lushbaugh, C. C. "Human depth-dose estimates in multidirectional gamma-ray fields." Physics in Medicine and Biology 15:144 (1970). (Abstract.)

Beck, W. L.; Stokes, T. R.; Cloutier, R. J.; and Lushbaugh, C. C. "Dosimetry for clinical total-body irradiation." AAPM Quarterly Bulletin 4:66 (1970). (Abstract.)

Bernard, S. R., and Hayes, R. L. "Dose to various segments of the gastrointestinal tract." In U.S. Atomic Energy Commission Symposium Series no. 20, CONF-691212, pp. 295-314. Washington, D.C.: U.S. Atomic Energy Commission, 1970.

Blank, M. L., and Snyder, F. "Long chain fatty alcohols in normal and neoplastic tissues." Lipids 5:337-41 (1970).

-----. "Specificities of alkaline and acid phosphatases in the dephosphorylation of phospholipids." Biochemistry 9:5034-36 (1970).

Blank, M. L.; Wykle, R. L.; Piantadosi, C.; and Snyder, F. "Biosynthesis of O-alkyl and O-alk-1 enyl ether-linked lipids in neoplastic cells." Proceedings of the American Society for Cancer Research 11:9 (1970). (Abstract.)

-----. "The biosynthesis of plasmalogens from labeled O-alkylglycerols in Ehrlich ascites cells." Biochimica et Biophysica Acta 210:442-47 (1970.)

1113845

Carlson, D. E., and Gengozian, N. "Radiation exposure-rate dependence of the immune response in mice." Radiology 97:433-38 (1970).

Chaskes, S., and Balish, E. "Immunoglobulins (I_gG, I_gA, and I_gM), complement (C'3), and transferrin in irradiated humans." Bacteriological Proceedings 70:77 (1970). (Abstract.)

Cloutier, R. J. "Symposium on medical radionuclides: radiation dose and effect." Nuclear Safety 11:475-81 (1970).

Cloutier, R. J.; Edwards, C. L.; and Snyder, W. S.; eds. Medical radionuclides: radiation dose and effects. U.S. Atomic Energy Commission Symposium Series no. 20, CONF-691212. Washington, D.C.: U.S. Atomic Energy Commission, 1970.

Cloutier, R. J., and Watson, E. E. "Radiation dose from radioisotopes in the blood." In U.S. Atomic Energy Commission Symposium Series no. 20, CONF-691212, pp. 325-46. Washington, D.C.: U.S. Atomic Energy Commission, 1970.

Comas, F. V. "The radiosensitivity of rat bone-marrow cells." International Journal of Radiation Biology 17:549-57 (1970).

Comas, F. V.; Edwards, C. L.; and Vodopick, H. "Splenic irradiation in chronic granulocytic leukemia: changes in leukocyte values." Radiation Research 42:413-23 (1970).

1113846

Corrill, L. S.; Stokes, T. R.; and Lushbaugh, C. C. "Accumulation rates of GI and marrow damage in pair-irradiated mice during continuous and fractionated daily exposures." Radiation Research 43:271 (1970). (Abstract.)

Cosgrove, G. E.; Humason, G.; and Lushbaugh, C. C. "Trichospirura leptostoma, a nematode of the pancreatic ducts of marmosets (Saguinus Spp.)." Journal of the American Veterinary Medicine Association 157:696-98 (1970).

Cosgrove, G. E.; Nelson, B. M.; and Self, J. T. "The pathology of pentastomid infection in primates." Journal of Laboratory Animal Care 20:354-60 (1970).

Debons, A. F.; Krimsky, I.; From, A.; and Cloutier, R. J. "Gold thioglucose induction of obesity: significance of focal gold deposits in hypothalamus." American Journal of Physiology 219:1403-8 (1970).

-----. "The histopathology of the gold thioglucose-induced destruction of the hypothalamic satiety center: evidence for direct participation of insulin in the functioning of the center." In Nutrition: Proceedings of the 8th International Congress of Nutrition, pp. 220-22. Amsterdam: Excerpta Medica, 1970.

-----. "Site of action of gold thioglucose in the hypothalamic satiety center." American Journal of Physiology 219:1397-1402 (1970).

1113847

Dickson, H.; Roberts, E., Jr.; Butler, H. M.; Cloutier, R. J.; Smithwick, G.; Watson, E. E.; Haywood, F. F.; and Berger, J. D. "Radiation Safety in the operation of a low-energy accelerator." In U.S. Atomic Energy Commission Report CONF-700322, pp. 441-58. Washington, D.C.: U.S. Atomic Energy Commission, 1970.

Edwards, C. L., and Hayes, R. L. "Scanning malignant neoplasms with gallium-67." Journal of the American Medical Association 212:1182-90 (1970).

-----. "Tumor scanning with ^{67}Ga citrate." In Year Book of Cancer, pp. 350-52. Chicago: Year Book Medical Publishers, 1970.

Edwards, C. L.; Hayes, R. L.; Nelson, B.; and Tehranian, N. "Clinical investigation of ^{67}Ga for tumor scanning." Journal of Nuclear Medicine 11:316-17 (1970). (Abstract.)

Edwards, C. L.; Nelson, B.; and Hayes, R. L. "Localization of gallium in human tumors." Clinical Research 18:89 (1970). (Abstract.)

Gengozian, N., and Merritt, C. B. "Effect of unilateral ovariectomy on twinning frequency in the marmoset." Journal of Reproduction and Fertility 23:509-12 (1970).

Gibbs, W. D.; Hodges, H. D.; Bailey, M.; and Lushbaugh, C. C. "Accurate whole-body quantitation of ^{131}I retention by counting a scatter window." Journal of Nuclear Medicine 11:487-90 (1970).

Goh, K. O. "Inner chromosomal structure of human leukemic metaphase: a light microscopic observation." Cytologia 35:465-70 (1970).

1113848

Goswitz, F. A., and Vodopick, H. "Pitfalls to avoid in the interpretation of CoB_{12} tests." Southern Medical Journal 63:1369 (1970). (Abstract.)

-----. "Radiocolloid scans in chronic granulocytic leukemia." Journal of Nuclear Medicine 11:630-31 (1970). (Abstract.)

Goswitz, F. A.; Vodopick, H.; and Clevenger, M. "The day one index and organ erythropoiesis." Southern Medical Journal 63:1368-69 (1970). (Abstract.)

Gottlieb, C. F., and Gengozian, N. "X-ray and neutron depression of the mouse immune system." Radiation Research 43:217 (1970). (Abstract.)

Hagen, P. O., and Blank, M. L. "Minor lipid components of Clostridium butyricum." Journal of the American Oil Chemists' Society 47:83A (1970). (Abstract.)

Hayes, R. L.; Byrd, B. L.; Carlton, J. E.; and Rafter, J. J. "Factors affecting the localization of ^{67}Ga in animal tumors." Journal of Nuclear Medicine 11:324 (1970).

Hayes, R. L.; Nelson, B.; Swartzendruber, D. C.; Carlton, J. E.; and Byrd, B. L. "Gallium-67 localization in rat and mouse tumors." Science 167:289-90 (1970).

Johnson, D. R.; Poston, J. W.; Auxier, J. A.; Brown, D. G.; Gramly, W. A.; Gibbs, W. D.; Hodges, H. D.; and Davy, D. R. "'Total' and 'exchangeable' sodium studies in swine and sheep using activation analysis and isotopic dilution." Health Physics 18:729-31 (1970). (Abstract.)

1113849

Kniseley, R. M.; Andrews, G. A.; Edwards, C. L.; and Hayes, R. L. "Bone marrow and skeletal scanning." In Year Book of Nuclear Medicine, p. 365. 1970.

Lee, T.-C. "The metabolism of lipids on smooth- and rough-surfaced membranes of rat liver microsomes." Federation of American Societies for Experimental Biology. Federation Proceedings 29:674 (1970). (Abstract.)

Lee, T.-C.; Swartzendruber, D. C.; Morris, H. P.; and Snyder, F. "Zonal centrifugation profiles of smooth- and rough-surfaced microsomes from normal and neoplastic tissues." In Tenth International Cancer Congress, pp. 278-79. 1970. (Abstract.)

Lushbaugh, C. C.; Corrill, L. S.; Stokes, T. R.; Humason, G.; and Lushbaugh, D. "Mouse splenic stem-cell response to protracted radiation exposure." Radiation Research 43:212-13 (1970). (Abstract.)

Medical Division, Oak Ridge Associated Universities. Research report, 1969, for the year ending December 31, 1969. Washington, D.C.: U.S. Atomic Energy Commission, 1970. (ORAU-110.)

Morris, A. C., Jr.; Barclay, T. R. and Lushbaugh, C. C. "Monitoring physiological responses during total-body irradiation therapy." Physics of Medicine and Biology 15:192 (1970). (Abstract.)

Nelson, B. "Postmortem studies of radionuclides in man." In U.S. Atomic Energy Commission Symposium Series no. 20, CONF-691212, pp. 103-13. Washington, D.C.: U.S. Atomic Energy Commission, 1970.

1113850

Nelson, B., and Kniseley, R. M. "Marrow fibrosis in myeloproliferative disorders." In U.S. Atomic Energy Commission Symposium Series no. 19, CONF-680529, pp. 533-55. Washington, D.C.: U.S. Atomic Energy Commission, 1970.

Pearson, T. A., and Balish, E. "Serum agglutinins and bacteriocidins from irradiated patients." Bacteriological Proceedings 70:111 (1970). (Abstract.)

-----. "Unusual Sphaerophorous species from the large intestine of man." Applied Microbiology 19:458-62 (1970).

Piantadosi, C.; Ishaq, K. S.; and Snyder, F. "Synthesis of O-alkyldihydroxyacetone and derivatives." Journal of Pharmaceutical Sciences 59:1201-2 (1970).

Piantadosi, C., and Snyder, F. "Plasmalogens and related derivaties: their chemistry and metabolism." Journal of Pharmaceutical Sciences 59:283-97 (1970).

Ricks, R. C., and Edwards, C. L. "The effect of dose rate and exposure fractionation on plasma iron kinetics in rats and man." Radiation Research 43:240-41 (1970). (Abstract.)

Ricks, R. C.; Lushbaugh, C. C.; and Frome, E. "Changes in the power spectrum of the impedance pneumograph trace during radiation-induced gastro-intestinal distress in man." Federation of American Societies for Experimental Biology. Federation Proceedings 29:45 (1970). (Abstract.)

Sansone, G.; Swartzendruber, D. C.; and Snyder, F. "Inclusions in mitochondria of preputial glands from mice: A combined biochemical and morphologic study." Biochimica et Biophysica Acta 201:401-9 (1970).

1113851

Snyder, F. Lipids and cancer, a bibliography: 1947-1970. Washington, D.C.: U.S. Atomic Energy Commission, 1970. (ORAU-111.)

-----. "Liquid scintillation radioassay of thin-layer chromatograms." In Proceedings of the International Symposium on the Current Status of Liquid Scintillation Counting; E. D. Bransome, ed.; pp. 533-55. New York: Grune and Stratton, 1970.

-----. "Thin-layer radiochromatography and related procedures." In Progress in Thin-layer Chromatography and Related Methods, A. Niederwieser and G. Pataki, eds.; vol. 1, pp. 52-73. Ann Arbor, Michigan: Humphrey Science Publishers, 1970.

Snyder, F.; Blank, M. L.; and Malone, B. "Requirement of cytidine derivatives in the biosynthesis of O-alkyl phospholipids." Journal of Biological Chemistry 245:4016-18 (1970).

Snyder, F.; Blank, M. L.; Malone, B.; and Wykle, R. L. "Identification of O-alkyldihydroxyacetone phosphate, O-alkylhydroxyacetone, and diacyl glyceryl ethers after enzymic synthesis." Journal of Biological Chemistry 245:1800-1805 (1970).

Snyder, F., and Malone, B. "Enzymic interconversion of fatty alcohols and fatty acids." Biochemical and Biophysical Research Communications 41:1382-87 (1970).

Snyder, F.; Malone, B.; and Blank, M. L. "Enzymic synthesis of O-alkyl bonds in glycerolipids." Journal of Biological Chemistry 245:1790-99 (1970).

1113852

Snyder, F.; Malone, B.; and Cumming, R. B. "Synthesis of glycerol ethers by microsomal enzymes derived from fibroblasts (L-M cells) grown in suspension cultures." Canadian Journal of Biochemistry 48:212-15 (1970).

Snyder, F.; Piantadosi, C.; and Malone, B. "The participation of 1- and 2-isomers of O-alkylglycerols as acyl acceptors in a cell-free system." Biochimica et Biophysica Acta 202:244-49 (1970).

Snyder, F.; Rainey, W. T., Jr.; Blank, M. L.; and Christie, W. H. "The source of oxygen in the ether bond of glycerolipids: ^{18}O studies." Journal of Biological Chemistry 245:5853-56 (1970).

Soodsma, J. F. "In vitro studies on the oxidative cleavage of alkyl glyceryl esters by rat liver." Federation of American Societies for Experimental Biology 29:931 (1970). (Abstract.)

Soodsma, J. F.; Piantadosi, C.; and Snyder, F. "The biocleavage of alkyl glyceryl ethers in Morris hepatomas and other transplantable neoplasms." Cancer Research 30:309-11 (1970).

Swartzendruber, D. C. "Electron microscopic studies of lymphoid germinal centers." In XIII International Congress of Hematology, p. 398. Munich: J. F. Lehmanns Verlag, 1970. (Abstract.)

Swartzendruber, D. C.; Byrd, B. L.; Hayes, R. L.; Nelson, B.; and Tyndall, R. L. "Preferential localization of gallium-67 citrate in tissues of leukemic mice." Journal of the National Cancer Institute 44:695-700 (1970).

1113853

Swartzendruber, D. C.; Hayes, R. L.; and Nelson, B. "Subcellular localization of gallium-67 by high resolution radioautography." Journal of Cell Biology 47:207a-8a (1970). (Abstract.)

Vodopick, H.; Rupp, E. M.; and Gengozian, N. "An in vitro histocompatibility test in a search for tumour antigen." In In Vitro Procedures with Radioisotopes in Medicine, pp. 199-208. Vienna: International Atomic Energy Agency, 1970.

Winchell, H. S.; Sanchez, P. D.; Watanabe, C. K.; Hollander, L.; Anger, H. O.; McRae, J.; Hayes, R. L.; and Edwards, C. L. "Visualization of tumors in humans using ^{67}Ga-citrate and the Anger whole-body scanner, scintillation camera and tomographic scanner." Clinical Research 18:145 (1970). (Abstract.) Also in Journal of Nuclear Medicine 11:378 (1970). (Abstract.) And Journal of Nuclear Medicine 11:459-66 (1970).

Wood, R. "Plasma membranes: structural analyses of neutral lipids and phospholipids of rat liver." Archives of Biochemistry and Biophysics 141:174-82 (1970).

-----. "Tumor lipids: identification of sterol ester species in Ehrlich ascites cells." Cancer Research 30:151-54 (1970).

Wood, R.; Anderson, N. G.; and Swartzendruber, D. C. "Tumor lipids: characterization of the lipids isolated from membranous material." Archives of Biochemistry and Biophysics 141:190-97 (1970).

Wood, R., and Harlow, R. D. "Tumor lipids: carbon number distribution of triglycerides and glyceryl ether diesters." Lipids 5:776-81 (1970).

1113854

-----. "Tumor lipids: structural analyses of the phospholipids." Archives of Biochemistry and Biophysics 141:183-89 (1970).

Wood, R., and Healy, K. "Liberation of aldehydes from alk-1-enyl-glyceryl ethers by acid hydrolysis." Lipids 5:661-63 (1970).

-----. "Tumor lipids: biosynthesis of plasmalogens." Biochemical and Biophysical Research Communications 38:205-11 (1970). Also in Journal of the American Oil Chemists' Society 47:79A (1970). (Abstract.) And in Journal of Biological Chemistry 245:2640-48 (1970).

Wood, R.; Walton, M.; Healy, K.; and Cumming, R. B. "Plasmalogen biosynthesis in Ehrlich ascites cells grown in tissue culture." Journal of the American Oil Chemists' Society 47:79A (1970). (Abstract.) Also in Journal of Biological Chemistry 245:4276-85 (1970).

Wykle, R. L.; Blank, M. L.; Piantadosi, C.; and Snyder, F. "Identification of intermediaries in the biosynthesis of O-alkyl-linked lipids." Federation of American Societies for Experimental Biology. Federation Proceedings 29:674 (1970). (Abstract.)

Wykle, R. L.; Blank, M. L.; and Snyder, F. "The biosynthesis of plasmalogens in a cell-free system." Federation of European Biochemical Societies. FEBS Letters 12:57-60 (1970).

Wykle, R. L., and Snyder, F. "Biosynthesis of an O-alkyl analogue of phosphatidic acid and O-alkyl glycerols via O-alkyl ketone intermediates by microsomal enzymes of Ehrlich ascites tumor." Journal of Biological Chemistry 245:3047-58 (1970).

1113855

MEDICAL 1971

Andrews, G. A. "Book review: Myeloproliferative Disorders of Animals and Man." Health Physics 21:342 (1971).

-----. "Total-body irradiation." In Primer of Radiology, R. J. Schulz, ed.; pp. 61-72. New York: GAF Corporation, 1971.

Andrews, G. A., and Haywood, F. F. "Clinical and Biological consequences of nuclear explosions." Practitioner 207:331-42 (1971).

Beck, W. L., Jr. K-shell ionization cross section for AG and L-shell ionization cross sections for Au, Bi, and U for protons from 1.0 to 5.0 MeV. Master's Thesis, University of Tennessee, 1971.

Beck, W. L., Jr.; Cloutier, R. J.; and Watson, E. E. "High-dose monitoring of personnel with film and thermoluminescent dosimetry." Health Physics 21(6):58 (1971). (Abstract.)

Beck, W. L., Jr.; Stokes, T. R.; Cloutier, R. J.; and Lushbaugh, C. C. "Dosimetry for clinical total-body irradiation." Physics of Medicine and Biology 16:165 (1971). (Abstract.)

Bell, O. E., Jr.; Blank, M. L.; and Snyder, F. "The incorporation of ^{18}O and ^{14}C from long-chain alcohols into the alkyl and alk-1-enyl ethers of phospholipids of developing rat brain." Biochimica et Biophysica Acta 231:579-83 (1971).

1113856

Blank, M. L.; Cress, E. A.; and Snyder, F. "The metabolism of fatty acids and fatty alcohols in fibroblasts (L-M cells) grown as monolayers." Journal of the American Oil Chemists' Society 48:100A (1971). (Abstract.)

Blank, M. L.; Cress, E. A.; Stephens, N.; and Snyder, F. "On the Analysis of long-chain alkane diols and glycerol ethers in biochemical studies." Journal of Lipid Research 12:638-40 (1971).

Blank, M. L.; Wykle, R. L.; and Snyder, F. "Enzymic synthesis of ethanolamine plasmalogens from an O-alkyl glycerolipid." Federation of European Biochemical Societies. FEBS Letters 18:92-94 (1971).

Brewen, J. G., and Gengozian, N. "Radiation-induced human chromosome aberrations: II. Human in vitro irradiation compared to in vivo irradiation of marmoset leukocytes." Mutation Research 13:383-91 (1971).

Carlson, D. E., and Gengozian, N. "The effect of acute radiation exposure rates on formation of hemagglutinating antibody in mice." Journal of Immunology 106:1353-62 (1971).

Carlton, J. E., and Hayes, R. L. "Rapid separation of generator-produced gallium-68 from EDTA eluate." International Journal of Applied Radiation and Isotopes 22:44-45 (1971).

Chaskes, S., and Kingdon, C. "Immunoglobulins (I G, I_gA and I_gM) in irradiated humans." Bacteriological Proceedings 71:73 (1971). (Abstract.)

1113857

Cloutier, R. J. "Book review: Protection in the management of patients who have received therapeutic amounts of radionuclides." Health Physics 21:343-44 (1971).

Cloutier, R. J., and Berger, J. D. "Health physics practices in laboratories using ^{3}H- and ^{14}C-labeled tracers." Journal of the American Oil Chemists' Society 48:330A (1971). (Abstract.)

Cloutier, R. J.; Watson, E. E.; Hayes, R. L.; and Nelson, B. "Radiation doses from isotopes of gallium." Journal of Nuclear Medicine 12:348 (1971). (Abstract.)

Edwards, C. L., and Hayes, R. L. "^{67}Ga for scanning and staging tumors." Journal of Nuclear Medicine 12:355 (1971). (Abstract.)

Edwards, C. L.; Hayes, R. L.; Ominsky, S.; Byrd, B. L.; and Rafter, J. J. "Intralymphatic injection of ^{67}Ga for visualizing abdominal lymph nodes." Journal of Nuclear Medicine 12:431 (1971). (Abstract.)

Gengozian, N. "Male and female cell populations in the chimeric marmoset." In Medical Primatology, 1970; E. I. Goldsmith and J. Moor-Janowski, eds.; pp. 926-38. Basel: S. Karger, 1971.

Gengozian, N.; Congdon, C. C.; Allen, E. A.; and Toya, R. E. "Immune status of allogeneic radiation chimeras." Transplantation Proceedings 3:434-36 (1971).

Gengozian, N., and Hübner, K. "'In situ' visualization of a graft-vs-host reaction." Journal of Immunology 106:1159-65 (1971).

1113858

Gengozian, N., and Porter, R. P. "Transplantation immunology in the marmoset." In Medical Primatology, 1970; E. I. Goldsmith and J. Moor-Jankowski, eds.; pp. 165-75. Basel: S. Karger, 1971.

Goh, K. O. "Choramphenicol, acute leukemia and chromosomal vacuolization." Southern Medical Journal 64:815-19 (1971).

-----. "Total body irradiation and human chromosomes: II. Cytogenetic studies of the cultured bone marrow cells seven years after total body irradiation." American Journal of Medical Science 262:43-49 (1971).

Goh, K. O., and Heusinkveld, R. S. "Contributions of cytogenetics to hematology." In Hematology for Internists; R. I. Weed, ed.; pp. 275-85. Boston: Little, Brown, 1971.

Goswitz, F.; Nelson, B.; Vodopick, H.; and Lushbaugh, C. "Human marrow changes after treatment with low-dose-rate total-body irradiation." Journal of Nuclear Medicine 12:359, (1971). (Abstract.)

Grigor, M. R.; Blank, M. L.; and Snyder, F. "Structural relationships between glycerides of pig serum and adipose tissue." Lipids 6:965-68 (1971).

Hagen, P. O. "The effect of low temperatures on microorganisms: conditions under which cold becomes lethal." In Inhibition and Destruction of Microbial Cells; W. B. Hugo, ed.; pp. 39-74. New York: Academic Press, 1971.

Hayes, R. L.; Byrd, B. L.; Carlton, J. E.; and Rafter, J. J. "Effect of scandium on the distribution of ^{67}Ga in tumor-bearing animals." Journal of Nuclear Medicine 12:437-38 (1971). (Abstract.)

1113859

Hayes, R. L.; Nelson, B.; Swartzendruber, D. C.; Brown, D. H.; Carlton, J. E.; and Byrd, B. L. "Studies of the intracellular deposition of ^{67}Ga." Journal of Nuclear Medicine 12:364 (1971). (Abstract.)

Kraus, L. M.; Rasad, A.; and Lushbaugh, C. C. "Fast moving hemoglobin (Hb) in C57BL/Cum mice: induced by continuous low level irradiation." In Abstracts of Papers, number 309. Washington, D.C.: American Chemical Society, 1971.

Lee, T.-C., and Snyder, F. "The measurement of lipid turnover in membranes by a double isotope technique." Journal of the American Oil Chemists' Society 48:330A (1971). (Abstract.)

Littlefield, L. G.; Goh, K. O.; Klepper, M. B.; and Joiner, E. E. "Chromosome breakages in women taking oral contraceptives: a two year study." In Fourth International Congress of Human Genetics, Paris 1971, Abstracts of Papers Presented, p. 113. Amsterdam: Excerpta Medica, 1971. (Abstract.)

Lumb, R. H., and Snyder, F. "A rapid isotopic method for assessing the biosynthesis of ether linkages in glycerolipids of complex systems." Biochimica et Biophysica Acta 244:217-21 (1971).

Lushbaugh, C. C.; Stokes, T. R.; and Corrill, L. S. "Dose-rate dependence of mouse endogenous splenic colony formation and proliferation during continuous and fractionated daily irradiation at low exposure rates." Radiation Research 47:344 (1971). (Abstract.)

1113860

McDow, A. E., Jr., and Ricks, R. C. "Uses of a time-shared computer in quantitative nuclear medicine." In U.S. Atomic Energy Commission Report CONF-710425, pp. 155-67. Washington, D.C.: U.S. Atomic Energy Commission, 1971.

Mardon, D. N.; Hurst, S. K.; and Balish, E. "Germ-tube production by Candida albicans in minimal liquid culture media." Canadian Journal of Microbiology 17:851-56 (1971).

Medical Division, Oak Ridge Associated Universities. Research report, 1970, for the year ending December 31, 1970. Oak Ridge, Tennessee: ORAU, 1971. (ORAU 113.)

Morris, A. C., Jr.; Barclay, T. R.; Tanida, R.; and Nemcek, J. V. "A miniaturized probe for detecting radioactivity at thyroid surgery." Physics of Medicine and Biology 16:397-404 (1971).

Nelson, B.; Hayes, R. L.; Edwards, C. L.; Kniseley, R. M.; and Andrews, G. A. "Distribution of ^{67}Ga in human tissues at autopsy." Journal of Nuclear Medicine 12:452 (1971). (Abstract.)

Otten, J. A.; Tyndall, R. L.; Estes, P. C.; and Swartzendruber, D. C. "Localization of gallium-67 citrate during embryogenesis." Proceedings of the American Association for Cancer Research 12:41 (1971). (Abstract.)

Piantadosi, C.; Ishaq, K. S.; Wykle, R. L.; and Snyder, F. "Synthesis and characterization of 1-O-alkyldihydroxy-acetone phosphates and derivatives." Biochemistry 10:1417-21 (1971).

Savage, N., and Balish, E. "Morphology, physiology, and virulence of some mutants of Candida albicans." Infection and Immunity 3:141-48 (1971).

1113861

Snyder, F. "The chemistry, physical properties, and chromatography of lipids containing ether bonds." In Progress in Thin-layer Chromatography and Related Methods, vol. 2, pp. 105-41. Ann Arbor, Michigan: Ann Arbor Science Publishers, 1971.

-----. "Glycerolipids in the neoplastic cell: methodology, metabolism, and composition." In Methods in Cancer Research vol. 4, pp. 399-436. New York: Academic Press, 1971.

Snyder, F.; Blank, M. L.; and Wykle, R. L. "The enzymic synthesis of ethanolamine plasmalogens." Journal of Biological Chemistry 246:3639-45 (1971).

Snyder, F.; Hibbs, M.; and Malone, B. "Enzymic synthesis of O-alkyl glycero-lipids in brain and liver of rats during fetal and postnatal development." Biochimica et Biophysica Acta 231:409-11 (1971).

Snyder, F., and Malone, B. "The biosynthesis of wax esters: enzymic interconversions of fatty acids and fatty alcohols." Journal of the American Oil Chemists' Society 48:85A (1971). (Abstract.)

Snyder, F., and Moehl, A. "Mass measurement in a liquid scintillation spectrometer: quantitation of sulfhydryl moieties in color quenching." In Organic Scintillators and Liquid Scintillation Counting; D. L. Harrocks and C.-T. Peng, eds.; pp. 419-24. New York: Academic Press, 1971.

Snyder, W. S.; Cloutier, R. J.; and Smith, S. "Dose to a developing fetus from a gamma emitter in the bladder." In U.S. Atomic Energy Commission Report ORNL 4720, pp. 119-20. Washington, D.C.: U.S. Atomic Energy Commission, 1971.

1113862

Swartzendruber, D. C., and Hübner, K. F. "Effect of irradiation on ^{67}Ga distribution in mouse tissues." In American Society for Cell Biology, Eleventh Annual Meeting, Abstracts of Papers, p. 296. 1971. (Abstract.)

Swartzendruber, D. C.; Nelson, B.; and Hayes, R. L. "Gallium-67 localization in lysomal-like granules of leukemic and nonleukemic murine tissues." Journal of the National Cancer Institute 46:941-52 (1971).

Wykle, R. L.; Blank, M. L.; and Snyder, F. "The enzymic synthesis of ethanolamine plasmalogens." Federation of American Societies for Experimental Biology. Federation Proceedings 30:1243 (1971). (Abstract.)

1113863

MEDICAL 1972

Barclay, T. R.; Morris, A. C., Jr.; and McDow, A. E., Jr. "Gamma-camera-to-computer interfacing--the easy way." In U.S. Atomic Energy Commission Report CONF-720430, pp. 369-75. Washington, D.C.: U.S. Atomic Energy Commission, 1972.

Beck, W. L.; Stokes, T. R.; and Lushbaugh, C. C. "Dosimetry for radiobiological studies of the human hematopoietic system." In NASA Report NASA TM X-2440, pp. 974-80. Washington, D.C.: U.S. National Aeronautics and Space Administration, 1972.

Beck, W. L.; Stokes, T. R.; and Wade, L., Jr. "Dosimetry for total-body irradiation accident." Health Physics 23:419 (1972). (Abstract.)

Berger, J. D. "Book review: Radiological Physics Examination Review Book." Health Physics 23:259 (1972).

Berger, J. D., and Cloutier, R. J. "Health physics practices in laboratories using ^{3}H- and ^{14}C-labeled tracers." Lipids 7:604-10 (1972).

Blank, M. L.; Kasama, K.; and Snyder, F. "Isolation and identification of an alkyldiacylglycerol containing isovaleric acid." Journal of Lipid Research 13:390-95 (1972).

Blank, M. L.; Wykle, R. L.; and Snyder, F. "The biosynthesis of ethanolamine plasmalogens by a postmitochondrial fraction from rat brain." Biochemical and Biophysical Research Communications 47:1203-8 (1972).

1113864

Brewen, J. G.; Preston, R. J.; and Littlefield, L. G. "Radiation-induced human chromosome aberration yields following an accidental whole-body exposure to ^{60}Co γ-rays." Radiation Research 49:647-56 (1972).

Brown, D. H.; Swartzendruber, D. C.; Carlton, J. E.; Byrd, B. L.; and Hayes, R. L. "Mechanism of gallium-binding in tumors: isolation and characterization of gallium-binding granules (GBG) in soft tissue tumors." Proceedings of the American Association for Cancer Research 13:37 (1972). (Abstract.)

Cloutier, R. J. "Health physics education and training: past, present, and future." In Health Physics Operational Monitoring, vol. 3, pp. 1305-44. New York: Gordon and Breach, 1972.

Duggan, J. L.; Beck, W. L.; Albrecht, L.; Munz, L.; and Spaulding, J. D. "Studies of x rays induced by charged particles." Advances in X-Ray Analysis 15:407-23 (1972).

Edwards, C. L., and Hayes, R. L. "Localization of tumors with radioisotopes." In U.S. Atomic Energy Commission Symposium Series no. 27, CONF-711101, pp. 618-39. Washington, D.C.: U.S. Atomic Energy Commission, 1972.

Edwards, C. L.; Hayes, R. L.; and Nelson, B. "The 'normal' ^{67}Ga scan." Journal of Nuclear Medicine 13:428-29 (1972). (Abstract.)

Gengozian, N. "A blood factor in the marmoset, Saguinus fuscicollis: its detection, mode of inheritance, and species specificity." Journal of Medical Primatology 1:272-86 (1972).

1113865

-----. "Inter- and intrasubspecies red cell immunizations in the marmoset, Saguinus fuscicollis ssp." Journal of Medical Primatology 1:172-92 (1972).

Goswitz, F. A. "Bone marrow imaging." In Continuing Education Lectures, 1972, pp. 10/1-10/15. Atlanta: Southeastern Chapter, Society of Nuclear Medicine, 1972.

-----. "Book review: Manual of Nuclear Medicine Procedures." Annals of Internal Medicine 76:1057-58 (1972).

Goswitz, F. A.; Andrews, G. A.; and Viamonte, M.; eds. Clinical uses of radionuclides: critical comparison with other techniques. U.S. Atomic Energy Commission Symposium Series no. 27, CONF-711101. Washington, D.C.: U.S. Atomic Energy Commission, 1972.

Goswitz, F.; Morris, A.; McDow, A.; Kim, K.; and Hodges, H. "A computer-interfaced four-probe counter and its application to a dynamic radiocolloid study." Journal of Nuclear Medicine 13:433 (1972). (Abstract.)

Goswitz, F. A., and Vodopick, H. A. "Dynamic radioisotopic studies in clinical hematology." In U.S. Atomic Energy Commission Symposium Series no. 27, CONF-711101, pp. 293-312. Washington, D.C.: U.S. Atomic Energy Commission, 1972.

Gottlieb, C. F., and Gengozian, N. "The humoral immune response in mice after neutron or x-irradiation at different dose rates." Journal of Immunology 109:711-18 (1972).

Gottlieb, C. F., and Gengozian, N. "Radiation dose, dose rate, and quality in suppression of the humoral immune response." Journal of Immunology 109:719-27 (1972).

1113866

Grigor, M. R.; Moehl, A.; and Snyder, F. "Occurrence of ethanolamine- and choline-containing plasmalogens in adipose tissue." Lipids 7:766-68 (1972).

Grigor, M. R.; Pratt, R. D.; and Snyder, F. "Acylation of cholesterol by microsomal enzymes from mouse preputial gland tumors." Archives of Biochemistry and Biophysics 150:371-75 (1972).

Hershman, J. M., and Edwards, C. L. "Serum thyrotropin (TSH) levels after thyroid ablation compared with TSH levels after exogenous bovine TSH: implications for ^{131}I treatment of thyroid carcinoma." Journal of Clinical Endocrinology and Metabolism 34:814-18 (1972).

Humason, G. L. Animal Tissue Techniques, 3rd edition. San Francisco: W. H. Freeman, 1972.

Kniseley, R. M. "Marrow studies with radiocolloids." Seminars in Nuclear Medicine 2:71-85 (1972).

Kniseley, R. M., and Goswitz, F. A. "Radiocolloid scanning." In U.S. Atomic Energy Commission Symposium Series no. 27, CONF-711101, pp. 293-312. Washington, D.C.: U.S. Atomic Energy Commission, 1972.

Lee, T.-C.; Piantadosi, C.; and Snyder, F. "The subcellular distribution of ether lipids in tumors." Proceedings of the American Association for Cancer Research 13:58 (1972). (Abstract.)

Littlefield, L. G. "An abnormal cell-line in a patient with acute granulocytic leukemia." Cancer 29:1281-86, (1972).

1113867

Lushbaugh, C. C. "Predicted levels of human radiation tolerance extrapolated from clinical studies of radiation effects." In Report NASA TM X-2440, pp. 398-415. Washington, D.C.: U.S. National Aeronautics and Space Administration, 1972.

Lushbaugh, C. C., and Ricks, R. C. "Some cytokinetic and histopathologic considerations of irradiated male and female gonadal tissues." In Frontiers of Radiation Therapy and Oncology, vol. 6, pp. 228-48. Basel: Karger, 1972.

McDow, A. E., Jr. "Code conversion by computer." In U.S. Atomic Energy Commission Report CONF-720430, pp. 335-41. Washington, D.C.: U.S. Atomic Energy Commission, 1972.

Medical Division, Oak Ridge Associated Universities. Research report, 1971, for the year ending December 31, 1971. Oak Ridge, Tennessee: ORAU, 1972. (ORAU-116.)

Morris, A. C., Jr.; Barclay, T. R.; Tanida, R.; and Nemcek, J. V. Design specifications for a miniaturized surgical probe. Washington, D.C.: U.S. Atomic Energy Commission, 1972. (ORAU-115.)

Morris, A. C., Jr.; Goswitz, F. A.; Kim, K. A.; McDow, A. E., Jr.; Aaron, P. A.; and Barclay, T. R. "Rapid analysis of dynamic radionuclide functions using the on-line computer." Journal of the Association for the Advancement of Medical Instrumentation 6:180 (1972).

Nelson, B.; Hayes, R. L.; Edwards, C. L.; Kniseley, R. M.; and Andrews, G. A. "Distribution of gallium in human tissues after intravenous administration." Journal of Nuclear Medicine 13:92-100 (1972).

1113868

Piantadosi, C.; Chae, K.; Ishaq, K. S.; and Snyder, F. "Synthesis of acyl dihydroxyacetone phosphates and related derivatives." Journal of Pharmaceutical Sciences 61:971-74 (1972).

Piantadosi, C.; Ishaq, K. S.; Blank, M. L.; and Snyder, F. "Synthesis of 1-O-alkyl-3-O-phosphorylethanolamine-2-propanone and related derivatives." Journal of Pharmaceutical Sciences 61:607-10 (1972).

Porter, R. P., and Gengozian, N. "In vitro proliferation and differentiation of hemic precursor cells from marrow and blood of naturally chimeric marmosets." Journal of Cellular Physiology 79:27-41 (1972).

-----. "Megakaryocytes cultured from blood lymphocytes of naturally chimeric marmosets." Blood 40:588-89 (1972). (Abstract.)

Ricks, R. C.; Lushbaugh, C. C.; and McDow, A. E., Jr. "Correlation of heart rate and CO_2 production with pulmonary impedance during exercise stress in man." Federation of American Societies for Experimental Biology. Federation Proceedings 31:311 (1972). (Abstract.)

-----. "Pulmonary impedance power spectral analysis: its correlation with heart rate and expired CO_2 during exercise stress in man." Journal of the Association for the Advancement of Medical Instrumentation 6:186 (1972). (Abstract.)

1113869

Ricks, R. C.; Lushbaugh, C. C.; McDow, A. E., Jr.; and Frome, E. "Pulmonary-impedance power spectral analysis: a facile means of detecting radiation-induced gastrointestinal distress and performance decrement in man." In Report NASA TM X-2440, pp. 238-48. Washington, D.C.: U.S. National Aeronautics and Space Administration, 1972.

Shively, J. M.; Brown, D. H.; Ball, F. L.; Caton, J. E.; Phares, E. F.; Brantley, J. N.; and Breillat, J. P. "Partial characterization of the polyhedral inclusion bodies of Thiobacillus neopolitanus." In U.S. Atomic Energy Commission Report ORNL-4771, pp. 182-84. Washington, D.C.: U.S. Atomic Energy Commission, 1972.

Snyder, F. "Enzymatic systems that synthesize and degrade glycerolipids possessing ether bonds." Advances in Lipid Research 10:233-59 (1972).

-----. "The enzymic pathways of ether-linked lipids and their precursors." In Ether Lipids: Chemistry and Biology; F. Snyder, ed.; pp. 121-56. New York: Academic Press, 1972.

-----. "Ether-linked lipids and fatty alcohol precursors in neoplasms." In Ether Lipids: Chemistry and Biology; F. Snyder, ed.; pp. 273-95. New York: Academic Press, 1972.

Snyder, F.; Wykle, R. L.; Blank, M. L.; Lumb, R. H.; Malone, B.; and Piantadosi, C. "Enzymic pathways for ether lipids." Federation of American Societies for Experimental Biology 31:454 (1972). (Abstract.)

Snyder, F., ed. Ether Lipids: Chemistry and Biology. New York: Academic Press, 1972.

1113870

Soodsma, J. F.; Piantadosi, C.; and Snyder, F. "Partial characterization of the alkylglycerol cleavage enzyme system of rat liver." Journal of Biological Chemistry 247:3923-29 (1972).

Stokes, T. R.; Lushbaugh, D.; Humason, G.; and Lushbaugh, C. C. "^{59}Fe studies on the erythroblastic response of normal and splenectomized mice to low level continuous radiation." Radiation Research 51:472-73 (1972). (Abstract.)

Swartzendruber, D. C., and Mateer, H. "Ultrastructural identification of intracellular lead by x-ray analysis on a scanning electron microscope." Journal of Cell Biology 55:255a (1972). (Abstract.)

Urso, P., and Gengozian, N. "Functional capacity of T, B, and A cells in allogeneic radiation chimeras." In Fourth International Congress of the Transplantation Society, Collected Abstracts, p. 300. New York: Grune & Stratton, 1972. (Abstract.)

Vodopick, H.; Rupp, E. M.; Edwards, C. L.; Goswitz, F. A.; and Beauchamp, J. J. "Spontaneous cyclic leukecytosis and thrombocytosis in chronic granulocytic leukemia." New England Journal of Medicine 286:204-90 (1972).

Watson, E. E.; Cloutier, R. J.; and Gibbs, W. "Whole body retention of gallium-67 citrate." Southern Medical Journal 65:1417 (1972). (Abstract.)

Webb, A. M. "Semiautomated determination of thyroxine (T_4) iodine." In Standard Methods of Clinical Chemistry, vol. 7, pp. 261-66. New York: Academic Press, 1972.

1113871

Wykle, R. L.; Blank, M. L.; Maline, B.; and Snyder, F. "Evidence for a mixed function oxidase in the biosynthesis of ethanolamine plasmalogens from 1-alkyl-2-acyl-Sn-glycero-3-phosphorylethanolamine." Journal of Biological Chemistry 247:5442-47 (1972).

Wykle, R. L.; Piantadosi, C.; and Snyder, F. "The role of acyldihydroxyacetone phosphate, reduced nicotinamide adenine dinucleotide, and reduced nicotinamide adenine dinucleotide phosphate in the biosynthesis of 0-alkyl glycerolipids by microsomal enzymes of Ehrlich ascites tumor." Journal of Biological Chemistry 247:2944-48 (1972).

Yuhas, J. M.; Stokes, T. R.; and Lushbaugh, C. C. "Multifactorial analysis of human blood cell responses to clinical total body irradiation." In NASA Report NASA TM X-2440, pp. 233-37. Washington, D.C.: U.S. National Aeronautics and Space Administration, 1972.

Yuhas, J. M.; Stokes, T. R.; and Lushbaugh, C. C. "Radiosensitivity and recovery potential of human blood-forming tissues." Radiology 105:641-44 (1972).

Zucker, S., and Webb, A. M. "Assay of muramidase activity in serum, plasma, or urine." In Standard Methods of Clinical Chemistry, vol. 7, pp. 9-17. New York: Academic Press, 1972.

1113872

SPECIAL TRAINING 1972

Collins, C. J.; Glover, I. T.; Eckart, M. D.; Raaen, V. F.; Benjamin, R. B.; and Benjamininov, B. S. "Molecular rearrangements. XXVII. Nitrous acid deamination of 3-exo-phenyl-3-hydroxy and 3-endo-phyenyl-3-hydroxy-2-endo-norbornylamines." Journal of the American Chemical Society 94:899 (1972).

Duggan, J. L.; Beck, W. L.; Albrecht, L.; Munz, L.; and Spaulding, J. D. "Studies of x-rays induced by charged particles." Advances in X-ray Analysis 15:407-23 (1972).

Duggan, J. L.; Carlton, R. F.; and Lin, J. "Cross sections for x-ray production via alpha particle bombardment." Bulletin of the American Physical Society 17:89 (1972).

Duggan, J. L.; Humphrey, D. L.; and Lin, J. "Ionization cross sections of As, Se, and Au for alpha particles from 1.5 to 12 MeV and Ag and Au for protons from 1 to 6 MeV." Bulletin of the American Physical Society 17:499 (1972).

Duggan, J. L.; Lin, J.; and Carlton, R. F. "X-ray production cross sections via proton and alpha bombardment." In Proceedings of the International Conference on Inner Shell Ionization Phenomena, Atlanta, Georgia, 1972. 1972.

Duggan, J. L.; Lin, J.; and Liu, H. H. "K shell ionization cross sections for Fe, Ni, Cu, Ge, Rb, and Zr for protons from 1 to 6 MeV." Bulletin of the American Physical Society 17:202 (1972).

Duggan, J. L.; Lin, J.; and Miller, P. D. "A study of the $^{11}B(^{3}He, \alpha)^{10}B$ reaction at 8, 10, and 12 MeV." Bulletin of the American Physical Society 17:112. (1972).

1113873

MEDICAL 1973

Akers, K. K.; Beck, W. L., Jr.; Cloutier, R. J.; and Dickson, H. W. "Health physics training at Oak Ridge Associated Universities." In DHEW Publication FDA 3-8029, pp. 281-87. Washington, D.C.: Department of Health, Education, and Welfare, 1973.

Andrews, G. A. "Book review: Biochemical Indicators of Radiation Injury in Man." Health Physics 24:455-56 (1973).

Andrews, G. A.; Gibbs, W. D.; Morris, A. C., Jr.; and Ross, D. A. "Whole-body counting." Seminars in Nuclear Medicine 3:367-88 (1973).

Bailey, O. T.; Benton, E. V.; Cruty, M. R.; Harrison, G. A.; Haymaker, W.; Humason, G.; Leon, H. A.; Lindberg, R. L.; Look, B. C.; Lushbaugh, C. C.; Philpott, D. E.; Samorajski, T.; Simmonds, R. C.; Suri, K. P.; Tremor, J. W.; Turnbill, C. E.; Vogel, F. S.; Winter, D. L.; and Zeman, W. "Biocore experiment." In Apollo 17 Preliminary Science Report, NASA Report SP-330. Washington, D.C.: U.S. National Aeronautics and Space Administration, 1973.

Barber, L. R.; Cloutier, R. J.; and Watson, E. E. Effective absorbed energies. Washington, D.C.: U.S. Atomic Energy Commission, 1973. (ORAU-120.)

Barclay, T. R.; Morris, A. C., Jr.; and Lucas, J. P. "A universal, solid-state attachment for the computer recording of rectilinear scanning data." In U.S. Atomic Energy Commission Report CONF-730627, pp. 183-89. Washington, D.C.: U.S. Atomic Energy Commission, 1973.

1113874

Beck, W. L.; Cloutier, R. J.; and Watson, E. E. "Personnel monitoring with film and thermoluminescent dosimeters for high exposures." Health Physics 25:421-25 (1973).

Beck, W. L.; Stokes, T. R.; and Lushbaugh, C. C. "Dosimetry for total-body irradiation therapy." In DHEW Publication FDA 73-8029, p. 423. Washington, D.C.: U.S. Department of Health, Education, and Welfare, 1973.

Bell, P. R.; McClain, W. J.; Ross, D. A.; McKeighen, R. E.; East, J. K.; Moore, E. C.; Edwards, C. L.; and Goswitz, F. A. A computer-based scanning system. Washington, D.C.: U.S. Atomic Energy Commission, 1973. (ORNL-TM-4038.)

Blank, M. L., and Snyder, F. "Ether-linked glycerol lipids: detection and identification of labeled intermediates and products formed in enzymic systems." Journal of the American Oil Chemists' Society 50:91A (1973). (Abstract.)

Blank, M. L.; Wykle, R. L.; and Snyder, F. "The retention of arachidonic acid in ethanolamine plasmalogens of rat tests during essential fatty acid deficiency." Biochimica et Biophysica Acta 316:28-34 (1973).

Brown, D. H.; Byrd, B.; Rafter, J.; and Hayes, R. L. "Subcellular localization of ^{67}Ga in rat hepatoma and normal host liver." Southern Medical Journal 66:1331-32 (1973). (Abstract.)

Brown, D. H.; Carlton, E.; Byrd, B.; Harrell, B.; and Hayes, R. L. "A rate-zonal centrifugation procedure for screening particle populations by sequential product recovery utilizing edge-unloading zonal rotors." Archives of Biochemistry and Biophysics 155:9-18 (1973).

1113875

Brown, D. H.; Swartzendruber, D. C.; Carlton, J. E.; Byrd, B. L.; and Hayes, R. L. "The isolation and characterization of gallium-binding granules from soft tissue tumors." Cancer Research 33:2063-67 (1973).

Chae, K.; Piantadosi, C.; and Snyder, F. "An alternate enzymic route for the synthesis of alkyl analog of phosphatidic acid involving alkylglycerol." Biochemical and Biophysical Research Communications 51:119-24 (1973).

-----. "Reductase, phosphatase, and kinase activities in the metabolism of alkyldihydroxyacetone phosphate and alkyldihydroxyacetone." Journal of Biological Chemistry 248:6718-23 (1973).

Clapp, N. K.; Tyndall, R. L.; and Cumming, R. B. "Hyperplasia of hepatic bile ducts in mice following long-term administration of butylated hydroxytoluene." Food and Cosmetics Toxicology 11:847-49 (1973).

Cloutier, R. J.; Smith, S. A.; Watson, E. E.; Snyder, W. S.; and Warner, G. G. "Dose to the fetus from radionuclides in the bladder." Health Physics 25:147-61 (1973).

Cloutier, R. J., and Watson, E. E. "Radiation doses from nuclear medicine procedures." In DHEW Publication FDA 73-8029, pp. 71-78. Washington, D.C.: U.S. Department of Health, Education, and Welfare, 1973.

Cloutier, R. J.; Watson, E. E.; Hayes, R. L.; Nelson, B.; and Smith, E. M. "Summary of current radiation dose estimates to humans from ^{66}Ga-, ^{67}Ga-, ^{68}Ga-, and ^{72}Ga-citrate." Journal of Nuclear Medicine 14:755-56 (1973).

1113876

Cloutier, R. J.; Watson, E. E.; Rohrer, R. H.; and Smith, E. M. "Calculating the radiation dose to an organ." Journal of Nuclear Medicine 14:53-55 (1973).

Congdon, C. C.; Payne, H. S.; Gengozian, N.; and Urso, P. "Spleen white pulp blurring in thymectomized radiation chimeras." Federation of American Societies for Experimental Biology. Federation Proceedings 32:870 (1973). (Abstract.)

Fliedner, T. M.; Bruch, C.; Calvo, W.; Flad, H. D.; Herbst, E.; Hügl, E.; Huget, R.; Nelson, B.; and Schnappauf, H. P. "Pattern of early hemopoietic regeneration in lethally irradiated dogs after transfusion of fresh and frozen blood leukocytes." Experimental Hematology 1:282 (1973). (Abstract.)

Fuhr, J. E., and Gengozian, N. "Coordination of heme and globin synthesis in primate reticulocytes." Biochimica et Biophysica Acta 320:48-53 (1973).

Garcia, Ana Maria. Cytogenetic changes in marrow cells from Syrian hamsters exposed to ^{60}Co total-body radiation. Master's thesis, São Paulo University, 1973.

Gengozian, N. "Book review: Primates in Medicine." Journal of Medical Primatology 2:254-55 (1973).

-----. "Book review: Transplantation Genetics of Primates." Journal of Medical Primatology 2:256 (1973).

Gengozian, N., and Congdon, C. C. "Immunological memory in radiation chimeras." Transplantation 16:32-40 (1973).

1113877

Gengozian, N.; Edwards, C. L.; Vodopick, H. A.; and Hübner, K. F. "Bone marrow transplantation in a leukemic patient following immunosuppression with antithymocyte globin and total body irradiation." Transplantation 15:446-54 (1973).

Gengozian, N., and Patton, M. L. "Identification of three blood factors in the marmoset, Saguinus fuscicollis ssp." In Medical Primatology 1972, pp. 349-60. Basel: S. Karger, 1973.

Gibbs, W. D.; Edwards, C. L.; and Hodges, H. D. "Linear scanner instrumentation and data handling." Southern Medical Journal 66:1330 (1973). (Abstract.)

Goh, K. O. "Total-body irradiation and human chromosomes: III. Cytogenetic studies in patients with malignant hematologic diseases treated with total-body irradiation." American Journal of the Medical Sciences 266:179-86 (1973).

Goswitz, F.; Lushbaugh, C.; and Vodopick, H. "Marrow changes in chronic granulocytic leukemia after treatment with total-body irradiation." Blood 42:984 (1973). (Abstract.)

Grigor, M. R., and Bell, I. C., Jr. "Synthesis of fatty acid esters of short-chain alcohols by an acyltransferase in rat liver microsomes." Biochimica et Biophysica Acta 306:26-30 (1973).

Grigor, M. R.; Blank, M. L.; and Snyder, F. "Cholesterol metabolism in rats bearing Morris hepatoma 7777." Cancer Research 33:1870-74 (1973).

Hansard, M. Investigation of the applicability of a digital filtering technique for electrocardiogram analysis. Master's thesis, University of Tennessee, 1973.

1113878

Hayes, R. L., and Byrd, B. L. "Factors influencing the distribution of rare earth radionuclides in normal and neoplastic tissue." Southern Medical Journal 66:1327-28 (1973). (Abstract.)

Hayes, R. L., and Carlton, J. E. "A study of the macromolecular binding of ^{67}Ga in normal and malignant animal tissues." Cancer Research 33:3265-72 (1973).

Hayes, R. L., and Edwards, C. L. "The effect of stable scandium on red blood cells and on the retention and excretion of ^{67}Ga in humans." Southern Medical Journal 66:1339-40 (1973). (Abstract.)

-----. "New applications of tumour-localizing radiopharmaceuticals." In Medical Radioisotope Scintigraphy, 1972, pp. 531-52. Vienna: International Atomic Energy Commission, 1973.

Hayes, R. L.; Rafter, J. J.; Washburn, L. C.; and Byrd, B. L. "Affinity of ^{253}einsteinium for tumor tissue." National News in Biology 246:23-25 (1973).

Hofer, K. G., and Swartzendruber, D. C. "^{67}Ga-citrate and ^{125}I-iododeoxyuradine as markers for in vivo evaluation of tumor cell metastasis and death." Journal of the National Cancer Institute 50:1039-45 (1973).

Huisman, T. H. J.; Schroeder, W. A.; Keeling, M. E.; Gengozian, N.; Miller, A.; Brodie, A. R.; Shelton, J. R.; Shelton, J. B.; and Apell, G. "Search for nonallelic structural genes for γ-chains of fetal hemoglobin in some primates." Biochemical Genetics 10:309-18 (1973).

1113879

Humason, G. "Hemopoietic tissues." In The Encyclopedia of Microscopy and Microtechnique; P. Grey, ed.; pp. 248-49. New York: Van Nostrand Reinhold Co., 1973.

-----. "Leukocytes." In The Encyclopedia of Microscopy and Microtechnique; P. Grey, ed.; pp. 289-92. New York: Van Nostrand Reinhold Co., 1973.

Kasama, K.; Rainey, W. T., Jr.; and Snyder, F. "Chemical identification and enzymatic synthesis of a newly discovered lipid class--hydroxyalkylglycerols." Archives of Biochemistry and Biophysics 154:648-58 (1973).

Kniseley, R. M. Coding index for tumor scanning. Washington, D.C.: U.S. Atomic Energy Commission, 1973. (ORAU-119.)

-----. Cooperative group to study localization of radiopharmaceuticals. Washington, D.C.: U.S. Atomic Energy Commission, 1973. (ORAU-118.)

Lee, T.-C., and Snyder, F. "Phospholipid metabolism in rat liver endoplasmic reticulum: structural analyses, turnover studies, and enzymic activities." Biochimica et Biophysica Acta 291:71-82 (1973).

Lee, T.-C.; Stephens, N.; Moehl, A.; and Snyder, F. "Turnover of rat liver plasma membrane phospholipids: comparison with microsomal membranes." Biochimica et Biophysica Acta 291:86-92 (1973).

Lee, T.-C.; Wykle, R. L.; Blank, M. L.; and Snyder, F. "Dietary control of stearyl CoA and alkylacylglycerophosphoryl-ethanolamine desaturases in tumor." Biochemical and Biophysical Research Communications 55:574-79 (1973).

1113880

Littlefield, L. G., and Goh, K. O. "Cytogenetic studies in control men and women: I. Variations in aberration frequencies in 29,709 metaphases from 305 cultures obtained over a three-year period." Cytogenetics and Cell Genetics 12:17-34 (1973).

Lombardi, M. H.; Beck, W. L., Jr.; and Cloutier, R. J. "Survey of radiopharmaceutical use and safety in sixty-nine hospitals." In DHEW Publication FDA 73-8029, pp. 227-35. Washington, D.C.: U.S. Deprtment of Health, Education, and Welfare, 1973.

Lushbaugh, C. C. "Book review: Manual of Radiation Haematology." Health Physics 24:456 (1973).

-----. "Human radiation tolerance." In Space Radiation Biology and Related Topics; C. A. Tobias and P. Todd, eds.; pp. 475-522. New York: Academic Press, 1973.

Medical Division, Oak Ridge Associated Universities. Research report, 1972, for the year ending December 31, 1972. Oak Ridge, Tennessee: ORAU, 1973. (ORAU-122).

Nelson, B.; Calvo, W.; Herbst, E.; Bruch, C.; Schnappauf, H. P.; and Fliedner, T. "Repopulation of dog lymphnodes after 1200 rads total-body irradiation and I.V. administration of autologous mononuclear blood cells." Experimental Hematology 1:282-83 (1973). (Abstract.)

Nelson, B., and Fliedner, T. M. "Lymphocytopoiesis after irradiation." Fortschritte auf dem Gebiete der Roentgenstrahlen und der Nuclear Medizin, supplement: pp. 290-92. (1973).

1113881

Nelson, B., and Pritchard, B. "Autoradiography with Polariod film." Beitraege zur Pathologie 149:206-10 (1973).

Otten, J. A.; Tyndall, R. L.; Estes, P. C.; Gude, W. D.; and Swartzendruber, D. C. "Localization of gallium-67 during embryogenesis." Proceedings of the Society for Experimental Biology and Medicine 142:92-95 (1973).

Piantadosi, C.; Chae, K.; Ishaq, K. S.; and Snyder, F. "Chemical synthesis of 1- ^{14}C-octadecyldihydroxyacetone phosphate and 1- ^{14}C-octadecyldihydroxyacetone." Journal of Pharmaceutical Sciences 62:320-22 (1973).

Porter, R. P., and Gengozian, N. "Immunological responsiveness and tolerance of marmoset lymphoid tissue in vitro." Transplantation 15:221-30 (1973).

-----. "Marmoset bone marrow." In Methods and Application of Tissue Culture; P. Krause and M. Patterson, eds.; pp. 93-97. New York: Academic Press, 1973.

Shively, J. M.; Ball, F.; Brown, D. H.; and Saunders, R. E. "Functional organelles in prokaryotes: polyhedral inclusions (carboxysomes) of Thiobacillus neapolitanus." Science 182:584-86 (1973).

Snyder, C.; Malone, B.; Nettesheim, P.; and Snyder, F. "Urethan-induced pulmonary adenoma as a tool for the study of surfactant biosynthesis." Cancer Research 33:2437-43 (1973).

Snyder, F. "Radioisotopes--introduction: Detection and chromatographic resolution of labeled lipid intermediaries formed in enzyme systems." Journal of Chromatography 78:141-47 (1973).

1113882

-----. "Thin-layer chromatographic behavior of glycerolipid analogs containing ether, ester, hydroxyl, and ketone groupings." Journal of Chromatography 82:7-14 (1973).

Snyder, F.; Clark, M.; and Piantadosi, C. "Biosynthesis of alkyl lipids: displacement of the acyl moiety of acyldihydroxyacetone phosphate with fatty alcohol analogs." Biochemical and Biophysical Research Communications 53:350-56 (1973).

Snyder, F.; Malone, B.; Nettesheim, P.; and Snyder, C. "Urethan pulmonary adenomas as a model for studying the biosynthesis of dipalmitoylglycerophosphorylcholine." Federation of American Societies for Experimental Biology. Federation Proceedings 32:561 (1973). (Abstract.)

Snyder, F.; Malone, B.; and Piantadosi, C. "Tetrahydropteridine-dependent cleavage enzyme of O-alkyl lipids: substrate specificity." Biochimica et Biophysica Acta 316:259-65 (1973).

Stemple, R. Bibliography of medical uses of technetium-99m 1965-1971. Washington, D.C.: U.S. Atomic Energy Commission, 1973. (ORAU-121.)

Swartzendruber, D. C., and Hübner, K. F. "Effect of external whole-body x-irradiation on gallium-67 retention in mouse tissues." Radiation Research 55:457-68 (1973).

Swartzendruber, D. C.; Wolfe, G.; and Hübner, K. F. "Gallium-67 localization in mouse peritoneal cells." Journal of the Reticuloendothelial Society 13:379-80 (1973). (Abstract.)

1113883

Tankersley, W. G., and Woodward, J. M. "Induction and isolation of non-replicative minicells of Salmonella typhimurium and their use as immunogens in mice." In Abstracts of the Annual Meeting of the American Society for Microbiology, p. 97. 1973. (Abstract.)

Urso, P., and Gengozian, N. "A, B, and T cell function in mouse allogeneic radiation chimeras." Federation of American Societies for Experimental Biology. Federation Proceedings 32:226 (1973). (Abstract.)

-----. "T cell deficiency in mouse allogeneic radiation chimeras." Journal of Immunology III:712-19 (1973).

Watson, E. E.; Cloutier, R. J.; and Gibbs, W. D. "Whole-body retention of ^{67}Ga-citrate." Journal of Nuclear Medicine 14:840-42 (1973).

Watson, E. E.; Cloutier, R. J.; Smith, S. A.; Snyder, W. S.; and Warner, G. G. "Dose to the fetus from radiopharmaceuticals in mother's bladder." Southern Medical Journal 66:1341 (1973). (Abstract.)

Wykle, R. L.; Blank, M. L.; and Snyder, F. "The enzymic incorporation of arachidonic acid into ether-containing choline and ethanolamine phosphoglycerides by deacylation-acylation reactions." Biochimica et Biophysica Acta 326:26-33 (1973).

1113884

Alpen, E. L.; Bateman, J. L.; Blair, H. A.; Brennan, J. T.; Hasterlik, R. J.; Lushbaugh, C. C.; Rust, J. H.; Leroy, G. V.; and Casarett, G. W. (Scientific Committee 14). Radiological factors affecting decision-making in a nuclear attack. Washington, D.C.: National Council on Radiation Protection and Measurements, 1974. (NCRP Report 42.)

Andrews, G. A. "Book review: Anticancer Agents Recently Developed in the People's Republic of China." Annals of Internal Medicine 81:863-64 (1974).

-----. "Radiation injury." In Encyclopaedia Britannica, 15th edition, pp. 417-21. Chicago: Encyclopaedia Britannica, 1974.

Blank, M. L., and Snyder, F. "A tissue culture system for studies of the regulation of ether-linked and ester-linked aliphatic moieties in glycerolipids." Archives of Biochemistry and Biophysics 160:100-105 (1974).

Blank, M. L.; Wykle, R. L.; Alper, S.; and Snyder, F. "Microsomal synthesis of the ether analogs of triacylglycerols acyl CoA: Alkylacylglycerol and Acyl CoA: Alk-1-enylacylglycerol acyltransferases in tumors and liver." Biochimica et Biophysica Acta 348:397-403 (1974).

Chaskes, S., and Phillips, A. W. "Pigmentation and autoflourescence of Candida species after growth on tryptophan media." Canadian Journal of Microbiology 20:595-603 (1974).

1113885

Clapp, N. K.; Tyndall, R. L.; Cumming, R. B.; and Otten, J. A. "Effects of butylated hydroxytoluene alone or with diethylnitrosamine in mice." Food and Cosmetics Toxicology 12:367-71 (1974).

Cloutier, R. J. "Book review: Nuclear Energy: Its Physics and Its Social Challenge." Health Physics 26:204 (1974).

Cloutier, R. J., and Watson, E. E. "Recent advances in dosimetry for nuclear medicine." American Nuclear Society. Transactions 19:43-44 (1974). (Abstract.)

Deland, F. H.; Sauerbrunn, B. J. L.; Boyd, C.; Wilkinson, R. H., Jr.; Friedman, B. I.; Moinuddin, M.; Preston, D. F.; and Kniseley, R. M. "^{67}Ga-citrate imaging in untreated primary lung cancer: preliminary report of a cooperative group." Journal of Nuclear Medicine 15:408-11 (1974).

Edwards, C. L., and Hayes, R. L. "Tumor detection with ^{67}Ga citrate." In Proceedings of the First World Congress of Nuclear Medicine, Japan, 1974, pp. 120-23. Tokyo, Japan: World Federation of Nuclear Medicine and Biology, 1974.

Gengozian, N.; Smith, T. A.; and Gosslee, D. G. "External uterine palpation to identify stages of pregnancy in the marmoset, Saguinus fuscicollis SSP." Journal of Medical Primatology 3:236-43 (1974).

Gibbs, W. D.; Edwards, C. L.; Hodges, H. D.; and Cloutier, R. J. "Measurement of temporal changes in whole-body radionuclide distribution with a profile scanner." In Dynamic Studies with Radioisotopes in Medicine 1974, pp. 75-84. Vienna: International Atomic Energy Agency, 1974.

1113886

Goh, K. O. "Exogenous deoxyribonucleoside triphosphates: II. Their effect on pulverized human chromosomes at the S phase." Proceedings of the Society for Experimental Biology and Medicine 145:938-43 (1974).

Goswitz, F. "Radiocolloid spleen scanning in lymphoma and chronic lymphocytic leukemia." Journal of Nuclear Medicine 15:496 (1974). (Abstract.)

Goswitz, F.; Morris, C.; Kim, K.; and Hansard, M. "Altered reticuloendothelial (RE) function in hematologic diseases." Journal of Nuclear Medicine 15:495-96 (1974). (Abstract.)

Greenlaw, R. H.; Weinstein, M. B.; Brill, A. B.; McBain, J. K.; Murphy, L.; and Kniseley, R. M. "^{67}Ga-citrate imaging in untreated malignant lymphoma: preliminary report of a cooperative group." Journal of Nuclear Medicine 15:404-7 (1974). (Abstract.)

Hayes, R. L.; Brown, D. H.; Byrd, B. L.; and Carlton, J. E. "A comparison of the tissues distribution of ^{67}Ga and the rare earth radionuclides." Journal of Nuclear Medicine 15:501 (1974). (Abstract.)

Hayes, R. L.; Brown, D. H.; and Carlton, J. E. "Comparison of the subcellular distribution of the tumor-localizing agents, ^{67}Ga, ^{111}In, ^{206}Bi, and ^{167}Tm. Journal of Nuclear Medicine 15:501 (1974). (Abstract.)

Hodges, H. D. "Applications and availability of whole-body counters to the nuclear medicine technologist." Journal of Nuclear Medicine Technology 2:102-4 (1974).

Hodges, H. D.; Gibbs, W. D.; Morris, A. C., Jr.; and Coffey, W. C., II. "An improved high-level whole-body counter." Journal of Nuclear Medicine Technology 15:610-12 (1974).

1113887

Hodges, H. D.; Goswitz, F. A.; and Berger, J. D. "Letter to the editor: Defective ^{198}Au-colloid." Journal of Nuclear Medicine Technology 2:18 (1974).

Johnston, G.; Benua, R. S.; Teates, C. D.; Edwards, C. L.; and Kniseley, R. M. "^{67}Ga-citrate imaging in untreated Hodgkin's disease: preliminary report of cooperative group." Journal of Nuclear Medicine 15:399-403 (1974).

Lee, T.-C., and Stephens, N. "Dietary effect of stearyl CoA desaturation in Morris hepatomas." Federation of American Societies for Experimental Biology. Federation Proceedings 33:1264 (1974). (Abstract 224).

Lee, T.-C.; Stephens, N.; and Snyder, F. "Dietary effects on stearyl coenzyme a desaturase in Morris hepatomas." Cancer Research 34:3270-73 (1974).

Lushbaugh, C. C. "Human radiation tolerance." In Space Radiation Biology and Related Topics; C. A. Tobias and P. Todd, eds.; Ch. 10, pp. 475-522. New York: Academic Press, 1974.

Lushbaugh, C. C., and Yuhas, J. M. "Pathological features of radiation-induced murine pulmonary carcinomas and their metastases." Radiation Research 59:222 (1974). (Abstract D-28-2.)

Morris, A. C., Jr.; Goswitz, F. A.; Kim, K. H.; McDow, A. E., Jr.; Aaron, P. A.; and Barclay, T. R. "Interface for direct on-line computer recording of dynamic radionuclide data." Medical and Biological Engineering 12:367-69 (1974).

1113888

Poggenburg, J. K., and Hayes, R. L. "Radiopharmaceuticals for function studies: Present and future." In Dynamic Studies with Radioisotopes in Medicine 1974, pp. 85-96. Vienna: International Atomic Energy Agency, 1974.

Ricks, R. C., and Lushbaugh, C. C. "The influence of exercise conditioning on the performance decrement effects of total-body irradiation." Health Physics 27(6):614 (1974). (Abstract P/12.)

-----. "Quantitation of radiation-induced changes in man." Radiation Research 59:39 (1974). (Abstract A-19-3.)

Rock, C. O., and Snyder, F. "Biosynthesis of 1-alkyl-Sn-glycero-3-phosphate via ATP: 2-alkyl-Sn-glycerol phosphotransferase." Federation of American Societies for Experimental Biology 33:1552 (1974). (Abstract 1858.)

-----. "Biosynthesis of 2-alkyl-Sn-glycero-3-phosphate via adenosine triphosphate: 2-alkyl-Sn-glycerol phosphotransferase." Journal of Biological Chemistry 249:5382-87 (1974).

Snyder, F.; Malone, B.; and Piantadosi, C. "Enzymic studies of glycol and glycerol lipids containing O-alkyl bonds in liver and tumor tissues." Archives of Biochemistry and Biophysics 161:402-7 (1974).

Tankersley, W. G., and Woodward, J. M. "Induction and isolation of a minicell-producing strain of Salmonella typhimurium." Proceedings of the Society for Experimental Biology and Medicine 145:802-5 (1974).

Urso, P., and Gengozian, N. "Variation in T and B cell deficiency in different mouse allogeneic radiation chimeras." Journal of Immunology 113:1770-79 (1974).

1113889

Vodopick, H., and Andrews, G. A. "Accidental radiation exposure." Archives of Environmental Health 28:53-56 (1974).

Vodopick, H.; Chaskes, S. J.; Solomon, A.; and Stewart, J. A. "Transient monoclonal gammopathy associated with cytomegalovirus infection." Blood 44:189-95 (1974).

Washburn, L. C.; Carlton, J. E.; Hayes, R. L.; and Yuhas, J. M. "Distribution of WR-2721 in normal and malignant tissues of mice and rats bearing solid tumors: Dependence on tumor type, drug dose and species." Radiation Research 59:475-83 (1974).

Washburn, L. C., and Hayes, R. L. "Thin layer chromatographic and colorimetric methods for monitoring the purity of S-2- (3-aminopropylamine)- ethylphosphorothioic acid (WR-2721)." Analytical Chemistry 46:2231 (1974).

Wykle, R. L., and Schremmer, J. M. "A lysophospholipase D pathway in the metabolism of ether-linked lipids in brain microsomes." Journal of Biological Chemistry 249:1742-46 (1974).

1113890

MEDICAL AND HEALTH SCIENCES DIVISION 1975

Allen, E. M., and Gengozian, N. "Effect of antithymocyte globulin pretreatment: immunological reconstitution of lethally irradiated animals." Transplantation 19:456-63 (1975).

Andrews, G. A., and Edwards, C. L. "Tumor scanning with gallium-67." Journal of the American Medical Association 233:1100-1103 (1975).

Barclay, T. R.; Cloutier, R. J.; Watson, E. E.; and Gilliam, P. L. "Interfacing a multichannel analyzer to a minicomputer." Nuclear Instruments and Methods 124:281-83 (1975).

Barnhart, D. D., and Gengozian, N. "An evaluation of the mixed lymphocyte culture reaction in marmosets." Transplantation 20:1107-15 (1975).

Blank, M. L.; Cress, E. A.; Piantadosi, C.; and Snyder, F. "A method for the quantitative determination of glycerolipids containing O-akyl and O-alkyl-1-enyl moieties." Biochimica et Biophysica Acta 380:208-18 (1975).

Blank, M. L.; Piantadosi, C.; Isaq, K. S.; and Snyder, F. "Modification of glycerolipid metabolism in L-M fibroblasts by an unnatural amino-alcohol, N-isopropylethanolamine." Biochemical and Biophysical Research Communications 62:983-88 (1975).

1113891

Blank, M. L., and Snyder, F. "Qualitative and quantitative aspects of thin layer chromatography in the analysis of phosphorus-free lipids." In Analysis of Lipids and Lipoproteins; E. G. Parkins, ed.; pp. 63-69. Champaign, Illinois: American Oil Chemists' Society, 1975.

Brown, R. C.; Blank, M. L.; Kostyu, J. A.; Osburn, P.; Kilgore, A.; and Snyder, F. "Analysis of tumor-associated alkyldiacylglycerols and other lipids during radiation-induced thymic leukemogenesis." Proceedings of the Society for Experimental Biology and Medicine 149:808-13 (1975).

Byrd, B. L.; Watson, E. E.; Cloutier, R. J.; and Hayes, R. L. "Effect of stable scandium on the long-term whole body retention of intravenously administered ^{46}Sc citrate in the rat." Health Physics 29:375-79 (1975).

Chaskes, S.; Kingdon, G. C.; and Balish, E. "Serum immunoglobulin levels in humans exposed to therapeutic total-body gamma irradiation." Radiation Research 62:145-58 (1975).

Chaskes, S., and Tyndall, R. L. "Pigment production by Cryptococcus neoformans from para- and ortho-diphenols: effect of the nitrogen source." Journal of Clinical Microbiology 1:509-14 (1975).

Edwards, C. L., and Hayes, R. L. "Gallium-67 citrate for tumor scanning." In Radiologic and Other Biophysical Methods in Tumor Diagnosis, Proceedings of the 18th Annual Clinical Conference on Cancer, 1973, pp. 39-56. Chicago: Year Book Medical Publishers, 1975.

1113892

El-Bassiouni, E. A.; Piantadosi, C.; and Snyder, F. "Metabolism of alkyldihydroxyacetone phosphate in rat brain." Biochimica et Biophysica Acta 388:5-11 (1975).

Ellis, J. T.; Kraft, L. M.; Lushbaugh, C. C.; Humason, G. L.; Hartraft, W. S.; Porta, E. A.; Bailey, O. T.; Greep, R. O.; Leach, C. S.; Lair, T.; Simmonds, R. C.; Vogel, F. S.; Dennis, R. L.; Brashear, H. R.; Talmage, R. V.; Harrison, G. A.; Corbett, R. L.; Klein, G.; Tilbury, T.; Suri, K.; and Haymaker, W. "The effects of cosmic particle radiation on pocket mice aboard Apollo XVII: appendix III: evaluation of viscera and other tissues." Aviation, Space, and Environmental Medicine 46:639-54 (1975).

Frenkel, J. K.; Nelson, B. M.; and Arias-Stella, J. "Immunosuppression and toxoplasmic encephalitis: Clinical and experimental aspects." Human Pathology 6:109-11 (1975).

Gengozian, N., and Batson, J. S. "Single-born marmosets without hemopoietic chimerism: naturally occurring and induced." Journal of Medical Primatology 4:252-61 (1975).

Goh, K. O. "Total-body irradiation and human chromosomes: V. Additional evidence of a transferable substance in the plasma of irradiated persons to induce chromosomal breakages." Journal of Medicine 6:51-60 (1975).

-----. "Total-body irradiation and human chromosomes: IV. Cytogenetic follow-up studies 8 and 10-1/2 years after total-body irradiation." Radiation Research 62:364-73 (1975).

1113893

Hayes, R. L., and Brown, D. H. "Biokinetics of radiogallium." In Nuklearmedizin: Fortschritte der Nuklearmedizin in Klinischer und technologischer Sicht, 12th Annual Meeting, Gesellschaft fur Nuklearmedizin, München, September 11-14, 1974; H. W. Pabst, ed. Stuttgart: Schattauer Verlag, 1975.

Hodges, H. D.; Morris, A. C., Jr.; and Gibbs, W. D. "Correlation of thyroid uptake with whole-body retention measurements." Journal of Nuclear Medicine Technology 3(2):72-75 (1975).

Hübner, K. F.; Gengozian, N.; and Gilman, T. A. "Suppression and recovery of the immune response and CFV potential of mice during and after chronic low-dose-rate gamma-irradiation." International Journal of Radiation Biology and Related Studies in Physics, Chemistry, and Medicine 28:301-12 (1975).

Hübner, K. F., and Littlefield, L. G. "Burkitt lymphoma in three American children." American Journal of Diseases in Children 129:1219-23 (1975).

Jones, J. B.; Lange, R. D.; Yang, T. J.; Vodopick, H.; and Jones, E. S. "Canine cyclic neutropenia: erythropoietin and platelet cycles after bone marrow transplantation." Blood 45:213 (1975).

Kateley, J. R., and Gengozian, N. "Rat-mouse radiation chimeras: characterization of an antibody-mediated graft-vs-host reaction." Journal of Immunology 114:125-32 (1975).

1113894

Lee, T.-C.; Blank, M. L.; Piantadosi, C.; Ishaq, K. S.; and Snyder, F. "Incorporation and subcellular distribution of an unnatural phospholipid base-analog, N-isopropylethanolamine, in rat liver." Biochimica et Biophysica Acta 409:218-24 (1975).

Littlefield, L. G.; Lever, W. E.; Miller, F. L.; and Goh, K.-O. "Chromosome breakage studies in lymphocytes from normal women, pregnant women, and women taking oral contraceptives." American Journal of Obstetrics and Gynecology 121:976-80 (1975).

Littlefield, L. G., and Mailhes, J. B. "Comparison of chromosome breakages in lymphocytes and fibroblasts from control women and women taking oral contraceptives." In Cytogenetics, Environment, and Malformation Syndromes; D. Bergsma and R. Neil Schimke, eds. The National Foundation March of Dimes Birth Defects original articles series, vol. 12. New York: Alan R. Liss, 1975. Also in Fertility and Sterility 26:828-32 (1975).

Medical and Health Sciences Division, Oak Ridge Associated Universities. Research report 1974-75. Oak Ridge, Tennessee: ORAU, 1975. (ORAU-127.)

Newsome, Y. L, and Littlefield, G. L. "Adriamycin-induced chromosome aberrations in human fibroblasts." Journal of the National Cancer Institute 55:1061-64 (1975).

Rock, C. O., and Snyder, F. "Metabolic interrelations of hydroxy-substituted ether-linked glycerolipids in the pink portion of the rabbit harderian gland." Archives of Biochemistry and Biophysics 171:631-36 (1975).

1113895

-----. "Purification of phospholipase A_2 from venoms by affinity chromatography." Federation of American Societies for Experimental Biology. Federation Proceeding, 34:525 (1975). (Abstract 1720.)

-----. "Rapid purification of phospholipase A_2 from Crotalus adamanteus venom by affinity chromatography." Journal of Biological Chemistry 250:6564-66 (1975).

-----. "A short-chain acyl-CoA: 1-alkyl-2-acyl-Sn-glycerol acyltransferase from a microsomal fraction of the rabbit harderian gland." Biochimica et Biophysica Acta 388:226-30 (1975).

Snyder, F., and Malone, B. "Acyltransferases and the biosynthesis of pulmonary surfactant lipid in adenoma alveolar type II cells." Biochemical and Biophysical Research Communications 66:914-19 (1975).

Snyder, F., and Snyder, C. "Glycerolipids and cancer." Progress in Biochemical Pharmacology 10:1-41 (1975).

Swartzendruber, D. C.; Buckland, C. H.; Lushbaugh, C. C.; Humason, G. L.; and Gengozian, N. "Ultrastructural abnormalities of marmoset colon cancer cells." Federation of American Societies for Experimental Biology. Federation Proceedings 34:825 (1975). (Abstract 3423.)

Swartzendruber, D. C., and Lushbaugh, C. C. "Intracellular microvilli in cystic colonic cancer cells." Journal of Cell Biology 67:423a (1975). (Abstract 846.)

1113896

Tyndall, R. L.; Colyer, S.; and Clapp, N. "Early alterations in plasma esterases with associated pathology following oral administration of diethylnitrosamine and butylated hydroxytoluene singly or in combination." International Journal of Cancer 16:184-92 (1975).

Tyndall, R. L., and Daniel, J. C., Jr. "Alterations in uterine and serum esterases in pregnant mammals." Fertility and Sterility 26:1098-1104 (1975).

Vodopick, H. "Erythropoietic hypoplasia after exposure to γ-benzene hexachloride." Journal of the American Medical Association 234:850-51 (1975).

Wykle, R. L., and Schremmer Lockmiller, J. M. "The biosynthesis of plasmalogens by rat brain: involvement of the microsomal electron transport system." Biochimica et Biophysica Acta 380:291-98 (1975).

1113897

MEDICAL AND HEALTH SCIENCES DIVISION 1976

Andrews, G. A. "History of radiopharmacy." In Radiopharmacy; Manuel Tubis and Walter Wolf, eds.; pp. 3-23. New York: John Wiley & Sons, 1976.

Andrews, G. A.; Hübner, K. F.; Washburn, L. C.; Wieland, B. W.; Gibbs, W. D.; Hayes, R. L.; and Butler, T. A. "Clinical tumour scanning with (^{11}C) carboxyl-labeled 1-aminocyclopentanecarboxylic acid (^{11}C ACPC)." In Proceedings of the 17th Annual Meeting. Louisville, Kentucky: Southeastern Chapter, Society of Nuclear Medicine, 1976. (Abstract.)

Armstrong, R. D., and Frome, E. L. "A branch and bound solution of a restricted least-squares problem." Technometrics 18:447-50 (1976).

-----. "The calculation of least absolute value estimators for two-way tables." In Proceedings of the Statistical Computing Section, American Statistical Association, pp. 101-6. Boston, Massachusetts: American Statistical Association, 1976.

-----. "A comparison of two algorithms for absolute deviation curve fitting." Journal of the American Statistical Association 71:328-30 (1976).

Baker, R. C.; Wykle, R. L.; and Lockmiller, J. S. "Identification of a soluble protein stimulator of microsomal cytochrome b_5-dependent desaturation reactions." Federation of American Societies for Experimental Biology. Federation Proceedings 35:1625 (1976). (Abstract 1357.)

1113898

Baker, R. C.; Wykle, R. L.; Lockmiller, J. S.; and Snyder, F. "Identification of a soluble protein stimulator of plasmalogen biosynthesis and stearoyl-coenzyme a desaturase." Archives of Biochemistry and Biophysics 177:299-306 (1976).

Blank, M. L.; Lee, T.-C.; Piantadosi, C.; Ishaq, K. S.; and Snyder, F. "Membrane lipid modification and stearoyl-coenzyme a desaturase activity in L-M cells." Archives of Biochemistry and Biophysics 177:317-22 (1976).

Blank, M. L.; Rainey, W. T., Jr.; Christie, W. H.; Piantadosi, C.; and Snyder, F. "Mass spectral analysis of a homologous series of S- and O-alkylglycerols." Chemistry and Physics of Lipids 17:201-6 (1976).

Brown, D. H.; Byrd, B. L.; Carlton, J. E.; Swartzendruber, D. C.; and Hayes, R. L. "A quantitative study of the subcellular localization of ^{67}Ga." Cancer Research 36:956-63 (1976).

Charnes, A.; Frome, E. L.; and Yu, P. L. "The equivalence of generalized least squares and maximum likelihood estimation in the exponential family." Journal of the American Statistical Association 71:169-72 (1976).

Dosado, E. A.; Hsie, A. W.; and Snyder, F. "Rapid screening of lipid metabolism in monolayer cell cultures." Journal of Lipid Research 17:285-87 (1976).

DuFrain, R. J.; Littlefield, L. G.; and Wilmer, J. L. Variations in the frequency of induced aberrations in rabbit somatic cells treated with a chemical clastogen. Paper presented at the Fifth International Congress of Human Genetics, Mexico City, October 10-15, 1976. Excerpta Medica, International Congress Series 397:120 (1976).

1113899

Frome, E. L.; Frederickson, E. L.; and Lushbaugh, C. C. "Power spectrum of the respiratory system." Biometrics 32:423-28 (1976).

Frome, E. L., and Yakatan, G. J. "Fitting the one compartment open model to bio-availability data." In Ninth International Biometric Conference, p. 19. Boston, Massachusetts: 1976. (Abstract.)

Gengozian, N.; Bazzell, S. J.; and Nickerson, D. "Histocompatibility antigens and antibody forming cells in the marmoset, a natural blood chimera." Federation of American Societies for Experimental Biology. Federation Proceedings 35:353 (1976). (Abstract 831.)

Gengozian, N.; Salter, B. L.; Basford, N. L.; and Kateley, J. R. "Characterization of the antibody response of the marmoset to sheep red blood cells." Clinical and Experimental Immunology 23:525-35 (1976).

Gengozian, N., and Urso, P. "Status of T- and B-cell cooperation in radiation chimeras: evidence for a suppressor effect." Transplantation Proceedings 8:631-35 (1976).

Goswitz, F. "Vitamin B_{12} absorption test and other studies." In Diagnostic Nuclear Medicine; A. Gottschalk and E. J. Potchen, eds.; pp. 186-90. Golden's Diagnostic Radiology; L. L. Robbins, ed.; section 20. Baltimore: The Williams and Wilkins Co., 1976.

1113900

Hayes, R. L. "Factors affecting uptake of radioactive agents by tumour and other tissues." In Proceedings of the IAEA Advisory Group Meeting on Tumour Localization with Radioactive Agents, Vienna, 1974, pp. 29-45. Vienna: International Atomic Energy Agency, 1976.

Hayes, R. L., and Byrd, B. L. "A comparison of the deposition of various tumor-localizing agents in inflammatory tissue." In Proceedings of the 17th Annual Meeting. Louisville, Kentucky: Southeastern Chapter, Society of Nuclear Medicine, 1976. (Abstract.)

Hayes, R. L.; Washburn, L. C.; Sun, T. T.; Rafter, J. J.; and Byrd, B. L. "Factors affecting the tissue distribution of (^{11}c) ACPC, a new tumor-localizing agent." In Proceedings of the 17th Annual Meeting. Louisville, Kentucky: Southeastern Chapter, Society of Nuclear Medicine, 1976. (Abstract.)

Hayes, R. L.; Washburn, L. C.; Wieland, B. W.; and Sun, T. T. "Carboxyl-labeled (^{11}C) ACBC, a possible new radiopharmaceutical for detection of cancer using positron tomography." Journal of Nuclear Medicine 18:639 (1976). (Abstract.)

Hayes, R. L.; Washburn, L. C.; Wieland, B. W.; Sun, T. T.; Turtle, R. R.; and Butler, T. A. "Carboxyl-labeled ^{11}C-1-aminocyclopentanecarboxylic acid, a potential agent for cancer detection." Journal of Nuclear Medicine 17:748-51 (1976).

Hilenski, L. L.; Walne, P. L.; and Snyder, F. "Aliphatic chains of esterified lipids in isolated eyespots of Euglena gracilis var. bacillaris." Plant Physiology 57:645-46 (1976).

1113901

Hodges, H. D., and Gibbs, W. D. "The participation of nuclear medicine technologists in radiation accident management." Journal of Nuclear Medicine Technology 4:95 (1976). (Abstract.)

Hodges, H. D., and Yaden, S. L. "Restraining rats with radiation-induced tail damage." Laboratory Animal Science 26:244 (1976).

Littlefield, L. G., and Joiner, E. E. Cytogenetic follow-up studies in 6 radiation accident victims. Paper presented at the Fifth International Congress of Human Genetics, Mexico City, October 10-15, 1976. Excerpta Medica, International Congress Series 397:137 (1976).

Lushbaugh, C. C.; Andrews, G. A.; Hübner, K. F.; Cloutier, R. J.; Beck, W. L.; and Berger, J. D. "REAC/TS: A pragmatic approach for providing medical care and physician education for radiation emergencies." In Diagnosis and Treatment of Incorporated Radionuclides, pp. 565-77. Vienna: International Atomic Energy Agency, 1976.

Lushbaugh, C. C., and Casarette, G. W. "The effects of gonadal irradiation in clinical radiation therapy: a review." Cancer 37:1111-20 (1976).

Lushbaugh, C. C., and Swartzendruber, D. C. "Histopathologic aspects of radiation effects on lymphatic tissues and malignancies." In Radiation and the Lymphatic System, proceedings of the 14th Annual Hanford Biology Symposium, 1974, pp. 28-35. Washington, D.C.: U.S. Energy Research and Development Administration, 1976. (CONF-740930.)

1113902

Machlin, L. J.; Garcia, F.; Kuenzig, W.; Richter, C. B.; Spiegel, H. E.; and Brin, M. "Lack of antiscorbutic activity of ascorbate 2-sulfate in the rhesus monkey." American Journal of Clinical Nutrition 29:825-31 (1976).

Mainwaring, H. R.; Swartzendruber, D. C.; Lushbaugh, C. C.; Idoyaga-Vargas, N. L.; and Watson, E. E. "Radiation effect on ^{67}Ga retention and distribution in mouse tissues." In Radiation and the Lymphatic System, proceedings of the 14th Annual Hanford Biology Symposium, 1974, pp. 28-35. Washington, D.C.: U.S. Energy Research and Development Administration, 1976. (CONF-740930.)

Medical and Health Sciences Division, Oak Ridge Associated Universities. Research report 1975-76. Oak Ridge, Tennessee: ORAU, 1976. (ORAU-128.)

Morris, A. C., Jr.; Barclay, T. R.; Akin, T. E.; Hansard, M. C.; Gibbs, W. D.; and Modzelewski, C. U. "14" x 17" film recorder for computer-enhanced scans." In Proceedings of the Sixth Symposium on Sharing of Computer Programs and Technology in Nuclear Medicine, Atlanta, 1976, pp. 401-11. 1976. Also published in ERDA Report CONF-760119.1, pp. 1-20. Washington, D.C.: U.S. Energy Research and Development Administration, 1976.

Morris, H. B.; Baker, R. C.; Wykle, R. L.; and Snyder, F. Effect of an unnatural phospholipid analog in microsomal membranes in cytochrome P-450. Paper presented at the 11th Annual Regional Lipid Conference, Winston-Salem, North Carolina, 1976.

Nelson, B. M., and Andrews, G. A. "Autologous stem-cell banks for restoring hemopoiesis." Advances in Radiation Biology 6:325-38 (1976).

1113903

Nelson, B.; Calvo, W.; Fliedner, T. M.; Herbst, E.; Bruch, C.; Schnappauf, H.-P.; and Flad, H.-D. "The repopulation of lymph nodes of dogs after 1200 whole-body x-irradiation and intravenous administration of mononuclear blood leukocytes." American Journal of Pathology 84:259-82 (1976).

Niblack, G. D., and Gengozian, N. "Identification of T and B lymphocytes in marmosets." Clinical and Experimental Immunology 23:536-43 (1976).

Nickerson, D. A., and Gengozian, N. "Primary in vitro antibody formation by blood leucocytes of a subhuman primate." Cell Immunology 27:171-76 (1976).

Palisano, J. R.; Walne, P. L.; and Brown, D. H. "Physico-chemical and ultrastructural characterization of isolated developing plastids of Euglena gracilis." Journal of Cell Biology 70(no. 2, part 2):166A (1976). (Abstract 498.)

Richter, C. B.; Humason, G. L.; and Lushbaugh, C. C. Edemic pneumocystis carinii infection in marmosets. Paper presented at the 27th Annual Session, American Association for Laboratory Animal Science, Houston, Texas, 1976.

Richter, C. B.; Humason, G. L.; and Tankersley, B. Acanthocephaliasis in caged marmosets. Paper presented at the 27th Annual Session, American Association for Laboratory Animal Science, Houston, Texas, 1976.

Ricks, R. C.; Cloutier, R. J.; Berger, J. D.; Beck, W. L., Jr.; and Lushbaugh, C. C. "REAC/TS: a radiation emergency assistance center/training site." In Program of the Twenty-first Annual Meeting of the Health Physics Society, San Francisco, 1976, p. 44. 1976. (Abstract Ja-9.)

1113904

Rock, C. O. Harderian glands: a model organ for the study of ether lipid metabolism in cancer cells. Ph.D. dissertation, University of Tennessee, 1976.

Rock, C. O.; Baker, R. C.; Fitzgerald, V.; and Snyder, F. "Stimulation of the microsomal alkylglycerol monooxygenase by catalase." Biochimica et Biophysica Acta 450:469-73 (1976).

Rock, C. O.; Fitzgerald, V.; Rainey, W. T., Jr.; and Snyder, F. "Mass spectral identification of 2-(O-acyl)hydroxy fatty acid esters in the white portion of the rabbit harderian gland." Chemistry and Physics of Lipids 17:207-12 (1976).

Rock, C. O. and Snyder, F. Localization of dihydroxyacetone phosphate acyltransferase. Paper presented at the 11th Annual Regional Lipid Conference, Winston-Salem, North Carolina, 1976.

-----. "Stimulation of alkyldihydroxyacetone phosphate synthesis detergents." Federation of American Societies for Experimental Biology. Federation Proceedings 35:1724 (1976). (Abstract 1861.)

Snyder, F. "Chromatographic analysis of alkyl and alk-1-enyl ether lipids and their derivatives." In Lipid Chromatographic Analysis; G. V. Marinetti, ed.; vol. 1, pp. 111-48. New York: Marcel Dekker, 1976.

Snyder, F., and Malone, B. "Transfer of methyl groups from N-dimethylnitrosamine to glycerolipids in rat liver." Chemico-Biological Interactions 13:237-41 (1976).

1113905

Tyndall, R. L.; Chaskes, S. J.; Carlton, J. E.; Nelson, B.; and Daniel, J. C. "Gallium-67 distribution in pregnant mammals." Journal of Experimental Zoology 195:417-24 (1976).

Urso, P., and Gengozian, N. "Status of T and B cell cooperation in radiation chimeras: evidence for a suppressor effect." Federation of American Societies for Experimental Biology. Federation Proceedings 35:788 (1976). (Abstract 3206.)

Voelker, D. R., and Lee, T.-C. "Fatty acid biosynthesis in pulmonary type II cell adenomas." Federation of American Societies for Experimental Biology. Federation Proceedings 35:1625 (1976). (Abstract 1354.)

Voelker, D. R.; Lee, T.-C.; and Snyder, F. "Fatty acid biosynthesis and dietary regulation in pulmonary adenomas." Archives of Biochemistry and Biophysics 176:753-56 (1976).

Washburn, L. C.; Coffey, J. L.; Watson, E. E.; Sun, T. T.; and Hayes, R. L. "Radiation dosimetry of some ^{11}C-labeled amino acid radiopharmaceuticals." In Radiopharmaceutical Dosimetry Symposium, proceedings of a conference; R. J. Cloutier, J. L. Coffey, W. S. Snyder, and E. E. Watson, eds.; pp. 441-51. Washington, D.C.: U.S. Department of Health, Education, and Welfare, 1976. (FDA 76-8044).

Washburn, L. C.; Rafter, J. J.; Hayes, R. L.; and Yuhas, J. M. "Prediction of the effective radioprotective dose of WR-2721 in humans through an interspecies tissue distribution study." Radiation Research 66:100-105 (1976).

Washburn, L. C.; Sun, T. T.; Rafter, J. J.; and Hayes, R. L. "^{11}C-labeled amino acids for pancreas visualization." Journal of Nuclear Medicine 17:557-58 (1976). (Abstract.)

1113906

Washburn, L. C.; Wieland, B. W.; Sun, T. T.; and Hayes, R. L. "Synthesis and preclinical investigations of DL-valine-1-^{11}C, a new agent for pancreatic imaging." In Proceedings of the 17th Annual Meeting. Louisville, Kentucky: Southeastern Chapter, Society of Nuclear Medicine, 1976. (Abstract.)

Wykle, R. L.; Malone, B.; and Snyder, F. Biosynthesis of dipalmitoyl-Sn-glycero-3-phosphocholine. Paper presented at the 11th Annual Regional Lipid Conference, Winston-Salem, North Carolina, 1976.

Wykle, R. L., and Snyder, F. "Microsomal enzymes involved in the metabolism of ether-linked glycerolipids and their precursors in mammals." In Enzymes of Biological Membranes, pp. 87-117. Biosynthesis of Cell Components; A. Martonosi, ed.; vol. 2. New York: Plenum Press, 1976.

Yang, W. K.; Tyndall, R. L.; and Daniel, J. C., Jr. "DNA- and RNA-dependent DNA polymerases: progressive changes in rabbit endometrium during preimplantation stage of pregnancy." Biology of Reproduction 15:604-13 (1976).

1113907

MEDICAL AND HEALTH SCIENCES DIVISION 1977

Andrews, G. A.; Hübner, K. F.; Washburn, L. C.; Wieland, B. W.; Gibbs, W. D.; Hayes, R. L.; Butler, T. A.; and Collman, I. R. "Clinical studies of ^{11}C-labeled amino acids." Journal of Nuclear Medicine 18:638 (1977). (Abstract.)

Armstrong, R. D., and Frome, E. L. Robust estimation of spline functions in data analysis. Paper presented at the Joint Central Regional Meeting, American Statistical Association and the Institute of Mathematical Statistics, Madison, Wisconsin, 1977.

-----. "A special purpose linear programming alogrithm for obtaining least absolute value estimators in a linear model with dummy variables." Communications in Statistics B6:383-98 (1977.

Cabot, M. C., and Gatt, S. "Rat brain microsomal lipase activity with an acid pH optimum." Paper presented at the Centre National de la Recherche Scientifique, International Colloquium on Enzymes of Lipid Metabolism; Strasbourg, France; 1977. In Proceedings of the Colloquium on Enzymes of Lipid Metabolism; P. Mandel, L. Freysz, and S. Gatt, eds. New York: Plenum Press, 1977.

Cabot, M. C., and Snyder, F. The incorporation of a cyclopentenyl fatty acid into cellular lipids of L-M cells: effects on growth and fatty acid composition. Paper presented at the 12th Annual Regional Lipid Conference, Helen, Georgia, 1977.

1113908

Chepenik, K. P.; Blank, M.; Malone, B.; Snyder, F.; and Waite, B. M. Some aspects of lipid metabolism during mammalian embryogenesis. Paper presented at the 12th Annual Regional Lipid Conference, Helen, Georgia, 1977.

Dosado, E. A.; Hsie, A. W.; and Snyder, F. "Modification of phospholipid metabolism in dibutyryl-cAMP-mediated morphological conversion of CHO cells." Biochemical and Biophysical Research Communications 78:1087-92 (1977).

Fuhr, J. E.; Gengozian, N.; and Overton, M. "In vitro stimulation of primate hemoglobin synthesis by L-thyroxine." Blood 49:407-13 (1977).

Gengozian, N.; Batson, J. S.; and Smith, T. A. "Breeding of the marmoset in the laboratory." In The Biology and Conservation of the Callithrichidae; D. G. Kleinman, ed. Washington, D.C.: Smithsonian Institution Press, 1977.

-----. "Breeding of tamarins (Saguinus ssp.) in the laboratory." In Biology and Conservation of the Callithrichidae, a Symposium; D. Kleinman, ed.; pp. 207-13. Washington, D.C.: Smithsonian Institution Press, 1977.

Gengozian, N. and McLaughlin, C. L. "Actively induced platelet-bound IgG associated with thrombocytopenia in the marmoset." Federation of American Societies for Experimental Biology. Federation Proceedings 36:379 (1977). (Abstract 578.)

Hayes, R. L. "The tissue distribution of gallium radionuclides." Journal of Nuclear Medicine 18:740-42 (1977).

1113909

Hayes, R. L.; Carlton, J. E.; and Kuniyasu, Y. "A ^{68}Ga albumin preparation for positron tomography of the liver." In Proceedings of the 18th Annual Meeting and Continuing Education Lectures, 1977. A Review of Nuclear Medicine, Part 2, section 3, p. 5. Abstracts of Scientific Sessions. Atlanta: Southeastern Chapter, Society of Nuclear Medicine, 1977. (Abstract.)

Hayes, R. L.; Rafter, J. J.; and Butler, T. A. "Copper-64 as a possible positron tomographic agent for detection of cancer." In Proceedings of the 18th Annual Meeting and Continuing Education Lectures, 1977. A Review of Nuclear Medicine, part 2, section, 3, p. 5. Abstracts of Scientific Sessions. Atlanta: Southeastern Chapter, Society of Nuclear Medicine, 1977. (Abstract.)

Highfill, R. R., and Gibbs, W. D. "Positron tomographic imaging of the abdomen." In Proceedings of the 18th Annual Meeting and Continuing Education Lectures, 1977. A Review of Nuclear Medicine, part 2, section 3, p. 6. Abstracts of Scientific Sessions. Atlanta: Southeastern Chapter, Society of Nuclear Medicine, 1977. (Abstract.)

Hodges, H. D.; Holloway, S.; and Gibbs, W. D. "Participation of nuclear medicine technologists in radiation accident management." Journal of Nuclear Medicine Technology 5:46-9 (1977).

-----. "Reducing Co_2 inhalation in clinical pulmonary investigations." Journal of Nuclear Medicine Technology 5:211-12 (1977).

1113910

Hübner, K. F.; Andrews, G. A.; Hayes, R. L.; Poggenburg, J. K., Jr.; and Solomon, A. "The use of rare-earth radionuclides and other bone seekers in the evaluation of bone lesions in patients with multiple myeloma or solitary plasmacytoma." Radiology 126:171-76 (1977).

Hübner, K. F.; Andrews, G. A.; Lushbaugh, C. C.; and Tompkins, E. "A follow-up study program for persons irradiated in radiation accidents." In Handling of Radiation Accidents 1977, Proceedings of a Symposium, pp. 57-70. Vienna, Austria: International Atomic Energy Agency, 1977.

Hübner, K. F.; Andrews, G. A.; Washburn, L.; Wieland, B. W.; Gibbs, W. D.; Hayes, R. L.; Butler, T. A.; and Winebrenner, J. D. "Tumor location with 1-aminocyclopentane [^{11}C] carboxylic acid: preliminary clinical trials with single-photon detection." Journal of Nuclear Medicine 18:1215-21 (1977).

Johnston, G. S.; Go, M. F.; Benua, R. S.; Larson, S. M.; Andrews, G. A.; and Hübner, K. F. "Gallium-67 citrate imaging in Hodgkin's disease: final report of cooperative group." Journal of Nuclear Medicine 18:692-98 (1977).

Lambremont, E. N.; Lee, T.-C.; and Blank, M. Effect of a choline analog, N-isopropylethanolamine, on lipid metabolism of L-M cells. Paper presented at the 12th Annual Lipid Conference, Helen, Georgia, 1977.

Lee, T.-C.; Baker, R. C.; and Stephens, N. "Evidence for participation of cytochrome b_5 in microsomal Δ-6 desaturation of fatty acids." Federation of American Societies for Experimental Biology. Federation Proceedings 36:672 (1977). (Abstract 2113.)

1113911

Lee, T.-C.; Baker, R. C.; Stephens, N.; and Snyder, F. "Evidence for participation of cytochrome b_5 in microsomal Δ-6 saturation of fatty acids." Biochimica et Biophysica Acta 489:25-31 (1977).

Lee, T.-C., and Snyder, F. "Cancer cells." In Lipid Metabolism in Mammals; F. Snyder, ed.; vol. 2, pp. 293-310. New York: Plenum Press, 1977.

McDermott, C. E. The effect of chronic irradiation on T and B lymphocytes. Ph.D. dissertation, University of Tennessee, 1977.

Medical and Health Sciences Division, Oak Ridge Associated Universities. Research report 1976-77. Oak Ridge, Tennessee: ORAU, 1977. (ORAU-135.)

Moore, C.; Lee, T.-C.; Blank, M.; Stephens, N.; and Snyder, F. Enzyme activities in lipid-modified membranes of rat liver. Paper presented at the 12th Annual Regional Lipid Conference, Helen, Georgia, 1977.

Niblack, C. D.; Kateley, J. R.; and Gengozian, N. "T- and B-lymphocyte chimerism in the marmoset." Immunology 32:257-63 (1977).

Phelps, M. E.; Hoffman, E. J.; Highfill, R. R.; and Kuhl, D. E. "A new emission computed axial tomograph for positron emitters." Journal of ~~Nucleonics~~ Nuclear Medicine 18:603 (1977). (Abstract.)

Richter, C. B.; Lushbaugh, C. C.; Humason, G. L.; and Swartzendruber, D. C. Adenocarcinoma of the colon in cotton-topped marmosets. Paper presented at the 1st Annual Meeting of the American Society of Primatologists, Seattle, Washington, 1977.

1113912

Rock, C. O. "The harderian gland." In Lipid Metabolism in Mammals; F. Snyder, ed.; vol. 2, pp. 311-21. New York: Plenum Press, 1977.

Rock, C. O.; Fitzgerald, V.; and Snyder, F. "Activation of alkyldihydroxyacetone phosphate synthase by detergents." Archives of Biochemistry and Biophysics 181:172-77 (1977).

-----. "Properties of dihydroxyacetone phosphate acyltransferase in the harderian gland." Journal of Biological Chemistry 252:6363-66 (1977).

Rock, C. O., and Snyder, F. "Localization and properties of dihydroxyacetone phosphate acyltransferase." Federation of American Societies for Experimental Biology. Federation Proceedings 36:850 (1977). (Abstract 3049.)

Schremmer, J. M.; Blank, M. L.; and Wykle, R. L. Studies of arachidonic acid release and prostaglandin synthesis by HSDM, C, cells, Paper presented at the 12th Annual Regional Lipid Conference, Helen, Georgia, 1977.

Scott, C. C.; Heckman, C. A.; Nettesheim, P.; and Snyder, F. "Lipid turnover in squamous-cell carcinoma cells and primary tracheal epithelial cells." Journal of Cell Biology 75:76a (1977). (Abstract 7235A.)

Sherman, M. I.; Miller, R. A.; and Richter, C. B. "Histologic analysis of experimental tumors from mouse blastocyst-derived cell lines." Journal of the National Cancer Institute 58:993-1002 (1977).

1113913

Snyder, F., and Rock, C. O. Detergent studies of microsomal enzymes involved in the synthesis of ether lipids. Paper presented at the Centre National de la Recherche Scientifique, International Colloquium on Enzymes of Lipid Metabolism; Strasbourg, France; 1977.

Snyder, F., ed. Lipid Metabolism in Mammals. New York: Plenum Press, 1977.

Urso, P., and Gengozian, N. "Immune competence of splenic lymphocytes following graft-vs-host disease in mouse allogeneic radiation chimeras." Journal of Immunology 118:657-61 (1977).

-----. "Suppression of GVH and PFC responses by spleen cells from radiation chimeras." Federation of American Societies for Experimental Biology. Federation Proceedings 36:1267 (1977). (Abstract 5302.)

Washburn, L. C.; Sun, T. T.; Anon, J. B.; and Hayes, R. L. "Effect of structural modifications on the tumor specificity of alicyclic α-amino acids." In Proceedings of the 18th Annual Meeting and Continuing Education Lectures, 1977. A Review of Nuclear Medicine, part 2, section 3, p. 9. Abstracts of Scientific Sessions, Atlanta: Southeastern Chapter, Society of Nuclear Medicine, 2977. (Abstract.)

Washburn, L. C.; Sun, T. T.; Wieland, B. W.; and Hayes, R. L. "[^{11}C] Tryptophan, a potential pancreas-imaging agent for positron tomography." Journal of Nuclear Medicine 18:638 (1977). (Abstract.)

Washburn, L. C.; Wieland, B. W.; Sun, T. T.; and Hayes, R. L. "^{11}C-Labeled amino acids as agents for tumor and pancreas visualization." Journal of Labelled Compounds 13:203 (1977). (Abstract.)

1113914

Wieland, B. W.; Highfill, R. R.; Lemon, R. A.; and Howell, R. S. "Applicability of a single-particle fixed-energy accelerator for production of short-lived, positron-emitting nuclides for clinical use." In Proceedings of the 18th Annual Meeting and Continuing Education Lectures, 1977. A Review of Nuclear Medicine, part 2, section 3, p. 10. Abstracts of Scientific Sessions. Atlanta: Southeastern Chapter, Society of Nuclear Medicine, 1977. (Abstract.)

Wieland, B. W.; Washburn, L. C.; Turtle, R. R.; Hayes, R. L.; and Butler, T. A. "Development of cyclotron targetry and remote radiochemical techniques for the continuous large-scale production of ^{11}C-labeled amino acids." Journal of Labelled Compounds 13:203 (1977). (Abstract.)

Wykle, R. L. "Brain." In Lipid Metabolism in Mammals; F. Snyder, ed.; vol. 1, pp. 317-66. New York: Plenum Press, 1977.

Wykle, R. L., and Kraemer, W. F. "Glycerol kinase activity in adenoma alveolar type II cells." Federation of European Biochemical Societies. FEBS Letters 78:83-5 (1977).

Wykle, R. L.; Kraemer, W. F.; and Schremmer, J. M. "Studies of lysophospholipase D of rat liver and other tissues." Archives of Biochemistry and Biophysics 184:149-55 (1977).

Wykle, R. L.; Malone, B.; and Snyder, F. "Biosynthesis of dipalmitoyl-Sn-glycero-3-phosphocholine by adenoma alveolar type II cells." Archives of Biochemistry and Biophysics 181:249-56 (1977).

1113915

Yakatan, G. J.; Smith, R. B.; Frome, E. L.; and Doluisio, J. T. "Pharmacokinetics of orally administered hydroflumethiazide in man." Journal of Clinical Pharmacology 17:37-47 (1977).

1113916

MEDICAL AND HEALTH SCIENCES DIVISION 1978

Andrews, G. A.; Hübner, K. F.; and Greenlaw, R. H. "Gallium-67 citrate imaging in malignant lymphoma: final report of cooperative group." Journal of Nuclear Medicine 19:1013-19 (1978).

Armstrong, R. D., and Frome, E. L. "A remark on algorithm AS108." Applied Statistics 27:378 (1978).

Blank, M. L.; Dalbey, W.; Nettesheim, P.; Price, J.; Creasia, D.; and Snyder, F. "Sequential changes in phospholipid composition and synthesis in lungs exposed to nitrogen dioxide." American Review of Respiratory Diseases 117:273-80 (1978).

Cabot, M. C., and Gatt, S. "The hydrolysis of triacylglycerol and diacylglycerol by a rat brain microsomal lipase with an acidic pH optimum." Biochimica et Biophysica Acta 530:508-12 (1978).

-----. "Lipases of rat brain microsomes." Advances in Experimental Medicine and Biology 101:101-11 (1978).

Cabot, M. C., and Snyder, F. "The assimilation of unnatural aliphatic moieties into complex lipids of neoplastic cells." In XII International Cancer Congress: Abstracts, Workshops, vol. XII, p. 323. Buenos Aires, Argentina, 1978. New York: Pergamon Press, 1979. (Abstract.)

-----. "The manipulation of fatty acid composition in L-M cell monolayers supplemented with cyclopentenyl fatty acids." Archives of Biochemistry and Biophysics 190:838-46 (1978).

1113917

Chaskes, S., and Tyndall, R. L. "Pigment production by cryptococcus neoformans and other cryptococcus species from aminophenols and diaminobenzenes." Journal of Clinical Microbiology 7:146-52 (1978).

-----. "Pigmentation and autofluorescence of cryptococcus species after growth on tryptophan and anthranilic acid media." Mycopathologia 64:105-112 (1978).

Chepenik, K. P.; Malone, B.; Blank, M.; Borst, D. E.; and Snyder, F. "Lipid metabolism during abnormal limb morphogenesis." Teratology 17:38A (1978). (Abstract.)

DuFrain, R. J.; Littlefield, L. G.; and Joiner, E. E. "Cytogenetic dosimetry for ^{241}Am alpha particle irradiation of G_0 stage human lymphocytes." Radiation Research 74:523 (1978). (Abstract.)

DuFrain, R. J.; Littlefield, L. G.; and Wilmer, J. L. "Chemically induced cytogenetic damage in germinal and somatic cells of the female rabbit." Mutation Research 53:103 (1978). (Abstract.)

Durum, S. K., and Gengozian, N. "The comparative radiosensitivity of T and B lymphocytes." International Journal of Radiation Biology and Related Studies in Physics, Chemistry, and Medicine 34:1-15 (1978).

Frome, E. L., and Armstrong, R. D. "A robust procedure for estimating the trend-cycle component of an economic time series." In Computer Science and Statistics: 10th Annual Symposium on Interface, 1977, pp. 271-75. Washington, D.C.: U.S. National Bureau of Standards Special Publications, 1978.

1113918

Frome, E. L., and DuFrain, R. J. "The analysis of dose-response curves for radiation-induced chromosome aberrations." Biometrics 34:731 (1978). (Abstract.)

Gengozian, N. "Immunology and blood chimerism of the marmoset." Primates in Medicine 10:173-83 (1978).

Gengozian, N.; Batson, J. S.; and Smith, T. A. "Breeding of marmosets in a colony environment." Primates in Medicine 10:71-8 (1978).

Gengozian, N.; Kately, J. R.; and Nickerson, D. A. "Marmoset species variation in the humoral antibody response: in vivo and in vitro studies." Immunology 35:549-58 (1978).

Gengozian, N., and McLaughlin, C. L. "Actively induced platelet-bound IgG associated with thrombocytopenia in the marmoset." Blood 51:1197-1210 (1978).

Gengozian, N., and Deinhardt, F., eds. Marmosets in Experimental Medicine. Primates in medicine, vol. 10; E. I. Goldsmith and J. Moor-Jankowski, eds. Basel, Switzerland: S. Karger, 1978.

Gibbs, W. D.; Holloway, S.; and Hodges, H. D. "An approach to quantitation of images obtained by positron emission tomography." Journal of Nuclear Medicine Technology 6:104 (1978). (Abstract.)

Hayes, R. L. "Chemistry and radiochemistry of metal ion nuclides commonly employed in radiopharmaceuticals." In The Chemistry of Radiopharmaceuticals; N. D. Heindel, H. D. Burns, T. Honda, and L. W. Brady, eds.; pp. 155-68. New York: Masson Publishing Company, 1978.

1113919

-----. "The medical use of gallium radionuclides: a brief history with some comments." Seminars in Nuclear Medicine 8:183-91 (1978).

Hayes, R. L.; Byrd, B. L.; and Rafter, J. H. "Studies of the mechanisms of ^{67}Ga uptake by tumor and normal tissue." In Proceedings of the 19th Annual Meeting, Southeastern Chapter, Society of Nuclear Medicine, p. 4. 1978. (Abstract.)

Hayes, R. L.; Byrd, B. L.; and Szymendera, J. "Effect of food intake on the tissue distribution of gallium-67." In Proceedings of the Second International Congress of the World Federation of Nuclear Medicine and Biology, p. 112. Washington, D.C., 1978. (Abstract.)

Hayes, R. L.; Washburn, L. C.; Wieland, B. W.; Sun, T. T.; Anon, J. B.; Butler, T. A.; and Callahan, A. P. "Synthesis and purification of [^{11}C] carboxyl-labeled amino acids." International Journal of Applied Radiation and Isotopes 29:186-87 (1978).

Hayes, R. L.; Washburn, L. C.; Wieland, B. W.; Sun, T. T.; Turtle, R. R.; and Butler, T. A. "Carboxyl-labeled ^{11}C-1-aminocyclopentanecarboxylic acid, a potential agent for cancer detection." In Year Book Cancer, pp. 236-37. 1978. Original publication: Journal of Nuclear Medicine 17:748-51 (1976).

Highfill, R. R. The use of cyclotron-produced radioisotopes in nuclear medicine. Paper presented at the 8th International Conference on Cyclotrons and their Applications, Bloomington, Indiana, 1978.

1113920

Highfill, R. R., and Wieland, B. W. "A choice of targetry to significantly reduce the size of medical cyclotrons for positron tomography." In Proceedings of the Second International Congress of the World Federation of Nuclear Medicine and Biology, p. 17. Washington, D.C., 1978. (Abstract.)

Hodges, H.; Gibbs, W. D.; and Holloway, S. "Letter to the editor." Journal of Nuclear Medicine Technology 6:96 (1978).

Hodges, H.; Gibbs, W. D.; and Holloway, S. "Letter to the editor." Journal of Nuclear Medicine Technology 6:96 (1978).

Hoeschele, J. D.; Johnson, N. P.; Rahn, R. O.; and Brown, D. H. "Comparative distribution/binding studies of ^{195m}Pt-labeled dichlorodiamine platinum (II), DDP, in the rat with emphasis on localization in DNA." Biochimie 60:1054 (1978). (Abstract.)

Hübner, K. F.; Andrews, G. A.; Gibbs, W. D.; Holloway, S.; Hayes, R. L.; and Washburn, L. C. "Initial diagnostic results with ^{11}C-labeled amino acids and the emission positron tomograph." In Proceedings of the Second World Federation of Nuclear Medicine and Biology, p. 13. Washington, D.C., 1978. (Abstract.)

Hübner, K. F.; Hayes, R. L.; Washburn, L. C.; Gibbs, W. D.; Byrd, B. L.; and Butler, T. A. "Scanning of the human pancreas with DL-valine-1-^{11}C and DL-tryptophan-1-^{11}C." Journal of Nuclear Medicine 19:686 (1978). (Abstract.)

1113921

Kateley, J. R.; Nickerson, D. A.; and Gengozian, N. "Mitogenic response of marmoset lymphocytes: cytokinetics and identification of responsive cells." Immunology 33:653-62 (1978).

Kuniyasu, Y.; Hayes, R. L.; and Carlton, J. E. "A ^{68}Ga albumin preparation for positron tomography of the liver." In Proceedings of the Second International Congress of World Federation of Nuclear Medicine and Biology, p. 90. Washington, D.C., 1978. (Abstract.)

Lambremont, E. N.; Blank, M. L.; Lee, T.-C.; and Snyder, F. "Regulation of glycerolipid synthesis in L-M fibroblasts by N-isopropylethanolamine, a choline analog." Journal of the American Oil Chemists' Society 55:254A (1978). (Abstract.)

Lambremont, E. N.; Lee, T.-C.; Blank, M. L.; and Snyder, F. "Δ-5 desaturation of fatty acids in L-M cells." Biochemical and Biophysical Research Communications 80:813-18 (1978).

Lawless, D.; Brown, D. H.; Hübner, K. F.; Colyer, S. P.; Carlton, J. E.; and Hayes, R. L. "Isolation and partial characterization of a ^{67}Ga-binding glycoprotein from Morris 5123C rat hepatoma." Cancer Research 38:4440-44 (1978).

Lee, T.-C.; Blank, M. L.; and Fitzgerald, V. "Oxidation of a fatty alcohol to fatty acid by rat liver microsomes." Federation of American Societies for Experimental Biology. Federation Proceedings 37:1704 (1978). (Abstract.)

Lee, T.-C.; Blank, M. L.; and Snyder, F. "Effect of a choline inhibitor (N-isopropylethanolamine) on cellular metabolism of L-M cells." Biochimica et Biophysica Acta 529:351-58 (1978).

1113922

Littlefield, L. G.; DuFrain, R. J.; and Colyer, S. P. "Sister chromatid exchanges in human lymphocytes exposed to ^{60}Co gamma radiation during G_0." Radiation Research 74:522-23 (1978). (Abstract.)

Littlefield, L. G., and Joiner, E. E. "Cytogenetic follow-up studies in six radiation accident victims (16 and 17 years postexposure)." In Late Biological Effects of Ionizing Radiation, Proceedings of a Symposium, vol. 1, pp. 297-308. Vienna, Austria: International Atomic Energy Agency, 1978.

Lushbaugh, C. C.; Hübner, K. F.; and Ricks, R. C. "Medical aspects of nuclear radiation emergencies." Emergency 10(9):32-35 (1978).

Lushbaugh, C. C.; Humason, G. L.; Swartzendruber, D. C.; Richter, C. B.; and Gengozian, N. "Spontaneous colonic adenocarcinoma in marmosets." Primates in Medicine 10:119-34 (1978).

Medical and Health Sciences Division, Oak Ridge Associated Universities. Research report 1977-78. Oak Ridge, Tennessee: ORAU, 1978. (ORAU-148.)

Moore, C.; Blank, M. L.; Lee, T.-C.; Benjamin, B.; Piantadosi, C.; and Snyder, F. "Membrane lipid modifications: biosynthesis and identification of phosphatidyl-N-methyl-N-isopropylethanolamine in rat liver microsomes." Chemistry and Physics of Lipids 21:175-78 (1978).

Moore, C.; Lee, T.-C.; Stephens, N.; and Snyder, F. "Enzyme activities in lipid-modified membranes of rat livers." Biochimica et Biophysica Acta 531:125-30 (1978).

1113923

Moore, C., and Snyder, F. Properties of acyl-CoA reductase from the mouse preputial gland. Paper presented at the 13th Annual Regional Lipid Conference, Long Beach, North Carolina, 1978.

Nelson, W. M.; Andrews, G. A.; and Watson, E. E. "Histopathologic studies of the liver following intravenous colloidal ^{198}Au therapy." Radiology 127:239-47 (1978).

Nénot, J. C.; Lushbaugh, C. C.; Lincoln, T. A.; Daw, H. T.; Komarov, E.; Djordjevic, D.; and Elder, W. M; comps. Manual on Early Medical Treatment of Possible Radiation Injury with an Appendix on Sodium Burns. Safety Series No. 47. Vienna, Austria: International Atomic Energy Agency, 1978.

Nickerson, D. A. Primary in vitro antibody formation by marmoset peripheral blood leucocytes. Ph.D. dissertation, University of Tennessee, 1978.

Nickerson, D. A., and Gengozian, N. "In vitro immune responses of marmoset peripheral blood T and B lymphocytes: species distinction." Federation of American Societies for Experimental Biology. Federation Proceedings 37:1487 (1978). (Abstract 1205.)

Parker, J. C.; Whiteman, M. D.; and Richter, C. B. "Susceptibility of inbred and outbred mouse strains to sendai virus and prevalence of infection in laboratory rodents." Infection and Immunity 19:123-30 (1978).

Polednak, A. P. "Age changes in differential leukocyte count among female adults." Human Biology 50:301-11 (1978).

-----. "Bone cancer among female radium dial workers: Latency periods and incidence rates by time after exposure." Journal of the National Cancer Institute 60:77-82 (1978).

1113924

-----. "Long-term effects of radium exposure in female dial workers: differential white blood cell count." Environmental Research 15:252-61 (1978).

Polednak, A. P.; Stehney, A. F.; and Rowland, R. E. "Mortality among women first employed before 1930 in the U.S. radium dial-painting industry. A group ascertained from employment lists." American Journal of Epidemiology 10:179-95 (1978).

Porcella, R. A.; Swartzendruber, D. C.; and Godbold, J. H., Jr. "A morphometric study quantifying the mucus content of proliferating colonic epithelial cells." Journal of Cell Biology 79:20a (1978). (Abstract.)

Richter, C. B.; Humason, G. L.; and Godbold, J. H., Jr. "Endemic Pneumocystis carinii in a marmoset colony." Journal of Comparative Pathology 88:171-80 (1978).

Richter, C. B.; Tankersley, W.; and Webb, A. Chronic recurrent colitis: a wasting syndrome in marmosets and tamarins. Paper presented at the Lab Animal Science Meeting, New York, 1978.

Rock, C. O.; Fitzgerald, V.; and Snyder, F. "Coupling of the biosynthesis of fatty acids and fatty alcohols." Archives of Biochemistry and Biophysics 186:77-83 (1978).

Rock, C. O., and Snyder, F. "Asymmetric localization of alkyldihydroxyacetone-P synthase and acyldihydroxyacetone-P acyltransferase in microsomal vesicles." Advances in Experimental Medicine and Biology 101:379-85 (1978).

1113925

Sauerbrunn, B. J. L.; Andrews, G. A.; and Hübner, K. F. "Gallium-67 citrate imaging in tumors of the genitourinary tract: report of cooperative study." Journal of Nuclear Medicine 19:470-75 (1978).

Scott, C.; Heckman, C.; and Snyder, F. "Ether-lipid regulation in cultured cells: relationship to glucose metabolism." Journal of Cell Biology 79:80a (1978). (Abstract.)

Shivers, C. A.; Gengozian, N.; Franklin, S.; and McLaughlin, C. L. "Antigen cross-reactivity between human and marmoset zonae pellucidae, a potential target for immunocontraception." Journal of Medical Primatology 7:242-48 (1978).

Tyndall, R. L.; Clapp, N. K.; Davidson, K. A.; Colyer, S. P.; and Burtis, C. A. "Effects of carcinogenic and noncarcinogenic chemicals on plasma esterases in BALB/c mice." Chemico-Biological Interactions 23:159-69 (1978).

Voelker, D. R. Pulmonary surfactant lipid metabolism in the alveolar type II cell adenoma. Ph.D. dissertation, University of Tennessee, 1978.

Voelker, D. R., and Snyder, F. "Subcellular site and mechanism of synthesis of pulmonary surfactant phosphatidylcholine in alveolar type II cell adenomas." Federation of American Societies for Experimental Biology. Federation Proceedings 37:1835 (1978). (Abstract.)

Washburn, L. C., and Hayes, R. L. "Importance of excess base in the synthesis of sodium phosphorothioate." In Inorganic Synthesis; A. G. MacDiarmid, ed.; vol. 17, pp. 193-94. New York: McGraw-Hill Book Co., 1978.

1113926

Washburn, L. C.; Sun, T. T.; Anon, J. B.; and Hayes, R. L. "Effect of structure on tumor specificity of alicyclic α-amino acids." Cancer Research 38:2271-73 (1978).

Washburn, L. C.; Sun, T. T.; Byrd, B. L.; Hayes, R. L.; and Butler, T. A. "Further preclinical studies of ^{11}C-DL-tryptophan, a potential pancreas-imaging agent." In Proceedings of the Second International Congress of the World Federation of Nuclear Medicine and Biology, p. 41. Washington, D.C. 1978. (Abstract.)

Washburn, L. C.; Wieland, B. W.; Sun, T. T.; Hayes, R. L.; and Butler, T. A. "[1-^{11}C] DL-Valine, a potential pancreas-imaging agent." Journal of Nuclear Medicine 19:77-83 (1978).

Wykle, R. L., and Schremmer, J. M. Biosynthesis of plasmalogens: influence of the composition of the 2-acyl constituent on desaturation of 1-alkyl-2-acyl-sn-glycero-3-phosphoethanolamine by tumor microsomes. Paper presented at the 13th Annual Regional Lipid Conference, Long Beach, North Carolina, 1978. Published in Society for Experimental Biology and Medicine 3:19 (1978). (Abstract.)

Yakatan, G. J.; Frome, E. L.; Leonard, R. G.; Shah, A. C.; and Doluisio, J. T. "Bioavailability of acetazolamide tablets." Journal of Pharmaceutical Sciences 67:252-55 (1978).

1113927

MEDICAL AND HEALTH SCIENCES DIVISION 1979

Armstrong, R. D., and Frome, E. L. "Least-absolute-value estimators for one-way and two-way tables." Naval Research Logistics Quarterly 26:79-96 (1979).

Armstrong, R. D.; Frome, E. L.; and Kung, D. S. "A revised simplex algorithm for the absolute deviation curve-fitting problem." Communications in Statistics 8B:175-190 (1979).

Arneson, R. M.; Geller, A. M.; and Byrne, W. L. "Binding of adenosine 5^1-monophosphate to bovine liver fructose 1,6-bisphosphatase." Enzyme 24:132-36 (1979.)

Blank, M. L., and Snyder, F. "A quantitative chromatographic method for the determination of low levels of nitrilotriacetic and ethylenediaminetetraacetic acids in diethylene triamine-pentaacetic acid." Journal of Chromatography 170:379-83 (1979).

Borman, L. S.; Johnson, D. O.; and Snyder, F. "Effects of a choline inhibitor on mammalian cell growth." In Vitro 15:223a (1979). (Abstract.)

Brown, A. J., and Snyder, F. "Solubilization of alkyldihydroxyacetone-P synthase from Ehrlich ascites cell microsomal membranes." Biochemical and Biophysical Research Communications 90:278-84 (1979).

Brown, D. H.; Carlton, J. E.; Rafter, J. J.; and Hayes, R. L. "A large scale extraction procedure for the purification of a ^{67}Ga binding glycoprotein." Journal of Nuclear Medicine 20:682 (1979). (Abstract.)

1113928

Digenis, G. A.; Casey, D. L.; Wesner, D. A.; Washburn, L. C.; and Hayes, R. L. "Preparation of optically active ^{11}C amino acids." Journal of Nuclear Medicine 20:662 (1979).

Duffey, D.; Beck, W. L.; Gleason, G. I.; and Wiggins, P. E. "Evaluation of dosimetry film by neutron activation and X-ray fluorescence." Journal of Nuclear Science and Technology 16:89-94 (1979).

DuFrain, R. J.; Littlefield, L. G.; Heffernan, K.; Wilmer, J. L.; and Batson, J. "Sister-chromatid in the genus Saguinus." Mammalian Chromosomes Newsletter 20:13 (1979). (Abstract.)

Frome, E. L., and DuFrain, R. J. "Estimation of the amount of exposure to an environmental clastogen using human cytogenetic dosimetry." In 1978 DOE Statistical Symposium; H. T. Davis, R. R. Prairie, and T. Truet, eds.; pp. 169-92. Albuquerque, New Mexico: U.S. Department of Energy, 1979. (DOE CONF-781108).

Gengozian, N., and Barton, B. A. "Isoimmunizations among marmosets to identify leucocyte antigens." Journal of Medical Primatology 8:113-21 (1979).

Hayes, R. L.; Rafter, J. J.; and Byrd, B. L. "Studies of the mechanism of gallium-67 uptake by tumor, abscess, and normal tissues." Journal of Nuclear Medicine 20:672-73 (1979). (Abstract.)

Hayes, R. L.; Szymendera, J. J.; and Byrd, B. L. "Effect of food intake on the tissue distribution of gallium-67: concise communication." Journal of Nuclear Medicine 20:938-40 (1979).

1113929

Highfill, R. R., and Phelps, M. E. "Positron tomography." IEEE Transactions on Nuclear Science NS-26:1632-34 (1979).

Highfill, R. R., and Wieland, B. W. "The medical applications of short-lived, cyclotron-produced radionuclides." IEEE Transactions on Nuclear Science NS-26:2220-22 (1979).

Hübner, K. F.; Andrews, G. A.; Buonocore, E.; Hayes, R. L.; Washburn, L. C.; Collman, I. R.; and Gibbs, W. D. "Carbon-11-labeled amino acids for the rectilinear and positron tomographic imaging of the human pancreas." Journal of Nuclear Medicine 20:507-13 (1979).

Hübner, K. F.; Buonocore, E.; Gibbs, W. D.; Holloway, S.; and Byrd, B. L. "Differentiation of pancreatic and other retroperitoneal tumors by positron emission computerized tomography (ECT)." Journal of Nuclear Medicine 20:631 (1979). (Abstract.)

Humason, G. L. Animal Tissue Techniques. Fourth edition. San Francisco: W. H. Freeman and Company, 1979.

Lambremont, E. N., and Wykle, R. L. "Wax synthesis by an enzyme system from the honey bee." Comparative Biochemistry and Physiology 63B:131-35 (1979).

Lee, T.-C. "Characterization of fatty alcohol: NAD^+ oxidoreductase from rat liver." Journal of Biological Chemistry 254:2892-96 (1979).

Littlefield, L. G.; Colyer, S. P.; Joiner, E. E.; and DuFrain, R. J. "Sister-chromatid exchanges in human lymphocytes exposed to ionizing radiation during G_0." Radiation Research 78:514-21 (1979).

1113930

Littlefield, L. G.; Colyer, S. P.; Sayer, A. M.; and DuFrain, R. J. "Sister-chromatid exchanges in human lymphocytes exposed during G_0 to four classes of DNA damaging chemicals." Mammalian Chromosomes Newsletter 20:25 (1979). (Abstract.) Also in Mutation Research 67:259-69 (1979).

Lushbaugh, C. C. "Letter to the editor." Emergency 11:6-7 (1979).

Lushbaugh, C. C., and Washburn, L. C. "FDA IND approval for Zn-DTPA, new clinical agent for decorporation therapy of actinides: letter to the editor." Health Physics 36:472 (1979). Also in Journal of Nuclear Medicine 20:73 (1979).

Moore, C., and Snyder, F. "Partial characterization of acyl-CoA reductase from mouse preputial gland." Federation of American Societies for Experimental Biology. Federation Proceedings 38:310 (1979). (Abstract.)

Polednak, A. P. "Long-term effects of radium exposure in female dial workers: liver function and liver disease." Environmental Research 18:454-65 (1979).

Polednak, A. P., ed. The Longevity of Athletes. Springfield, Illinois: Charles C. Thomas, 1979.

Porcella, R. A.; Swartzendruber, D. C.; and Godbold, J. H., Jr. "A morphometric study quantifying the mucous content of proliferating colonic epithelial cells." The American Journal of Anatomy 155:103-10 (1979).

Richter, C. B., and Buyckmichi, N. "Squamous-cell carcinoma of the epidermis in an aged white-lipped tamarin (Saguinus fuscicollis leucogenys Gray)." Veterinary Pathology 16:263-65 (1979).

1113931

Rundo, J.; Polednak, A. P.; Brues, A. M.; Lucas, H. F.; Patten, B. C.; Rowland, R. E.; and Stehney, A. F. "A study of radioactivity and health status of former thorium workers." Environmental Research 18:94-100 (1979).

Scott, C. C.; Heckman, C. A.; Nettesheim, P.; and Snyder, F. "Metabolism of ether-linked glycerolipids in cultures of normal and neoplastic rat respiratory tract epithelium." Cancer Research 39:207-14 (1979).

Tankersley, W. G.; Richter, C. B.; and Batson, J. S. "Therapy of filariasis in tamarins." Laboratory Animal Science 29:107-10 (1979).

Voelker, D. R., and Snyder, F. "Subcellular site and mechanism of synthesis of disaturated phosphatidylcholine in alveolar type II cell adenomas." Journal of Biological Chemistry 254:8628-33 (1979).

Washburn, L. C.; Sun, T. T.; Byrd, B. L.; Hayes, R. L.; and Butler, T. A. "DL-[carboxyl-^{11}C] tryptophan, a potential agent for pancreatic imaging; production and preclinical investigations." Journal of Nuclear Medicine 20:857-864 (1979).

Wieland, B. W.; Highfill, R. R.; and King, P. H. "Proton accelerator targets for the production of ^{11}C, ^{13}N, ^{15}O, and ^{18}F." IEEE Transactions on Nuclear Science NS-26:1713-17 (1979).

Wieland, B. W., and Howell, R. A. "Computed yields of ^{11}C, ^{13}N, ^{15}O, and ^{18}F for proton bombardment of enriched stable isotope targets." Journal of Labelled Compounds 16:103-5 (1979). (Abstract.)

1113932

Wykle, R. L., and Schremmer, J. M. "Biosynthesis of plasmalogens by the microsomal fraction of Fischer R-3259 sarcoma. Influence of specific 2-acyl chains on the desaturation of 1-alkyl-2-acyl-*Sn*-glycero-3-phosphoethanolamine." *Biochemistry* 18:3512-17 (1979).

1113933

PUBLICATIONS FOR THE MEDICAL AND HEALTH SCIENCES DIVISION (FY-80)

Full-length journal articles

Blank, M. L., Snyder, F., Byers, L. W., Brooks, B., and Muirhead, E. E.
Antihypertensive activity of an alkyl ether analog of phosphatidylcholine
Biochem. Biophys. Res. Commun. 90, 1194-1200, 1979

Buonocore, E. and Hubner, K. F.
Positron-emission computed tomography of the pancreas: A preliminary study
Radiology 133, 195-201, 1979

Buonocore, E., Hubner, K. F., and Collmann, I. R.
Differentiation of retroperitoneal tumor using positron emission computed tomography
J. Comput. Assist. Tomogr. 3, 825-828, 1979

Buyukmihci, N. and Richter, C. B.
Prevalence of ocular disease in a colony of tamarins and marmosets
Lab. Anim. Sci. 29, 800-804, 1979

Cabot, M. C. and Snyder, F.
Manipulation of alkylglycerolipid levels in cultured cells. Fatty alcohol versus alkylglycerol supplements
Biochim. Biophys. Acta 617, 410-418, 1980

Chepenik, K. P., Blank, M., Snyder, F., and Waite, B. M.
On the presence of plasmalogens in developing rat embryos
Int. J. Biochem. 11, 605-607, 1980

DuFrain, R. J., Littlefield, L. G., and Wilmer, J. L.
Cyclophosphamide-induced sister chromatid exchanges in rabbit lymphocytes
Environ. Mutagenesis 1, 283-286, 1979

DuFrain, R. J., Littlefield, L. G., and Wilmer, J. L.
The effect of washing lymphocytes after in vivo treatment with streptonigrin on the yield of chromosome and chromatid aberrations in blood cultures
Mutat. Res. 69, 101-105, 1980

DuFrain, R. J., Littlefield, L. G., Joiner, E. E., and Frome, E. L.
Human cytogenetic dosimetry: A dose-response relationship for alpha particle radiation from ^{241}Am
Health Phys. 37, 279-289, 1979

DuFrain, R. J., Heffernan, K., Wilmer, J. L., Batson, J., and Littlefield, L. G.
Sister-chromatid exchange and mitotic stimulation in lymphocytes from four species of the genus Saguinus
J. Med. Primatol. 9, 233-239, 1980

Frome, E. L. and Yakatan, G. J.
Statistical estimation of the pharmokinetic parameters in the one compartment open model
Commun. Statist.-Simula. Computa. B9, 201-222, 1980

1113934

Fuhr, J. E. and Gengozian, N.
Fetal hemoglobin: in vivo stimulation by D-thyroxine in adult marmosets
Blood Cells 5, 471-474, 1979

Gengozian, N. and McLaughlin, C. L.
IgG+ platelets in the marmoset: Their induction, maintenance, and survival
Blood 55, 885-890, 1980

Gengozian, N., Brewen, J. G., Preston, R. J., and Batson, J. S.
Presumptive evidence for the absence of functional germ cell chimerism in the marmoset
J. Med. Primatol. 9, 9-27, 1980

Godbold, J. H., Jr. and Tompkins, E. A.
A long-term mortality study of workers occupationally exposed to metallic nickel at the Oak Ridge Gaseous Diffusion Plant
J. Occup. Med. 21, 799-806, 1979

Hayes, R. L., Byrd, B. L., Rafter, J. J., and Carlton, J. E.
The effect of scandium on the tissue distribution of ^{67}Ga in normal and tumor-bearing rodents
J. Nucl. Med. 21, 361-365, 1980

Hodges, H. D. and Aldridge, R. E.
Radiation safety in the nuclear medicine laboratory
J. Nucl. Med. Technol. 8, 87-89, 1980

Lee, T-c. and Fitzgerald, V.
Phase transitions of alkyl ether analogs of phosphatidylcholine
Biochim. Biophys. Acta 598, 189-192, 1980

Lee, T-c., Hougland, A. E., and Stephens, N.
Perturbation of lipid metabolism in L-M cultured cells by elaidic acid supplementation: formation of fatty alcohols
Biochem. Biophys. Res. Commun. 91, 1497-1503, 1979

Lee, T-c., Fitzgerald, V., Stephens, N., and Snyder, F.
Activities of enzymes involved in the metabolism of ether-linked lipids in normal and neoplastic tissues of rat
Biochim. Biophys. Acta 619, 420-423, 1980

Littlefield, L. G., Colyer, S. P., and DuFrain, R. J.
Comparison of sister-chromatid exchanges in human lymphocytes after G_0 exposure to mitomycin in vivo vs. in vitro
Mutat. Res. 69, 191-197, 1980

McDermott, C. A. and Gengozian, N.
The effect of low-exposure-rate gamma irradiation on T and B lymphocyte function in the mouse
Int. J. Radiat. Biol. 37, 415-428, 1980

1113935

Palisano, J. R., Walne, P. L., and Brown, D. H.
Ultrastructure and physical characteristics of proplastids and chloroplasts isolated by zonal centrifugation from Euglena gracilis var. bacillaris
Eur. J. Cell Biol. 21, 305-312, 1980

Polednak, A. P.
Mortality among men occupationally exposed to phosgene in 1943-45
Environ. Res. 22, 357-367, 1980

Schremmer, J. M., Blank, M. L., and Wykle, R. L.
Bradykinin-stimulated release of [^{3}H]arachidonic acid from phospholipids of $HSDM_1C_1$ cells: Comparison of diacyl phospholipids and plasmalogens as sources of prostaglandin precursors
Prostaglandins 18, 491-505, 1979

Scott, C. C., Heckman, C. A., and Snyder, F.
Regulation of ether lipids and their precursors in relation to glycolysis in cultured neoplastic cells
Biochim. Biophys. Acta 575, 215-224, 1979

Urso, P. and Gengozian, N.
Nonspecific suppressor elements in murine allogeneic radiation chimeras
Cell. Immunol. 47, 19-31, 1979

Urso, P. and Gengozian, N.
Depressed humoral immunity and increased tumor incidence in mice following in utero exposure to benzo(α)pyrene
J. Toxicol. Environ. Health 6, 569-576, 1980

Washburn, L. C., Sun, T. T., Byrd, B. L., Hayes, R. L., and Butler, T. A.
1-Aminocyclobutane[^{11}C]carboxylic acid, a potential tumor-seeking agent
J. Nucl. Med. 20, 1055-1061, 1979

Wykle, R. L., Malone, B., and Snyder, F.
Acyl-CoA reductase specificity and synthesis of wax esters in mouse preputial gland tumors
J. Lipid Res. 20, 890-896, 1979

Wykle, R. L., Malone, B., Blank, M. L., and Snyder, F.
Biosynthesis of pulmonary surfactant: Comparison of 1-palmitoyl-sn-glycero-3-phosphocholine and palmitate as precursors of dipalmitoyl-sn-glycero-3-phosphocholine in adenoma alveolar type II cells
Arch. Biochem. Biophys. 199, 526-537, 1980

Wykle, R. L., Kraemer, W. F., and Schremmer, J. M.
Specificity of lysophospholipase D
Biochim. Biophys. Acta 619, 58-67, 1980

1113936

Chapters, review articles, and other publications

Frome, E. L. and Hudson, D. R.
A jackknife procedure for estimating standaridzed mortality ratios
In: Proceedings of the Statistical Computing Section of the American Statistical Association, 1979, Washington, D.C., pp. 323-325, 1980

Gengozian, N.
The marmoset as a model for twinning, chimerism, and immunologic tolerance
In: Spontaneous Animal Models of Human Disease, Vol. 1, (Andrews, E. J., Ward, B. C., and Altman, N. H., eds.), pp. 222-224, Academic Press, New York, 1979

Hodges, H. D.
NCRP Report No. 57: Instrumentation and monitoring methods for radiation protection. A review
J. Nucl. Med. Technol. 7, 245, 1979

Hubner, K. F., Andrews, G. A., Washburn, L., Wieland, B. W., Gibbs, W. D., Hayes, R. L., Butler, T. A., and Winebrenner, J. D.
Tumor location with 1-aminocyclopentane [^{11}C]carboxylic acid; preliminary clinical trials with single-photon detection (Original publication: J. Nucl. Med. 18, 1215-1221, 1977)
Year Book Cancer, 1979, 237-239

Littlefield, L. G. [Contributor]
Chromosome abberations in somatic cells
In: Influence of Dose and Its Distribution in Time on Dose-Response Relationships for Low-LET Radiations, pp. 23-37, National Council on Radiation Protection and Measurements, Washington, D. C., NCRP Report No. 64, 1980

Polednak, A. P. and Frome, E. L.
Mortality among men employed between 1943 and 1947 at a uranium-processing plant
In: Proceedings of the 1979 DOE Statistical Symposium, Gatlinburg, Tennessee, 1979, (Gardiner, D. A. and Truett, T., eds.), pp. 116-127, U.S. Department of Energy Report CONF-791016, 1980

Ricks, R. C.
A training course for radiation accident management in the health physics/medical environment
In: Health Physics Training; Proceedings of the Health Physics Society 13th Midyear Topical Symposium, 1979, Honolulu, Hawaii, (Yanger, W. L. and Hanly, P. J., eds), pp, 7-15, Hawaii Chapter, Health Physics Society, Honolulu, Hawaii, 1980

Ricks, R. C., Beck, J., and Berger, J.
Response to Radioactive Materials Transport Accidents, Washington, D. C., Department of Transportation, (DOT/RSPA/MTB-79/8) (Interim Edition), Various paging, 1980

1113937

Snyder, F., Lee, T-c., Blank, M. L., and Moore, C.
In vivo modification of phospholipid polar head groups and alterations in membrane activities and cellular events
In: Membrane Fluidity. Biophysical Techniques and Cellular Regulation, (Kates, M. and Kuksis, A., eds.), pp. 307-323, The Humana Press, Inc., Clifton, New Jersey, 1980

Swartzendruber, D. C., Miller, P. N., and Richter, C. B.
Ultrastructure of colonic neoplastic cells in metastases of tamarins
In: Proceedings for the 38th Annual Meeting of the Electron Microscope Society of America, (Arceneaux, C. J., ed.), San Francisco, California, 1980, pp. 730-731, Claitor's Publishing Division, Baton Rouge, Louisiana, 1980

Washburn, L. C., Sun, T. T., Byrd, B. L., Hayes, R. L., Butler, T. A., and Callahan, A. P.
High-level production of [^{11}C]carboxyl-labeled amino acids
In: Radiopharmaceuticals II: Proceedings of the 2nd International Symposium on Radiopharmaceuticals, 1979, Seattle, Washington, pp. 767-777, Society of Nuclear Medicine, New York, New York, 1979

1113938

Abstracts (published) of papers presented at meetings

Blank, M. L., Snyder, F. L., Byers, L. W., Brooks, B., Smith, K. A., and Muirhead, E. E.
Similarities in the antihypertensive action of an alkyl ether analog of phosphatidylcholine and a phospholipid derived from the renal medulla
Clin. Res. 27, 781A, 1979

Brown, A. J. and Snyder, F.
Solubilization of alkyldihydroxyacetone-P synthase from Ehrlich ascites cell microsomal membranes
Soc. Exp. Biol. Med. (S.E. Sect.) 4, 17, 1979

Brown, A. J. and Snyder, F.
Properties of membrane-bound and solubilized alkyldihydroxyacetone-P synthase
Fed. Proc. 39, 1993, 1980

Cabot, M. C. and Welsh, C. J.
Alterations in lipid metabolism induced by 12-O-tetradecanoylphorbol-13-acetate in differentiating human myeloid leukemia
Fed. Proc. 39, 2188, 1980

DuFrain, R. J., Wilmer, J. L., and Littlefield, L. G.
Analysis of cyclophosphamide-induced sister-chromatid exchange
Environ. Mutagenesis 1, 176, 1979

DuFrain, R. J., Frome, E. L., and Littlefield, L. G.
Dose response, distribution, and dispersion analyses of streptonigrin-induced cytogenetic abnormalities in somatic cells of rabbit
Environ. Mutagenesis 2, 256-257, 1980

DuFrain, R. J., Frome, E. L., Littlefield, L. G., and Joiner, E. E.
Application of the generalized Poisson distribution to alpha particle-induced chromosome aberrations in human lymphocytes
Radiat. Res. 83, 486-487, 1980

Ehrenkaufer, R. L. E., Fowler, J. S., MacGregor, R. R., Ruth, T. J., Wieland, B., and Wolf, A. P.
Production of carrier free, anhydrous $H^{18}F$ by deuteron irradiation of H_2/Ne target gas
In: Second Chemical Congress of the North American Continent, San Francisco, California, 1980. Astracts of papers, Pt. I, NUCL No. 89, American Chemical Society, Washington, D. C., 1980

Fishman, J. B., Blank, M. L., and Snyder, F.
Accumulation of O-alkylacyl ethanolamine phospholipid in tumor tissues
Soc. Exp. Biol. Med. (S.E. Sect.) 4, 13, 1979

Gengozian, N., Ostby, D. A., and Rankin, J.
Active induction of immune thrombocytopenia in the marmoset
In: Abstracts, Fourth International Congress of Immunology, International Union of Immunological Societies, Paris, France, 1980. Abstract 15.5.06. Societe Francaise d'Immunologie, Paris, 1980

1113939

Huff, V., Hutton, D. G., DuFrain, R. J., and Littlefield, L. G.
Comparison of chromosome lesion frequency in rabbit bone marrow following a single or double injection of cyclophosphamide
Soc. Exp. Biol. Med. (S.E. Sect.) 4, 19, 1979

Huff, V., Hutton, D. G., DuFrain, R., Littlefield, L. G., and Wilmer, J.
Streptonigrin and cyclophosphamide-induced chromosome lesions in somatic cells vs. oocytes of the rabbit
Environ. Mutagenesis 2, 254, 1980

Kabalka, G. W., Gooch, E. E., Sun, T. T., and Washburn, L. C.
Rapid and mild syntheses of radioiodinated estrogen derivaties via organoborane technology
In: Second Chemical Congress of the North American Continent, San Francisco, California, 1980. Abstracts of papers, Pt. I, NUCL No. 91, American Chemical Society, Washington, D. C., 1980

Lee, T-c. and Stephens, N.
Increased formation of fatty alcohols by trans fatty acid supplementation in cultured L-M cells
Fed. Proc. 39, 1724, 1980

Littlefield, L. G., Colyer, S. P., and DuFrain, R. J.
Sister-chromatid exchanges in human lymphocytes after G_0 exposure to Mitomycin C (MMC): Effects of concentration and exposure time
Environ. Mutagenesis 2, 262, 1980

Moore, C. and Snyder, F.
Synthesis of long chain alcohols by acyl-CoA reductase from mouse preputial gland
Soc. Exp. Biol. Med. (S.E. Sect.) 4, 15, 1979

Morrison, W. D., Huff, V., Colyer, S., Littlefield, G., and DuFrain, R.
Cytogenetic effects of cis-platinum(II)diaminedichloride (cis-PPD) on rabbit and human cells
Environ. Mutagenesis 2, 298-299, 1980

Partain, C. L., Hubner, K. F., Staab, E. V., Scatliff, J. H., Miller, G. F., and Gibbs, W. D.
CSF Kinetics: Comparison of nuclear medicine, contrast enhanced CT, and positron emission tomography
Invest. Radiol. 14, 377, 1979

Renooij, W., Wykle, R. L., Blank, M. L., Lee, T-c., Malone, B., Fitzgerald, V., and Snyder, F.
Metabolism of 1-alkyl-2-acetoyl-sn-glycero-3-phosphocholine, an antihypertensive phospholipid
Fed. Proc. 39, 2187, 1980

Richter, C. B., Swartzendruber, D. C., and Littlefield, L. G.
Neoplastic disease of the large bowel of the cotton-topped tamarin
J. Am. Med. Vet. Assoc. 176, 880, 1980

1113940

Sayer, A. M., Littlefield, L. G., Richter, C. B., DuFrain, R. J., and Batson, J. S.
Mutagen-induced chromosome lesions in lymphocytes of Saguinus oedipus and Saguinus fuscicollis
Soc. Exp. Biol. Med. (S.E. Sect.) 4, 18, 1979

Sayer, A. M., Littlefield, L. G., DuFrain, R. J., and Richter, C. B.
Mutagen-induced chromosome lesions in lymphocytes of Saguinus oedipus - A possible genetic marker for animals at risk for colon cancer
Environ. Mutagenesis 2, 297, 1980

Urso, P. and Gengozian, N.
Suppression of humoral and cell-mediated immune response after in utero exposure to benzo(α)pyrene
Fed. Proc. 39, 775, 1980

Urso, P. and Gengozian, N.
Depressed immunity and increased tumor incidence in progeny of pregnant mice exposed to benzo(α)pyrene
In: Abstracts, Fourth International Congress of Immunology, International Union of Immunological Societies, Paris, France, 1980. Abstract 17.1.41. Societe Francaise d'Immunologie, Paris, 1980

Washburn, L. C., Sun, T. T., Byrd, B. L., and Hayes, R. L.
^{11}C-Labeled branched-chain amines, potential agents for positron tomographic lung function studies
J. Nucl. Med. 21, 13, 1980

1113941

 List of Publications from Research Report

PUBLICATIONS

Full-length journal articles

Armstrong, R. D., Frome, E. L., and Sklar, M. G.
Linear programming in exploratory data analysis (Work performed at the University of Texas, Austin)
J. Educ. Stat. (in press)

Arneson, R. M., Hinds, J. L., and Wander, J. D.
Antioxidants in neoplastic cells: IV. Evidence that the phenolic antioxidant A274 is 9-(4-hydroxyphenyl)xanthene, an artifact in tissue culture media
Lipids 16, 82-86, 1981

Bair, J. K., Miller, P. D., and Wieland, B. W.
Neutron yields from 4- to 12-MeV proton bombardment of ^{11}B, ^{13}C, and ^{18}O as related to the production of ^{11}C, ^{13}N, and ^{18}F
Int. J. Appl. Radiat. Isot. (in press)

Beck, W. L.
Radiation accident dosimetry
Nucl. Instrum. Methods 175, 150-152, 1980

Berger, M. E., Thompson, D. W., Ricks, R. C., and Kaufman, D.
The medical technologist and the radiation-accident victim
Am. J. Med. Technol. (in press)

Blank, M. L., Cress, E., Whittle, T., and Snyder, F.
In vivo metabolism of a new class of biologically active phospholipids: 1-alkyl-sn-glycero-3-phosphocholine, a platelet activating-hypotensive phospholipid
Life Sci. (in press)

Blank, M. L., Lee, T-c., Fitzgerald, V., and Snyder, F.
A specific hydrolase for 1-alkyl-2-acetyl-sn-glycero-3-phosphocholine (a hypotensive-platelet activating lipid)
J. Biol. Chem. 256, 175-178, 1981

Blank, M. L., Cress, E. A., Byrd, B. L., Washburn, L. C., and Snyder, F.
Liposomal encapsulated Zn-DTPA for removing intracellular ^{169}Yb
Health Phys. 39, 913-920, 1980

Borman, L. S.
Modulation of mammalian cell growth by a choline analog, N-isopropylethanolamine
In Vitro (in press)

Cabot, M. C. and Goucher, C. R.
Chaulmoogric acid: Assimilation into the complex lipids of Mycobacteria
Lipids 16, 146-148, 1981

Cabot, M. C. and Lumb, R. H.
The activity of a low temperature lipase in the larvae of Sarcophaga bullata (Diptera:Sarcophagidae) (Work performed at Western Carolina University, Cullowhee, North Carolina)

1113942

Comp. Biochem. Physiol. 68B, 325-328, 1981

Cabot, M. C. and Welsh, C. J.
Ether lipid studis in mouse C3H/10T1/2 cells and a 3-methylcholine transformed clone
Arch. Biochem. Biophys. (in press)

Cabot, M. C., Welsh, C. J., Callaham, M. F., and Huberman, E.
Alterations in lipid metabolism induced by 12-O-tetradecanoylphorbol-13-acetate in differentiating human myeloid leukemia cells
Cancer Res. 40, 3674-3679, 1980

Casey, D. L., Digenis, G. A., Wesner, D. A., Washburn, L. C., Chaney, J. E., Hayes, R. L., and Callahan, A. P.
Preparation and preliminary tissue studies of optically active C-11- D- and L-phenylalanine
Int. J. Appl. Radiat. Isot. (in press)

DuFrain, R. J. and Garrand, T. J.
The influence of incorporated halogenated analogues of thymidine on the sister chromaid exchange frequency in human lymphocytes
Mutat. Res. 91, 233-238, 1981

DuFrain, R. J., Littlefield, L. G., and Wilmer, J. L.
Evaluation of chemically induced cytogenetic lesions in rabbit oocytes. I. The test system and the effects of streptonigrin
Mutat. Res. 85, 147-160, 1981

Fox, L. L., Gengozian, N., Shivers, C. A., and Sieg, P.
Marmoset response to immunization with porcine zonae pellucidae: Measurement of antibody activity with an enzyme-linked immunosorbent assay
J. Med. Primatol. (in press)

Gengozian, N. and Ostby, D. A.
Antibodies selectively reactive to autologous and host-type platelets are obtained following interspecies immunizations in marmosets
Clin. Exp. Immunol. 43, 128-134, 1981

Hayes, R. L.
The interaction of gallium with biological systems
J. Nucl. Med. Biol. (in press)

Hayes, R. L., Carlton, J. E., and Kuniyasu, Y.
A new method for labeling mirospheres with ^{68}Ga
Eur. J. Nucl. Med. (in press)

Hayes, R. L., Rafter, J. J., Byrd, B. L., and Carlton, J. E.
Studies of the in vivo entry of ^{67}Ga into normal and malignant tissue
J. Nucl. Med. 22, 325-332, 1981

Hübner, K. F., Krauss, S., Washburn, L. C., Gibbs, W. D., and Holloway, E. C.
Tumor detection with 1-aminocyclopentane and 1-aminocyclobutane [^{11}C]carboxylic acid using positron emission computerized tomography
Clin. Nucl. Med. 6, 249-252, 1981

1113943

King, P. H., Hübner, K., Gibbs, W., and Holloway, E.
Noise identification and removal in positron imaging systems
IEEE Trans. Nucl. Sci. NS-28, 148-151, 1981

Huff, V., Littlfield, L. G., DuFrain, R. J., and Wilmer, J. L.
Factors affecting the sensitivity of rabbit lymphoid and bone marrow cells to streptonigrin-induced chromosome aberrations
Cytogenet. Cell Genet. (in press)

Lee, T-c. and Snyder, F.
Phase transition of an unnatural analog of phosphatidylcholine: Phosphatidyl-N-isopropylethanolamine
Lipids 16, 75-76, 1981

Lee, T-c., Blank, M. L., Fitzgerald, V., and Snyder, F.
Substrate specificity in the biocleavage of the O-alkyl bond: 1-alkyl-2-acetyl-sn-glycero-3-phosphocholine (a hypotensive and platelet-activating lipid) and its metabolites
Arch. Biochem. Biophys. 208, 353-1981

Leonard, R. B. and Ricks, R. C.
Emergency department radiation-accident protocol
Ann. Emerg. Med. 9, 462-470, 1980

Littlefield, L. G., Colyer, S. P., and DuFrain, R. J.
Physical, chemical, and biological factors affecting sister-chromatid exchange induction in human lymphocytes exposed to mitomycin C prior to culture
Mutat. Res. 81, 377-386, 1981

Morrison, W. D., Huff, V., Colyer, S. P., DuFrain, R. J., and Littlefield, L. G.
Cytogenetic effects of cis-platinum(II)diamminedichloride in vivo
Environ. Mutagenesis (in press)

Nickerson, D. A. and Gengozian, N.
Functional capabilities of marmoset T and B lymphocytes in primary in vitro antibody formation
Cell. Immunol. 57, 408-419, 1981

Polednak, A. P.
Mortality among welders, including a group exposed to nickel oxides
Arch. Environ. Health (in press)

Polednak, A. P. and Frome, E. L.
Mortality among men employed between 1943 and 1947 at a uranium-processing plant
J. Occup. Med. 23, 169-178, 1981

Polednak, A. P. and Keane, A. T.
Long half-life component of uranium retention: Implications for potential health effects among early uranium workers
Health Phys. (in press)

1113944

Renooij, W. and Snyder, F.
Biosynthesis of 1-alkyl-2-acetyl-sn-glycero-3-phosphocholine (platelet activating factor and a hypotensive lipid) by cholinephosphotransferase in various rat tissues
Biochim. Biophys. Acta 663, 545-556, 1981

Sayer, A. M., Littlefield, L. G., DuFrain, R. J., and Richter, C. B.
Analysis of mutagen-induced chromosome damage in a primate species (Saguinus oedipus oedipus) at risk for spontaneous adenocarcinoma of the colon
Cancer Genet. Cytogenet. 3, 161-169, 1981

Swartzendruber, D. C. and Richter, C. B.
Mucous and argentaffin cells in colonic adenocarcinomas of tamarins and rats
Lab. Invest. 43, 523-530, 1980

Tardif, S. D. and Richter, C. B.
Competition for a desired food in family groups of the common marmoset (Callithrix jacchus) and the cotton-top tamarin (Saguinus oedipus)
Lab. Anim. Sci. 31, 52-55, 1981

Wykle, R. L., Malone, B., and Snyder, F.
Enzymatic synthesis of 1-alkyl-2-acetyl-sn-glycero-3-phosphocholine, a hypotensive and platelet aggregating lipid
J. Biol. Chem. 255, 10256-10260, 1980

1113945

Chapters, review articles, and other publications

Andrews, G. A., Hübner, K. F., Fry, S. A., Lushbaugh, C. C., and Littlefield, L. G.
Report of 21-year medical follow-up of survivors of the Oak Ridge Y-12 accident
In: The Medical Basis for Radiation Accident Preparedness, (Hübner, K. F. and Fry, S. A., eds.), pp. 59-79, Elsevier North-Holland, New York, 1980

Beck, W. L., Jr., Berger, C. D., Berger, J. D. and Goans, R. E.
Instrumentation for detection and measurement of ionizing radiation
In: Instrumentation and Controls Handbook, Marcel Dekker Publishing Co., New York (in press)

DuFrain, R. J., Littlefield, L. G., Joiner, E. E., and Frome, E. L.
In vitro human cytogenetic dose response systems
In: The Medical Basis for Radiation Accident Preparedness, (Hübner, K. F. and Fry, S. A., eds.), pp. 357-374, Elsevier North-Holland, New York, 1980

Frome, E. L.
PREG: A Computer Program for Poisson Regression Analysis, 37 p., (ORAU-178), Oak Ridge Associated Universities, Oak Ridge, Tennessee, 1981

Frome, E. L. and Hudson, D. R.
Interval estimation for X predictions when the dependent variable follows the Poisson distribution
In: 1980 Proceedings, Statistical Computing Section, American Statistical Association, Houston, Texas, pp. 294-297, published by The Association, Washington, D. C., 1981

Frome, E. L. and Hudson, D. R.
A general statistical data structure for epidemiologic studies of DOE workers
In: Proceedings of the 1980 DOE Statistical Symposium, Oakland, California (in press)

Frome, E. L. and Khare, M.
Comments on Broksky's statistical methods for evaluating epidemiological results (Letter to the Editor)
Health Phys. 39, 695-697, 1980

Fry, S. A.
The United States radiation accident and other registries of the REAC/TS registry system: their functions and current status
In: The Medical Basis for Radiation Accident Preparedness, (Hübner, K. F. and Fry, S. A., eds), pp. 451-468, Elsevier North-Holland, New York, 1980

Hansard, M. S. and Wray, M. L.
A SAS job stream generator
In: Proceedings of Statistical Analysis System Users Group, International Conference, 1981, Lake Buena Vista, Florida (in press)

Hayes, R. L., Byrd, B. L., Rafter, J. J., Carlton, J. E., and Coffey, J. L.
Ytterbium-169 citrate for detection of inflammatory lesions
In: Proceedings of the IAEA International Symposium on Medical Radionuclide Imaging, Heidelberg, Germany, 1980, (in press)

1113946

Hemplemann, L. H., Lushbaugh, C. C., and Voelz, G. L.
What happened to the survivors of the early Los Alamos nuclear accidents?
In: The Medical Basis for Radiation Accident Preparedness, (Hübner, K. F. and Fry, S. A., eds), pp. 17-32, Elsevier North-Holland, New York, 1980

Hodges, H. D. [Reviewer]
Perceptions of Risk, Proceedings No. 1, NCRP, Washington, D. C., 1979
J. Nucl. Med. Technol. (in press)

Holly, F. E. and Beck, W. L.
Dosimetry studies for an industrial radiography accident
In: The Medical Basis for Radiation Accident Preparedness, (Hübner, K. F. and Fry, S. A., eds.), pp. 265-277, Elsevier North-Holland, New York, 1980

Hübner, K. F. [Reviewer]
NCRP Report No. 65: Management of persons accidentally contaminated with radionuclides
J. Nucl. Med. (in press)

Hübner, K. F. and Fry, S. A. [Editors]
The Medical Basis for Radiation Accident Preparedness, 545 p. Elsevier North-Holland, New York, 1980

Hübner, K. F., King, P., Gibbs, W. D., Partain, C. L., Washburn, L. C., Hayes, R. L., and Holloway, E.
Clinical investigations with ^{11}C-labeled amino acids using positron emission computerized tomography in patients with neoplastic diseases
In: Proceedings of the IAEA International Symposium on Medical Radionuclide Imaging, Heidelberg, Germany, 1980, (in press)

Janardan, K. G., Schaeffer, D. J., and DuFrain, R. J.
A stochastic model for the study of the distribution of chromosome aberrations in human and animal cells exposed to radiation or chemicals
In: Statistical Distributions in Scientific Work (Tallie, G., Patil, G. P., and Baldessari, B., eds.) 1981, D. Reidel Publishing Co., Boston (in press)

Kabalka, G. W., Gooch, E. E., Hsu, H. C., Washburn, L. C., Sun, T. T., and Hayes, R. L.
Rapid and mild syntheses of radioiodinated estrogen derivaties via organoborane technology
In: Applications of Nuclear and Radiochemistry, Pergamon Press, New York (in press)

Littlefield, L. G., Joiner, E. E., DuFrain, R. J., Hübner, K. F., and Beck, W. L.
Cytogenetic dose estimates from in vivo samples from persons involved in real or suspected radiation exposures
In: The Medical Basis for Radiation Accident Preparedness, (Hübner, K. F. and Fry, S. A., eds.), pp. 375-390, Elsevier North-Holland, New York, 1980

Lushbaugh, C. C., Fry, S. A., Hübner, K. F., and Ricks, R. C.
Total-body irradiation: a historical review and follow-up
In: The Medical Basis for Radiation Accident Preparedness, (Hübner, K. F. and

1113947

Fry, S. A., eds.), pp. 3-15, Elsevier North-Holland, New York, 1980

Mauderly, J., Hahn, F., Martin, C. J., and Richter, C.
Animal models of diseases of the human elderly: Chronic bronchitis and emphysema
In: Mammalian Models for Research on Aging. Institute of Laboratory Animal Resources (ILAR) Committee on Animal Models for Research on Aging, National Research Council, DHEW, publisher, (in press)

Parker, J. C. and Richter, C. B.
Respiratory (Sendai, PVM, K)
In: The Mouse in Biomedical Research, (H. L. Foster, J. D. Small, and J. G. Fox, eds.), Academic Press, New York, New York (in press)

Polednak, A. P.
Long-range studies of uranium workers and the Oak Ridge radiation worker population
In: The Medical Basis for Radiation Accident Preparedness, (Hübner, K. F. and Fry, S. A., eds.), pp. 401-409, Elsevier North-Holland, New York, 1980

Richter, C. B.
Diagnostic Exercise [Mucinous adenocarcinoma of the decending colon]
Lab. Anim. Sci. 31, 137-138, 1981

Richter, C. B., Lushbaugh, C. C., and Swartzendruber, D. C.
Cancer of the colon in the cotton-topped tamarins
In: Comparative Pathology of Zoo Animals, (Montali, R. J. and Migaki, G., eds.), pp. 567-571, Proceedings of a Symposium, 1978, Washington, D. C., The Smithsonian Institution Press, 1980

Ricks, R. C.
REAC/TS: its role as a specialty referral center and training site
In: The Medical Basis for Radiation Accident Preparedness, (Hübner, K. F. and Fry, S. A., eds.), pp. 291-296, Elsevier North-Holland, New York, 1980

Ricks, R. C. [Reviewer]
NCRP Report No. 65: Management of persons accidentally contaminated with radionuclides
Radiat. Res. (in press)

Ricks, R. C., Beck, J., and Berger, J.
Response to Radioactive Materials Transport Accidents, Washington, D. C., Department of Transportation, (DOT/RSPA/MTB-79/8) (Interim Edition), Various paging, 1980

Sagan, L. A. and Fry, S. A.
Radiation accidents: A conference review
Nucl. Saf. 21, 562-569, 1980

Wieland, B. W.
Target development problem areas in the accelerator production of ^{11}C, ^{13}N, ^{15}O, and ^{18}F for application in diagnostic nuclear medicine
In: Proceedings of the 1980 World Conference of International Nuclear Target Development Society, Gatlinburg, Tennessee. Special Edition of Nuclear

1113948

Instruments and Methods (Kobisk, E. H. and Adair, H. L., eds.), Elsevier North Holland, New York (in press)

1113949

Abstracts (published) of papers presented at meetings

Blank, M. L., Lee, T-c., Cress, E. A., Whittle, T., Fitzgerald, V., and Snyder, F.
In vivo metabolism of a new class of phospholipid, 1-alkyl-2-acetyl-*sn*-glycero-3-phosphocholine, a platelet activating-hypotensive lipid
Fed. Proc. 40, 1806, (Abstract 1534), 1981

Borman, L. S., Swartzendruber, D. C., and Littlefield, L. G.
Establishment of a cell system from rat colonic carcinoma
In Vitro (in press)

Brown, A. J. and Snyder, F.
Partial purification of alkyl synthase
Fed. Proc. 40, 1806, (Abstract 1535), 1981

Cabot, M. D. and Welsh, C. J.
Fatty acid metabolism in tetradecanoylphorbol-13-acetate-treated human leukemia cells
Fed. Proc. 40, 1590, (Abstract 290), 1981

Cookfair, D., Frome, E., and Patten, B.
Methodological problems in occupational studies of female workers
Am. J. Epidemiol. (in press)

DuFrain, R. J.
A conformation based hypothesis for the mechanism of sister chromatid exchange formation
Mamm. Chromosome Newslett. (in press)

DuFrain, R. J.
The influence of streptonigrin exposure on the SCE frequency in rabbit lymphocytes
Environ. Mutagenesis (in press)

DuFrain, R. J., Littlefield, L. G., Frome, E. L., Wilmer, J. L., Huff, V., Hutton, D., and Morrison, W. D.
Cytogenetic evaluation of embryos and somatic cells from female rabbits treated with streptonigrin
Mamm. Chromosomes Newslett. 21, 17, 1980

Dupree, E. A.
Mortality among workers at a uranium refining and processing plant
Am. J. Epidemiol. 112, 446, 1980

Frome, E. L. and DuFrain, R. J.
Determination of overdispersion of dicentric chromosome aberrations that are assumed to follow Poisson distribution
Biometrics 37, 183, 1981

Fry, S. A., Lushbaugh, C. C., and Hübner, K. F.
An overview of radiation accidents and injuries
Int. J. Nucl. Med. Biol. (in press)

1113950

Hayes, R. L. and Byrd, B. L.
Transfer of ^{67}Ga from the hamster dam to fetus and offspring
In: Proceedings of the Third International Radiopharmaceutical Dosimetry Symposium, Oak Ridge, Tennessee, 1980, (Watson, E. E., Schlafke-Stelson, A., Coffey, J. L., and Cloutier, R. J., eds.), Bureau of Radiological Health, Food and Drug Administration, Rockville, Maryland, (in press)

Hayes, R. L., Rafter, J. J., and Carlton, J. E.
Toxicity and tissue distribution of ^{99}Tc pertechnetate
In: Proceedings of the 21st Annual Meeting and Continuing Education Lectures, Southeastern Chapter, Society of Nuclear Medicine, [Abstract Section] p. 8, 1980

Hayes, R. L., Rafter, J. J., Carlton, J. E., and Byrd, B. L.
The in vivo entry of ^{67}Ga into an experimental abscess
In: Proceedings of the 21st Annual Meeting and Continuing Education Lectures, Southeastern Chapter, Society of Nuclear Medicine, [Abstract Section] p. 1, 1980

Hübner, K. F., King, P., Gibbs, W. D., Washburn, L. C., and Hayes, R. L.
Positron emission computerized tomography: A potential tool for in vivo quantitation of the distribution of radiopharmaceuticals
In: Proceedings of the Third International Radiopharmaceutical Dosimetry Symposium, Oak Ridge, Tennessee, 1980, (Watson, E. E., Schlafke-Stelson, A., Coffey, J. L., and Cloutier, R. J., eds.), Bureau of Radiological Health, Food and Drug Administration, Rockville, Maryland, (in press)

Hübner, K. F., Partain, C. L., Robertson, J., Mahaley, M. S., Purvis, J., and Gibbs, W. D.
Brain tumor imaging by positron emission computerized tomography (ECT) using ^{11}C-labeled amino acids
In: Proceedings of the 21st Annual Meeting and Continuing Education Lectures, Southeastern Chapter, Society of Nuclear Medicine, [Abstract Section] p. 2, 1980

Hudson, D. R., Frome, E. L., Dupree, E. A., Hansard, M. S., Beck, W. L., and Lushbaugh, C. C.
Exploratory analysis of mortality in a cohort of nuclear material workers
Am. J. Epidemiol. (in press)

Jay, M., Digenis, G. A., Chaney, J. E., Washburn, L. C., Byrd, B. L., Hayes, R. L., and Callahan, A. P.
Synthesis and brain uptake of carbon-11 phenethylamine
J. Labelled Compd. Radiopharm. 18, 137, 1981

Kabalka, G. W., Gooch, E. E., Sun, T. T., and Washburn, L. C.
A rapid and mild method for labeling functionally substituted molecules with iodine radionuclides
J. Labelled Compd. Radiopharm. 18, 117-118, 1981

King, P. H. and Wieland, B. W.
Computer modeling of accelerator beam window failures
J. Labelled Compd. Radiopharm. 18, 225-226, 1981

1113951

Littlefield, L. G., DuFrain, R. J., Joiner, E. E., and Colyer, S. P.
Overdispersion of two-break chromosome lesions in cultured lymphocytes from a person internally contaminated with ^{241}Am
Environ. Mutagenesis (in press)

Littlefield, L. G., Colyer, S. P., Joiner, E. E., DuFrain, R. J., and Cohen, M. M.
Chromosomal radiation sensitivity in lymphoblastoid cell lines from patients with ataxis telangiectasia
Mamm. Chromosome Newslett. (in press)

Littlefield, L. G., DuFrain, R. J., Joiner, E., Colyer, S., Batson, J., and Welter, D. J.
Cytogenetic dose response kinetics in lymphocytes of persons with Down's syndrome following in vitro exposure to low LET radiation
Mamm. Chromosomes Newslett. 21, 16, 1980

Lushbaugh, C. C.
Pathophysiology of ionizing radiation injuries
J. Occup. Med. 22, 276, 1980

Partain, C. L., Hübner, K. F., Mahaley, M. S., Rollo, F. D., Price, R. R., and Scatliff, J. H.
Brain tumor imaging based on ^{11}C-labeled amino acid utilization using positron emission tomography
Invest. Radiol. 15, 380, 1980

Partain, C. L., Hübner, K. F., Mahaley, M. S., Rollo, F. D., Price, R. R., and Scatliff, J. H.
Brain tumor imaging: Positron emission tomography using ^{11}C-labeled amino acids
J. Comput. Assist. Tomogr. 4, 702, 1980

Partain, C. L., Price, R. R., James, A. E., Jr., Hübner, K. F., Mahaley, M. S., Scatliff, J. H., and Robertson, J. T.
Positron emission tomography: Brain tumor imaging using carbon-11 amino acids
In: Proceedings of the IAEA International Symposium on Medical Radionuclide Imaging, Heidelberg, Germany, 1980, (in press)

Polednak, A. P.
Studies of workers exposed to internal radiation (uranium and thorium)
Am. J. Epidemiol. 112, 445, 1980

Richter, C. B., Tankersley, W. G., Davis-Tardiff, S., and Carson, R. L.
Preference for high sugar diets by the common marmoset
Am. J. Primatol. (in press)

Rudnick, S., Shy, C., Fry, S., and Robie, D.
Study of health effects in DOE workers occupationally exposed to >5 rem/year
Am. J. Epidemiol. (in press)

Urso, P. and Gengozian, N.
In utero exposure to benzo(α)pyrene (BP) decreases the immune response and increases sensitivity to tumor induction
Fed. Proc. 40, 1037, 1981

1113952

Washburn, L. D., Ringenberg, R. E., Sun, T. T., and Hayes, R. L.
^{11}C-Labeled 1-aminocyclohexanecarboxylic ([^{11}C]ACHC), a potential agent for studies of amino acid transport in the brain
J. Labelled Compd. Radiopharm. 18, 13-14, 1981

Washburn, L. C., Sun, T. T., Byrd, B. L., and Callahan, A. P.
Resolution of [^{11}C]DL-valine by high-performance liquid chromatography
J. Nucl. Med. (in press)

Washburn, L. C., Dees, L., Byrd, B. L., Sun, T. T., and Hayes, R. L.
Comparison of [^{68}Ga]EDTA, [^{11}C]α-aminoisobutyric acid, and [^{99m}Tc]pertechnetate for diagnosis of blood-brain barrier disruption.
J. Nucl. Med. (in press)

Washburn, L. C., Dees, L., Byrd, B. L., Sun, T. T., and Hayes, R. L.
^{11}C-labeled α-aminoisobutyric acid, a potential agent for positron tomographic assessment of blood-brain barrier disruption
In: Proceedings of the 21st Annual Meeting and Continuing Education Lectures, Southeastern Chapter, Society of Nuclear Medicine, [Abstract Section] p. 2, 1980

Washburn, L. C., Sun, T. T., Byrd, B. L., Ringenberg, R. E., and Hayes, R. L.
^{11}C-Labeled amino acids for the study of brain function
In: Abstracts of the 182nd National American Chemical Society Meeting, 1981, New York, (in press)

Wieland, B. W., Schlyer, D. J., Ruth, T. J., and Wolf, A. P.
Deuteron beam penetration in a neon gas target for producing fluorine-18
J. Labelled Compd. Radiopharm. 18, 27-29, 1981

1113953

July 15, 1981

Mr. Howard L. Rosenberg
1401 16th St. NW
Washington, D. C. 20036

Dear Mr. Rosenberg:

This letter will confirm that the Department of Energy (DOE) Oak Ridge Operations (ORO) is in receipt of your Freedom of Information Act (FIOA) request dated July 10, 1981. This letter will also confirm the telephone conversation between you and David G. Darugh of the ORO Office of Chief Counsel on July 14, 1981, at which time you reformulated your request and granted DOE a five (5) workday time extension for response.

It is my understanding that your reformulated FOIA request now asks for DOE ORO to provide the following information concerning records related to medical radiation therapy conducted here:

1. All radiation therapy proposals submitted for review to the "ORAU/ORNL Committee on Human Studies." Specifically, all proposals/protocols, committee notes, minutes, recommendations and actions; and, all interim, progress or final reports submitted to the Committee concerning the therapy or course of treatment.

2. A list of published reports or articles resulting from therapy approved or reviewed by the Committee. Additionally, DOE will attempt to identify sources of unpublished reports resulting from therapy approved or reviewed by the Committee.

3. One ORAU Annual Report published prior to 1975 for your review.

Your request for a wavier of fees because the release of this information will primarily benefit the public is approved. Your request, as modified above, has been deemed to be accepted for processing as of this date.

PERSONNEL

DOE F 1325.10
(7-79)

OFFICIAL FILE COPY

1113954

Accordingly, your reformulated request has been forwarded to the Authorizing Official, who will respond within fifteen (15) working days.

Sincerely,

Wayne Range
Freedom of Information Officer

CC-10:DGD

bcc: J. L. Foutch, CC-10
W. R. Bibb, ER-13
Dr. C. Hubner, ORAU
R. Benson, ER-13

CC-10:DGDarugh:mh:61213:7/15/81

CONCURRENCE
RTG. SYMBOL CC-10
INITIALS/SIG. DGD
DATE 7/15/8
RTG. SYMBOL M-4
INITIALS/SIG. WR
DATE 7/15/8
RTG. SYMBOL
INITIALS/SIG.
DATE

1113955

PS Form 3811, Jan. 1979

RETURN RECEIPT, REGISTERED, INSURED AND CERTIFIED MAIL

SENDER: Complete items 1, 2, and 3.
Add your address in the "RETURN TO" space on reverse.

1. The following service is requested (check one.)
- [X] Show to whom and date delivered ..... ¢
- [ ] Show to whom, date and address of delivery ..... ¢
- [ ] RESTRICTED DELIVERY
  Show to whom and date delivered ..... ¢
- [ ] RESTRICTED DELIVERY.
  Show to whom, date, and address of delivery $ ____

(CONSULT POSTMASTER FOR FEES)

2. ARTICLE ADDRESSED TO:
Howard L. Rosenberg
1401 16th St., NW
Washington, D.C. 20036

3. ARTICLE DESCRIPTION:

REGISTERED NO.	CERTIFIED NO.	INSURED NO.
	P158767602	

(Always obtain signature of addressee or agent)

I have received the article described above.
SIGNATURE [ ] Addressee [X] Authorized agent

4. DATE OF DELIVERY JAN 19 1981 — POSTMARK

5. ADDRESS (Complete only if requested)

6. UNABLE TO DELIVER BECAUSE: — CLERK'S INITIALS

GPO : 1979-300 459

P15 8767

RECEIPT FOR CERTIFIED MAIL

NO INSURANCE COVERAGE PROVIDED—
NOT FOR INTERNATIONAL MAIL
(See Reverse)

SENT TO
Howard Rosenberg
STREET AND NO
1401 16th St., NW
P.O., STATE AND ZIP CODE
Washington, D.C. 20036

POSTAGE				$
CONSULT POSTMASTER FOR FEES	CERTIFIED FEE			¢
	OPTIONAL SERVICES	SPECIAL DELIVERY		¢
		RESTRICTED DELIVERY		¢
		RETURN RECEIPT SERVICE	SHOW TO WHOM AND DATE DELIVERED	¢
			SHOW TO WHOM, DATE AND ADDRESS OF DELIVERY	¢
			SHOW TO WHOM AND DATE DELIVERED WITH RESTRICTED DELIVERY	¢
			SHOW TO WHOM, DATE AND ADDRESS OF DELIVERY WITH RESTRICTED DELIVERY	¢
TOTAL POSTAGE AND FEES				$
POSTMARK OR DATE				

PS Form 3800, Apr. 1976

1113956

JACK ANDERSON
1401 16th Street, N.W., Washington, D.C 20036

FREEDOM OF INFORMATION OFFICE

February 13, 1981

FEB 18 AM 9:19

Ltr 3/5/81

Mr. Wayne Range
Freedom of Information Officer
Department of Energy
Oak Ridge Operations
P.O. Box E
Oak Ridge, Tenn. 37830

Dear Mr. Range:

Thank-you for your letter of Feb. 2 and the materials you forwarded to me on Feb. 6. However, I am still hoping to receive a number of other explanatory documents. I asked Dr. C.C. Lushbaugh for those materials when I visted Oak Ridge last month. However, so far I have received none. Since that time I have learned that many of the documents I seek are available through FOIA. Therefore, I will amend my FOIA request of Jan. 27, 1981 to include them.

Specifically, I am also interested in receiving more detailed financial plans regarding the operations of the ORAU Medical Division than those I received. As Dr. Bibb explained, the plans are "probably not now in existence." Are they in existence or are they not? I believe that federal records management procedures require that they remain on file or available.

Under the provisions of the Freedom of Information Act, 5 U.S.C. 522, I am requesting access to the records listed below by letter on attachment "A".
As you know, the act permits you to reduce and waive fees when the release of the information is considered as primarily benefiting the public. Since I am requesting this information as part of an on-going inquiry into the effects of radiation on man, and into the U.S. government's efforts to quantify those effects, and since these questions are still in debate within the scientific community and within the populace at large, I believe this request fits that category and I therefore ask you to waive any fees. I was gratified to note that you have already determined my request "to be appropriate for a fee waiver," as you pointed out in your letter of Feb. 2, 1981

If all or any part of this request is denied, please cite the specific examp ion(s) which you think justifies your refusal to release the information, and inform me of the appeal procedures available to me under the law. I would appreciate your handling this request, if possible as part of my earlier request of Jan. 27. I look forward to hearing from you within 10 days, as the law stipulates.

Sincerely,

Howard L. Rosenberg
Staff Associate

1113957

PERSONNEL

FOIA

12614

MAR 5 1981

Mr. Howard L. Rosenberg
Staff Associate
Jack Anderson
1401 16th Street, N.W.
Washington, D. C. 20036

Dear Mr. Rosenberg:

Please accept this letter in response to your Freedom of Information Act ("FOIA") request of February 13, 1981, which was received on February 18, 1981, by the Oak Ridge Freedom of Information Officer. Your request for a fee waiver was granted on February 20, 1981, and your FOIA request was deemed received for processing as of that date.

Your statement that you wished us to handle this request as part of your earlier request is confusing, since such treatment would appear to impact only time of response and fees. If we treated it as such, response would have been late the date we received your request. Therefore, since we received two requests, for different documents, we have taken the logical approach of treating them as separate requests.

The documents identified as being responsive to your February 13, 1981, request are listed below. We have used the same alphabetical designations as your request for ease of reference.

(a) Six pages of information on the membership of the ORAU/ORNL Committee on Human Studies are enclosed. We assume this is the committee you had in mind in using the title "Human Use Committee."

(b) Three pages of research projects that have been reviewed by the Committee on Human Studies are enclosed. The listing is chronological, earliest to latest. We are sure your use of the phrase "human experimentation" is simply loose terminology. You realize, of course, that ORAU practiced medical therapy, sometimes using experimental substances or experimental procedures, but it never engaged in "human experimentation."

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

PERSONNEL -1

1113958

DOE F 1325.10
(7-79)

OFFICIAL FILE COPY

(c) No protocols existed for what you refer to as the "LETBI/METBI studies." These were treatment programs based on individual needs, not experiments, so "protocols" would not be expected. The use of these devices was guided by a board certified, properly licensed radiotherapist, who was assisted by board certified internists, hematologists and nuclear medicine experts.

(d) There were no formal "criteria for determining patients admitted for LETBI/METBI therapy." Licensed physicians in private practice who knew of ORAU's therapeutic research expertise and long success in developing beneficial application of nuclear radiation in medicine referred their patients to the ORAU medical staff. There were no "self-referrals" and no solicitations for patients. The patients received the kind of radiation therapy their disease and its stage required, as determined by an in-house staff backed by medical consultants from various other institutions.

(e) Enclosed are two typical "consent forms," taken from existing records, with the identifying information deleted.

(f) There are no existing "financial plans" for the ORAU Medical and Health Sciences Division for the period you desire, as has previously been explained to you. In response to your statement that you "believe that federal records management procedures require that they remain on file or available," enclosed please find a one-page excerpt from Order DOE 1324.2, Subject: "Records Disposition," Attachment IV-I, which shows a three-year retention period for Financial Plan files under item 2 of Records Schedule 5.

(g) In addition to USAEC Report ORAU 112, which was provided you earlier, we know of two other "statistical analyses." These are NASA-CR-144439 and NASA TM-X-2440, and are available from NTIS, Springfield, Virginia 22151. The cost of the former document is $7.50; the cost of the latter document is $10.00.

(h) Information on NASA TM-X-2440 is provided in (g), above. Enclosed are three documents representing ORAU's contribution to that document.

(i) We understand that a report of the 1966 proceedings is available directly from IAEA, or from UNIPUB, 345 Park Avenue South, New York, New York 10010.

1113959

(j) Form 990's submitted to the IRS by ORAU are not records of DOE, and are beyond the scope of a request addressed to this agency. Since we are not familiar with the status of such filings under IRS's implementation of the FOIA, we suggest you request these documents of IRS, if you still desire them.

(k) Enclosed are Schedules 189 for August 1, 1977, October 1, 1977, and October 1, 1978, plus Field Task Proposal/ Agreements for October 1, 1978, and October 1, 1979, all for ORAU epidemiological studies. The August 1, 1977, schedule marked the entry of ORAU into the Health and Mortality Study.

(l) The requested report is enclosed.

(m) Enclosed are four photographs and diagrams of the LETBI/METBI facilities: a photograph of a model of the METBI facilities; two diagrams of the LETBI facilities (one in both small glossy and large reproduced formats); and one diagram of the LETBI/METBI facilities.

There have been no deletions from the documents furnished in this response. You will note that we have responded that no documents exist for your items (c), (d) and (f). Under DOE's regulations implementing the FOIA, a determination under 10 CFR §1004.4(d)(1) that a document does not exist gives rise to the right to appeal the determination to the Office of Hearings and Appeals. Appeals are required to be by written notice addressed to the Director, Office of Hearings and Appeals, Department of Energy, 2000 M Street, NW, Washington, D. C. 20461, within thirty (30) days of receipt of the initial denial letter. Both the envelope and letter must be clearly marked "Freedom of Information Appeal." Judicial review is available after appeal in the district in which you reside or have a principal place of business, or in which the records are situated, or in the District of Columbia.

Sincerely,

Original Signed by
W. T. Hamstead
William T. Hamstead
Acting Assistant Manager
for Administration
Authorizing Official

CC-10:JLF

Enclosures:
As stated

bcc w/o enc: Wayne Range, M-4

CC-10:JLFoutch:mh:61204:3-4-81

CONCURREN
RTG. SYMBO CC-10
INITIALS/SIG JLF
DATE 3/4/81
RTG. SYMBO ER-13
INITIALS/SIG REB
DATE 3/4/8
RTG. SYMBO ER-13
INITIALS/SIG MRB
DATE 3/4/8
RTG. SYMBO AD-40
INITIALS/SIG WTH
DATE 3/4/8
RTG. SYMBO
INITIALS/SIG
DATE
RTG. SYMBO
INITIALS/SIG
DATE
RTG. SYMBO
INITIALS/SIG
DATE
RTG. SYMBO
INITIALS/SIG
DATE
RTG. SYMBO
INITIALS/SIG
DATE

HOWARD L. ROSENBERG
FOIA REQUEST OF J. ARY 27--FEBRUARY 13, 1981

ATTACHMENT "A"

a) Membership list of the Human Use Committee jointly operated by ORAU and ORNL for the years 19[illegible]-1981.

b) Projects of human experimentation reviewed by the Human Use Committee between its inception and as of January 1981.

c) Protocols issued for LETBI/METBI studies, including those issued for reviewed by the Human Use Committee. (Therapy protocols)

d) Criteria for determining patients admitted for LETBI/METBI therapy.

e) Sample of consent forms given to patients involved in LETBI/METBI therapy.

f) Copies of all "financial plans," for ORAU Medical and Health Sciences Division for FY 57 through FY 75.

g) Any statistical analyses prepared of patients who received TBI at the LETBI/METBI facilities.

h) NASA TM-X 2440

i) Proceedings of a panel on Total Body Irradiation in Humans at IAEA Vienna 196[illegible].

j) Form 990s filed with the IRS for years 1965 through 1981.

k) Form 189s, also known as "work packages" for epidemiological studies of the Oak Ridge data from FY 1974 through the current year.

l) Report entitled "Recent Progress in Assessment of Human Resistance to TBI--In Proceedings on Recovery from Nuclear War. Fort Monroe, Va. November 1967." (Not available in the open literature.)

m) Copies of photographs and diagrams (in reproducible form) available of the Oak Ridge LETBI/METBI facilities.

'81 FEB 18 AM 9:19
FREEDOM OF INFORMATION

1113961

February 23, 1981

Dr. Benson:

As you requested, I am addressing each of the 13 FOI requests of Mr. Rosenberg's Attachment "A" for you to use in responding to DOE's legal department's needs.

a) I find that a membership list of the ORAU Human Studies Committee can be made available for the years 1967 to date. There was no formal committee as such before 1967.

b) We did not do "human experimentation" ever. A list of research projects that were reviewed by our committee on research involving human subjects can be made available, but it would have to be constructed from the minutes. Committee deliberation notes and proposals themselves are not available to the public because they would require voluminous explanations of the science that I do not have time or staff to rewrite.

Chron - Failed to letter.

c) No formal protocols as such exist for the so-called LETBI/METBI studies. The use of these devices was guided by a board certified radiotherapist properly licensed who was assisted by board certified internists, hematologists, and nuclear medical experts. Not experiment, treatment program based on [illegible]

d) Criteria for "determining patients admitted" for LETBI/METBI therapy: Patients were not admitted for LETBI/METBI therapy. They were referred to our medical staff by licensed physicians in private practice who knew of our therapeutic research expertise and our long success in developing beneficial applications of nuclear radiations in medicine. There were no "self-referrals" and no solicitations for patients. The patients received the kind of radiation therapy their disease and its stage required as determined by an in-house staff backed up by medical consultants from various other institutions.

e) Nurse Sipe will make a copy of a "consent form" of a patient who received therapy in the LETBI facility next week. These voluminous records are stored in a secured warehouse and protected under both the Federal Privacy Act and the constraints of medical privacy.

f) Copies of all financial plans for this Division for FY 1957 through FY 1975 are not available to me.

g) "Any statistical analyses", etc are available to the public in NASA-CR-144439 from NTIS for $7.50. Also NASA TM-X 2440 and USAEC Report ORAU 112

h) I am not aware of what NASA TM-X 2440 is. NTIS, Springfield, Va. 22151 @ $10

i) This Proceeding is available from IAEA or UNIPUB, 345 Park Avenue South, New York, NY 10010.

j) The request for Forms 990 is being taken care of by Mr. Joyce, ORAU legal consultant for William Countiss.

1113962

k) Form 189s, also known as "work packages" for epidemiological studies of the Oak Ridge data from FY 1974 to present are not available from my office. The current ones are working drafts subject to change and under discussion, and so are not available under an FOI.

l) A copy of the report entitled Recent Progress in Assessment of Human Resistance to Total-Body Irradiation is attached.

m) Copies of photographs and diagrams of the LETBI and METBI facilities are contained in NASA-CR-144439 available from NTIS (see above). If Mr. Rosenberg intends to reproduce these in print, he will need my written permission as well as that of any original publisher. Since some photos are of simulated patients and former staff, the publication of photographs of people can only occur with permission of the persons involved.

Please have someone inform Mr. Rosenberg that my permission for him to take a picture of me in my office did not include my permission for him to publish it free of a charge to be set by me or my heirs.

We will prepare a package of this material for your use, as directed, on my return to Oak Ridge on March 2.

C. C. Lushbaugh

Typed in Dr. Lushbaugh's absence.

1113963

h) NASA TM-X 2440 is:

Proceedings of the National Symposium on Natural and Manmade Radiation in Space, held at Los Vegas, March 1-5, 1971.

Editor: Warman, E. A.
Published January 1972 - Aeroject Nuclear Systems, Sacramento. NTIS CONF NO 710304, 132 pages.

NTIS, Springfield, Va. 22151 @ $10
[illegible] particle radiation reflected in [illegible]

1113964

ORAU/ORNL COMMITTEE ON HUMAN STUDIES - FEBRUARY 1980

William Calhoun, Ph.D.
Professor and Head
Department of Psychology
The University of Tennessee
Knoxville, Tennessee 37916

H. R. Friedman, Ph.D.
Clinical Psychologist
The Regional Mental Health Center
240 West Tyrone Road
Oak Ridge, Tennessee 37830

Shirley A. Fry, M.B., Ch.B.
Medical and Health Sciences Division
Oak Ridge Associated Universities
P. O. Box 117
Oak Ridge, Tennessee 37830

A. Seaton Garrett, Jr., M.D.
Medical Director
Oak Ridge National Laboratory
Building 4500 N
Oak Ridge, Tennessee 37830

Donald W. Goodwin, Ph.D.
Minister, United Church
Chapel-on-the-Hill
85 Kentucky Avenue
Oak Ridge, Tennessee 37830

R. Griesemer, Ph.D., D.V.M.
Biology Division
Oak Ridge National Laboratory
Oak Ridge, Tennessee 37830
(Y-12 Area, Building 9207)

Martha S. Hansard, Ph.D.
Medical and Health Sciences Division
Oak Ridge Associated Universities
P. O. Box 117
Oak Ridge, Tennessee 37830

Karl F. Hübner, M.D.
Chief Clinician
Medical and Health Sciences Division
Oak Ridge Associated Universities
P. O. Box 117
Oak Ridge, Tennessee 37830

Melvin E. Koons, J.D.
Y-12 Area
Union Carbide Corporation
P. O. Box Y
Building 9704-2
Oak Ridge, Tennessee 37830

Robert Lange, M.D. (Chairman)
Director, The University of Tennessee Memorial Research Center
Center for the Health Sciences, Knoxville Units
1924 Alcoa Highway
Knoxville, Tennessee 37920

Steve Lawrence
Manager for Administration
Oak Ridge Associated Universities
P. O. Box 117
Oak Ridge, Tennessee 37830

Clarence C. Lushbaugh, M. D.
Chairman, Medical and Health Sciences Division
Oak Ridge Associated Universities
P. O. Box 117
Oak Ridge, Tennessee 37830

L. Clifford McKee, Jr., M. D.
Metropolitan Nashville General Hospital
72 Hermitage Avenue
Nashville, Tennessee 37210

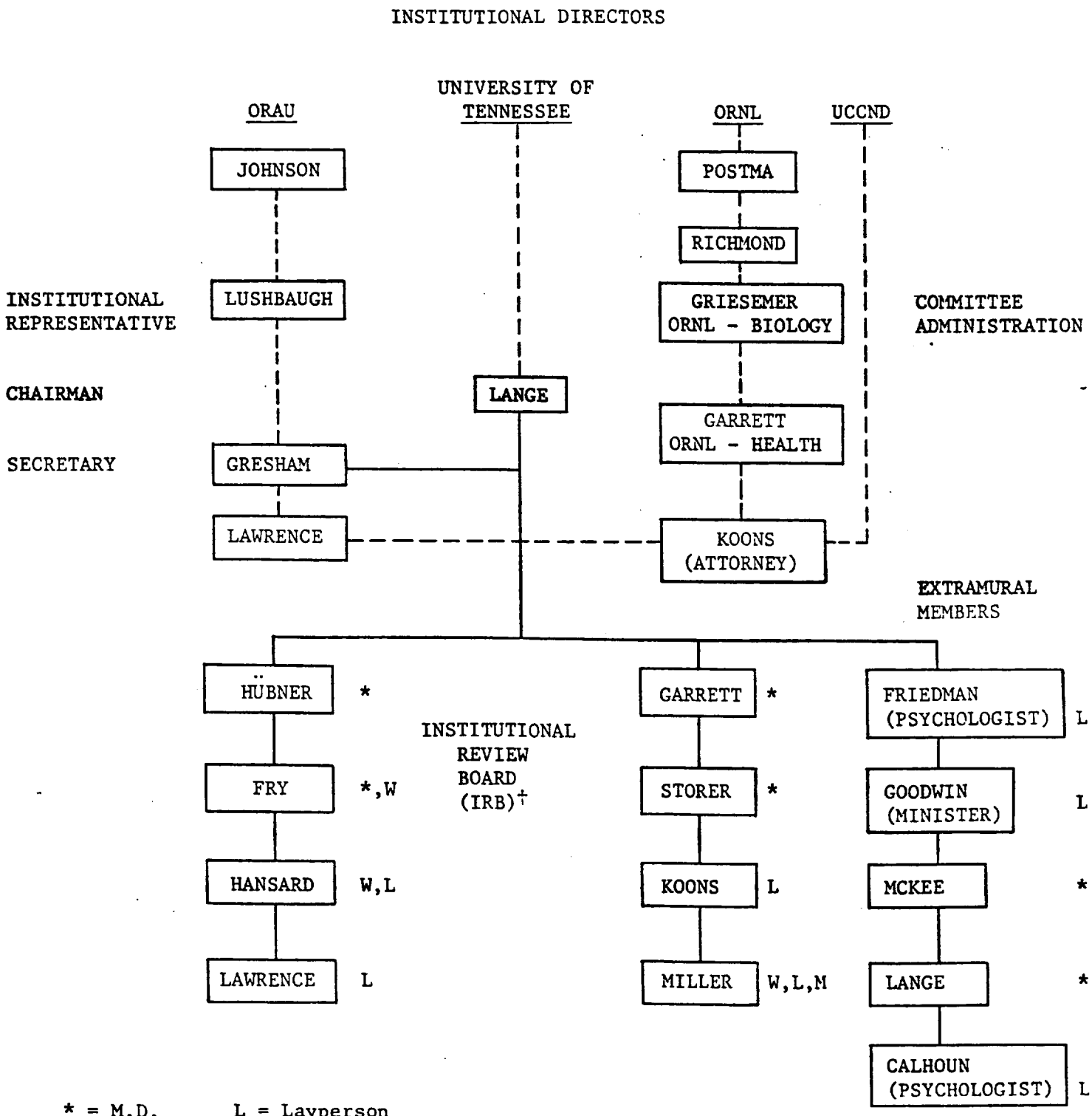
Ruby Miller, B.S.
Public Relations Representative
Union Carbide Corporation - Nuclear Division
Oak Ridge National Laboratory
P. O. Box X, Building 4500 N
Oak Ridge, Tennessee 37830

John B. Storer, M.D.
Director, Biology Division
Oak Ridge National Laboratory
Oak Ridge, Tennessee 37830
(Y-12 Area, Building 9207)

1113965

Block diagram of the bi-institutional Committee structure, administration, lines of authority and present membership and functional identities.

BLOCK DIAGRAM OF ADMINISTRATIVE AND MEMBERSHIP STRUCTURE OF ORAU/ORNL COMMITTEE ON HUMAN STUDIES



* = M.D. L = Layperson
W = Woman M = Minority

†ON ORNL PROPOSALS, ORNL AFFILIATES DO NOT VOTE; ON ORAU PROPOSALS, ORAU AFFILIATES DO NOT VOTE; EXTRAMURAL MEMBERS VOTE ON ALL PROPOSALS.

†VOTING MEMBERS

1113966

ORAU/ORNL COMMITTEE ON HUMAN STUDIES MEMBERS

1967 - Present

G. A. Andrews, M.D.
E. Balish, Ph.D.
A. B. Brill, M.D.
*W. Calhoun, Ph.D.
R. J. Cloutier
C. L. Edwards, M.D.
*H. R. Friedman, Ph.D.
*S. A. Fry, M.B., Ch.B.
*A. S. Garrett, M.D.
*D. W. Goodwin, Ph.D.
R. O. Goh, M.D.
*R. Griesemer, Ph.D., D.V.M.
*M. S. Hansard, Ph.D.
H. Harmon
R. Heyssel, M.D.
*K. F. Hübner, M.D.
R. M. Kniseley, M.D.
*M. E. Koons, J.D.
*R. D. Lange, M.D.
*S. Lawrence
S. Lawyer, J.D.
T. A. Lincoln, M.D.
*C. C. Lushbaugh, M.D.
*L. C. McKee, M.D.
*R. Miller
B. M. Nelson, M.D.
*J. B. Storer, M. D.
E. Tompkins
J. B. Woods, M.D.

*Current Membership

2/23/81

1113967

ORAU/ORNL COMMITTEE ON HUMAN STUDIES

January 1977

Gould A. Andrews, M.D. (Secretary)
Director of Clinical Applications
Medical and Health Sciences Division
Oak Ridge Associated Universities
P. O. Box 117
Oak Ridge, Tennessee 37830

Telephone 483-8411, Ext. 359

A. Bertrand Brill, M.D., Ph.D.
Associate Professor, Dept. of Medicine
Division of Nuclear Medicine & Physics
Vanderbilt University School of Medicine
Nashville, Tennessee 37203

FTS: 8, 8, 852-5022, #322-2394

Donald W. Goodwin, Ph.D.
Minister, United Church, Chapel-on-the-Hill
85 Kentucky Avenue
Oak Ridge, Tennessee 37830

482-1016 - Office; 482-1850 - Home

Karl F. Hübner, M.D.
Chief of Outpatient Clinical Studies
Medical and Health Sciences Division
Oak Ridge Associated Universities
P. O. Box 117
Oak Ridge, Tennessee 37830

483-8411, Ext. 285

Melvin E. Koons, J.D.
Y-12 Area
Union Carbide Nuclear Company
P. O. Box Y
Building 9704-2
Oak Ridge, Tennessee 37830

483-8611, Ext. 3-5979

Robert D. Lange, M.D. (Chairman)
Assistant Director
University of Tennessee Memorial
Research Center & Hospital
1924 Alcoa Highway
Knoxville, Tennessee 37920

971-3235

Michael Scott Lawyer, J.D.
Staff Attorney, Oak Ridge Associated
Universities, P. O. Box 117
Oak Ridge, Tennessee 37830

483-8411, Ext. 207

Thomas A. Lincoln, M.D.
Director, Health Division
Oak Ridge National Laboratory
Building 4500-N, Room K-122
Oak Ridge, Tennessee 37830

483-8611, Ext. 3-6681

Clarence C. Lushbaugh, M.D.
Chairman, Medical and Health Sciences
Division
Oak Ridge Associated Universities
P. O. Box 117
Oak Ridge, Tennessee 37830

483-8411, Ext. 215

John B. Storer, M.D.
Director, Biology Division
Oak Ridge National Laboratory
Oak Ridge, Tennessee 37830
(Y-12 Area, Building 9207)

483-8611, Ext. 3-7135

1113968

Oak Ridge Associated Universities

Post Office Box 117
Oak Ridge, Tennessee 37830
Telephone 615 483-8411

Medical and Health Sciences Division

Oak Ridge Associated Universities and Oak Ridge National Laboratory
Committee on Human Studies

Gould A. Andrews, M. D., Secretary
Director of Clinical Applications
Medical and Health Sciences Division
Oak Ridge Associated Universities
P. O. Box 117
Oak Ridge, Tennessee 37830

A. Bertrand Brill, M. D., Ph.D.
Associate Professor, Dept. of Medicine
Division of Nuclear Medicine & Physics
Vanderbilt University School of Medicine
Nashville, Tennessee 37203

Donald W. Goodwin, Ph.D.
Minister
United Church
Chapel-on-the-Hill
Oak Ridge, Tennessee 37830

Karl F. Hübner, M. D.
Chief of Outpatient Clinical Studies
Medical and Health Sciences Division
Oak Ridge Associated Universities
P. O. Box 117
Oak Ridge, Tennessee 37830

Melvin E. Koons, J. D.
Union Carbide Nuclear Company
Y-12 Area, P. O. Box Y
Building 9704-2
Oak Ridge, Tennessee 37830

Robert D. Lange, M. D., Chairman
Assistant Director
University of Tennessee
Memorial Research Center & Hospital
1924 Alcoa Highway
Knoxville, Tennessee 37920

Thomas A. Lincoln, M. D.
Director, Health Division
Oak Ridge National Laboratory
Building 4500-N, Room K-122
Oak Ridge, Tennessee 37830

Clarence C. Lushbaugh, M. D., ex officio
Chairman, Medical and Health Sciences Div
Oak Ridge Associated Universities
P. O. Box 117
Oak Ridge, Tennessee 37830

John B. Storer, M. D.
Director, Biology Division
Oak Ridge National Laboratory
Y-12 Area
Building 9207
Oak Ridge, Tennessee 37830

Joan B. Woods, M. D.
Psychiatrist
Oak Ridge Mental Health Center
Oak Ridge, Tennessee 37830

1113969

11-75

Formation of Committee on Human Studies

April 6, 1967:

Dr. Robert Heyssel

Dr. Robert Lange

Dr. Gould Andrews

Dr. Lowell Edwards (Ex Officio)

Sept. 15, 1967: (added)

Dr. Edward Balish

Dr. Kong-oo Goh

July 10, 1969: (2 replacements, 2 new members added)

Dr. A. B. Brill (to replace Dr. Heyssel)

Dr. John B. Storer (to replace Dr. Goh)

Mr. Melvin Koons

Dr. Bill Nelson

Jan. 1970: Dr. T. A. Lincoln (to replace Dr. Balish)

Aug. 13, 1971: Membership remains the same, but Dr. Lange asked to be relieved of duties of Chairman and Secretary. It was decided that Dr. G. A. Andrews assume the duties of these offices.

1113970

PROPOSALS - ORAU/ORNL COMMITTEE ON HUMAN STUDIES

Clinical Trial of $^{113}In^{m}$ as a Kidney and Bone Scanning Agent

Clinical Trial of ^{68}Ga-Labeled Hydrous Ferric Oxide Colloid

Immunotherapy of Acute Leukemia

Marrow Grafting Following TBI

Use of Radioiodine in Surgical Removal of Thyroid Cancer
(No formal proposal)

Use of Small Tracer Doses of Rare Elements in Human Volunteers
(No formal proposal)

A Study of Infections in Cancer Patients

Study of Granulocyte Kinetics in Myeloproliferative Diseases

Tumor Scanning with Gallium-67

Studies of TBI in Patients with Hematologic Disorders

Blood Lymphocyte Survival and Distribution in Patients with Lymphoproliferative Disorders

Scanning Tumors of the Retroperitoneal Lymph Nodes after Intralymphatic Injection of Radioactive Gallium

Therapeutic Allogeneic Transplantation of Human Bone Marrow

Proposal to Visualize Lymph Node Drainage after Scanning Doses of Gallium-67

Histologic Changes in the Skin Related to the Graft-vs-Host Reaction after Marrow Transplantation

Changes in Blood Enzyme Levels Following Exercises and/or TBI in Man

Chromosomal Breakages in Fibroblasts from Women Taking Oral Contraceptives

Scandium Augmented Gallium Localization in Tumors - Phase I and Phase II Studies

Regulation of Granulopoiesis

Use of a Radioprotective Drug in Radiation Therapy: Metabolism of ^{35}S Labeled WR-2721

Mechanism of Immunotherapy of Human and Animal Cancers by Intralesional Injection of *Mycobacterium Bovis* (BCG)

1113971

Comparison of ^{111}In, ^{67}Ga, ^{206}Bi as Tumor Scanning Agents

Evaluation of Heart and Lung by the Use of an External Radioisotope

Human Performance Testing of Cancer Patients as Controls for a Study of Uremia

Clinical Testing of ^{85m}Sr as a Bone Scanning Agent

Tracer Studies on ^{47}Sc (Proposal not presented)

Application of Computer-Interfaced Gamma-Ray Spectrometer for Dynamic Function Tests

Comparison of Indium-111 Chloride and Indium-111 Sulfur Colloid in Evaluation of Bone Marrow Disorders

Effect of Splenectomy and TBI on Onset of Blast Crisis and Survival in Chronic Granulocytic Leukemia

Fate of Labeled Mononuclear Blood Cells in Tissues Especially in Lymph Nodes, Spleen, and Marrow

Feasibility of Measuring Cognitive and Psychomotor Functions after TBI in Man

Female Reaction to Sperm Histocompatibility Antigens

Erbium-171 as a Clinical Scanning Agent for Detection of Osseous and Non-osseous Tumors

Thulium-167 as a Clinical Scanning Agent for Detection of Osseous and Non-osseous Tumors

Dysprosium-157 as a Clinical Scanning Agent for Detection of Osseous and Non-osseous Tumors

Esterase Activity and Mammalian Reproduction

Carbon-11 Labeled Compounds for Organ and Tumor Localization

Clinical Use of ^{11}C-Labeled 1-Aminocyclopentane-Carboxylic Acid for Tumor Detection

Clinical Use of ^{11}C-Labeled DL-Tryptophan for Pancreas Imaging

Lipid Markers in Human Leukemic Cells

Clinical Testing of a Line Scanning Proportional Counter Camera

Plasma Esterase Analysis in Cyclic Neutrophenic Humans

Morphogenesis of Colon Cancer: Electron Microscopic Study of Human Adenocarcinomas

1113972

DOE RECORDS SCHEDULE 5

BUDGET PREPARATION, PRESENTATION, AND APPORTIONMENT RECORDS

Budget and apportionment records include the various files accumulated in the course of formulating the budget for submission to the Office of Management and Budget and to the Congress, in defending requests for funds before both bodies, and after enactment of an appropriation bill, in ensuring that the funds are used in such a way as to suffice for the appropriate period of time. The funds are made available by the Office of Management and Budget (OMB). DOE must indicate and justify regularly to OMB the proposed rate of expenditure. After the funds have been made available, DOE's controls over the funds are in the expenditure accounting records (schedule 7) and detailed information relative to expenditures is contained in the accountable officers' account (schedule 6).

This schedule applies to records of budget preparation, presentation, and apportionment except that records created prior to 1-1-21 must be offered to the National Archives and Records Service before applying the disposition instructions.

Budget records are created at various organizational levels. Budget proposals reflect the input of operating levels, as well as the coordinating work done by formally organized budget offices. The records consist of detailed workpapers and budgetary statements developed by operating units, the more significant budget statements and related papers representing consolidated submissions prepared at higher levels and forwarded to the budget officer, and the records at the highest level pertaining to the budget submission.

The budget presentation system is standardized by the OMB, which prescribes format and procedures for all Federal agencies. However, the internal reports and papers which support the budget and are used in its preparation vary from agency to agency. The budget submission, a record copy of which is designated by DOE, is a duplicate of the set of papers submitted to the OMB. These include summary statements of appropriations and expenditures, statements of contract authorizations, statements of receipts, narrative summary statements which highlight the principal features of the request, and immediately related supporting documents. The narrative presents the policies and programs which the budget request and supplemental requests support. In addition to the summaries, the submission includes schedules of obligations and statements pertaining to each type of appropriation and fund under which DOE operates. Finally, OMB requires additional supporting data pertaining to objects of expenditure, particular programs, and figures based on the cost of various types of service operations, such as personnel and payrolling activities.

DOE RECORDS SCHEDULE 5

ITEM NO.	DESCRIPTION OF RECORDS	RETENTION PERIOD
1.	**BUDGET FILES** accumulated by Headquarters and field organizations in the course of budgetary activities, including contractor, field organizations, and internal budget submissions covering construction, operations, equipment, and other cost estimates; instructions on budget preparation, workpapers, together with related documents, and correspondence.	
	a. Budget files, Office of the Controller.	
	(1) File copy of instructions on budget preparation.	Permanent.
	(2) Budget estimates, narrative statements, related schedules, and data submitted to OMB and the Congress, including amendments and supplementals, assenting and dissenting commentary by major DOE divisions, and relevant documentation.	Permanent.
	(3) All other Office of the Controller budget files.	6 years after close of fiscal year covered by budget.
	b. All other budget files.	6 years after close of fiscal year covered by budget.
2.	**FINANCIAL PLAN FILES** consisting of authorization from the Controller to field and Headquarters organizations and national laboratories setting forth by programs the amount of funds available for the fiscal year, together with papers accumulated in connection with proposed revisions and with mid-year reviews. (Exclusive of DOE files, Office of the Controller files.)	3 fiscal years after close of fiscal year covered by plan.

In: Proceedings of the National Symposium on Natural and Manmade Radiation in Space, Las Vegas, 1971, E. A. Warman, ed. NASA TM X-2440, 1972, pp.238-248.

Pulmonary-Impedance Power Spectral Analysis: A Facile Means of Detecting Radiation-Induced Gastrointestinal Distress and Performance Decrement in Man[1]

Robert C. Ricks, C. C. Lushbaugh, Earl McDow

Oak Ridge Associated Universities

and

Edward Frome

Emory University

DO NOT REMOVE

INTRODUCTION

It is common practice in routine physiologic monitoring of patients in intensive care units to measure respiratory rate and amplitude along with other vital signs by electronic means. In most respiratory studies the data are obtained through the use of impedance pneumography. This technique of measuring respiratory phenomena by means of electrical impedance has been previously described (refs. 1 and 2). These devices and techniques provide continuous analog and digital records of the patient's functional status and constantly updated visual displays of the data. Most often the values for the various vital sign measurements are displayed numerically on a cathode ray tube so that the nurse or physician can make assessments of pulse, respiratory rate, and temperature as often as desired without having to count the number of waves per time interval. In precarious clinical situations upper and lower bound alarms are used to alert the staff when changes occur that could require responsive action. Such systems, while serving well their purpose of continuous surveillance of the patient, produce large amounts of taped data that contain a wealth of clinical information often difficult to analyze in retrospect. Usually these data are stored until the tapes are needed for recording the data of other cases when they are erased. Little of them have been put to use in physiologic research or applied physiology because few methods have as yet been developed for reducing the data into a condensed form that provides clinically useful information beyond that of the analog trace itself.

Recently we reported preliminarily (ref. 3) a data reduction and analytical system for the electronic impedance pneumograph. This computerized analysis provides the investigator a power spectrum of the respiratory trace from the patient over a chosen time interval. Since, as is well known, respiratory rate and amplitude can be modified by direct, as well as reflex neural pathways from other systems, changes in impedance pneumograph traces are not unique for each kind of systemic stress that modifies breathing. These changes, however, can indicate that respiratory activity is being modified by external stimuli or extra-respiratory stresses. Examples include the common ear cough that results from irritation of the sensory endings of the auricular nerve by plugs of wax in the auditory meatus; altered respiratory patterns caused by sudden immersion in cold water, painful stimuli, nausea, vomiting, muscular effort, and blood pH and gas changes. These changes in respiratory amplitude and frequency are mediated through autonomic neural elements in the various organs concerned and are presumed to be primarily of parasympathetic (vagal) origin, best described as "vagal looping."

The purpose of our study was to see if pulmonary-impedance power spectral

[1]Research supported jointly by USAEC and NASA.

1113974

analysis could be used to detect the onset and course of gastrointestinal distress induced pharmacologically or by total-body irradiation; to see how typical the computed power spectra and their variances were for such well defined respiratory states as exercise induced hyperpnea, respiratory acidosis, and hyperventilation in volunteers and in patients exposed to therapeutic levels of total-body irradiation; and, if possible, to use this system to detect radiation induced decrements in physical performance to study their relation to exposure rate.

These observations could have some medical usefulness during extended manned-space missions (e.g., orbiting platforms and interplanetary expeditions) in a potentially hostile environment. The potential hazards of space radiation (proton fluxes, heavy primaries, X- and gamma-radiations, solar activity) have been previously reviewed by others (refs. 4, 5, 6, and 7). In addition to potentially high-flux space radiation, on-board power reactors will increase the environmental background and crew exposures on extended manned space missions. While the types and intensities of space radiation are well defined, if not predictable, the response of man to these ionizing events is not well known because of the absence of experimental observations. However, the general sequence of events involved in the radiation prodrome (nausea, vomiting, fatigue) are well documented for man (refs. 6, 8, 9, and 10), but the majority of quantitatively related radiation-induced changes have been studied in lower animals where psychological testing was primarily involved (refs. 11 and 12). The effects of radiation on the performance of rats subjected to swim tests, however, have shown that exposures of 300-1000 R depressed performance ability in a dose-rate dependent manner (ref. 13). Thoma and Wald (ref. 14) reviewed the clinical signs and symptoms of radiation accident victims and report that postexposure fatigue may be evident for 4 days to several months following exposures estimated to have been 240-600 rads to the total body. Fatigue was not measured quantitatively nor produced by objective testing; each victim described his own feeling of malaise.

A review of pertinent literature on human performance ability after radiation exposure has been published by Zellmer (ref. 15). Psychological testing of patients receiving total-body irradiation therapy has been reported by Payne (16) and demonstrates that no decrement occurs in man's ability to perform well-directed tests (e.g., USAF SAM rotary pursuit test and USAF SAM complex coordination test) after exposures of 15-50 R of X rays (0.95/min). Likewise, the same conclusions were reached after exposures of patients to 25-200 R given in 25 R fractions at 3.8 R/min. All individuals (ages 23-76 yr) exposed were being treated for malignancies (ref. 16).

Our studies, on the other hand, dealt with nondirected tests (bicycle ergometry) for assessing performance abilities during and after radiation exposure. While highly motivated individuals (e.g., trained astronauts) might be expected to demonstrate continued performance on well-directed duties even in the event of accidental incapacitating radiation exposures, their ability to perform nondirected (general activities) might be reduced. This is one question our investigation seeks to answer.

METHODS

Traces of pulmonary impedance were obtained before, during (in the case of exposure protraction), and after therapeutic levels of total-body irradiation of leukemic patients with ^{137}Cs or ^{60}Co gamma rays. The radiation facilities used have been previously described (refs. 17, 18, 19, and 20). Briefly, fractionated exposures of 30 R/day were carried out in a ^{137}Cs

1113975

total-body irradiator at a rate of 1.5 R/min, while protracted (30 R/day) and fractionated (10 R/day) exposures were administered utilizing a ^{60}Co total-body irradiator at the rate of 1.5 R/hr. An electronic physiologic monitoring system[2] was used to obtain the pulmonary impedance traces. Three surface (skin) electrodes were attached to the subject, one to each anterior lateral axillary line on each side of the subjects chest and over the xyphoid sternal process. The impedance of a 100 μamp current passing between the axillary electrodes is measured simultaneously with the cardiac current changes (EKG). The xyphoid electrode is the grounding circuit. This configuration of electrodes has been described previously by others using it to monitor the physiologic status of astronauts in space flight or in simulated tests (refs. 21, 22, 23, 24, 25, and 26). Impedance pneumograph traces were also obtained on a normal volunteer who ingested an emetic (ipecac); on normal unirradiated volunteers and patients (undergoing total-body therapeutic irradiation) all of whom exercised periodically on a bicycle ergometer. The voltage changes in pulmonary impedance were recorded on strip chart and on analog tape from which 4-minute data segments were selected, converted into digital form and analyzed using an IBM-1800 computer. In our system, in its present stage of development, digital data processing can be done in real time or in retrospect. After digital conversion, the data were processed with a power spectral analysis program which computed power spectral estimates and respiratory variances that were graphed automatically.

RESULTS

Selected impedance pneumograph traces obtained from a patient receiving 30 R/20 hr day at an exposure rate of 1.5 R/hr are shown in Fig. 1. The total exposure was 250 R over an 8-day period. These traces illustrate that normal, regular breathing occurred throughout all monitoring periods. The regularity of these impedance pneumographs is reflected by low-power spectra and nonvarying frequencies as shown in Fig. 2. During the entire exposure the patient, who had received no previous radiation therapy, felt well and did not develop nausea or loss of appetite. In Fig. 3 the pre- and postexposure pulmonary impedance traces are shown for a patient who received rapidly-delivered fractionated exposures of 30 R/day (1.5 R/min) on each of 5 consecutive days for a total exposure of 150 R. The pulmonary impedance traces became increasingly irregular postexposure with increasing exposure accumulation up through day 4. The effect of the last fractional dose (30 R) appears to have been suppressed by 20 mg chlorpromazine administered prior to exposure. The changes in pulmonary impedance are more easily visualized in the power spectra computed from them (Fig. 4). All 5 postexposure pulmonary impedance traces were obtained within 30 min after irradiation. Subjective levels of postexposure gastrointestinal distress experienced by the patient are shown in Table 1. These symptoms correlate well with the strip chart traces and the changes in their power spectral reductions. There is (Fig. 4) a progressive increase in the shift of pulmonary impedance waves to lower frequency and higher amplitude and power as radiation exposure accumulates. The patient reported that recovery from the postexposure nausea, reflected by these changes, occurred 2-8 hours later. The relative absence of symptoms and pathologic pulmonary-impedance patterns and power spectra also correlated, as seen in Figs. 3 and 4, for day 5. The daily pretreatment pulmonary impedance traces and their power spectra are remarkably uniform and normal, substantiating, apparently, the patient's

[2]Beckman Type R dynograph, Beckman Instrument, Inc. Palo, Alto, California.

1113976

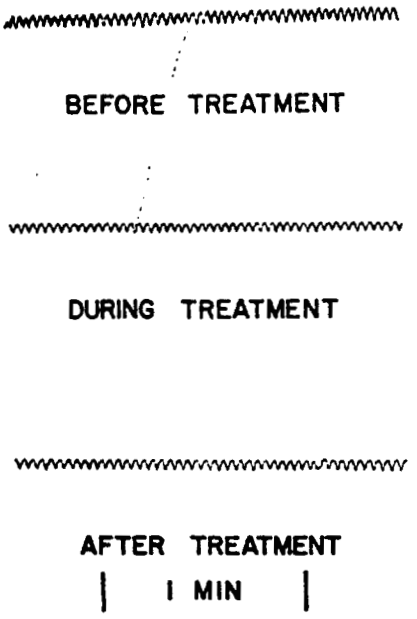


Figure 1. Strip chart tracings of pulmonary impedance recorded before, during (mid-treatment), and after treatment with 30 R daily at 1.5 R/hr.

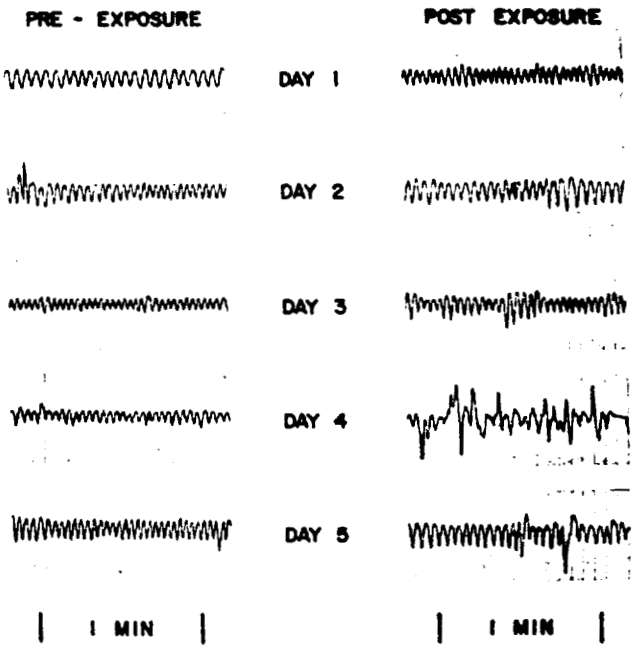


Figure 3. Strip chart tracings of pulmonary impedance following 150 R in 5 equal daily fractions at an exposure rate of 1.5 R/min.

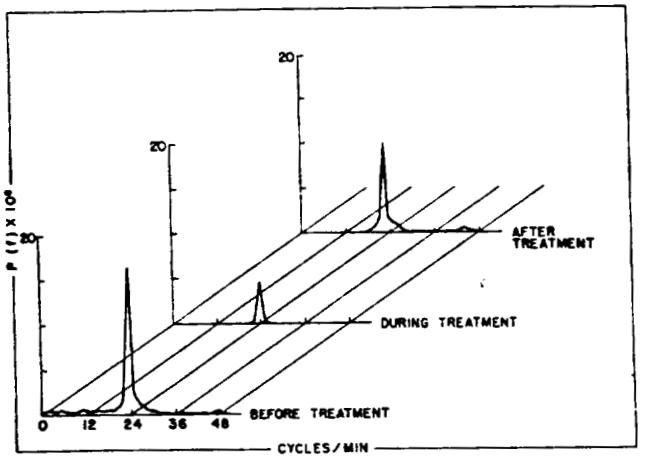


Figure 2. Graphic representation of pulmonary impedance power spectra obtained before, during (mid-treatment), and after treatment with 30 R daily for 8 days at 1.5 R/hr for a total exposure of 250 R.

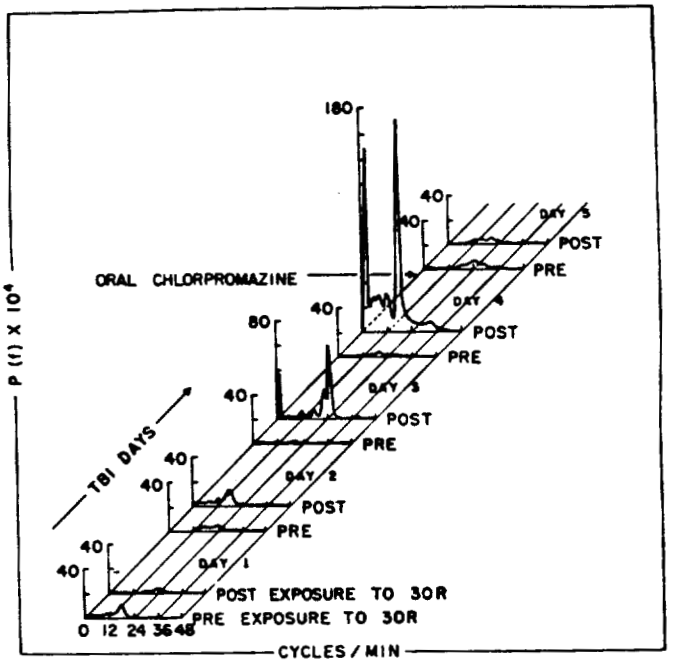


Figure 4. Graphic correlation of severity of nausea with pulmonary impedance power spectra before and 15 minutes after 20-minute exposure to 30 R (1.5 R/min on 5 consecutive days, total exposure 150 R). On the 5th day the patient was administered oral chlorpromazine (20 mg) therapy for radiation sickness.

1113977

claim that symptoms of radiation sickness were absent at those times.

TABLE I

PATIENT EVALUATION OF GI DISTRESS THAT FOLLOWED TREATMENT WITH 30 R (1.5 R/MIN) DAILY FOR 5 DAYS

Accumulated Exposure	Described GI Distress
Post 30 R	None
" 60 R	Mild
" 90 R	Moderate
" 120 R	Severe
" 150 R	Mild

The comparison of dose rate effects was enhanced by the fact that the patient who received the fractionated radiation therapy (see above) returned for additional radiation treatment but the exposure (150 R) was protracted (1.5 R/hr) over a 5-day period. Pulmonary impedance strip chart traces recorded before, during, and immediately after the therapeutic irradiation period indicate that respiratory alterations occurred prior to and early into treatment and consisted primarily of high amplitude (deep) breathing (Fig. 5). Power spectra of pulmonary-impedance wave forms (Fig. 6) reflect these findings and show that no significant pulmonary alterations occurred throughout exposure after the initial changes. No low-frequency components are present in the power spectra obtained in relation to this dose protraction, however, low frequency shifts did occur in this same patient when the exposure (150 R) was fractionated (see above). These findings are interpreted as being due to psychologically-induced nausea related to the severe nausea experienced previously by this same patient when given fractionated irradiation therapy 6 months prior. The fractionated exposure (150 R) which induced nausea in this experiment is well below the 300 rad dose (single exposure) reported by Lushbaugh, et al. (ref. 10) that resulted in a mean vomiting-onset time of 144 ± 66 min. Gerstner (ref. 9) has previously indicated that nausea and vomiting, if present, will occur approximately 6 hrs after doses below 600 rads. While this particular patient may have a low radiation-induced GI distress threshold, the dose rate influence on the human radiation prodrome is illustrated.

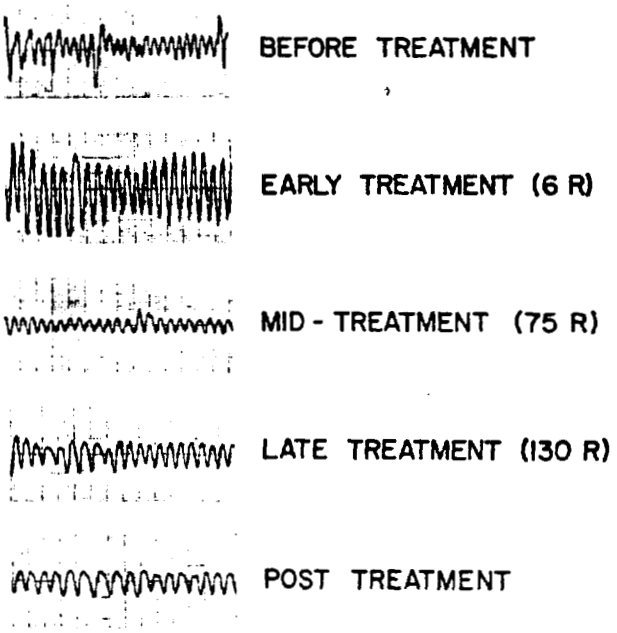


Figure 5. Pulmonary impedance tracings from patient exposed to 150 R (30 R daily) at 1.5 R/hr. Figures in parenthesis indicate accumulated R at time of pulmonary monitoring.

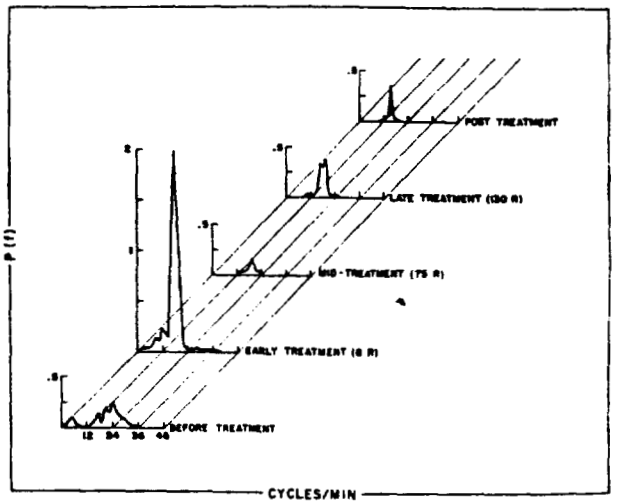


Figure 6. Power spectra of pulmonary impedance wave forms obtained at specific intervals before, during, or immediate after exposure to 150 R (30 R/day) at 1.5 R/hr. Figures in parenthesis indicate accumulated R at time of pulmonary monitoring.

1113978

In order to compare radiation and pharmacologically induced gastrointestinal distress, we obtained power spectra of pulmonary impedance wave forms from a normal male volunteer, aged 22, who was administered an emetic (ipecac). Power spectra of these pulmonary traces are shown in Fig. 7 and illustrate shifts to high-power, low-frequency components at those times when the subject experienced severe nausea (17-20 min) and when emesis occurred (49-52 and 57-60 min, respectively). These data demonstrate similar respiratory phenomena occurred (as measured by our method of analysis) in our experiments when gastrointestinal distress occurred regardless of its means of induction. The quantity of analog data obtained in this experiment encouraged us to modify the computer program to afford greater data reduction. This modification is based on the fact that the area under a pulmonary impedance power spectrum is the total variance in terms of amplitude and frequency of respiration. This single number can be computed and used as a one-dimensional expression of the level of respiratory efforts.

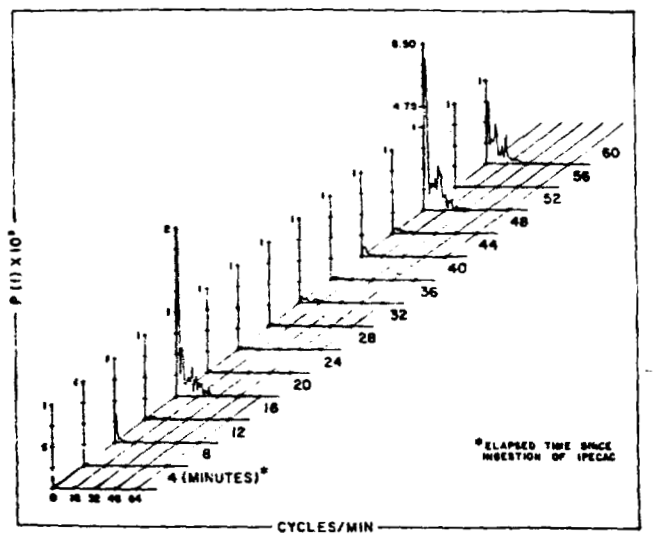


Figure 7. Power spectra of pulmonary impedance wave forms obtained over a 1 hr time period in a normal volunteer following administration of an emetic (ipecac).

When this number is plotted as it changes with time, a continuous graph is produced of the variance in respiratory effort throughout the monitoring period. This new method requires one-half the previous computing time; the output consists of two indices (a mean and the variance of the power spectrum) that can be used without graphing the individual power spectrum. In this case, the mean is the average transthoracic voltage as measured by the impedance pneumograph coupler, while the variance is directly proportional to the area under the power spectrum. The power spectrum of the pulmonary impedance wave form is not graphed in this new system unless requested by the investigator or clinician. In addition, this new method provides separate analysis of each of 4 consecutive minutes of pulmonary impedance data instead of one combined analysis of 4 minutes of data. An average mean and average variance (four 1-minute data periods /4) also is provided. We have defined the minute-by-minute variance as the continuous variance and its average over 4 minutes as the average variance.

Data obtained from the volunteer with pharmacologically induced GI distress (see above) and analyzed by the new method are shown in Fig. 8. Increased continuous variance corresponds exactly to the minute with the occurrence of severe nausea (18th min) and emesis (50th and 59th min). These changes in respiratory function are also well protrayed by the average variance which tends to smooth the data without losing fidelity. Inferences drawn from data analyzed by both the old and new methods would be the same.

We anticipated this new method would have a useful purpose in the analysis of long-term pulmonary studies and have applied it to pulmonary impedance data obtained from patients receiving total-body therapeutic irradiation, all of whom exercised on a bicycle ergometer. Figure 9 illustrates the pulmonary impedance variance obtained from a normal volunteer

1113979

before, during, and after exercising to tolerance (~8 min) against a work load of 75 watts. Shifts in both continuous and average variance occurred during the initial phases of exercise and increased to a maximum late in the exercise period. Post-exercise variances decreased periodically returning to preexercise levels at about 35 minutes.

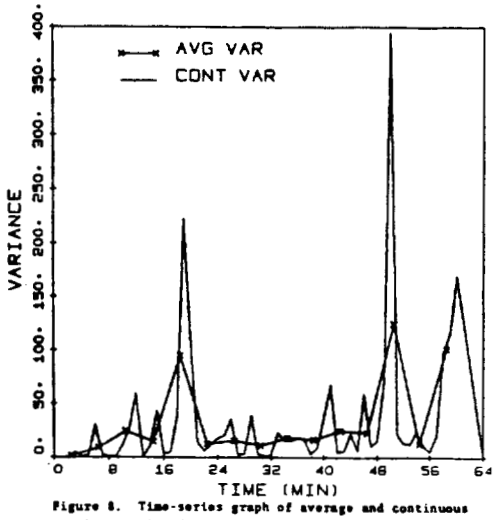


Figure 8. Time-series graph of average and continuous pulmonary impedance power spectral variances obtained over a 60 minute period in a normal subject following ingestion of ipecac.

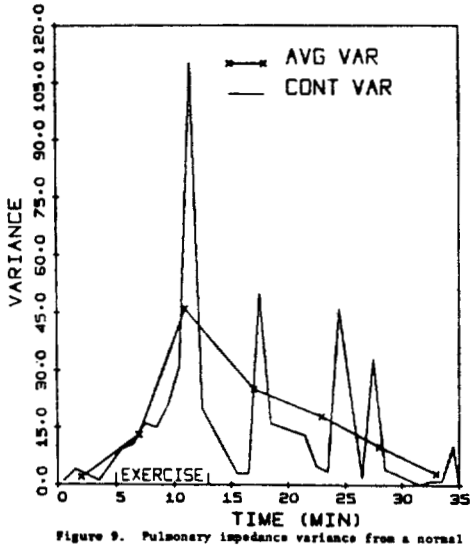


Figure 9. Pulmonary impedance variance from a normal individual obtained before, during, and after exercise on a bicycle ergometer. The exercise work load was 75 watts; pedaling speed was 60 RPM.

In order to determine the effect of total-body irradiation on performance decrement, pulmonary impedance data were obtained from selected patients receiving protracted or fractionated exposures (1.5 R/hr) and who exercised periodically before, during, and after exposure. Patients were selected on the basis of their willingness and ability to exercise and that their disease was not acutely debilitating. No aspects of radiation-induced fatigue were ever discussed with these patients. Data from two patients exposed to protracted radiation therapy (30 R/20 hr day) at a rate of 1.5 R/hr are shown in Figs. 10 and 11. Only the average variance of the pulmonary impedance power spectral data is illustrated. Increased respiratory demand during and immediately after exercise was reflected by changes in pulmonary impedance wave forms in both patients studied and closely resembled changes noted in exercising volunteers. Increased power at various respiratory rates (generally >20/min), seen as a large increase in total variance, was amplified after total-body exposures of 100-150 R. A decrement in performance ability was indicated by a greater increase in respiratory variance, after radiation, when measured at 3 and 10 days postirradiation in one patient who received 100 R (Fig. 10), and at 5 days in another patient who received 150 R (Fig. 11).

Radiation-induced performance decrement was also studied in two patients receiving fractionated exposures of 10 R daily at a rate of 1.5 R.hr and who exercised on a bicycle ergometer. The results are shown in Fig. 12. Subject A is the same individual exposed (6 months earlier) to 100 R (30 R/day) at 1.5 R/hr and who demonstrated no decrement until 3 days postirradiation. Subject B received a total exposure of 140 R (10 R/day) at 1.5 R/hr but postexposure exercise was not accomplished due to unexpected thrombophlebitis. While no postexposure performance decrement was noted, slight increases in respiratory variance did occur during exposure of both patients. The signficance of these changes is not understood at this time.

These data demonstrate that pulmonary impedance power spectral analysis is capable of detecting and predicting the onset and severity of radiation-induced gastrointestinal distress. The approach also serves

1113980

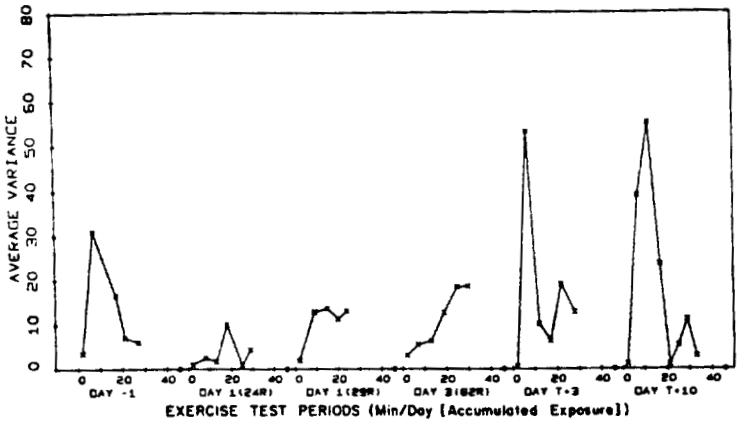


Figure 10. Pulmonary impedance variances obtained from a 62-year-old patient exercising on a bicycle ergometer before, during, and after total-body exposure (100 R) at 30 R/day (1.5 R/hr). The exercise work load was 50 watts; pedaling speed was 60 RPM. Exercise lasted 8 min for each test period.

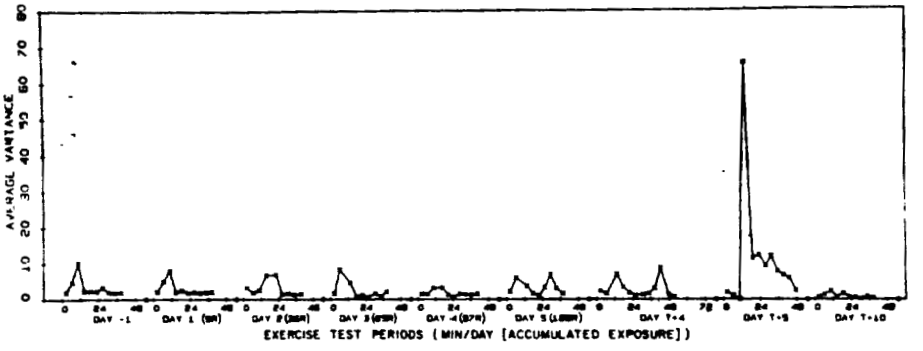


Figure 11. Pulmonary impedance variances obtained from a 65-year-old patient exercising on a bicycle ergometer before, during, and after total-body exposure (150 R) at 30 R/day (1.5 R/hr). The exercise work load was 25 watts; pedaling speed was 40 RPM. Exercise lasted 5 min for each test period.

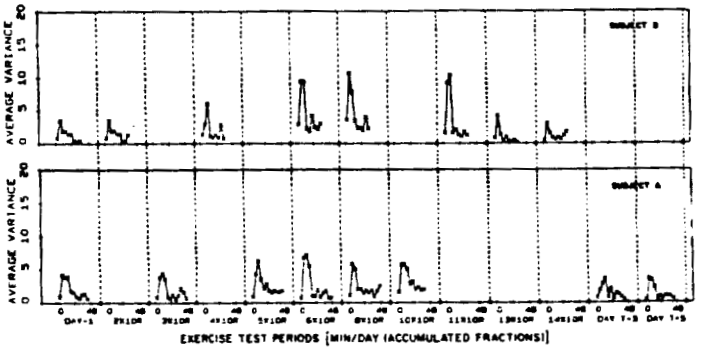


Figure 12. Treatment windows showing pulmonary impedance variance obtained from two patients before, during, and after total-body exposure to daily ^{60}Co fractions of 10 R at 1.5 R/hr. Subject A (aged 62 yr) received a total exposure of 100 R; subject B (aged 70 yr), 140 R. Each patient exercised periodically on a bicycle ergometer before and during exposure. Subject A exercised after exposure. The exercise work loads for A and B were 50 watts, 60 RPM and 40 watts, 40 RPM, respectively. Exercise lasted 5 min during each test period.

1113981

to illustrate the dose-rate influence on the human radiation prodrome and reflects the effectiveness of its chemotherapeutic control. In addition, it provides a facile means of measuring the performance decrement effects of total-body irradiation in man. The results indicate the necessity for similar studies over more extended post-irradiation time periods and a correlation of the data with biochemical changes. In experiments underway with unirradiated volunteers and with patients who receive total-body irradiation we are attempting to correlate these changes in the pulmonary impedance pneumograph during controlled exercise with levels of expired CO_2, plasma lactic acid dehydrogenase, plasma creatine phosphokinase, and plasma glutamic-oxalacetic transaminase.

SUMMARY AND CONCLUSIONS

Changes in respiratory variance revealed by power spectral analysis of the pulmonary impedance pneumogram can be used to detect and measure stresses directly or indirectly affecting human respiratory function.

When gastrointestinal distress occurred during a series of 5 total-body exposures of 30 R at a rate of 1.5 R/min, it was accompanied by typical shifts in pulmonary impedance power spectra. These changes did not occur after protracted exposure of 250 R (30 R daily) at 1.5 R/hr that failed to cause radiation sickness.

This system for quantitating respiratory effort can also be used to detect alterations in one's ability to perform under controlled exercise conditions. Performance decrement due to various stresses is difficult to quantitate because of a lack of objectivity in most tests and bias due to different levels of motivation. In our tests the end point of increased respiratory variance and the method of measuring it is too obtuse for the test subject to recognize and falsify. Increased fatigability has been reported after total-body irradiation but little is known about doses required and the time for its occurrence. Using pulmonary impedance power spectral analysis we found while observing 4 irradiated patients that increased fatigability could occur during prolonged fractionated exposures to 10 R daily and after completion of continuous exposures to 30 R/day for 5 days. The performance decrement detected by this means occurred at lower total doses than previously reported for radiation-induced fatigue and at lower exposure rates than those that cause gastrointestinal distress.

REFERENCES

1. Geddes, L. A.; and Hoff, H. E.: The Measurement of Physiologic Events by Electrical Impedance. A Review. Am. J. Med. Electron., vol. 3, 1964, pp. 16-17.
2. Geddes, L. A.; Hoff, H. E.; Hickman, D. M.; and Moore, A. G.: The Impedance Pneumograph. Aerosp. Med., vol. 33, 1962, pp. 28-33.

1113982

3. Lushbaugh, C. C.; Frome, E. L.; Davis, H. T.; and Bibler, D. S.: Power Spectrum of the Impedance Pneumograph: A Data Reduction System Producing an Analytical Parameter of Potential Clinical Usefulness. Aerosp. Med., vol. 40, 1969, pp. 425-429.
4. Langham, W. H.: Implications of Space Radiations in Manned Space Flights. Aerosp. Med., vol. 30, 1959, pp. 410-417.
5. Newell, Homer, E.; and Naugle, John E.: Radiation Environment in Space. Science, vol. 132, 1960, pp. 1465-1472.
6. Langham, Wright H.; Brooks, Phillips M.; and Grahn, Douglas (editors). Radiation Biology and Space Environmental Parameters in Manned Spacecraft Design and Operations. Aerosp. Med., vol. 36, No. 2, Section 2, 1965, pp. 1-55.
7. Odland, Lawrence T.; and Michaelson, Sol M. Space Travel: A Suggested Method for Predicting Human Response to Ionizing Radiation. Aerosp. Med., vol. 34, 1963, pp. 62-66.
8. Jenkinson, E. L.; and Brown, W. H.: Irradiation Sickness: A Hypothesis Concerning the Basic Mechanism and a Study of the Therapeutic Effect of Amphetamine and Dextro-Desoxyephedrine. Amer. J. Roentgenol. Radium Therp. Nucl. Med., vol. 51, 1944, pp. 496-503.
9. Gertsner, H. B.: Reaction to Short-Term Radiation in Man. Annu. Rev. Med., vol. 11, 1960, pp. 289-302.
10. Lushbaugh, C. C.; Comas, F.; and Hofstra, R.: Clinical Studies of Radiation Effects in Man: A Preliminary Report of a Retrospective Search for Dose-Relationships in the Prodromal Syndrome. Radiat. Res. Suppl., vol. 7, 1967, pp. 398-412.
11. Kaplan, S. J.; Gentry, G.; Melching, W. H.; and Delit, M.: Some Effects of a Lethal Dose of X-Radiation Upon Retention in Monkeys. NP 5413 (Aug. 1954).
12. Zellmer, Robert; Culver, James; and Pickering, John E.: Proton-Irradiation Effects in Primates. Radiat. Res. Suppl., vol. 7, 1967, pp. 325-329.
13. Kimeldorf, D. J.: Jones, D. C.; and Castanera, T. J.: Effect of X-irradiation Upon the Performance of Daily Exhaustive Exercise by the Rat. Amer. J. Physiol., vol. 174, 1953, pp. 331-335.
14. Thomas, G. E., Jr.; and Wald, N.: The Diagnosis and Management of Accidental Radiation Injury. J. Occup. Med., vol. 1, 1959, pp. 421-447.
15. Zellmer, Robert W.: Human Ability to Perform After Acute Sublethal Radiation. Mil. Med., vol. 126, 1961, pp. 681-687.
16. Payne, Robert B.: Effects of Ionizing Radiation on Human Psychomotor Skills. U. S. Armed Forces Med. J., vol. 10, 1959, pp. 1009-1021.

1113983

17. Brucer, M.: A Total-Body Irradiator. Int. J. Appl. Radiat., vol. 10, 1961, pp. 99-105.

18. Morris, A. C., Jr.: Measurements in a Total-Body Irradiation Facility. Int. J. Appl. Radiat., vol. 11, 1961, pp. 108-113.

19. Andrews, G. A.; Beck, W. L.; Cloutier, Roger J.; Morris, A. C., Jr.; Barclay, T. R.; Comas, Frank V.; Edwards, C. L.; and Lushbaugh, C. C.: The Low-Exposure-Rate Total-Body Irradiation Facility (LETBI). In ORAU Medical Division Research Report, 1967, ORAU-106 (1968), pp. 13-18.

20. Morris, A. C., Jr.; Barclay, T. R.; and Lushbaugh, C. C.: Physiologic Monitoring in the Low-Exposure Total-Body Irradiation Facility. In ORAU Medical Division Research Report, 1967, ORAU-106 (1968), pp. 23-27.

21. Pacela, Allan F.: Impedance Pneumography - A Survey of Instrumentation Techniques. Med. Biol. Eng., vol. 4, 1966, pp. 1-15.

22. Day, J. L.; and Lippitt, M. W., Jr.: A Long-Term Electrode System for Electrocardiography and Impedance Pneumography. Psychophysiol., vol. 1, 1964, pp. 174-182.

23. Geddes, L. A.; Hoff, H. E.; Vallbona, C.; Harrison, G.; Spencer, W. A.; and Canzoneri, J.: Numerical Indication of Indirect Systolic and Diastolic Blood Pressures, Heart and Respiratory Rate. Anestheosiol., vol. 25, 1964, pp. 861-866.

24. Geddes, L. A.: The Acquisition of Physiological Data. Int. Anesthesiol. Clin., vol. 3, 1965, pp. 379-405.

25. Montes, L. F.; Day, J. L.; and Kennedy, Lofton: The Response of Human Skin to Long-Term Space Flight Electrodes. J. Invest. Dermatol., vol. 49, 1967, pp. 100-102.

26. Day, J. L.: Review of NASA-MSC Electroencephalogram and Electrocardiogram Electrode Systems Including Application Techniques. NASA Technical Note, NASA TN D-4398, 1968.

1113984

Proceedings of the National Symposium on Natural and Manmade Radiation in Space, Las Vegas, 1971, E. A. Warman, ed. NASA Report NASA TM-2400, 1972, pp. 398-415. Predicted Levels of Human Radiation Tolerance Extrapolated from Clinical Studies of Radiation Effects

FILE COPY
DO NOT REMOVE

C. C. Lushbaugh

Medical Division

Oak Ridge Associated Universities[1]

INTRODUCTION

Whatever the merits of the pros and cons of present day debates concerning manned space exploration, results of clinical studies of radiation effects in man himself do not support the contention that man is too radiosensitive an animal for this task. Man, other animals, electrical components, machines, etc. are all radiosensitive but have different tolerance levels that can be measured by the failure probabilities of variously performing systems. These may be immediately or only remotely important biologically or operationally. Evaluation of the space radiation hazards to man depend equally upon the accuracy of our physical knowledge of the levels and kinds of radiation that he may encounter and our biological knowledge of human radiation responses. Biologically, our knowledge is qualitatively good but not quantitatively accurate for man. Most quantitative radiobiologic estimates must be extrapolated from or with the aid of studies in animals where radiation exposures can be controlled experimentally and radiation effects quantitated by destructive techniques not applicable to clinical studies. The suitability of these animal models for prediction of the kinds and levels of human responses has been gauged by many clinical studies of victims of radiation accidents and of patients undergoing elective radiation exposure in the therapy of their disease. Unfortunately, for our purposes, there have been few radiation accidents where men have been exposed to known amounts of radiation. On the other hand, in therapeutic exposures, although the dose is well known, the radiation effects are often confused by the preexisting disease process.

Never the less, my associates[2] and I have been directing the major part of our efforts at the Medical Division in Oak Ridge toward defining human radiosensitivity from such clinical studies of radiation effects (refs. 1 - 9). These studies were begun in 1959 when our first human total-body irradiator was constructed for radiotherapy of patients with uniform exposures to omnidirectional beams from an array of gamma ray emitting radioisotope sources. Since then, with the continuing support of the AEC and with support from NASA commencing in 1964, we have expanded these studies of human therapeutic and biologic effects of single rapidly delivered exposures with low dose

[1]The studies upon which this chapter is based have been supported since 1959 chiefly by the USAEC and augmented by NASA since 1964.

[2]Gould A. Andrews, R. M. Kniseley, C. Lowell Edwards, R. Tanida, F. Goswitz, Frank Comas, H. Vodopick, E. Balish, G. Kingdon, G. Littlefield, R. Ricks, W. Beck, T. Stokes, P. Aaron, E. Frome, E. McDow, A. Webb, A. Sipe, Mrs. Sutliff, and support staff.

11113985

rate exposure studies of protracted or fractionated radiation effects. Here we are now using another facility (Fig. 1) constructed solely for such exposures which in some instances have taken as long as ten days -- about the time for a round-trip lunar exploration. Coincidentally, the skin dose from ^{60}Co gamma rays in this low-exposure-rate total-body irradiation facility ("LETBI") accumulates with 1.5 R/hr exposures: the same rate that skin dose from protons would have, according to Dye and Wilkinson (ref. 10), in the worst week ever recorded for solar flare activity in space. As can be seen in Figure 2, derived from their study, the intestinal doses from the therapeutic and solar forms of irradiation and their respective rates of accumulation are widely divergent. The relatively small accumulated intestinal dose from solar protons offers little or no chance for untoward physiologic effects occurring from such radiation exposures in space.

We have broadened these direct therapeutic observations where possible by retrospective studies of clinical data obtained from other American and Canadian investigators and radiotherapists who kindly made these data available to this project. To obtain some basis for relating these results obtained with photons to those that might occur after exposure to high LET particles, we have been following closely the continuing studies of the ABCC staff at Hiroshima on the effects of mixed fission neutron and gamma irradiation that occurred in the Japanese atom bombings (see later).

This paper could end right here if the question to be answered for determining permissible exposures in space was only: What is the photon flux that "man" can "tolerate" and function in, while living under almost continuous exposure

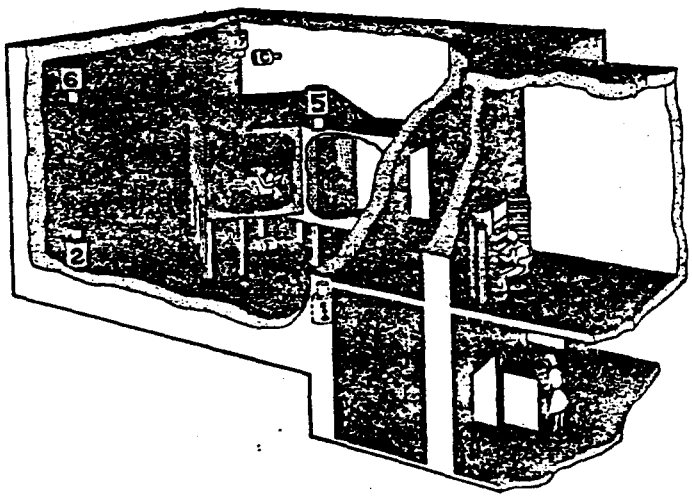
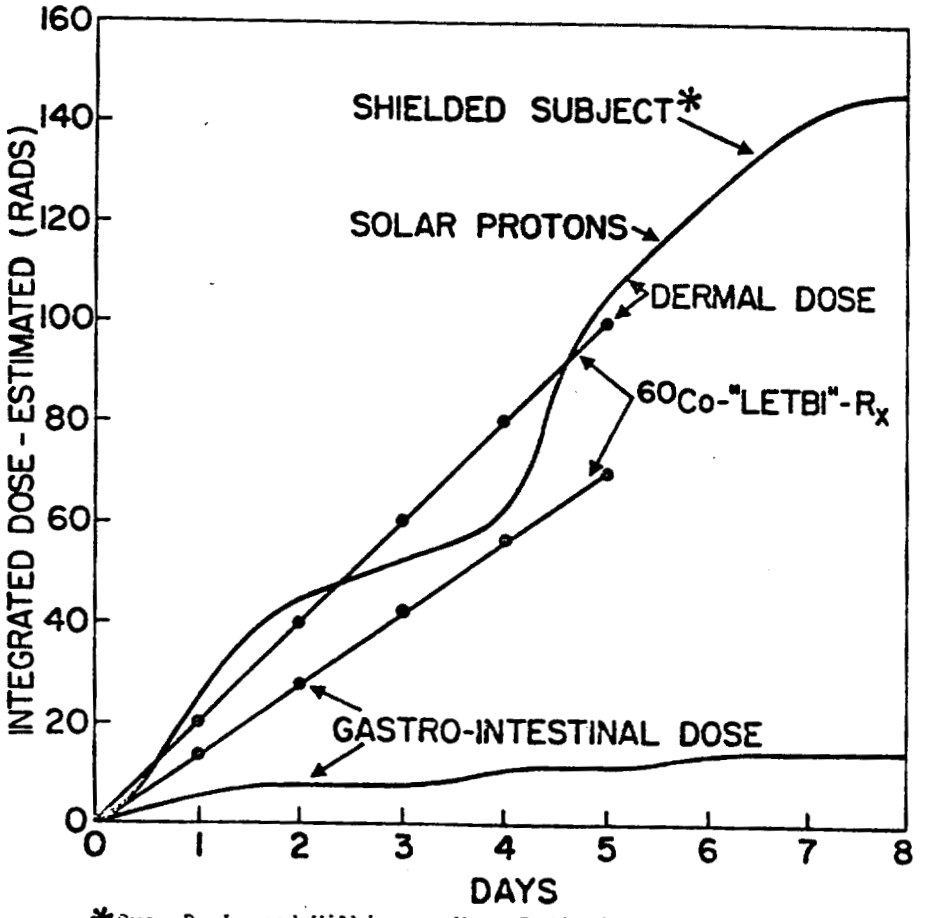


Figure 1. Cut-away diagram of the low dose-rate, total-body irradiation facility used in Oak Ridge to study the effects of protracted exposures (100 to 250 R of ^{60}Co gamma rays accumulated at 1.5 R/hr for 5 to 10 days). The location of some of the eight 26 Ci sources are shown (numbered) with the smaller trimming sources (C and F) surrounding the inner treatment room where the patient resides. The control room and data processing areas are adjacent to the 36 x 36 x 18 ft radiation containment room.

1113986



*Dye, D. L. and Wilkinson, M.: Radiation Hazards in Space, Science 147:19-25, 1 January 1965.

Figure 2. The rate of dose accumulations in the skin and intestinal tract of patients exposed to 1.5 R of ^{60}Co gamma rays/hr contrasted with those estimated for those organs of an hypothetical astronaut shielded by a space vehicle in the solar proton fluxes that occurred between 10 and 17 July 1959.

1113987

conditions? We know that patients rs as well as others) "tolerate" total accumulated exposures of photons up to 250 R (average [estimated] bone marrow doses of 150 rads) and daily exposures at rates of 28 to 33 R at 1.5 R/hr. "Toleration" here, of course, is used by me at the subjective level; only a rare patient under these exposure conditions has shown gastrointestinal distress or complained of being sick or tired. Hematologically, however, exposures of this magnitude cause therapeutic depressions in blood leukocyte or platelet levels; percentage-depressions that would not be desirable from an occupational medicine point of view. Recently, as reported in another paper (ref. 11) in this symposium, we have demonstrated, using physiologic monitoring, that, unbeknowst to the patient being irradiated at these "tolerance" levels, he becomes exercise-intolerant or more easily fatigable even though no symptoms of the prodromal radiation syndrome or GI sickness occur. Although we believe we are defining in these retrospective and on-going studies a less-than-ten-day continuous irradiation "tolerance" level for man, we also know that many more human observations are needed before we can predict with certainty how radiosensitivity of various biologic systems change when exposures occur slowly over extremely large time periods and to relatively non-reparable high LET radiations. The late biologic consequences of irregular, numerous small exposures to high, as well as low, LET particular radiations remain our most serious problem because they are the restrictive criteria on which safe levels of occupational exposures must rest.

The word "tolerance," of course, has many definitions and many inferences that change in relation to the bodily functions being considered. The term is used by me as the b: gic summation of initial response, recovery from damage, and ignorable damage remaining in the total body or a specific organ system for various periods of time. For example, the one most commonly used level of radiation tolerance for any animal species is its radiation-induced lethality expressed in terms of the exposure (R) or dose (rads) that is expected to kill 50% of that kind of animals within 30 or more days ($LD_{50/30}$; $LD_{50/60}$).

THE HUMAN LETHAL DOSE PROBLEM

There is world-wide willingness to accept the estimate that the dose that will kill the unattended normal man with 50 percent certainty within 60 days of exposure ($LD_{50/60}$) is 450 R and that the mechanism of death is damage to his hematopoietic system and defense mechanisms against infection. The degree of acceptance of this 450-R value is surprisingly high in view of its history and its lack of valid support from reported human data (ref. 12). The importance of establishing this number for man was recognized during and immediately after World War II (ref. 13). It is the obvious point of reference for relating the radiosensitivity of man to that of other mammals whose radiation sensitivity has been well established by years of extensive research - most commonly by determining precisely the LD_{50} and its confidence limits for the species (ref. 14). This number, which is reproducible experimentally in laboratories around the world for each species, has rightly become the simpliest expression for mammalian radiosensitivity. Because of the ease of its experimental determination, it has also become the end point most commonly used in radiobiological studies of relative effectiveness of various kinds of ionizing and nonionizing radiations and various kinds of radioprotective

1113988

agents and postirradiation therapy.

Just how this estimate of 450 R for man's total-body radiation tolerance was made has never been revealed publically. The assumption has been made (ref. 15) that Warren and Bowers based their estimate on lethality data obtained by the Joint Commission of the Medical Departments of the U. S. Army, Navy, and the Manhattan Engineering District in Japan during 1945. Most such accounts must be apocryphal since there was a tenfold error in the Hiroshima bomb-yield estimates that would have biased this number upwards and made it impossible to reconcile with the lower exposures in Nagasaki. These corrections, called "T65 doses" (ref. 16) are the ones now in use at ABCC in retrospective evaluation of human responses in these bombings.

Attempts to increase this estimate to 600 R, in the belief that the suggested human $LD_{50/60}$ implied a depth dose of 450 rads of photon energy, have been fought off successfully by several investigators, notably by Cronkite and Bond (ref. 17) on the basis of their observations of the hematopoietic responses of the Marshallese natives, inadvertently irradiated by fallout after a Bikini atom bomb test (ref. 18).

The LD_{50}, by definition, forms the best single measurement of the upper or acute lethal boundary of total-body radiation tolerance (see Fig. 3). There have been several attempts to check the 450-R estimate from human case histories after both accidental and intentional radiation exposures. These are tabulated in Table 1 to show how all studies have produced values lower than the original estimate and seem to indicate that 450 R is too high to be considered an estimate of midline depth-dose (absorbed radiation energy). The table also includes the results of two recent attempts to obtain

Table 1

EDUCATED GUESSES AND SOME CLINICAL AND STATISTICAL ESTIMATES OF HUMAN TOTAL-BODY RADIATION TOLERANCE

	$LD_{50/60}$ Exposure	$LD_{50/60}$ Dose
A. NORMAL MAN		
1. Warren and Bowers (ref. 12)	450 R	
2. Cronkite and Bond (ref. 17)	350 rad	
3. Langham (ref. 15)	430 R	(285 rad)
4. Jablon et al. (ref. 19)	405 rem*	
B. PATIENTS		
1. Mathé et al. (ref. 20)	400 R	
2. Langham (ref. 15)	380 R	(250 rad)
3. Lushbaugh et al. (ref. 4)	370 R	(245 rad)
C. NORMAL MAN + BLAST AND BURN TRAUMA		
1. Lushbaugh and Auxier (ref. 21)	260 rem†	

*RBE for fission neutron component = 5.

†RBE for fission neutron component = 2.

1113989

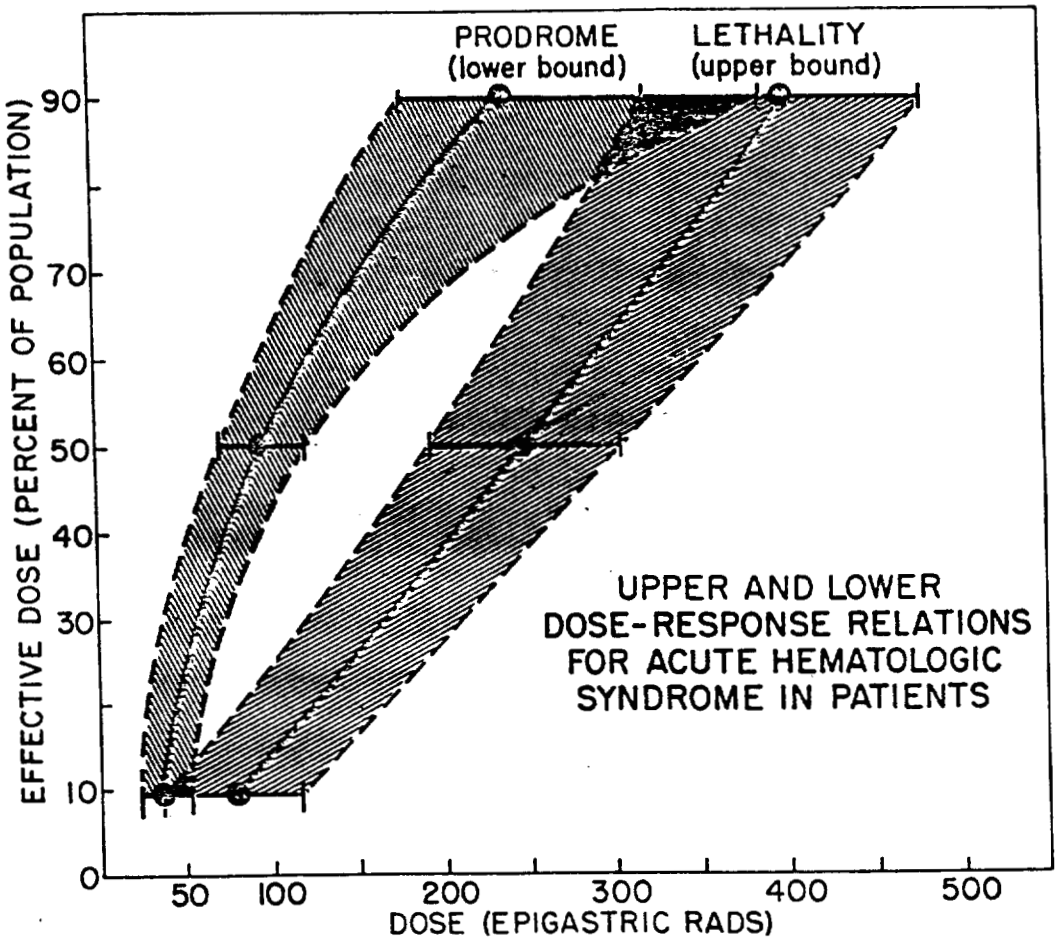


Figure 3. Acute hemopoietic syndrome is defined graphically by estimates of effective single doses for radiation-induced anorexia and lethality in patients. The probit regression lines have shaded fiducial limits. Depth dose is shown in "epigastric" rads to indicate that it is the fraction of the free field of photon radiation absorbed in the midline, midplane of the upper abdomen. This reference dose is usually 64 to 68 percent of the exposure in an average-sized man.

1113990

estimates of the human LD_{50} from the Hiroshima-Nagasaki exposures to mixed fission neutrons and gamma radiation (refs. 21 and 19). Many large animal experiments using fission neutrons, particularly those of Alpen (ref. 22) and Bond (ref. 23) and co-workers have provided a strong basis for forming the opinion that in "large" animals like man, dogs, swine, and cattle the RBE or QF for high LET radiation is 1.0 for acute hematopoietic death (ref. 15). In studies of human dermal responses to fast neutrons (refs. 24 and 25), RBE values of from 2 to 4 are needed, as in lower animals, to equate neutron dose for skin erythema with that of the reference (low LET) radiation. A QF value of 3 for high LET radiation (>3.5 keV/μ) has, however, been suggested only for damage to skin, intestines, and germinal epithelium (and not for prodromal responses, early hematologic responses, as well as hematopoietic death [ref. 15]). This recommendation seems to me to depreciate the well-known, experimentally-proven fact that sublethal cellular injury induced by high LET radiations is irreparable and as permanent as the cell in which it occurred. It would seem biologically more conservative, particularly from a safety point of view, to assume that in human tissues, including marrow, the damage caused by a dose of high LET radiation would be poorly repaired as it is in similar small animal tissues, and that hematopoietic as well as skin and intestinal crypt stem-cells would suffer equally in respect to actual dose from the same high LET radiation.

The answer to this problem is still disputable, but the more recent observations in the Japanese lend weight to the other side of the question for the first time. Lushbaugh and Auxier (ref. 21) used data from an unpublished study of the effects of various kinds of shielding upon survival in both cities in relation to the T-65 dose estimates of the free-field fluxes at the 50 percent survival points. They obtained an LD_{50} estimate of 260 rem using an RBE of 2. This estimate was expected to be low because it should reflect the additive effects of heat and blast combined with radiation-induced damage. The more recent study by Jablon et al. (ref. 19), relates the estimated individualized doses received by ∿100,000 survivors in the two cities with their clinical history of epilation and oropharyngeal hemorrhages. The human pharyngeal-epithelial and tonsillar-adenoidal barriers to infection have not been given much consideration in recent discussions of the acute hematopoietic syndrome. Yet it is an excellent objective end point for measurement. This painful, hemorrhagic sore throat is a symptom complex known as agranulocytic angina that stems from pharyngeal ulceration, bacterial invasion, granulocytopenia, and thrombocytopenia. By using this system complex as the measurable quantum of damage from total-body irradiation, any additive effect of other forms of concomitant trauma was avoided in the ABCC study. As can be seen in Table 2, the isoeffective exposures are only equal in rem when an RBE much greater than unity is used for the neutron component of the exposures. The isoeffective exposure dose (ED_{50}) of 405 rem that was found is remarkably close to the original human LD_{50} estimate. It is an even closer estimate of the exposure field strength that would be required for a mid-line human dose of 285 to 300 rads suggested as the possible human $LD_{50/60}$ by Langham (ref. 15) and Cronkite and Bond (ref. 17). The 310 rem, estimated as the isoeffective estimated dose for epilation in both cities using an RBE of 4 for neutrons, is likewise remarkably close to the widely accepted clinical value of 300 R

Table 2

FIFTY-PERCENT ISOEFFECTIVE EXPOSURE DOSES FOR HUMAN SKIN AND BONE-MARROW DAMAGE, ESTIMATED IN SURVIVORS OF NEUTRON AND GAMMA IRRADIATION IN HIROSHIMA (H) AND NAGASAKI (N)

	Neutron RBE Used	Resulting Estimates of Isoeffective Doses*	
		H	N
		(rem)	
Epilation	1	190	300
	4	→310	310←
	5	350	310
Hemorrhage	1	200	375
	4	360	390
	5	→405	405←

*Approximated from graphic data of ABCC Study by Jablon et al. (ref. 19).

of X radiation as the radiation exposure causing epilation in man. These correspondences seem to demonstrate an internal consistency in the data and their analyses that indicates, to me at least, that neutrons do have an RBE greater than 1.0 for acute hematologic, as well as for skin, effects in man. It would seem difficult to pass the ABCC study off lightly because it does not agree with large animal observations. We should not ignore Mathé's observation (ref. 20) that the man who died after neutron exposure in the Yugoslavian radiation accident had much more extensive marrow destruction than was to be expected on the basis of his estimated dose of 430 rads. There seems to be less official reluctance to accept the use of a large RBE for neutrons and other high LET radiation when late-effect end points are considered. Most fractional-cell-survival studies demonstrate well the relative irreparability of sublethal cellular damage after high LET radiation exposure and provide a firm experimental basis for assuming a large QF for such effects as genetic damage, leukemogenesis, and carcinogenesis after single exposures. When coupled with the decrease in "damage efficiency" that occurs in most biologic systems with increasing protraction or fractionation of the same total exposure, the RBE increases further (ref. 26). There is not much clinical information about high LET radiation in man other than that about the well-known effects of alpha-particle exposures in victims of radium poisoning and in uranium miners. The data under study by ABCC provides unquestionable verification for the large QF for fission neutrons for leukemogenesis and thyroid carcinogenesis (ref. 27) after single exposures.

In Figure 3 the acute hematopoietic syndrome of irradiated man is defined as the probability of of response estimates in respect to total-body photon exposures. Here, probability of lethality forms the upper bound and that of acute GI distress of the prodromal syndrome forms the lower bound of the envelope. How these dose-response relations shift when exposure is prolonged or fractionated is our continuing problem.

Retrospective studies of a large volume of clinical data extracted from hospital charts of 2000 patients given therapeutic total-body irradiation have given us dose-response relations for the symptoms and signs of the prodromal syndrome. The statistically determined single exposures that can be expected to produce these symptoms in 50 percent of the patients so exposed are shown in Table 3 along with the increased levels of the exposure required for the same incidence when the exposure period is lengthened.

When total-body exposure occurs promptly in less than one day, the effective dose for 50 percent incidence of these response (ED_{50}) are: anorexia, 147 R; nausea, 210 R; vomiting, 277 R; and diarrhea, 348 R. The log-normal frequency distribution of these responses in respect to dose indicates that

1113992

Table 3

ACCUMULATED ESTIMATED EXPOSURES* FOR

50 PERCENT INCIDENCE OF PHYSIOLOGIC SYMPTOMS

	Exposure Length (Number of Patients)		
	<1 Day (504)	<8 Days (105)	>8 Days (1083)
		(R)	
Anorexia	147	309	600?
Nausea	210	397	750?
Vomiting	277	745	>900?
Fatigue	223	400?	
Diarrhea	348	800	

*Midline upper abdominal dose (RAD = 0.66 Exposure R).

? = Guesstimate; 20 to 30 R/day is apparent threshold of dose rate.

the exposures required for their 10-percent incidence would be about one-fourth of that for a 50-percent incidence (ref. 4). The probability dose-response curves predicting the population incidence of these responses are steepest for anorexia and become progressively less steep for nausea, vomiting, and diarrhea in that order. This family-like relationship of the probability curves for the occurrence of the effects from mild to severe suggests that individual variation in ability to repair the underlying physiologic damage is progressively greater for each step in severity. If true, this analysis predicts that a radiosensitive person who shows, for example, nausea at a low dose would be more likely to show other symptoms and signs of greater damage per unit of irradiation than a radioresistant person in whom nausea did not occur without a much greater exposure. Except for the low-radiation-damage threshold of the human spermatogonia type B of about 15 rads, these gastrointestinal physiologic effects are the most radioresponsive. In the context of space exploration, these early gastrointestinal effects appear to be the most likely symptoms to occur with small exposures and therefore to be the most likely to reduce performance capabilities. Their occurrence would be improbable, however, when the exposing radiation flux was less than 20-30 R/day and the radiation was poorly penetrating, two conditions that, on the basis of previous space radiation measurements, seem to have a high probability. Nothing is known to suggest an RBE for high LET radiation for production of these physiologic effects. Although one might guess that the quality factor (QF) might be greater than three, the results of studies on the effect of dose protraction upon the size of the effective exposure dose (shown in Table 3) in 1,085 patients given small, daily total-body exposures, suggest that between 20-30 R/day are required for 30 or more days to cause these symptoms; exposures of from 10 to 20 R/day produced nausea infrequently even when these exposures were delivered rapidly at approximately daily intervals for three to four weeks; exposures of about 5 to 6 R.day were physiologically symptomless.

Although all of our statistically validated human information in this area is derived from exposures to photons, there is no reason to believe that fission neutrons delivered in small daily doses for prolonged periods to the sensitive midabdominal trigger-zone would produce damage that would ever summate in the acute onset of gastrointestinal distress. This opinion would seem correct, particularly if chronic exposures are constrained by current planning limits of 0.15 rem/day through reactor shields (ref. 15).

Recent observations obtained during the physiologic monitoring of patients in our LETBI unit during and after low-exposure rate (less than

1113993

1.5 R/day and low total daily ex ıre of less than 30 R/day) confirm these analyses of patients' charted histories that reveal the absence of acute GI distress under these conditions (ref. 11). They indicate, however, that increased fatigability can occur with small daily exposures of this magnitude. These studies are still too fragmentary to be considered a statistically sound basis for predicting the incidence of radiation-induced fatigue at low-exposure rates. So far, however, using bicycle ergometry, we have observed performance capability has decreased after single, prompt exposures (150 R) and after low-exposure rate, fractionated, 15 daily exposures of 10 R (150 R). These measurements, based on pulmonary impedance pneumography, seem to show that this form of performance decrement follows a cyclic-time course with a periodicity depending on the initial rate of induction of radiation damage. The long duration of the effect after one exposure could conceivably be enhanced by subsequent, remotely-spaced exposures but we are uncertain of this. This effect could be a threat to performance during long-duration space missions if small radiation exposures and muscular inactivity worked together to reduce physical strength and conditioning.

EFFECT OF MULTIPLE EXPOSURES ON LETHALITY

Almost nothing is known in truly quantitative terms about the effect of protraction or fractionation of human exposures upon the size of the isoeffective lethal dose. The Space Radiation Study Panel used an unpublished study of Focht, Nickson, and Langham in its evaluation of this problem (ref. 15) to see if clinical data obtained from the medical records of the Heublein total-body irradiation unit, Memorial Hospital, could be fitted to a Strandqvist-type of mathematical model. In this retrospective s y the relative roles of the basic disease and of the protracted low-dose-rate radiation in causing death could not be determined. Whether or not a patient died during or within 60 days of his treatment was recorded only as yes or no quantal information and graphed in relation to total accumulated exposure and duration of exposure. The three graphic areas defined by exposure and time were delineated by the incidences for >90% death, 50% death, <10% death. The best fit of these data to three parallel lines for the 90, 50, and 10% probabilities of death were then computed by Langham (unpublished) using a "Strandqvist" (ref. 28) power function model:

Isoeffective (fractionated) $LD_{50} = 345\ t^{0.26}$

Where 345 is the assumed nominal single lethal dose in rads (midline absorbed photon energy) for a single protracted exposure to about 530 R of X radiation over one week; t is used for exposures longer than 1 week's duration and the exponent of t is the power-function or slope constant of the log-log regression line.

This model and its parameters were graphed (Fig. 4) by the author to show how this model predicts these isoeffective lethal dosage levels (90, 50, and 10%) will increase with increasing durations of exposure up to a year. The amount of repair predicted by this model for photon irradiation is remarkable. It is of interest that the power function (or slope constant) derived from the best fits was 0.26, a number remarkably similar to that factor for normal skin damage and tumor cures (ref. 28) and hematologic damage (ref. 29). As shown in the figure, this model predicts 50% survival at 18 rads/wk or ∿3 rads (marrow dose)/day/year. The slope of this regression line for increase in LD_{50}, as marrow

1113994

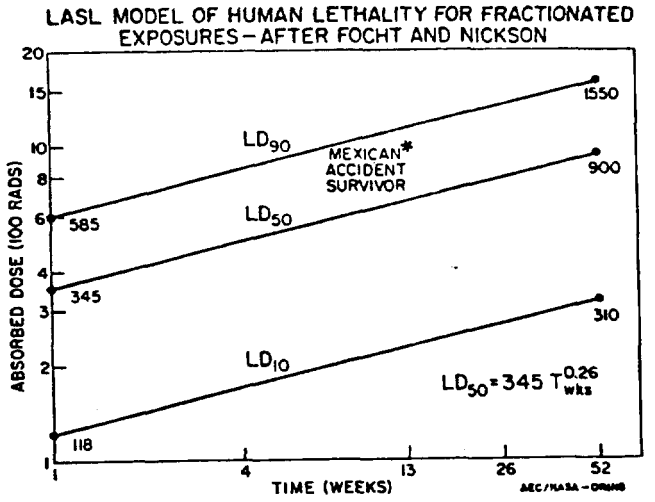


Figure 4. The Los Alamos Scientific Laboratory (LASL) model for human lethality computed from clinical total-body irradiation data of Focht and Nickson using the method of Strandqvist to determine the power function for duration of exposure in weeks.

dose is protracted, would be steeper if fatal diseases were not present in the study population. A recent study of clinical and accident data indicates that this slope may be increased as much as 2 or 3 times if the exposed persons have normal-health hematopoietic systems (ref. 29).

Low-dose-rate exposure at the rate suggested by these combined observations (about 10 R/day if the Yuhas correction of 3 is accepted) is, however, apparently not tolerable for man for a year. In fact, the events in the 1964 Mexican accident can be interpreted as demonstrating that in only 100 days of such irradiation an exposure close to that for lethality will be accumulated at ∿10 R/day (ref. 30). One of the victims in this accident was literally irradiated to death in 115 days, during which time she received an estimated 2,000 to 3,000 rem of cobalt-60 gamma radiation (15 to 25 R/day [see Table 4]). Her husband, who is still surviving at the time of this writing seven years after the accident (shown by the asterisk in Figure 4) received his daily exposures (984 to 1,717 rem in 106 days) during the night while sleeping. His wife and his mother were irradiated continuously day and night as they worked about the house where an unrecognized radiography ^{60}Co source was stored. The four deaths in this family of five were found at autopsy to be from severe hematopoietic damage that led to hemorrhage and infection. All but the survivor acted as though they had a plague-like disease. The survivor, however, had surprisingly few symptoms and signs of illness in contrast to the severe radiation-induced atrophy of his bone marrow that was subsequently demonstrated by marrow biopsy. What symptoms he had were chiefly referrable to his low-grade anemia rather than his severe leukopenia.

Table 4

1964 MEXICAN ^{60}CO RADIATION ACCIDENT

(Martinez et al., 1964)

	Exposure (days)	Estimated Exposure (rem)	Approximate Exposure Rate Ranges (rem/day)	(rem/hr)	After Survival (days)
Son	24	2940-5165	125-250	5-12	18
Wife	115	1996-2938	17-26	0.7-1	2
Daughter	99	1373-1872	14-19	0.5-0.8	30
Mother	90	1818-2897	20-32	0.8-1.3	80
Survivor* (Husband)	106	984-1717	9-16	0.4-0.6	(7+ years)

*April 1971.

1113995

In Figure 5, two ways are s. . in which the dose-response relations may shift when exposure is protracted. There are: (a) a decrease in the slopes of the shifted probability lines caused by greater repair of radiation damage accumulated slowly (revealed as a greater variation in the response rates of the population); and (b) a simple displacement of dose-response envelope without a change in the slope of the lines for the probability of response. This dose-response displacement is to be expected when exposure is to high LET radiation where cellular damage is nonreparable. In Figure 6, the results are shown when the LASL study is used to predict the level of human lethality for the exposure rates of 6, 20, and 30 rads/wk. This probability estimate, shown by the solid line superimposed on those of Figure 5, supports the many observations made in mice irradiated at low-dose rates that the hematopoietic system has a remarkable ability to recover from slowly delivered photon irradiation. Recently, Yuhas, et al. (ref. 29) obtained additional evidence supporting this remarkable reparability of the normal human hematopoietic system when its exposure is made in small fractions. He derived a multifactorial regression model for human blood-cell responses to multiple as well as single total-body therapeutic exposures using approximately 2,000 clinical case histories. Individual charts were carefully selected that met strict criteria for numbers of blood examinations, dosimetry, precise diagnoses, and evidence that the individual was not in the terminal stage of his disease. The dose-response patterns of 123 single exposures and 395 multiple exposures were studied in four diagnostic groups of patients: chronic myelogenous

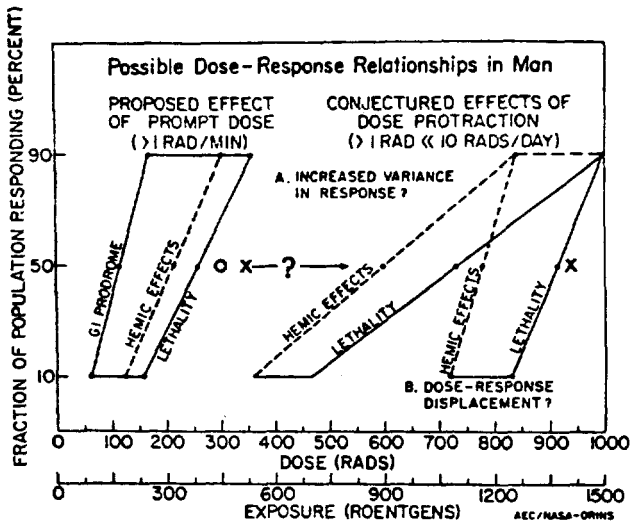


Figure 5. A graphic representation of two possible ways that clinically recognizable lower and upper dose-response probability boundaries of the hematopoietic syndrome may shift when exposure is protracted over a year.

A. Variance in the incidence of a response is increased as reparability increases as after low LET photon irradiation.

B. The dose-response envelope is displaced upwards without change in the slope of probability lines, commensurate with proliferation capacity of unhit target cells in the presence of irreparably damaged targets as after exposure to high LET particles. The prodromal symptomatology, lower bound of the prompt exposure probability envelope becomes undetectable when the daily fraction of the exposure is less than 15 R and therefore is replaced by symptoms referable to anemia or infection. (See Table 3.)

leukemia (CML), chronic lymphocytic leukemia (CLL), lymphosarcoma (LS), and nonleukemic patients with normal blood values. The percent of WBC remaining at the nadir was found to be related to a power function on total exposure and the duration of the therapy in days:

$$\% \text{ WBC} = K\,[100] \cdot [D]^{-b_1} \cdot [T]^{b_2}$$

K = a constant, required for extrapolation to the ordinate at zero dose because no effect was seen below 25 R

D = total exposure in R

b_1 = the slope of % WBC on D

T = the time of protraction in days

b_2 = the slope of % WBC on a given D or T

1113996

The slope of percent WBC on exposure was found to be essentially equal to -1.0 in all diagnostic groups (Table 5). In persons with normal marrow, percent WBC on time (T) at a given exposure (D) increased as the 0.63 power of the number of days separating the first and last fractional exposures used. In CML, CLL, and LS this exponent was found to be 0.39, 0.23, and 0.22.

Table 5

SLOPE CONSTANTS AND TESTS OF THE STATISTICAL SIGNIFICANCE OF THE YUHAS MODEL (REF. 29)

Diagnostic Group	Single Exposures		Multiple Exposures		
	b_1	Correlation Coefficients	b_2	Correlation Coefficients	P Value
"Normal"	1.04	0.57	0.63	0.535	<0.025
CML	0.999	0.82	0.392	0.569	<0.0001
CLL	0.917	-	0.221	0.583	<0.0001
LS	1.119	0.42	0.231	0.567	<0.0005

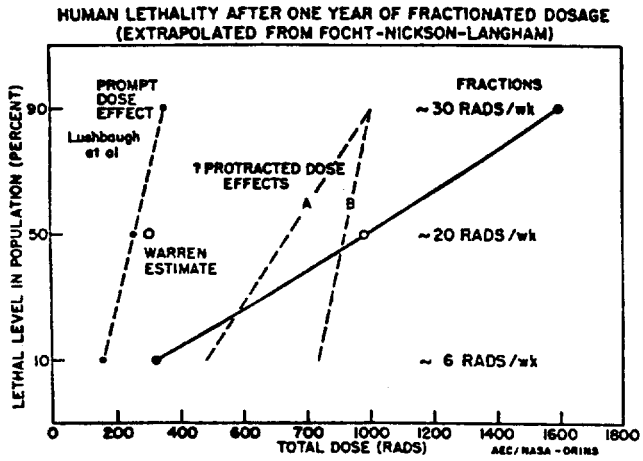


Figure 6. The conjectured effect of a year-long dose protraction upon the displacement and slope of dose-response probability regression lines (shown in Figure 5) contrasted with the prediction of the LASL model using actual data. (For further explanation, see text.)

The values for the slope constants shown in Table 5 have biological implications: The negativity of b_1 indicates that as dose increases, the percent survival of peripheral WBC decreases. The correspondence of this value for each group to 1.0 may indicate that, in the different cellular systems involved in these diseases, differences in radiosensitivity are not significant. This result is surprising in view of the widely held clinical belief that the leukocytes in CLL, for example, are much more radiosensitive than the cells comprising the WBC in CML or in "normal" persons. This apparent deviation from clinical "fact," however, can be explained by the significant differences found in the values for b_2. The larger this positive slope constant the more effective the length of exposure protraction is in increasing percent survival; according to these values, in the "normal," protection of the white blood cell level by dose protraction is three times that found in CLL and LS (see Fig. 7). In the latter groups, dose protraction should not, according to this analysis, decrease the effectiveness of the total dose as much as in the "normal" group and as, to a lesser extent, it will in the CML group. These interpretations implied by the analytical results agree well with most clinical observations and suggest, in keeping with experimental observations, that normal tissues are spared more than abnormal ones by dose protraction. This concept is in fact the rationale for fractionation and protraction of

1113997

radiation therapy of malignant tissues admidst normal ones. These observed differences in peripheral WBC survival, after the same radiation exposure, probably result more from different efficiencies of recovery mechanisms than from inately different cellular radiosensitivities in these diseases (ref. 29).

It is commonly assumed that hematologic effects reflected by changes in peripheral blood counts correlate quantitatively with lethality. This correlation, however, has not been demonstrated either clinically or experimentally. Therefore, a regression model for the effect of dose-rate upon hematologic parameters, such as blood granulocyte levels, cannot be used with much assurance as the regression model relating dose-rate and lethality. The obverse is also true. Bateman (ref. 31), however, has shown well, at least in my opinion, that dose-rate data for such end effects as human dermal responses, and lethality of mouse, rat, swine, and sheep can be fit as a linear function of the reciprocal cube root of dose rate. This empirical observation stems in large part from the way the Strandqvist model and its numerous modifications all approximate the power-function exponent of 0.33. Applying the model to the data of others where a dose-rate effect is easily demonstrable, Bateman showed that:

$$ED_{R_1} = D_{\infty} \left(1 + \frac{k}{\sqrt[3]{R_1}}\right)$$

where D_{∞} is the single dose requirement when exposure is at an infinitely rapid rate, ED_{R_1} is the isoeffective dose at some lesser rate (R_1). The size of k, the slope constant for dose-rate effect as a function of the cube root of R, seems to be related to the size of the single-exposure

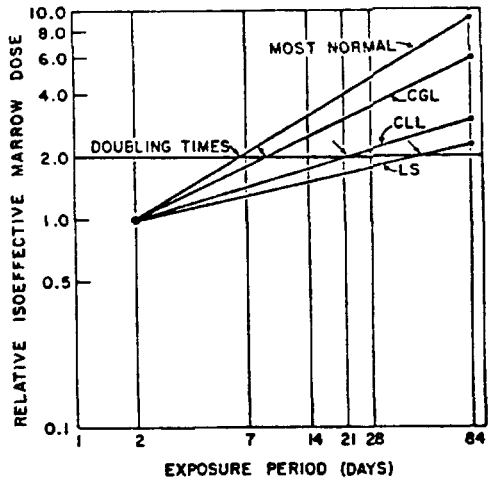


Figure 7. Graph of the rate of blood cell recovery predicted by the Yuhas multifactorial dose - WBC response model based on clinical data of total-body irradiated patients with no marrow disease ("most normal"), chronic granulocytic leukemia (CGL), chronic lymphocytic leukemia (CLL), and lymphosarcoma (LS). The data have been normalized to relative isoeffective marrow dose for two-day protraction for each set to compare the relative doubling times (straight arrows) in terms of exposure duration: 7 days, normal; 9 days, CGL; 22 days, CLL; and 42 days, LS.

dose given at conventionally rapid (therapeutic) rates. The size of k also expresses the recovery kinetics of the animal species and the cellular system involved. For example, in Bateman's study of lethality, k was 1.6 for swine, a species known to have remarkably efficient total-body repair, and 0.65 for sheep, an animal model of slow, inefficient radiation repair kinetics. Also, apparently the more radiosensitive a biologic system is (i.e., the smaller the dose is that is required to be effective) the less well it repairs the effects of this small dose; thus the size of k is variable within the same species, as it depends on the specific recovery mechanisms and kinetics of the damaged biologic system.

1113998

The Bateman model was used to construct a nomogram for human dose-rate tolerance using some of the biologic end points whose derivation and validity have been discussed above. This nomogram is shown in Fig. 8. Some of the assumptions are based on animal observations when normal human observations are not available. The extrapolations extend beyond 100 days even though the observations upon which they are based do not extend this far. They are extended to a year in the figure to correspond to the temporal requirement of deep-space exploration. Extrapolations of clinical data using the models of Strandqvist, Yuhas, and Casarett (refs. 32, 33) do not fit this reciprocal of the cube root scale of dose rate beyond one to three months after which they curve rapidly upward, away from the lines shown in the figure, indicating again perhaps the surprisingly great reparability that most tissues have of acute radiation damage induced at extremely low dose rates. Such a conclusion is, however, too optimistic for occupational radiation protection and long-mission planning guidelines since it predicts that no discernible acute responses will occur in marrow, gut, or skin below rather high dose-rate thresholds. In the absence of much objective clinical support for the quantitative relations implied by the nomogram, such reparability on the part of all men cannot be assumed. Even so, the extrapolations for the dose-rate response relation of infertility and sterility, severe hematologic effects, and hematopoietic death shown in the figure are more conservative than those of the Yuhas model, for example, as shown in Figure 7, that predict a ninefold increase in an isoeffective dose for hematologic damage to normal human marrow if exposure were fractionated over a 3-month period.

Until we obtain additional evidence that normal human marrow can actually repair as rapidly as this, the clinically conservative approach is to accept the worst predictions of the model; the doubling times of 21 to 42 days for CLL and LS, which, interestingly enough, approximate the rate that the Bateman model predicts in the nomogram (Fig. 8) by the line for "severe" hematologic response for patients.

In the dose-rate nomogram the accumulated isoeffective exposures are shown in the figure in R of photons. The encircles star, ⊛, however, along with the line for "Late Effects," which has no slope, should be considered as dose in rem. The Late Effects lines are intended to define on the nomogram the dose-rate tolerance boundary or the safe occupational upper limits for human tolerance to low-dose-rate exposure if remote and late effects, rather than prompt effects, must be considered (ref. 34). The other steeper lines in the nomograph indicate possible dose-rate effect on the size of accumulated doses for such undesirable prompt effects as the 50 percent risk of death within 60 days. Such exposures have a low probability of ever occurring in space exploration, but, as we have indicated, are the kind on which we have the most clinical information. Much more clinical information, however, is needed before the creditability of any of these lines, their slopes, and dose-rate relations can be established statistically. The nomogram does, however, support the opinion that, except for the remote possibility of some unforeseen, uncontrollably large exposure, man is more than sufficiently radioresistant to make the risks of an early acute radiation effect on one short space mission intangibly small in relation to the other non-radiation risks involved.

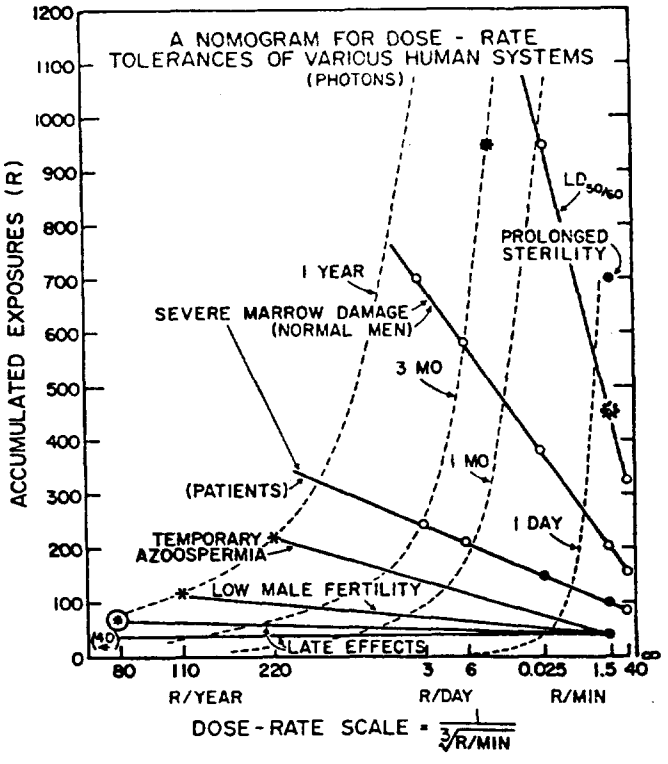


Figure 8. A nomogram predicted by the Bateman model of the effect of one-day, one-month, three-month, and one-year-long exposures on the size of accumulated exposure required to produce constant levels of several kinds of somatic damage; 60-day lethality, severe damage to normal marrow, assuming man and sheep are equally radiosensitive large animals. The smaller asterisk at ∿1000 R on the 3-month isotime line locates the Mexican radiation accident survivor (see text). The lines for severe marrow damage are extrapolated from clinical data points (solid circles) and computed points (open circles) to show damage to diseased marrow, temporary (reparable) cessation of sperm production, reduced male fertility and late effects such as increased rate of cancer induction. The largest asterisk represents the original $LD_{50/60}$ estimate for man and has a regression line with a slope constant k = 0.65 running through it. Constants (k) are assumed of 0.24 for the recovery capability of diseased and 2 x 0.24 for for normal hematopoietic systems. The lines for sterility and low fertility are based on the human data (ref. 15 [solid circles]) and canine data (small asterisks) on the one-year isotime line of Casarett and Hursh (refs. 32 and 33). The "Late Effects" lines are extracted from the Space Science Board Report (ref. 34).

1114000

REFERENCES

1. Andrews, G. A.; Lushbaugh, C. C.; Kniseley, R. M.; White, D. A.; and Friedman, B. I.: Effects of Ionizing Radiations on Hematopoietic Tissue, International Atomic Energy Agency, Vienna, 1967, p. 75.
2. Andrews, G. A.: Radiat. Res. Suppl., vol. 7, 1967, p. 390.
3. Andrews, G. A.; Comas, F. V.; Edwards, C. L.; Kniseley, R. M.; Lushbaugh, C. C.; and Vodopick, H.: Oak Ridge Associated Universities, USAEC Report, ORAU-112, 1970.
4. Lushbaugh, C. C.; Comas, F.; Saenger, E. L.; Jacobs, M.; Hofstra, R.; and Andrews, G. A.: Radiat. Res., vol. 27, 1966, p. 487.
5. Fanger, H.; and Lushbaugh, C. C.: Arch. Path., vol. 83, 1967, p. 446.
6. Lushbaugh, C. C.; Comas, F.; Edwards, C. L.; and Andrews, G. A.: Proceedings of a Symposium on Dose Rate in Mammalian Radiation Biology, UT-AEC Agricultural Research Laboratory, USAEC Report Conf-680410, 1969, p. 17.1.
7. Lushbaugh, C. C.: Advances in Radiation Biology, vol. 3, Academic Press, Inc., New York, 1969, p. 277.
8. Oakes, W. R.; and Lushbaugh, C. C.: Radiology, vol. 59, 1952, p. 737.
9. Shipman, T. L.; Lushbaugh, C. C.; Petersen, D. F.; Langham, W. H.; Harris, P. S.; and Lawrence, J. N. P.: J. Occup. Med., Suppl. 3, 1961, p. 145.
10. Dye, D. L.; and Wilkinson, M.: Science, vol. 147, 1965, p. 19.
11. Ricks, R. C.; Lushbaugh, C. C.: McDow, E.; and Frome, E.: This symposium. (In press.)
12. Warren, S.; and Bowers, J. Z.: Ann. Int. Med., vol. 32, 1950, p. 207.
13. Oughterson, A. W.; and Warren, S., eds: Medical Effects of the Atomic Bomb in Japan, McGraw-Hill Book Co., New York, 1956.
14. Bond, V. P.: Fleidner, T. M.: and Archambeau, J. O.: Mammalian Radiation Lethality, A Disturbance in Cellular Kinetics, Academic Press, New York, 1965.
15. Langham, W. H., ed.: Radiobiological Factors in Manned Space Flight, National Academy of Sciences, NRC Publication 1487, 1967.
16. Auxier, J. A.; Cheka, J. S.; Haywood, F. F.; Jones, T. D.; and Thorngate, J. H.: Health Phys., vol. 12, 1966, p. 425.

1114001

17. Cronkite, E. P.; and Bond, V. P.: U. S. Armed Forces Med. J., vol. 11, 1960, p. 249.

18. Cronkite, E. P.; Bond, V. P.; Conard, R. A.; Shulman, N. R.; Farr, R. S.; Cohn, S. H.; Dunham, C. L.; and Browning, L. E.: J. Amer. Med. Assoc., vol. 159, 1955, p. 430.

19. Jablon, S.; Fujita, S.; Fukushima, K., Ishimaru, T.; and Auxier, J. A.: Symposium on Neutrons in Radiobiology, UT-AEC Agricultural Research Laboratory and Oak Ridge National Laboratory, USAEC Report Conf-691106, 1969, p. 547.

20. Mathé, G.; Amiel, J. L.; and Schwarzenberg, L.: Ann. N. Y. Acad. Sci., vol. 114, 1964, p. 368.

21. Lushbaugh, C. C.; and Auxier, J.: Radiat. Res., vol. 39, 1969, p. 526.

22. Alpen, E. L.; Shill, O.; and Tochilin, E.: Radiat. Res., vol. 9, 1958, p. 85.

23. Bond, V. P.; Carter, R. E.; Robertson, J. S.; Seymour, P. H.; Hechter, H. H.: Radiat. Res., vol. 4, 1956, p. 139.

24. Stone, R. S.; and Larkin, J. C., Jr.: Radiology, vol. 39, 1942, p. 608.

25. Sheline, G.; Phillips, T. L.; Field, S. B.; Brennan, J. T.; and Raventos, A.: Amer. J. Roentgenol. Radium Ther. Nucl. Med., vol. 111, 1971, p. 31.

26. Field, S. B.: Radiology, vol. 92, 1969, p. 381.

27. Wood, J. W., Tamagaki, H., Neriishi, S.; Sato, T., Sheldon, W. F.; Archer, P. G.; Hamilton, H. B.; and Johnson, K. G.: Am. J. Epid., vol. 89, 1969, p. 4.

28. Strandqvist, M.: Acta Radiol., Suppl., vol. 55, 1944, p. 1.

29. Yuhas, J. M.; Stokes, T. R.; and Lushbaugh, C. C.: This symposium. (In press.)

30. Martinez G., R.; Cassab H., G.; Ganem G., G.; Guttman K., E.; Lieberman L., M.; Vater B., L.; Linares M., M.; and Rodriquez M., H.: Rev. Med. Inst. Mex. Seguro Social, vol. 3, Suppl 1, 1964, p. 14.

31. Bateman, J. L. A.: Proceedings of Symposium on Dose Rate in Mammalian Radiation Biology, USAEC Report Conf-680410, 1968, p. 23.1.

32. Casarett, G. W.; and Eddy, H. A.: Ibid, p. 14.1.

33. Casarett, G. W.; and Hursh, J. B.: Proc. Int. Conf. Peaceful Uses of Atomic Energy, Geneva, vol. II, 1955, p. 184.

34. Space Science Board: Radiation Protection Guides and Constraints for Space Mission and Vehicle-Design Studies Involving Nuclear Systems, National Academy of Sciences, Washington, D. C., 1970.

1114002

1972

Proceed. s of the National Symposium on tural and Manmade Radiation in Space, Las Vegas, 1971, E. A. Warman, ed. NASA Report NASA TM X-2440, 1972, pp. 974-980.

DOSIMETRY FOR RADIOBIOLOGICAL STUDIES OF THE HUMAN HEMATOPOIETIC SYSTEM[1]

W. L. Beck, T. R. Stokes, and C. C. Lushbaugh

Oak Ridge Associated Universities

FILE C
DO NOT REM

INTRODUCTION

At present, physical measurements of radiation exposure field fluxes are considerably more accurate than retrospective biologic estimates of the radiation dose in any particular exposure incident. However, wide individual variation in clinical response to radiation exposure often creates an apparent disagreement between physical and biological dose estimates. This disparity is largely caused by biologic variations in radiosensitivity and systemic repair but is also the result of individually different depth-dose distributions owing to body size differences or orientation geometry occurring during otherwise equal exposures.

Medical appraisal of the range of human biological variation in hematologic responses is needed, but has not been made because dosimetric information about the real depth doses to the bone marrow of individual patients is not available. The wide spatial distribution of bone marrow in the human skeleton makes the determination of the total averaged dose or any local bone marrow dose difficult and at present requires an empirical approach. This study was performed to devise a system for estimating individual bone marrow doses in therapeutic radiation exposures of leukemic patients. These measurements are needed to make dose-response correlations and to study the effect of dose protraction on peripheral blood cell levels. Such correlations are basic to medical management of irradiated persons since the bone marrow is one of man's most important radiosensitive tissues; lethality within 60 days of acute exposures from 200 to about 1000 R usually results from hematopoietic failure. Some studies (refs. 1 and 2) have shown that in selected patient populations the human $LD_{50/60}$ may approach a low of 250 rads average body-dose, but confidence in these estimates is poor.

During extended space explorations there may be little risk of receiving such sizeable doses acutely but there is a real chance of accumulating doses to the marrow that may be biologically significant. True correlation and variation of human hematologic responses to total-body irradiation (TBI) are sorely needed to help in establishing workable limits for these occupational exposures during missions in outer space. While the studies we have made were primarily intended for clinical uses, the data obtained is applicable to some of the dosimetric and shielding problems of space medicine.

In the Oak Ridge Associated Universities (ORAU) Medical Division program of therapeutic TBI, three irradiators with different exposure rates are in use: the ORAU low-exposure-rate total-body irradiator (LETBI) and medium-exposure-rate total-body irradiator (METBI), and the University of Tennessee-AEC Variable Dose Rate Irradiation Facility (VDRIF). Each of these irradiators was specifically designed to produce a uniform field of high-energy-gamma radiation for total-body exposures of large animals and man.

[1]Research supported jointly by U.S. AEC and NASA.

1114003

THE IRRADIATORS

The LETBI facility consists of a large outer room (Fig. 1B) in which a smaller exposure room (Fig. 1A) is centrally positioned. Eight cobalt-60 sources of 16 Curies each are located in the outer room and they irradiate the treatment room from all sides. This arrangement provides a radiation field uniform to within ±10% in the living volume (16×16×8 ft) occupied by the patient. Treatments given at an average exposure rate of 1.5 R/hr have ranged from 3 to 8 days duration to provide total protracted exposures up to 250 R. During exposure the patient is free to move about the exposure room while being irradiated for 18 to 22 hr per day. This facility is described in more detail by Andrews, et al. (ref. 3).

A model of the METBI facility is sho in Fig. 2. The control room is connect by a curved hallway to the 8×8×8 foot treatment room. Eight cesium-137 sourc of 500 Curies each, located in the walls irradiate the centrally suspended treat bed. The radiation field in the 2×2×6 f volume occupied by the patient on the be is uniform to within ±5% of the 1.5 R/mi exposure rate in the volume center. Exp sure times here range from a few minutes a few hours for total exposures of 20 to 350 R. A complete description of this f cility has been published by Brucer (ref 4).

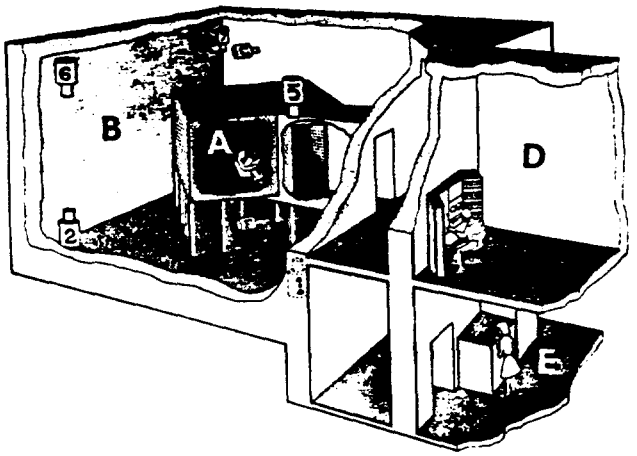


Figure 1.—Cutaway drawing of the low-exposure-rate total-body irradiation facility (LETBI) showing:
(A) Centrally positioned radiation exposure/living room.
(B) Concrete shielded radiation containment room.
(D) The remote control room for operation of the ^{60}Co sources (only sources No. 1,2,5,6,7, C and F are shown), radiation exposure level supervision, nursing and physiologic surveilance of the patient.
(E) The on-line and data processing room.

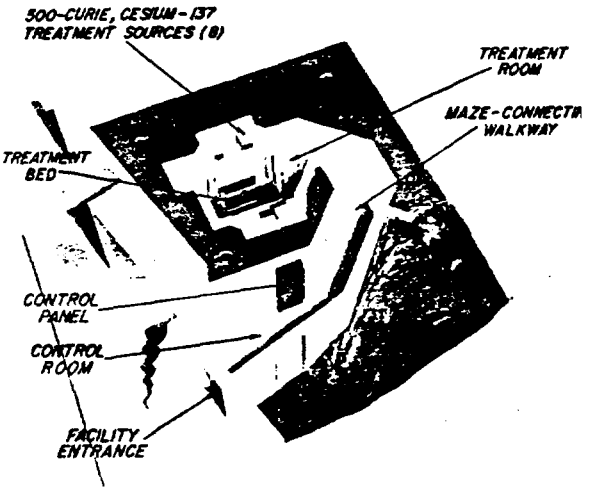


Figure 2.—Cutaway model of the medium-exposure-rate total-body irradiation facility (METBI).

1114004

The floor plan of the third irradiator (VDRIF) used in this therapy program is shown in Fig 3. Six cobalt-60 sources of 7700 Curies each are arranged in a rectangular array with 20 ft between adjacent sources. Exposures are done with the patient lying on his side on a hospital stretcher in the center of the source array. During patient therapy five sources are used to provide exposure over the stretcher at a rate of 40 R/min ±5%. To minimize the radiation hazard to hospital attendants, who might be required to aid the patient in case of equipment failure, we do not use source No. 1, which is nearest the entrance to the exposure room. A more complete description of this irradiator is given by Checka, et al. (ref. 5).

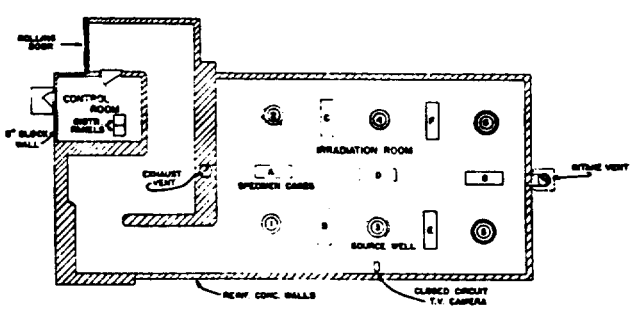
The radiation characteristics and dimensions of these irradiators are summarized in Table 1.

TABLE 1

RADIATION CHARACTERISTICS AND DIMENSIONS OF THREE TOTAL-BODY IRRADIATORS

FACILITY	SOURCES	RADIATION (Gamma)	EXPOSURE VOLUME	EXPOSURE RATE TREATMENT VOLUME	MODE OF EXPOSURE	SOURCE TO CENTER EXPOSURE VOLUME
LETSI	8 ^{60}Co	1.25 MeV	16×16×8' (room)	1.5 R/hr (±10%)	Multilateral	10.5'
METSI	8 ^{137}Cs	0.662 MeV	6×2×1' (above bed)	1.5 R/min (±5%)	Multilateral	5.8'
VDRIF*	5* ^{60}Co	1.25 MeV	6×2×1' (above bed)	40 R/min (±5%)	Bilateral	10' (Sources 3,4) 22.5' (Sources 3,5,6)

*This irradiator belongs to the UT-AEC Agricultural Research Laboratory.
VDRIF has 6 sources, but only 5 are used during therapy to patients.



VARIABLE DOSE RATE FACILITY —— FLOOR PLAN

Figure 3.—Floor plan of the University of Tennessee-Atomic Energy Commission (UT-AEC) Agricultural Research Laboratory Variable Dose Rate Irradiation Facility (VDRIF). Source positions are indicated by No. 1-6.

THE PHANTOM

An Alderson Rando phantom (ref. 6) was used as a patient analogue. This standard-man-sized phantom is constructed of isocyanate rubber, equivalent to tissue in interactions with ionizing radiation. A human skeleton and density-adjusted lungs are contained within the otherwise solid phantom. The phantom is sliced into transverse sections 2.5 cm thick with holes of 5 mm diameter arranged in a 3×3-cm grid to provide positions for thermoluminescent dosimeters (TLD). When not in use as dosimeter sites, the holes are filled with removable plugs of tissue-equivalent material.

Each of the 137 dosimeter sites located within the bone-marrow loci, identified from radiographs of the 34 transverse sections of the phantom, contained an individually calibrated TLD during periods of irradiation similar to the exposure of the patients.

1114005

DOSIMETERS

Extruded lithium fluoride dosimeters[2] (1.4×1.4×7 mm) were used to make all measurements within the phantom. These dosimeters are well suited for this application because of their small size, energy independence, approximately tissue equivalence, sensitivity, reusability, and ease of handling. They have a linear response from 10^{-2} to 10^{3} rads and a slightly supralinear response from 10^{3} to about 5×10^{5} rads when radiation damage becomes a limiting factor. In our laboratory we found the response of freshly calibrated dosimeters to be reproducible with a standard deviation of the order of 1-2% when exposed under calibration conditions. Repeated measurements in the same position in the phantom rarely disagree by more than 5%. We have previously reported details for calibrating, annealing (processing for reuse), and analyzing these dosimeters (ref. 7).

MARROW DOSE CALCULATIONS

Since the active marrow is not uniformly distributed within the body in a simple, well-defined volume, it was necessary to know the spatial distribution of the marrow to determine average marrow dose. The distribution of active marrow for normal adults as estimated by Ellis (ref. 8) is expressed as the percent of the total amount located in a particular anatomical marrow compartment, e.g., the ribs or skull. The distribution of the dosimeters in the marrow compartments defined by Ellis was not proportionate to the amount of marrow therein. For example, 19% of the 137 dosimeters were located in ribs which contained only about 8% of the total active marrow. Therefore, average total dose to marrow had to be calculated by first determining the average dose for a specific compartment and then using its percentage of total marrow as a weighting factor. Table 2 lists the average compartment dose and its range per 100 R of exposure from each of the three irradiators. Table 3 summarizes the average marrow dose calculations.

TABLE 2

MARROW COMPARTMENT AVERAGE DOSE IN RADS/100 R

	IRRADIATORS					
	LETBI		METBI		VDRIF	
Marrow Compartment	Average Dose	Range	Average Dose	Range	Average Dose	Range
Head	82	73-89	78	71-85	68	61-74
Upper Limb Girdle	69	58-75	66	58-73	78	70-82
Sternum	75	73-77	69	65-71	77	74-77
Ribs	63	46-76	68	62-72	75	70-84
Vertebrae	58	47-75	65	59-80	70	63-78
Sacrum	45	41-46	54	50-56	75	67-83
Lower Limb Girdle	52	44-62	59	52-71	72	63-77

TABLE 3

CALCULATIONS OF AVERAGE BONE-MARROW DOSE IN RADS/100 R

		LETBI		METBI		VDRIF	
Bone Marrow Compartment	Percent Active Bone Marrow	Average Dose	Weighted* Factor	Average Dose	Weighted* Factor	Average Dose	Weighted* Factor
Head	13.1	82	1074	78	1022	68	891
Upper Limb Girdle	6.4	69	442	66	422	78	499
Sternum	2.3	75	173	69	159	77	177
Ribs	7.9	63	498	68	537	75	593
Vertebrae	28.4	58	1647	65	1846	70	1988
Sacrum	13.9	45	626	54	751	75	1043
Lower Limb Girdle	26.1	52	1357	59	1570	72	1879
Totals	98.1†		5820		6277		7070
Average Weighted Dose‡		59		64		72	

* Weighted factor = average dose × percent bone marrow.
† Average weighted dose = Σ weighted factors ÷ total percent active bone marrow.
‡ Total percent is 98.1 because 1.9% of the marrow is located in the heads of the humeri where no measurements could be made.

[2]Dosimeter available from Harshaw Chemical Company, Cleveland, Ohio.

1114006

The compartment dose es .ates in Table 2 indicate that the marrow dose distribution is different in each of these irradiators. The most unexpected result is that the LETBI ^{60}Co gamma irradiator produces a smaller marrow dose than the METBI ^{137}Cs gamma irradiator. The other irradiator (VDRIF) produces the largest marrow dose as would be expected on the basis of relative penetrability of the gamma rays involved. This apparent paradox between the LETBI and METBI doses can be explained only on the basis of the distance the radiation travels in the body to the deep-seated marrow sites In the VDRIF about 80% of the radiation is incident at 90° to the long axis of the body and passes through the body's least thickness, the anterior-posterior diameter. This geometry provides the minimum radiation-path length to all marrow sites and therefore the largest average depth dose.

In the METBI facility the ^{137}Cs gamma rays are incident on the body's long axis at angles from 78-90° and they penetrate the body at an angle of approximately 30° to its larger lateral (side to side) diameter. The average length of radiation path in this geometry, somewhat greater than in the VDRIF, and the lower energy radiation explain the smaller marrow dose from the METBI exposures. However, other depth dose studies (refs. 9 and 10) have shown a less than 5% difference in average marrow dose from ^{137}Cs and ^{60}Co gamma rays under equal exposure geometries.

In the LETBI the exposure geometry is complicated by the patient's freedom to move about the large exposure room. We have calculated the angle of incidence for two typical positions of the patient; when he is standing near the room center, the average angle of incidence is about 70°; lying on the bed, the average angle of incidence is only about 25°. If we make the assumption that the average angle of incidence is the average for these two positions, or about 45°, then by simple geometry the length o he radiation path is 40% greater in this geometry than it would be for radiation incident at 90°. Because of this geometry, the LETBI average marrow dose is the lowest of the three irradiators studied.

The large dependence of average marrow dose on the angle of incidence of radiation is shown also by the study of Clifford (ref. 11), who measured this average dose in a rotating phantom first exposed at 90° and then at several angles down to 15° with the long axis of the body. Radiation energies of 60, 100, 212, and 660 keV were used. His results indicate that average dose to the marrow is reduced by a factor of two for exposures at 15° compared with 90° for all radiation energies. In addition, he also shows that marrow dose for 90° exposures varies by only about ±10% over the energy range from 60 to 660 keV and is maximum at about 100 keV.

Since the LETBI and METBI facilities produce essentially omnidirectional fields, we can compare the marrow dose estimates in LETBI of 0.59 and METBI of 0.64 rads/R with that predicted from Clifford's measurements (integrated over the angular region of 0° to 90°) of 0.62 rads/R. This agreement is surprisingly good considering that his estimates were based on measurements in only eight positions in his phantom and were primarily intended for evaluation of potential hazards of radiations from atomic weapons for civil defence planning.

The International Commission on Radiological Protection (ICRP) (ref. 12) has defined the active marrow dose as the appropriate radiation criterion for relating not only short-term hematopoietic effects but also certain late somatic biological effects to radiation exposures. To simplify its calculations to estimate marrow dose, the ICRP determined that the active marrow is located at an average depth of 5 cm. To test the validity of this simplification, we determined the average 5-cm dose to the phantom in each of the three irradiators.

1114007

The circumferential 5-cm depth line was defined in each of the 34 phantom sections and divided by radii at every 30°. The depth dose at the intercepts of the radii and the 5-cm depth line was determined by interpolation of the depth-dose data obtained from dosimeters located in surrounding grid positions. These were averaged for each section and then weighted by the mass of the section to obtain the overall average 5-cm depth dose. The comparisons of these dose estimates with the average marrow doses are shown in Table 4.

TABLE 4

COMPARISON OF ESTIMATED DOSE TO BONE MARROW WITH AVERAGE BODY DOSE AT 5-cm DEPTH

	Average Active Bone-Marrow Dose (in rads/100 R)	Average 5-cm Depth Dose (in rads/100 R)	Ratio $\frac{\text{5-cm Depth Dose}}{\text{Marrow Dose}}$
LETBI	59	68	1.15
METBI	64	66	1.03
VDRIF	72	73	1.01

These data indicate that the 5-cm dose approximates the average marrow dose quite closely in the ^{137}Cs gamma-ray field (METBI) and the high-flux ^{60}Co gamma-ray field (VDRIF) where the incident radiation is principally at right angles to the stationary body. The agreement, while adequate, is not as good for the low-exposure-rate cobalt irradiator (LETBI) where the incident radiation is from both above and below a standing patient and where the angles change as the patient sits down, reclines, or walks about, changing his geometric relationship to each source.

These results also suggest that a dosimeter, capable of indicating simultaneously dose rate and total accumulated dose, located in the center of a 5-cm radius sphere of tissue-equivalent material could be used to approximate the astronaut's average marrow dose received during space flight. The dose-rate signal from this dosimeter could also be used to indicate when maximum shielding from unidirectional exposures, such as solar flares, is needed and to indicate what vehicle orientation provides the maximum shielding.

This study also shows clearly that average dose to the marrow is strongly dependent on the length of the radiation path in the body. It is therefore obvious that for equal exposure conditions, a very large person will receive a relatively smaller dose to the marrow than a very small person. To determine how large this variation due to body size will be, we are extending these studies to determine body self-shielding factors for a particular individual rather than the idealized 70-kg man. The exposure rate from a small radioactive source is first measured in air and then at the center point of phantoms of different sizes by a high-sensitivity whole-body counter containing an array of eight 5×4-in. sodium iodide crystals. The ratio of the counts from within the phantom to the counts in air can be used to indicate the body's self-shielding factor. The results of this study are still incomplete but the feasibility studies indicate that this experimental approach has merit. From these studies we should obtain correction curves relating average marrow dose to self-shielding factor for each of our irradiator geometries and type of source. The self-shielding factor for each individual or patient could then be obtained by having him swallow a less than 1.0-microcurie radioactive source, then counting him in the whole-body counter when the source is located at the center of the patient's body.

Accurate dosimetric information relevant to the biological effects under study are essential for improving the reliability of established human dose-response relations. This is particularly true when the effects considered are the changes in peripheral

1114008

blood-cell levels. These studies are limited to medical exposures because changes in the blood-cell levels are related to the preirradiation levels. For these reasons, we are seeking to obtain truly adequate dosimetry information from which we can deduce dose-response relations which will aid in space mission planning, management of radiation accident victims, and will improve the usefulness of TBI therapy of disseminated diseases.

REFERENCES

1. Lushbaugh, C. C.; Comas, F.; and Hofstra, R.: Radiation Res., suppl. 7, 1967, pp. 398-412.
2. Lushbaugh, C. C.; Comas, F.; Edwards, C. L.; and Andrews, G. A.: USAEC Report CONF-680410, 1968, pp. 17.1-17.23.
3. Andrews, G. A.; Beck, W. L.; Cloutier, R. J.; Morris, Jr., A. C.; Barclay, T. R.; Comas, F. V.; Edwards, C. L.; and Lushbaugh, C. C.: USAEC Report ORAU-106, 1967, pp. 13-18.
4. Brucer, M.: Int. J. Appl. Radiation Isotop., vol. 10, 1961, pp. 99-105.
5. Checka, J. S.; Robinson, E. M.; Wade, Jr., L.; and Gramly, W. A.: Health Phys. (in press).
6. Alderson, S. W.; Lanzl, L. H.; Rollins, M.; and Spira, J.: Amer. J. Roentgenol. Radium Therap. Nucl. Med., vol. 87, 1962, pp. 185-195.
7. Beck, W. L.; Callis, E. L.; and Cloutier, R. J.: USAEC Report CONF-680920, 1968, pp. 976-989.
8. Ellis, R. E.: Phys. Med. Biol., vol. 5, 1961, pp. 255-258.
9. Facey, R. A.: Health Phys., vol. 14, 1968, pp. 557-568.
10. Jones, A. R.: Health Phys., vol. 12, 1966, pp. 663-671.
11. Clifford, C. E.; and Facey, R. A.: Health Phys., vol. 18, 1970, pp. 217-225.
12. Recommendations of the International Commission on Radiological Protection (Adopted September 17, 1965), ICRP Publication 9, New York Pergamon, 1966.

SCHEDULE 189

ADDITIONAL EXPLANATION FOR OPERATING COSTS

Oak Ridge Operations
Field Office or Laboratory

RT 01 01
Budget Activity No.

1a. Contractor:

Oak Ridge Associated Universities

1b. Contract No.:

E-(40-1)-GEN-33

2. Project Title:

ERDA HEALTH AND MORTALITY STUDY

3. Project No.:

4. Starting Date of Project:

August 1, 1977 (Phase-in)
October 1, 1977 (Operation)

5. Date Schedule Prepared:

May 12, 1976

6. Method of Reporting:

Annually

7. Working Location:

Oak Ridge, Tennessee

8a. Person in Charge:

C. C. Lushbaugh

8b. Principal Investigator(s):

C. C. Lushbaugh
E. Tompkins
J. Godbold
R. Ricks

9. Man Years:

	Actual Last Year FY 1976	Estimated FY 1976A	Est. This Fiscal Yr. FY 1977	Est. Next Fiscal Yr. FY 1978
	0	0	0.9	5.60

10. Costs:

ERDA Health and Mortality Study	$ 0	$ 0	$40	$480

1114010

2. Project Title:
D. ERDA HEALTH AND MORTALITY STUDY

3. Project No.:

11. Dates and Titles of Publications:

Not applicable. (See Progress Report No. 12, "Study of the Lifetime Health and Mortality Experience of Employees of AEC Contractors," Contract No. CH AT (11 - 1)-3428.

12. Objective and Scope:

The objective of this program is to use modern epidemiologic technology as the means for monitoring large populations of workers in industries related to fuel and energy production to detect any harmful effects of these occupations as soon as possible so that health protection can be constantly improved.

Project 1. ERDA Health and Mortality Study

The objective of the Health and Mortality Study is to evaluate on a continuing basis the disability and mortality experience of persons with a history of employment in selected installations associated with the nuclear industry. The primary purpose of the study is to determine if such employment histories are associated with an increase in age, sex specific mortality in general, or with an increase in age, sex specific mortality due to selected causes of death. Some determinant factors to be studied are: the adequacy of comparison populations to predict the expected mortality experience of the defined study population; the type, level, and dose rate of radiation exposure of the study population; and the length of time elapsed from first employment in a nuclear industry to morbidity and mortality.

Project 2. Prospective Studies of Newly Emerging or Rapidly Expanding Industries Related to Energy Production from Non-Nuclear Fuels

The objective of this program is to devise efficient, easily operated systems for industries needing to manage on an ongoing basis their occupational health and industrial hygiene records to provide an early-warning system for untoward effects. (Development of this project will not begin until late FY 78.)

13. Relationship to Other Projects:

This program during FY 76 and FY 77 up through July 31, 1977 is collaborative with the extramural program at the University of Pittsburgh; Study of the Lifetime Health and Mortality Experience of Employees of AEC Contractors (CH AT (11-1)-3428). It is budgeted as part of the REAC/TS program through July 31, 1977. On August 1, 1977, through September 30, 1977, the management and direction of the ERDA Health and Mortality Study at Pittsburgh will be transferred to ORAU and the two staffs merged. Beginning FY 78 this reorganized epidemiologic study will be collaborative with three BER programs:

(1) Transuranium Registry; Hanford Environmental Health Foundation;
(2) Analysis of Radionuclides in Human Tissues; Pacific Northwest Laboratory and Los Alamos Scientific Laboratory;
(3) Epidemiological Study of Plutonium Workers; Los Alamos Scientific Laboratory.

2. Project Title:
D. ERDA HEALTH AND MORTALITY STUDY

3. Project No.:

13. Relationship to Other Projects: (continued)

In addition, these programs and staff have collaborative interactions with ORNL staff in Health Physics, Statistics, Energy, and Biology Divisions.

14. Progress and Accomplishments in FY 76:

Our progress in epidemiologic studies is reported in the REAC/TS program under Follow-Up and Mortality Studies.

15. Program Plans in FY 77:

Our program plans for epidemiologic studies up to the August 1, 1977 merger with the ERDA Health and Mortality Study are described in the REAC/TS sub-189 on Radiation-Accident Management.

Program Plans for FY 77 (August - September 30):

It is our understanding that the change in scientific direction and program management of the ERDA Health and Mortality Study (H &M) will be completed soon after August 1. As described in the REAC/TS program 189 most of the time in the preceding months will have been used by our epidemiologic staff to become acquainted with the Health and Mortality staff and their goals. Our staff will need to work with H & M scientific leadership (Dr. T. Mancuso), Chief Consultant in Statistics (Dr. B. Sanders), and Consultant Health Physicist (Mr. Al Becher). The consultant services and advice of these men are necessary for a smooth transition and the completion of such ongoing projects as the acturial longevity study and the proportionate mortality studies. Use of these endpoints will then be held in abeyance after completion of work in progress to await updated definitions of control populations for comparative purposes and concentration of our efforts on mortality-rate studies. Dr. Sanders' help will be required in establishing working relations with our present staff and the Social Security System for uninterrupted identification of deceased employees and our subsequently obtaining their death certificates. The fiscal problems presently involved in this collection process will be transferred from UCN to ORAU. UCN will remain involved with the data-management portion of these studies under a subcontract arrangement.

16. Program Plans for FY 78:

Project 1. ERDA Health and Mortality Study

The identification of populations of workers at Hanford and at Oak Ridge will be completed and preliminary analyses using these data reviewed. Systems

2. Project Title: 3. Project No.:
D. ERDA HEALTH AND MORTALITY STUDY

16. Program Plans for FY 78: (continued)

will be developed to permit the monitoring of the mortality experience of these populations on a continuing routine basis. The systems will provide for: addition of new employees; addition of new deaths by cause; updating of exposure data; and categorization of the study populations into cohorts according to age, sex, years of employment, year of first radiation exposure, years of survival, level and type of radiation exposure; and place of employment. A comparison population, or preferably different comparison populations to adequately predict the expected mortality experience of the Hanford and Oak Ridge workers will be defined. The comparison populations will be as similar in socioeconomic and environmental characteristics to the worker population as possible. Means will be developed to obtain the necessary information about comparison populations in a timely and continuing way at reasonable cost and have the resulting population of sufficient size to provide sensitivity in analysis. Several potential comparison populations will be evaluated. These will include: the U. S. population and the population of Tennessee; the population of a cluster of states around and including Tennessee for Oak Ridge and similarly the state of Washington for Hanford; siblings of employee; non-state, and other occupational groups including selected samples for social security files. The best candidate comparison populations will be selected and systems developed to obtain the necessary data on these populations. Currently all survival and death information is obtained through the social security administration. These procedures will be reviewed in depth toward developing more efficient methods of obtaining the necessary information in the future. The size of the populations currently under study will be evaluated to determine the statistical sensitivity available to detect changes in mortality patterns in this population. Sample-size requirements to provide meaningful analyses on various cohorts will be determined. This information will be the basis of setting priorities on data acquisition, data analysis, and population expansion in subsequent years.

Project 2. Prospective Studies of Newly Emerging or Rapidly Expanding Industries Related to Energy Production from Non-Nuclear Fuels

The application of modern epidemiologic monitoring and nuclear medical techniques for earlier detection of disease must also be provided for fossil-fuel-related industry. While coal workers comprise only about 1% of all U. S. workers "covered" by Workmen's Compensation, they receive more than 40% of all available U. S. funds for job-incurred illness! If these statistics were to apply today to nuclear industrial workers, the potential for nuclear-fuel-generated power-production would be at or near zero. A major problem of almost insurmountable proportions is the coal-mining industry's apparent acceptance of the occupational medical problems involved. Worse yet, the more sophisticated coal-power industries like those involved in oil production from coal liquefaction still follow the struthious principle that "head-in-sand can avoid fiscal and moral responsibility." It is our understanding that ERDA recognizes its biomedical mandate for developing better health protection standards for fossil and other non-nuclear sources of energy production. We understand further that industry-wide monitoring systems for measuring noxious chemicals need to be developed. In addition, however, the priceless medical epidemiologic experience of a laissez-faire industry being allowed to run wild by an indifferent public,

2. Project Title:
D. ERDA HEALTH AND MORTALITY STUDY

16. Program Plans for FY 1978: (continued)

should be recorded by modern scientific methods, so that later generations may evaluate our relative concerns for nuclear and non-nuclear fuel production and their consequences. Accordingly, industry-wide health management systems comprising the most modern approaches of epidemiology and biostatistics must be designed and made available for application to these ERDA contractors involved in research and development of energy production. In this project, as time permits, such systems will be developed and tailored for industries with specific toxicant dangers. First priority will be given to the needs of ERDA pilot plants now only in planning stages.

SCHEDULE 189

ADDITIONAL EXPLANATION FOR OPERATING COSTS

Oak Ridge Operations
Field Office or Laboratory

RK 02 01 01
Budget Activity No.

1a. Contractor:

Oak Ridge Associated Universities

1b. Contract No.:

EY-76-C-05-0033

2. Project Title:

ERDA HEALTH AND MORTALITY STUDIES

(1) ERDA Health and Mortality Study

3. Project No.:

4. Starting Date of Project:

October 1, 1977

5. Date Schedule Prepared:

May 2, 1977

6. Method of Reporting:

Annually

7. Working Location:

Oak Ridge, Tennessee

8a. Person in Charge:

C. C. Lushbaugh

8b. Principal Investigator(s):

E. Tompkins
E. Frome
J. Godbold
C. C. Lushbaugh
R. Ricks

9. Man Years:	Actual Last Year FY 1977	Est. This Fiscal Year FY 1978	Est. Next Fiscal Year FY 1979
	2.0	14.7	13.5

10. Costs:

	$40	$480	$450

1114015

2. **Project Title:**
A. ERDA HEALTH AND MORTALITY STUDIES
Sub 189 (1) ERDA Health and Mortality Study

11. Dates and Titles of Publications:

Not applicable. (See Progress Report No. 12., "Study of the Lifetime Health and Mortality Experience of Employees of ERDA Contractors", Thomas F. Mancuso, Contract No. E (11-1) - 3428.

12. Objective and Scope:

The objective of this program is to use modern epidemiologic technology as the means for monitoring large populations of workers in industries related to fuel and energy production to detect any harmful effects of these occupations as soon as possible so that health protection can be constantly improved.

Project 1. ERDA Health and Mortality Study

The objective of the Health and Mortality Study is to evaluate on a continuing basis the disability and mortality experience of persons with a history of employment in selected installations associated with the nuclear industry. The primary purpose of the study is to determine if such employment histories are associated with an increase in age, sex-specific mortality in general, or with an increase in age, sex-specific mortality due to selected causes of death. Some determinant factors to be studied are: the adequacy of comparison populations to predict the expected mortality experience of the defined study population; the type, level, and dose rate of radiation exposure of the study population; the type and level of exposure to non-nuclear occupational toxicants; and the length of time elapsed from first employment in a nuclear industry to morbidity and mortality.

Project 2. Prospective Studies of Newly Emerging or Rapidly Expanding Industries Related to Energy Production from Non-Nuclear Fuels

The objective of this program is to devise efficient, easily operated systems for industries needing to manage on an ongoing basis their occupational health and industrial hygiene records to provide an early-warning system for untoward effects. The newly emerging coal conversion industry will be exposing workers to known carcinogens. Plans for medical surveillance of workers are being designed to provide early detection of malignant (or pre-malignant) changes toward successful medical intervention. Plans for industrial hygiene programs are being designed to minimize exposure of workers to carcinogens. To measure the success of these programs, continuing analysis of exposure and health data on an industry-wide basis will be necessary. Data collection protocols and forms will be developed and field tested; data-management systems will be designed; and analysis protocols will be written and tested. (Development of this project will not begin until late FY 78.)

13. Relationship to Other Projects:

The ERDA Health and Mortality Study is collaborative with three BER programs:
(1) Transuranium Registry; Hanford Environmental Health Foundation
(2) Analysis of Radionuclides in Human Tissue; Pacific Northwest Laboratory and Los Alamos Scientific Laboratory
(3) Epidemiologic Study of Plutonium Workers; Los Alamos Scientific Laboratory

In addition, these programs and staff have collaborative interactions with ORNL

2. Project Title:
A. ERDA HEALTH AND MORTALITY STUDIES
Sub 189 (1) ERDA Health and Mortality Study

3. Project No.:

13. Relationship to Other Projects: (continued)

staff in Medical and Industrial Hygiene, in Health Physics, Statistics, Energy, and Biology Divisions, and with Medical and Industrial Hygiene staff at ORGDP and other ERDA installations.

14. Progress and Accomplishments in FY 77:

The professional staff of epidemiologists and statisticians needed to conduct the ERDA Health and Mortality study have been recruited and the staff has become familiar with existing data banks. A study of the mortality experience of workers exposed to metallic nickel at ORGDP has been implemented, and a study of the mortality experience of workers at the Savannah River Plant has been completed. The special search for missing death certificates for workers in the Oak Ridge population who are known to have died has continued, and 30 percent of the "missing" certificates have been located.

15. Program Plans for FY 78:

Project 1. ERDA Health and Mortality Study

The identification of populations of current and former workers at Hanford, Oak Ridge, Mound, and Mallinckrodt will be completed. A comparison population, of preferably different comparison populations, to adequately predict the expected mortality experience of the Hanford and Oak Ridge workers will be defined. The comparison populations will be as similar in socioeconomic and environmental characteristics to the worker population as possible. Means will be developed to obtain the necessary information about comparison populations in a timely and continuing way at reasonable cost and have the resulting population of sufficient size to provide sensitivity in analysis. Several potential comparison populations will be evaluated. These will include: the U.S. population and the population of Tennessee; the population of a cluster of states around and including Tennessee for Oak Ridge, and similarly the State of Washington for Hanford; siblings of employees, non-state and other occupational groups, including samples from Social Security files. The best candidate comparison populations will be selected and systems developed to obtain the necessary data on these populations. Currently, all survival and death information is obtained through the Social Security Administration and State Departments of Vital Statistics. These procedures will be reviewed in depth toward developing more efficient methods of obtaining the necessary information in the future. The size of the populations currently under study will be evaluated to determine the statistical sensitivity available to detect changes in mortality patterns in this population. Sample-size requirements to provide meaningful analyses on various cohorts will be determined. This information will be the basis of setting priorities on data acquisition, data analysis, and population expansion in subsequent years. Under a subcontract with Union Carbide Nuclear to provide data management support for this study, data-management systems will be developed and implemented to permit the monitoring of the mortality experience of these populations on a continuing routine basis. The systems will provide for: addition of new employees; addition of new deaths by cause; updating of exposure data; and categorization of the study populations into cohorts according to age, sex, years of employment, year of first radiation exposure, years of survival, level and type of radiation exposure, and place of employment. Social Security records will be screened for deaths occurring in

2. Project Title: 3. Project No.:

A. ERDA HEALTH AND MORTALITY STUDIES

Sub 189 (1) ERDA Health and Mortality Study

15. Program Plans for FY 78: (continued)

1974-76, and the search for death certificates continued with priority being given to deaths of workers hired before 1950. All data files will be screened and tested for misinformation and corrections will be made as necessary. The study of mortality of workers exposed to metallic nickel will be completed and submitted for publication.

Project 2. Prospective Studies of Newly Emerging or Rapidly Expanding Industries Related to Energy Production from Non-Nuclear Fuels

In cooperation with the medical staff at Oak Ridge National Laboratory, forms for collection of data on clinical findings and medical, occupational, and family histories for coal-conversion workers will be designed. The forms will be designed to provide for ease and accuracy in completion, coupled with economy in conversion to automatic data processing. A search will be implemented to define populations of workers who have been employed in pilot coal-conversion operations in the past. Planning for epidemiologic investigation of workers exposed in the past will begin as time permits.

16. Program Plans for FY 79:

Project 1. ERDA Health and Mortality Study

The first analyses of mortality of workers in Oak Ridge employed before 1950 will be completed. To evaluate the effect of latency, analyses plans will be developed to permit definitive investigation of changes in mortality patterns with time. These analyses techniques will be tested on the pre-1950 Oak Ridge cohort using cut-off dates of 1965, 1970, and 1975. Any possible health problems suggested by these analyses or the study of nickel workers will be examined in depth in the various sub-populations toward developing etiologic hypotheses to be tested in other populations included in the Health and Mortality rosters.

The possibilities for evaluating morbidity in the nuclear workers will be examined. The use of Social Security disability payments to workers as an indication of morbidity has been suggested.

The files of workers will be maintained on a current basis and streamlined methods for obtaining death certificates will be implemented as they are developed.

Project 2. Prospective Studies of Newly Emerging or Rapidly Expanding Industries Related to Energy Production from Non-Nuclear Fuels

The forms and protocols designed for collection of health data on coal-conversion workers will be field tested in selected industrial health departments (probably ERDA installations) and redesigned as indicated. Forms and protocols for easy and efficient collection of exposure data will be designed with the cooperation of the industrial hygienists at Oak Ridge National Laboratory.

2. Project Title:
A. ERDA HEALTH AND MORTALITY STUDIES
Sub 189 (1) ERDA Health and Mortality Study

3. Project No.:

16. Program Plans for FY 79: (continued)

The identified populations of workers in coal-conversion pilot plants of the past will be screened for mortality experience. Historical qualitative exposure data will be developed as far as feasible. Any potential health-problem areas suggested by these data will be incorporated into the health-data and exposure-data protocols.

The planning for an industry-wide health surveillance system will start. The planning will provide for data-management systems; methods for obtaining current health and occupational exposure information on current employees, retired employees, continuing epidemiologic analysis of the data; and continual feedback to participating industries.

SCHEDULE 189

ADDITIONAL EXPLANATION FOR OPERATING COSTS

Oak Ridge Operations
Field Office or Laboratory

RK 02 01 01
Budget Activity No.

1a. Contractor:

Oak Ridge Associated Universities

1b. Contract No.:

EY-76-C-05-0033

2. Project Title:

ERDA HEALTH AND MORTALITY STUDIES

(2) Applied Human Toxicology (Non-Nuclear)

3. Project No.:

4. Starting Date of Project:

October 1, 1977

5. Date Schedule Prepared:

May 2, 1977

6. Method of Reporting:

Annually

7. Working Location:

Oak Ridge, Tennessee

8a. Person in Charge:

C. C. Lushbaugh

8b. Principal Investigator(s):

E. Tompkins
E. Frome
J. Godbold
C. C. Lushbaugh
Toxicologist

9. Man Years:	Actual Last Year FY 1977	Est. This Fiscal Year FY 1978	Est. Next Fiscal Year FY 1979
	0	0	2.3

10. Costs:

	$0	$0	$150

1114020

2. Project Title:
A. ERDA HEALTH AND MORTALITY STUDIES
Sub 189 (2) Applied Human Toxicology (Non-Nuclear)

3. Project No.:

11. Dates and Titles of Publications:

Not applicable.

12. Objective and Scope:

It is expected that our epidemiologic studies in FY 77 and FY 78 will identify and define deficiencies in present exposure surveillance systems that need correction. New exposure measurement systems will be needed for specific chemicals and other agents to generate data that can be used to quantitate low-level chronic industrial exposures. Toxicologic knowledge and industrial hygiene technology must be available for application to such problems as they arise.

This program will not be instituted in FY 78 because this activity will depend upon the recruitment during the year of a human-oriented toxicologist of senior staff level and an associated clinical pathologist. This staff nucleus is needed to generate the detailed program plans for FY 79.

13. Relationship to Other Projects:

This project will be directly related to the ERDA Health and Mortality Study.

14. Progress and Accomplishments in FY 77:

Not applicable.

15. Program Plans for FY 78:

A toxicologist with an interest in industrial toxicants and experience in industrial hygiene will be recruited at the senior staff level. A clinical pathologist will also be recruited.

16. Program Plans for FY 79:

Our present studies in the biochemistry of surfactant and in cytogenetics suggest that these biological monitors can be useful as exposure-measurement tools in industries involving chemical exposures of workers. These bioassay techniques will be field tested in several non-nuclear energy-production plants with different types of chemical exposures and dose-response curves developed.

1114021

MILESTONES

FY 77

4/4: Complete Savannah River Plant mortality study.

FY 78

1/4: Complete identification of ERDA Health and Mortality population.

1/4: Complete death certificate acquisition plan.

2/4: Complete ORGDP nickel worker study.

2/4: Establish Health and Mortality data management system.

3/4: Define appropriate Health and Mortality comparison population.

3/4: Define populations employed in coal-conversion plants in the past.

4/4: Evaluate Hanford mortality experience.

4/4: Design non-nuclear medical surveillance forms.

FY 79

2/4: Determine feasibility of Health and Mortality morbidity surveillance.

2/4: Establish procedures for continuing surveillance and reporting of mortality experience of workers.

2/4: Define appropriate factors to determine chemical exposures of workers in coal conversion.

3/4: Complete design of non-nuclear surveillance forms and field test.

3/4: Complete mortality analysis of Oak Ridge workers.

3/4: Field test surfactant as a lung burden dosimeter.

4/4: Complete mortality study of past coal-conversion workers.

4/4: Field test cytogenetics as a chemical exposure dosimeter.

4/4: Present provisional dose response curve for surfactant.

SCHEDULE 189

ADDITIONAL EXPLANATION FOR OPERATING COSTS

Oak Ridge Operations Field Office or Laboratory	GK 01 02 01 1 Budget Activity No.

1a. Contractor: Oak Ridge Associated Universities	1b. Contract No.: EY-76-C-05-0033
2. Project Title: HUMAN HEALTH EFFECTS FROM ENERGY GENERATORS A. Health and Mortality Studies	3. Project No.: 002493
4. Starting Date of Project: October 1, 1978	5. Date Schedule Prepared: March 24, 1978
6. Method of Reporting: Annually	7. Working Location: Oak Ridge, Tennessee
8a. Person in Charge: C. C. Lushbaugh	8b. Principal Investigator(s): E. Tompkins E. Frome J. Godbold C. C. Lushbaugh (Epidemiologist) (Toxicologist)

9. Man Years:

Actual Last Year FY 1978	Est. This Fiscal Year FY 1979	Est. Next Fiscal Year FY 1980
9.90	12.10	12.10

1114023

	FY 1978	FY 1979	FY 1980
10a. Operating Obligations (BA):			
Total Estimated BO.....	480	600	645
Less: Beginning BA Balance.....	136	180	194
Add Ending BA Balance.....	180	194	207
Total BA/Obligations.....	524	614	658
10b. Operating Budget Outlay (BO):			
1. Direct Salaries	$101	$130	$137
2. Fringe Benefits	18	24	26
3. Consultant Fees	25	10	10
4. Travel	6	6	8
5. Trans & Comm	9	10	11
6. Materials	14	11	14
7. Sundries	0	1	1
8. Technical Services	10	10	12
9. Computer Costs	136	205	220
10. Hosp. & Medical Costs	0	0	0
11. Bldg. Operating Costs	13	13	14
12. Division Distributed Expense	80	101	108
13. ORAU Administrative Expense	68	79	84
Total BO	$480	$600	$645
10c. Capital Equipment Obligations (BA)			
	$5		
Miscellaneous		$2	$3
	$5	$2	$3

1114024

2. Project Title:
A. HEALTH AND MORTALITY STUDIES

3. Project No.:
002493

11. Dates and Titles of Publications:

(See Final Report No. 13, August 1, 1976 - July 31, 1977, *Study of the lifetime health and mortality experience of employees of ERDA contractors,* Thomas F. Mancuso, Contract No. EY-76-S-02-3438).

Armstrong, R. D. and Frome, E. L. *A special purpose linear programming algorithm for obtaining least absolute value estimators in a linear model with dummy variables.* Communications in Statistics (In press).

Frome, E. L. and Armstrong, R. D. *A robust procedure for estimating the trend-cycle component of an economic time series.* Proc. Tenth Annual Symposium on Computer Science and Statistics (In press).

Richter, C. B., Humason, G. L. and Godbold, J. H., Jr. *Endemic pneumocystis carinii in a marmoset colony.* J. Comparative Path. (In press).

Armstrong, R. D. and Frome, E. L. *Robust estimation of spline functions in data analysis.* Presented at the Joint Central Regional Meeting, American Statistical Association and the Institute of Mathematical Statistics, Madison, Wisconsin, 1977.

Armstrong, R. D. and Frome, E. L. *A comparison of two algorithms for absolute deviation curve fitting.* J. Am. Stat. Assoc. 71: 328-330, 1976.

Armstrong, R. D. and Frome, E. L. *The calculation of least absolute value estimators for two-way tables.* In Proc. Stat. Computing Section, Am. Stat. Assoc., Boston, Massachusetts, pp. 101-106, 1976.

Armstrong, R. D. and Frome, E. L. *A branch and bound solution of a restricted least squares problem.* Technometrics 18: 447-450, 1976.

Charnes, A., Frome, E. L. and Yu, P. L. *The equivalence of generalized least squares and maximum likelihood estimation in the exponential family.* J. Am. Stat. Assoc. 71: 169-172, 1976.

Frome, E. L. and Yakatan, G. J. *Fitting the one compartment open model to bioavailability data.* In Ninth International Biometric Conference, Boston Massachusetts, p. 19, 1976, Abstract.

Godbold, James H., Jr. *Small sample t intervals for comparisons suggested by the data.* Dissertation, Johns Hopkins University, Baltimore, MD, 1976.

---

12. Objective and Scope:

This program uses modern epidemiological and statistical methods to monitor the occupational exposures and health experience of populations of workers with histories of employment in industries related to fuel and energy production. These surveillance systems provide early warning of possible harmful effects associated with the work environment of these industries so health protection of the workers can be constantly improved.

11 1 4 0 2 5

2. Project Title:
A. HEALTH AND MORTALITY STUDIES

3. Project No.:
002493

12. Objective and Scope: (continued)

Project a. Mortality Studies of Nuclear Workers (Formerly ERDA Health and Mortality Study)

The mortality study of workers in selected installations associated with the nuclear industry is designed to provide, on a continuing basis, an evaluation of the mortality experience of workers with a history of employment in the plants under study. This study determines if employment in these installations is associated with an increase in age, sex-specific mortality in general, or with an increase in age, sex-specific mortality due to specific causes of death. Some determinant factors studied are: The adequacy of comparison populations to predict the expected mortality experience of the defined study population; the type, level, and dose rate of radiation exposure of the study population; the type and level of exposure of the population to non-nuclear industrial toxicants; and the length of time elapsed from first employment in a nuclear in dustry to mortality.

Project b. Studies of Health Effects in Workers Employed in Newly Emerging or Rapidly Expanding Industries Related to Energy Production from Non-Nuclear Fuels

The newly emerging coal conversion industry is exposing workers to known carcinogens. Plans for medical surveillance of workers are being designed to provide early detection of malignant (or pre-malignant) changes to enable successful medical intervention. Systems are needed to evaluate the effectiveness of current preventive measures. These systems depend upon continuing analyses of exposure and health data on a U.S. industry-wide basis. An evaluation of the mortality experience of workers with a history of past exposure to the toxicants formed in coal conversion processes will be made. Concurrently, an efficient, easily operated system for managing on an ongoing basis, occupational health and industrial hygiene records will be devised. Data-collection protocols and forms will be developed and field tested; data-management systems will be designed; and analysis protocols will be written and tested. (Development of this project will begin late in FY 78.

Project c. Applied Human Toxicology (Non-Nuclear)

New exposure-measurement systems are needed to quantitate individual exposures and low-level chronic industrial exposures of workers to specific chemicals or mixtures of several chemicals. As the epidemiology studies identify deficiencies in present exposure surveillance systems, new measurement systems will be developed. In addition, as possibly useful biological monitors are developed in other programs, they will be field tested in populations with different types of chemical exposures. For those biological monitors which are promising, dose-response curves will be developed.

2. Project Title:
A. HEALTH AND MORTALITY STUDIES

3. Project No.:
002493

13. Relationship to Other Projects:

The Health and Mortality Studies are collaborative with four BER programs:
(1) Health and Mortality Study of Hanford Workers - Hanford Environmental Health Foundation and Biology Division, Pacific Northwest Laboratory
(2) Transuranium Registry; Hanford Environmental Health Foundation
(3) Analysis of Radionuclides in Human Tissue; Los Alamos Scientific Laboratory
In addition, these programs and staff have collaborative interactions with ORNL staff in Medical and Industrial Hygiene, and in the Health Physics, Statistics, Energy, and Biology Divisions, and with Medical and Industrial Hygiene staff at ORGDP and other DOE installations.

14. Progress and Accomplishments in FY 78:

A study of mortality in workers exposed to elemental nickel at Oak Ridge Gaseous Diffusion Plant has been completed. The mortality due to respiratory cancer in workers exposed to nickel was compared with mortality in a sample of ORGDP employees with no exposure to nickel. There is no evidence of increased respiratory cancer in workers exposed to elemental nickel.

Operational procedures have been developed and a manual written which defines and describes all interactions with Social Security Administration for the identification of deceased workers and with state health departments for the acquisition of death certificates for these workers. The procedures for death-certificate retrieval are currently being tested using deaths identified in the Mortality Study of Nuclear Workers. These procedures will become the bases for the operation of the DOE Central Office for Death Certificate Retrieval in FY 79.

The responsibility for the conduct of the ERDA Health and Mortality Study (now called the Mortality Studies of Nuclear Workers) was transferred to ORAU in August, 1977. Initial exploratory use of the computer files containing the data for this study uncovered an unacceptable error rate in the computerized data files (as high as 10 per cent for some variables). A massive data "clean-up" program is underway to make the collected data useable for future analyses. Concurrently, data collection and editing procedures are being developed which will preclude incorporation of erroneous data into the computerized data files in the future.

The biostatistical and data-management expertise of this program has provided support in these two disciplines for the other occupational medicine programs in the Medical and Health Sciences Division.

A toxicologist with a broad interest in industrial toxicants and experience in industrial hazards is being recruited at the senior staff level.

15. Program Plans for FY 79:

Project a. Mortality Studies of Nuclear Workers

The existing computer files containing data on workers in the two Oak Ridge pro-

2. Project Title:
A. HEALTH AND MORTALITY STUDIES

3. Project No.:
002493

15. Program Plans for FY 79: (continued

duction plants, Oak Ridge National Laboratory, Mound Laboratory, and the Fernal Plant of National Lead of Ohio will be validated. The validation will include verification of "correctness" of data, as well as completeness of employee rosters for the listed sites.

Potential populations to be used as controls in these studies will be evaluated and a control population(s) selected. The populations of the U.S., Tennessee, Ohio, Southeastern U.S., and selected occupational groups will be evaluated for timely availability of data as well as applicability of the data to the program.

Procedures for the continuing surveillance and reporting of the mortality experience of these workers on a routine basis will be established. Data management systems to provide for editing and updating of files as well as statistical analyses will be developed and tested. Statistical analysis techniques will be devised to evaluate the effect of latency. Analyses plans will be developed to permit definitive investigation of changes in mortality patterns with time.

The first analyses of mortality of workers in Oak Ridge employed before 1950 will be initiated.

In cooperation with REECO, the roster of civilians involved in operations at the Nevada and Pacific Test Sites will be made as complete as possible, Social Security numbers sought, and the first Social Security Administration search for deceased individuals started.

Project b. Studies of Health Effects in Workers Employed in Newly Emerging or Rapidly Expanding Industries Related to Energy Production from Non-Nuclear Fuels

Populations previously employed in coal-conversion-type activities will be identified, and a study of their mortality experience will be initiated. Although an increased risk of skin cancer is an accepted occupational hazard in the industry, mortality from causes which might also be associated with these occupations will be delineated. Historical qualitative exposure data will be developed as far as feasible, to relate to observed mortality.

In cooperation with the medical staff at Oak Ridge National Laboratory, forms for the collection of data on clinical findings and medical, occupational, and family histories for coal-conversion workers will be designed. The forms will be designed to provide for ease and accuracy in completion, coupled with economy in conversion to automatic data processing. The field testing of these forms and protocols in selected industrial health departments (probably DOE installations) will be initiated and the forms redesigned as indicated. Forms and protocols for easy and efficient collection of exposure data will be designed with the cooperation of the industrial hygienists at Oak Ridge National Laboratory.

Project c. Applied Human Toxicology (Non-Nuclear)

The newly acquired toxicologist will start developing a program toward the identification of potentially hazardous exposures in selected work places. The definition of appropriate factors to determine exposure of workers to various chemicals associated with coal conversion will have the first priority.

2. Project Title:

A. HEALTH AND MORTALITY STUDIES

3. Project No.: 002493

16. Program Plans for FY 80:

Project a. Mortality Studies of Nuclear Workers

The analyses of mortality of workers who were hired in Oak Ridge before 1950 will be completed. The analyses techniques to evaluate latency will be tested on the pre-1950 Oak Ridge cohort using cut-off dates of 1965, 1970, and 1975. Any possible health problems suggested by these analyses will be examined in depth in the various sub-populations included in the Mortality Study rosters.

The first analyses of mortality of workers in Oak Ridge who were hired after 1950 and of employees of National Lead and of Mound Laboratory will be initiated. The data for Mallinkrodt will be evaluated for suitability for analysis. Development of procedures and protocols for the continuing surveillance and reporting of the mortality experience of workers with a history of employment in selected nuclear installations will be completed and ready for implementation in FY 81. Current death information for all employees will be obtained from the Social Security Administration and the search for death certificates initiated.

The efforts to identify civilians present at Nevada and Pacific Test Sites will continue as necessary in cooperation with REECO.

Project b. Studies of Health Effects in Workers Employed in Newly Emerging or Rapidly Expanding Industries Related to Energy Production from non-Nuclear Fuels

The preliminary analyses of the mortality of workers in coal-conversion-like industries will be completed. Any potential health-problem areas suggested by the study of these employees will be incorporated into the health-data and exposure-data protocols for the industry-wide surveillance system.

The planning for an industry-wide health surveillance system will start. The planning will provide for data-management systems: Methods for obtaining current health and occupational-exposure information on current employees and retired employees, continuing epidemiologic analysis of the data, and continual feedback to participating industries. The forms and protocols for collection of exposure data in coal-conversion plants will be field tested.

Project c. Applied Human Toxicology (Non-Nuclear)

Present studies in the biochemistry of surfactant and cytogenetics suggest that these biological monitors can be useful as exposure-measurement tools in industries involving chemical exposures of workers. These bioassay techniques will be field tested in several non-nuclear energy-production plants with different types of chemical exposures. If these biological monitors can detect chemical exposure, specific chemical exposures in selected workers will be defined and the development of dose-response curves initiated.

SCHEDULE 189

ADDITIONAL EXPLANATION FOR OPERATING COSTS

Oak Ridge Operations	GK 01 02 01 1
Field Office or Laboratory	Budget Activity No.

1a. Contractor:	1b. Contract No.:
Oak Ridge Associated Universities	EY-76-C-05-0033
2. Project Title:	3. Project No.:
HUMAN HEALTH EFFECTS FROM ENERGY GENERATORS B. DOE/Central Office for Death Certificate Retrieval	
4. Starting Date of Project:	5. Date Schedule Prepared:
October 1, 1978	March 24, 1978
6. Method of Reporting:	7. Working Location:
Annually	Oak Ridge, Tennessee
8a. Person in Charge:	8b. Principal Investigator:
C. C. Lushbaugh	E. Tompkins E. Frome J. Godbold C. C. Lushbaugh R. Ricks

9. Man Years:

Actual Last Year FY 1978	Est. This Fiscal Year FY 1979	Est. Next Fiscal Year FY 1980
0	1.30	2.70

1114030

	FY 1978	FY 1979	FY 1980
10a. Operating Obligations (BA):			
Total Estimated BO.....	0	35	155
Less: Beginning BA Balance.....	0	0	47
Add Ending BA Balance.....	0	47	54
Total BA/Obligations.....	0	82	162
10b. Operating Budget Outlay (BO):			
1. Direct Salaries.....	$ 0	$ 10	$ 19
2. Fringe Benefits.....	0	2	4
3. Consultant Fees.....	0	0	0
4. Travel.....	0	0	4
5. Trans & Comm.....	0	0	1
6. Materials.....	0	10	72
7. Sundries.....	0	0	0
8. Technical Services.....	0	0	1
9. Computer Costs.....	0	0	0
10. Hosp & Medical Costs.....	0	0	0
11. Bldg. Operating Costs.....	0	0	0
12. Division Distributed Expense.....	0	6	25
13. ORAU Administrative Expense.....	0	7	29
Total BO	$ 0	$ 35	$155
10c. Capital Equipment Obligations (BA)			
	$0	$0	$0

1114031

2. Project Title:
B. DOE/CENTRAL OFFICE FOR DEATH CERTIFICATE RETRIEVAL

3. Project No.:

11. Dates and Titles of Publications:

Not applicable.

12. Objective and Scope:

This office provides the nation-wide focus for interactions of all DOE epidemiology programs with the Social Security Administration to determine "alive-or-dead" status of individuals enrolled in various DOE/BER/Epidemiologic research studies. When such an individual is found to be deceased, the death certificate is located, a copy obtained from the appropriate State Health Department and transmitted to the requesting investigative group.

13. Relationship to Other Projects:

This office functions in support of epidemiology programs throughout DOE. Major programs, at present, are located at Hanford Environmental Health Foundation, Pacific Northwest Laboratory, Los Alamos Scientific Laboratory, and Oak Ridge Associated Universities.

14. Progress and Accomplishments in FY 78:

Not applicable. (As part of the ERDA Health and Mortality Studies, the system for the operation of this office has been developed and tested).

15. Program Plans for FY 79:

As requested by Manager, Human Health Studies Programs, DOE, this office will submit to Social Security Administration rosters of names obtained from Research Program Manager to be screened for alive-or-dead status. When informed that an individual is dead, the office will try to determine the place of death and then to obtain a copy of the death certificate which will be provided to the appropriate research study office. Working on a state-by-state basis, attempts will be made to develop the most efficient search techniques feasible consistent with the specific applicable laws and the file systems of the state Vital Statistics Departments.

The stated budget covers the retrieval of death certificates for Rocky Flats worker population and the worker populations of Hanford and Oak Ridge. The first alive-or-dead Social Security Administration screen of civilians involved in test operations at Nevada and in the Pacific will be initiated.

16. Program Plans for FY 80

Efforts to improve efficiency of death certificate search techniques will continue.

Death certificates will be obtained for the civilian test-site population and retrieval continued on Oak Ridge, Hanford, and Rocky Flats populations. The Oak Ridge population will be rescreened through Social Security Administration.

DOE F 1 .m 5120.2
(12-78)

U.S. DEPARTMENT OF ENERGY

FIELD TASK PROPOSAL/AGREEMENT

1. WP BIN NUMBER	2. TASK NO.	3. REV. NO.	4. PROJECT NO.	5. DATE PREPARED (mm dd yy)	6. CONTRACTOR NUMBER
		0		4-01-79	2493

7. TASK TITLE	8. WORK PACKAGE TITLE
HEALTH AND MORTALITY STUDIES	

9. BUDGET AND REPORTING CODE	10. TASK TERM Begin: (mm dd yy)	End: (mm dd yy)	11. CONTRACTOR NAME	12. CODE (see instructions)
GK 01 02 01 1	10-01-78	Open	Oak Ridge Associated Universities	ORH

13. CONTRACTOR TASK MANAGER (Name, FTS No.)	14. PRINCIPAL INVESTIGATORS
Dr. C. C. Lushbaugh FTS: 626-3090	Dr. Anthony Polednak Dr. Ed Frome Dr. Martha Hansard

15. WORK LOCATION (See instructions): Name of facility, City, State, ZIP Code	16. Does this task include any management services efforts?
Oak Ridge, TN 37830	☐ YES ☒ NO

17. TASK DESCRIPTION (Approach, relation to work package, in 200 words or less)

Epidemiologic studies are being conducted on populations of DOE (or DOE Contractor) workers whose occupations involve exposure to internal and external radiation, along with other agents. Current work concerns the mortality of workers at uranium processing plants in Tennessee (Oak Ridge) and several other states, starting with about 60,000 workers at the Y-12 facility in Oak Ridge (in operation from 1943 to the present). These studies are aimed at assessing the long-term health effects of exposure to external radiation and inhalation of uranium. Statistical methods are being assessed or developed and include examining the effects of confounding factors (e.g., demographic variables, smoking, and exposure to other toxic agents). Statistics appropriate for analyses involving multiple control groups (internal and external) are being developed.

Special groups of workers exposed to toxic agents (such as mercury, beryllium, and nickel) are studied to assess confounding factors in studies of radiation effects, but the results are also relevant to non-nuclear energy techniques.

18. CONTRACTOR TASK MANAGER

(Signature) 04-01-79 (Date)

19 DETAIL ATTACHMENTS: (See instructions)

- ☒ a. Facility Requirements
- ☒ b. Publications
- ☒ c. Purpose
- ☐ d. Background
- ☐ e. Approach
- ☒ f. Technical progress
- ☐ g. Future accomplishments
- ☐ h. Relationships to other projects
- ☐ i. Environmental assessment
- ☐ j. Explanation of milestones
- ☐ k. Other (specify):

1114033

(12-78)

TASK REQUIREMENTS FOR OPERATING/EQUIPMENT

COSTS AND OBLIGATIONS

CONTRACTOR NAME

Oak Ridge Associated Universities

BIN NUMBER	TASK NO.	REV. NO.	DATE PREPARED	CONTRACTOR NUMBER
		0	4-01-79	2493

20. STAFFING (in staff years)	FY 1979	FY 1980 PRESIDENT'S	FY 1980 REVISED	AUTHORIZED	FY 1981
a. SCIENTIFIC	6.40		7.60		7.60
b. OTHER DIRECT	3.10		3.60		3.60
c. TOTAL DIRECT	9.50		11.20		11.20
21. OBLIGATIONS AND COSTS (in Thousands)					
a. TOTAL COSTS	700	645	1,230		1,695
b. TOTAL OBLIGATIONS	889		1,370		1,730
22. EQUIPMENT (in Thousands)					
a. EQUIPMENT COSTS	42		3		4
b. EQUIPMENT OBLIGATIONS					
23. OTHER COSTS (specify)					
aDirect Salaries & Ben.	209		275		294
bSupporting Services	104		116		130
cMaterials & Other Direct	294		707		1,114
dIndirect Expenses	93		132		157

24. OPTIONAL FIVE-YEAR PLAN (in Thousands) Constant BY dollars	BY +1	BY +2	BY +3	BY +4
a. TOTAL OPERATING COSTS				
b. TOTAL OPERATING OBLIGATIONS				
c. TOTAL EQUIPMENT COSTS				
d. TOTAL EQUIPMENT OBLIGATIONS				

25. MILESTONE SCHEDULE	PROPOSED SCHEDULE	AUTHORIZED SCHEDULE
Complete preliminary mortality of of Tennessee-Eastman workers with 1973 SSA death search.	January-June 1979	
Complete mortality study of TEC workers with SSA death search of 1979.	June-December, 1979	
Complete preliminary analysis of Y-12 (UCCND) mortality workers.	June-October, 1979	
Validate exposure data and complete mortality Y-12 study.	June,1979-January,1980	
Complete mortality study of early workers at uranium processing plants (Mallinckrodt, NLO).	June,1979-June,1980	
Complete mortality study of other Oak Ridge nuclear workers (X-10,K-25)	June, 1979-Sept.,1980	
Complete mortality study of UCCND welders.	January,1979-Nov.1979	
Feasibility studies on workers exposed to mercury and beryllium.	Feb.,1979-March, 1980	
Obtain medium-sized computer, make computer operational, and interface with UCCND Computer Science Division	Dec., 1979-March,1980	
Complete rosters and data bases at Bettis and KAPL sites for complete mortality studies.	April, 1979-April, 1980	
Complete up-dated analysis of mortality among TEC and Y-12 workers with 1981 SSA death search results.	June, 1981-Jan,1982	

1114034

36

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No.	Date Prepared	Contractor Number
		0	4-01-79	2493

Enter headings in accordance with Item 19.

19a. Facility Statement

The Epidemiology Staff will be housed in the Tyrone Road Building during FY 79. A modification of the building designed to develop additional office space and toxicology laboratories is scheduled for completion during FY 79, and in FY 80 the staff will occupy this new space. To proceed with work scheduled for FY 80 and 81 in the task proposal entitled "DOE/Data Processing Support Facility Program," additional office space may be required. If so, it may be necessary to remodel an additional section of the building into office space.

19b. Publications:

Armstrong, R. D., Frome, E. L., and Kung, D. S. *A revised simplex algorithm for the absolute deviation curve fitting problem.* Commun. Statist. 1979 (to appear).

DuFrain, R. J., Littlefield, L. G., Joiner, E. E., and Frome, E. L. *Human cytogenetic dosimetry: A dose response relationship for alpha particle radiation from americium-241.* Health Physics, 1979 (to appear).

Armstrong, R. D. and Frome, E. L. *Least absolute value estimates for one- and two-way tables.* Naval Research Logistics Quarterly, 1979 (in press).

Frome, E. L. and DuFrain, R. D. *The analysis of dose-response curves for radiation induced chromosome aberrations.* Biometrics 34, 731, 1978, Abstract 2766.

Armstrong, R. D. and Frome, E. L. *A remark on algorithm AS108.* Appl. Statist, 1979 (in press).

Armstrong, R. D. and Frome, E. L. *A special purpose linear programming algorithm for obtaining least absolute value estimators in a linear model with dummy variables.* Commun. Statist.-Simula, Computa B6(4), 383-398, 1977.

Polednak, A. P. *Bone cancer among female radium dial workers. Latency periods and incidence rates by time after exposure.* J. Natl. Cancer Inst. 60, 77-82, 1978. (Work performed at Argonne National Laboratory, Chicago).

Polednak, A. P. *Long-term effects of radium exposure in female dial workers: Differential white blood cell count.* Environ. Res. 15, 151-161, 1978. (Work performed at Argonne National Laboratory, Chicago).

Polednak, A. P., Stehney, A. F., and Rowland, R. E. *Mortality among women first employed before 1930 in the U. S. radium dial-painting industry. A group ascertained from employment lists.* Am. J. Epidemiol. 107, 179-195, 1978 (Work performed at Argonne National Laboratory, Chicago).

1114035

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No.	Date Prepared	Contractor Number
		0	4-01-79	2493

Enter headings in accordance with Item 19.

19b. Publications (continued)

Polednak, A. P. *Long-term effects of radium exposure in female dial workers: Liver disease and liver function.* Environ. Res. (in press). (Work performed at Argonne National Laboratory, Chicago).

Dupree, E. A. *The role of risk factors in the complications of diabetes mellitus.* Thesis, The Johns Hopkins University, Baltimore, Maryland, 1978.

Godbold, J. H., Jr. and Tompkins, E. A. *A long-term mortality study of workers occupationally exposed to metallic nickel at the Oak Ridge Gaseous Diffusion Plant.* J. Occup. Med. (in press).

Hansard, M. S. *Automatic encoding of natural language medical problems.* Ph.D. dissertation, 1978, Georgia Institute of Technology, Atlanta, Georgia.

19c. Purpose:

The purpose of the task is to evaluate the long-term health effects of occupational exposure to low levels of ionizing radiation. The objectives are to perform mortality studies of specific populations of DOE/DOE contractor employees occupationally exposed to radiation and to various chemicals or toxic agents and to analyze and interpret these data. This will lead to a significant increase in the scientific evidence for evaluating the health effects of occupational exposures to low levels of ionizing radiation through studies of several occupational groups. The results of these studies can be interpreted in the light of the findings of other (limited) evidence from similar studies on occupational groups and the extensive data on Japanese atomic-bomb survivors. In meeting these objectives, consideration of the effects of concomitant exposures to chemicals and other toxic agents will be evaluated. The latter work is needed both to assess the possible confounding effect of these other exposures in the analysis of radiation-exposure effects and to contribute to knowledge regarding the health effects of substances which may also be relevant to other energy technologies.

19f. Technical Progress:

FY 78-79

In FY 78, the feasibility of conducting a mortality study of workers employed at the Oak Ridge Y-12 facility during the period 1943-47 (Tennessee Eastman Company)

1114036

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No.	Date Prepared	Contractor Number
		0	4-01-79	2493

Enter headings in accordance with Item 19.

19f. Technical Progress (continued)

FY 78-79

was established. The Tennessee Eastman population is comprised of about 40,000 persons who worked during the 1943-47 period in the uranium-processing facility at Y-12. It offers the advantage of long follow-up from employment--i.e., 31 to 35 years, to 1978 which is the cut-off year for determination of vital status by the latest Social Security Administration search.

Also, exposures to uranium dust was potentially high. External radiation exposure (film badge) data do not exist, but uranium urinalysis results were located (in late FY 78) on a sample of long-term workers. A search is being conducted to locate information on the operation of the facility, including air-sampling data descriptions of the operation of electromagnetic-separation process, and information on work areas and job descriptions. Medical examination records, including an extensive pre-employment examination form and chest radiographs were made available to ORAU late in FY 78, along with the original hard-copy payroll records. Data obtained from payroll records, including work histories, have been computerized and are in the process of being edited and verified.

Data from medical recordings, including use of tobacco and past diseases and hospitalizations, are being evaluated and may be computerized in FY 79.

A complete roster of Tennessee-Eastman employees was sent to Social Security Administration (SSA) in January, 1979. The results of this search will be available in several months when states are to be searched for death certificates. Preliminary analyses are scheduled for completion June 1, 1979 using results of a late 1973 SSA search. At present, copies of death certificates, on file for over 92.5% of the approximately 7,000 deaths identified in the 1973 SSA search, are being verified and the search for missing certificates is continuing.

Along with the study of Tennessee-Eastman workers at Y-12, a study was initiated (in early FY 79) of persons employed at Y-12 after Union Carbide took over operations in 1947. This population has a shorter period of follow-up relative to the Tennessee-Eastman group, but data on individual exposure to radiation and other substances are more extensive. Film-badge and uranium-urinalysis data from about 1950 are available on Union Carbide computers, and data-analysis files for mortality studies are being prepared from them. The completeness and validity of these data on external- and internal-radiation exposure with respect to time and specific individuals is scheduled to be ascertained in FY 79. Data-analysis files containing these data, along with work-history data, are being prepared using K-25 computer facilities. In addition to these data on individual

1114037

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No.	Date Prepared	Contractor Number
		0	4-01-79	2493

Enter headings in accordance with Item 19.

19f. Technical Progress (continued)

FY 78-79

exposures to radiation, air-sampling data (uranium) by location are being studied to determine environmental levels and to estimate individual exposures during time periods when individual monitoring was done.

The first (preliminary) analysis of mortality among Y-12 (Union Carbide) workers is to be completed by June 1979, based on the results of the 1973 Social Security Administration (SSA) search for deaths.

FY 80-81

A more extensive mortality study will be completed in FY 80, which should include validated radiation-exposure data and deaths reported by the SSA in the 1979 search for deaths. At the request of, and by agreement with, Union Carbide Nuclear Division, a study of all Carbide employees who ever worked as welders has been initiated. The preliminary roster includes about 1345 persons, most of whom worked at the K-25 facility. The availability of industrial hygiene data on substances to which welders may be exposed (various gases, toxic metal fumes, and metallic dusts) was explored in FY 79. A roster of these welders was sent to the Social Security Administration in January 1979 for identification of deceased persons. This mortality study is scheduled to be completed in November 1979, FY 80. Mercury and its compounds are still widely used in industry, and mercury is also released through combustion of fossil fuels. The long-term effects of human exposure to mercury (especially inorganic mercury) have not been studied extensively, while the effects of large doses of mercury compounds have been known for some time (due to previous pharmacological uses). An as yet undetermined number of Oak Ridge workers (probably a few thousand) have worked with inorganic mercury. The use of mercury began at Y-12 under Tennessee Eastman's operation when vacuum gauges were cleaned with large amounts of mercury. Mercury (Hg^{++}) urinalysis data are available on (at least) a small group of these early workers (1944-1945). The total number of workers potentially exposed to mercury at Y-12 (Tennessee Eastman, 1943-1947) will be determined in FY 79. After Union Carbide took over operations of Y-12, between one and two thousand workers reportedly worked with mercury between 1957 and 1966. Some 28,000 records (many persons having multiple samples) of urinary mercury determinations have been computerized, and we are obtaining access to these data. At K-25, a few hundred workers have reportedly been exposed to mercury since 1948. Mortality studies of these workers are

1114038

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No. 0	Date Prepared 4-01-79	Contractor Number 2493

Enter headings in accordance with Item 19.

19f. Technical Progress (continued)

FY 80-81

planned for FY 80-81, using procedures outlined for the study of nuclear workers at Oak Ridge, of which the mercury workers are a subgroup.

For adequate scientific evaluation of the possible effects of external and internal radiation exposure, the role of various "confounding" factors must be determined and taken into account in analyses of mortality from specific causes. Statistical methods developed by various investigators are being evaluated, and possible alternative methods (or the application of other existing statistical methods) were studied in FY 79. (This work was conducted by Dr. E. Frome, with consultants from Emory University, University of North Carolina.) Necessary computer support for these activities, and for all data analyses involved in the studies mentioned above, is being examined by Dr. M. Hansard in consultation with outside computer scientists at the University of Tennessee and elsewhere.

A 200 megabyte disk drive for on-line data storage was purchased and installed at the Computer Sciences Division of Union Carbide. This development helped support immediate computer needs for FY 79. In FY 80 our long-term computer needs will include a medium-sized computer dedicated to real-time processing and accessing the large masses of data of the Health and Mortality Study. Presently (FY 79) data input into the Health and Mortality files at the Computer Science Division is largely by key punch; data retrieval, data reduction (as into tables) data editing and corrections are by batch processing obtained by purchase requests to the Computer Science Division, Union Carbide Nuclear Division). Therefore the present system is too slow and cumbersome to obtain the acceleration of data processing and analysis needed in this project. A device in the size range of a DEC VAX 11/780 and accessories (less than $400,000) will be installed to overcome these difficulties. Proposal writing to substantiate this need was under way in early FY 79.

Staff statisticians, computer scientists, and epidemiologists will have begun to develop a health surveillance data model. This model will be used to establish the availability of various types of data for each DOE population and to formulate data acquisition, conversion, management, and analysis plans.

The more extensive mortality analyses of Y-12 (Tennessee-Eastman) and Y-12 (Union Carbide) workers will be completed in early 1980. Mortality studies of

1114039

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No. 0	Date Prepared 4-01-79	Contractor Number 2493

Enter headings in accordance with Item 19.

19f. Technical Progress (continued)

FY 80-81

other Oak Ridge workers (at X-10 and K-25) should be completed in FY 80 and FY 81. Mortality studies of workers at several early (World War II) uranium-processing plants, in addition to the Y-12 (Tennessee-Eastman) facility, should also be completed in FY 80 and 81; this work is being conducted by E. A. Dupree, Associate Epidemiologist.

Since many members of the early occupational cohorts (Tennessee-Eastman) are reaching age groups with high mortality rates, continued follow-up is necessary to fully evaluate the long-term effects of radiation exposure. Thus, the roster of Tennessee-Eastman workers will be resubmitted to the Social Security Administration in late FY 80 or early FY 81.

Pilot studies planned to evaluate the completeness of ascertainment of deaths by the Social Security Administration will include complete searches of state indexes of death for all names on rosters of the Health and Mortality Study (e.g., Y-12 workers) and possibly more direct follow-up by contact through former employers. We have been in contact with Dr. James Stebbings, Jr., at the Los Alamos Scientific Laboratory, and with Dr. Sidney Marks, Hanford Environmental Research Foundation, regarding this important problem, and collaboration with these investigators is most helpful.

Further investigations planned of workers exposed to various chemicals will include a study of beryllium workers to be completed by FY 1981.

1114040

DOE F .m 6120.2
(12-78)

U.S. DEPARTMENT OF ENERGY

FIELD TASK PROPOSAL/AGREEMENT

1. WP BIN NUMBER	2. TASK NO.	3. REV. NO.	4. PROJECT NO.	5. DATE PREPARED (mm dd yy)	6. CONTRACTOR NUMBER
		0		4-01-79	3034

7. TASK TITLE	8. WORK PACKAGE TITLE
DOE DEATH CERTIFICATE RETRIEVAL OFFICE	

9. BUDGET AND REPORTING CODE	10. TASK TERM Begin: (mm dd yy)	End: (mm dd yy)	11. CONTRACTOR NAME	12. CODE (see instructions)
GK 01 02 01 1	10-01-78	Open	Oak Ridge Associated Universities	ORH

13. CONTRACTOR TASK MANAGER (Name, FTS No.)	14. PRINCIPAL INVESTIGATORS
Dr. C. C. Lushbaugh FTS: 626-3090	Dr. Anthony Polednak

15. WORK LOCATION (See instructions): Name of facility, City, State, ZIP Code	16. Does this task include any management services efforts?
Oak Ridge, TN 37830	☐ YES ☒ NO

17. TASK DESCRIPTION (Approach, relation to work package, in 200 words or less)

The Death Certificate Retrieval Office (DCRO) is in operation to facilitate mortality studies supported by the Department of Energy. The office provides a single point of contact with the Social Security Administration (SSA) for identification of deceased DOE/DOE-contractor workers being followed up in several epidemiologic studies. After deceased persons have been identified, the DCRO conducts searches for copies of death certificates using information provided by the SSA, death indexes from certain states, and other search methods developed by the DCRO. All information obtained using these methods is provided to the investigators conducting epidemiologic studies. The operation of the DCRO should be improved by closer collaboration with these investigators, by development of more systematic search procedures, and by more extensive use of computers.

18. CONTRACTOR TASK MANAGER

(Signature) 04-01-79 (Date)

19. DETAIL ATTACHMENTS: (See instructions)

- ☐ a. Facility Requirements
- ☐ b. Publications
- ☒ c. Purpose
- ☐ d. Background
- ☐ e. Approach
- ☒ f. Technical progress
- ☐ g. Future accomplishments
- ☐ h. Relationships to other projects
- ☐ i. Environmental assessment
- ☐ j. Explanation of milestones
- ☐ k. Other (specify):

1114041

DOE Form 61[illegible] (Page 2)
(12-78)

TASK REQUIREMENTS FOR OPERATING EQUIPMENT COSTS AND OBLIGATION

CONTRACTOR NAME

Oak Ridge Associated Universities

BIN NUMBER	TASK NO.	REV. NO.	DATE PREPARED	CONTRACTOR NUMBER
		0	4-01-79	3034

20. STAFFING (in staff years)	FY 1979	FY 1980 PRESIDENT'S	FY 1980 REVISED	AUTHORIZED	FY 1981
a. SCIENTIFIC	1.00		1.00		1.00
b. OTHER DIRECT	2.60		3.00		3.00
c. TOTAL DIRECT	3.60		4.00		4.00
21 OBLIGATIONS AND COSTS (in Thousands)					
a. TOTAL COSTS	155	155	167		180
b. TOTAL OBLIGATIONS	195		171		184
22. EQUIPMENT (in Thousands)					
a. EQUIPMENT COSTS	0		0		0
b. EQUIPMENT OBLIGATIONS					
23. OTHER COSTS (specify)					
aDirect Salaries & Ben.	44	48	51		55
bSupporting Services	30	29	31		33
cMaterials & Other Direct	55	51	57		62
dIndirect Expenses	26	27	28		30

24 OPTIONAL FIVE-YEAR PLAN (in Thousands) Constant BY dollars	BY +1	BY +2	BY +3	BY +4
a. TOTAL OPERATING COSTS				
b. TOTAL OPERATING OBLIGATIONS				
c. TOTAL EQUIPMENT COSTS				
d. TOTAL EQUIPMENT OBLIGATIONS				

25 MILESTONE SCHEDULE	PROPOSED SCHEDULE	AUTHORIZED SCHEDULE
FY 1979		
A. Complete search for death certificates of decedents and supply copies to DOE participants.	Jan., 1979-May, 1979	
B. Expand present methods of searching for death certificates and develop computerized retrieval system.	Feb., 1979-Jan., 1980	
C. Develop cooperative efforts with the Social Security Administration (SSA) to ascertain completeness of ascertainment of deaths.	March, 1979-Jan.,1980	
D. Complete search for death certificates based on June, 1979, SSA submission.	June,1979-Dec., 1979	
FY 1980		
A. Complete search for death certificates based on rosters sent to SSA in November.	Nov., 1979-May, 1980	
B. Complete search for death certificates based on results of June, 1980, SSA submission.	June, 1980-Dec.,1980	
FY 1981		
A. Complete search for death certificates based on results of November, 1980, SSA submission.	Nov., 1980-May, 1981	

1114042

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No.	Date Prepared	Contractor Number
		0	4-01-79	3034

Enter headings in accordance with Item 19.

19b. Publications

None

19c. Purpose

The DOE/Death Certificate Retrieval Office (DCRO) is organized to provide a central office for facilitating mortality studies of DOE workers supported by DOE. The DCRO provides DOE/Human Health and Assessments Divisions a single liason between the Social Security Administration (SSA) and all DOE mortality studies. Semiannually, SSA identifies deceased persons from rosters supplied by DCRO. DCRO provides assistance to DOE participants in ascertaining the place (state) of death, in obtaining and verifying copies of death certificates, and in coding the underlying cause of death. The system is intended to avoid unnecessary duplication of these efforts by DOE-supported epidemiologic follow-up studies.

19f. Progress FY 1978

The Death Certificate Retrieval Office began operation by searching the states for death certificates of Hanford employees previously identified as dead by Social Security searches. A roster of employees (Rocky Flats, Los Alamos, and Baneberry test site) was sent to Social Security in June, 1978, and deceased persons identified. Copies of death certificates have been obtained for most of these decedents. An in-house, five-day course in modern death-certificate nosology was given by Reba Dent (formerly at NCHS) for DCRO staff. Efforts were begun to obtain indexes of deaths from State Vital Statistics Offices. Thus far, DCRO has indexes for 15 states on hand; several others have agreed to supply an index; while about 20 states have replied negatively to our request.

FY 1979

In January, 1979, a computer tape containing approximately 100,000 names of DOE employees was sent to the Social Security Administration (SSA) for ascertainment of deaths reported to the SSA system. The population included Oak Ridge (Tennessee Eastman Co. and Y-12 plants), Hanford, and Los Alamos workers and a small group of workers being studied at Argonne National Laboratory. After deceased persons have been identified by SSA, DCRO will begin to obtain copies of death certificates from State Vital Statistics Offices. Various state indexes of deaths available to DCRO will be used in this process.

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No.	Date Prepared	Contractor Number
		0	4-01-79	3034

Enter headings in accordance with Item 19.

19f. FY 1979 (continued)

The next submission to SSA, scheduled for June, 1979, includes Oak Ridge (K-25, X-10), Mallinckrodt and National Lead employees, and other groups as determined by other DOE participants using DCRO services.

Efforts to obtain indexes of deaths from State Vital Statistics Offices continued.

Steps were underway to systematize and computerize the process of certifying death certificates as much as possible.

Planned Progress FY 1980, 1981

Future submissions to SSA will include resubmissions by DOE participants (Hanford, Los Alamos, Oak Ridge) for more recent determinations of deaths in order to prepare mortality studies with the most recent follow up of DOE employees. The DCRO will continue to obtain copies of death certificates for deceased persons in all of these populations. Close cooperation is planned with DOE participants using DCRO services to provide the most efficient means of accomplishing the ultimate goal of DCRO which is to facilitate epidemiologic studies of DOE workers.

The problem will be addressed of ascertaining completeness of reporting of deaths through the Social Security Administration (SSA) searches alone. Arrangements to be made with the SSA for cooperative efforts will enable solution of this important problem. The efficiency of the entire operation of DCRO will be enhanced by increased use of computers for storage of all information, including causes of death obtained from the death certificate.

DOE F 1 .m 6120.2
(12-78)

U.S. DEPARTMENT OF ENERGY

FIELD TASK PROPOSAL/AGREEMENT

1. WP BIN NUMBER	2. TASK NO.	3. REV. NO.	4. PROJECT NO.	5. DATE PREPARED (mm dd yy)	6. CONTRACTOR NUMBER
		0		4-01-79	NEW

7. TASK TITLE: DOE/DATA PROCESSING SUPPORT FACILITY PROGRAM

8. WORK PACKAGE TITLE:

9. BUDGET AND REPORTING CODE	10. TASK TERM Begin: (mm dd yy)	End: (mm dd yy)	11. CONTRACTOR NAME	12. CODE (see instructions)
GK 01 02 01 1	10-01-79	Open	Oak Ridge Associated Universities	ORH

13. CONTRACTOR TASK MANAGER (Name, FTS No.)

Dr. C. C. Lushbaugh

FTS: 626-3090

14. PRINCIPAL INVESTIGATORS

A. Polednak, Ph.D., Epidemiologist
D. Robie, B.S. - Data Processing Support Manager

15. WORK LOCATION (See instructions) Name of facility, City, State, ZIP Code

Oak Ridge, TN 37830

16. Does this task include any management services efforts?

☐ YES
☒ NO

17. TASK DESCRIPTION (Approach, relation to work package, in 200 words or less)

This program provides the technical support necessary for developing the data bases for DOE Health and Mortality Studies including all former as well as present DOE laboratories, plants and DOE-contractor sites (∿ 101 sites). Specialists trained in data collection, data validation, quality control, and data processing obtain personnel and occupational data for past and current employees of DOE/DOE contractors at sites where employment and radiation exposure data are not now part of the DOE Health and Mortality studies. Using modern data management practices, this staff prepares the data for computerization, vital status searches, biostatistical and epidemiologic analyses. Trained staff work as three to four man teams in the field at various sites where, with local cooperation, they microfilm raw data, if not obtainable in machine readible computerized formats. These copies are then returned to a centralized data-processing facility where along with experts in health physics, industrial hygiene and work history profiles, the data are abstracted and encoded in uniform formats for computerization. Quality control of data collection, validation of radiation and other exposure data, as well as sampling for completeness, editing for error detection and consistency is directed by the epidemiologists, statisticians and computer scientists of DOE Health and Mortality Study Program.

18. CONTRACTOR TASK MANAGER

(Signature) 04-01-79 (Date)

19. DETAIL ATTACHMENTS (See instructions)

- ☐ a. Facility Requirements
- ☐ b. Publications
- ☒ c. Purpose
- ☐ d. Background
- ☐ e. Approach
- ☒ f. Technical progress
- ☐ g. Future accomplishments
- ☐ h. Relationships to other projects
- ☐ i. Environmental assessment
- ☐ j. Explanation of milestones
- ☐ k. Other (specify):

1114045

DOE Form 5130.2 (Page 3) (12-78)

TASK REQUIREMENTS FOR OPERATING/EQUIPMENT COSTS AND OBLIGATION

CONTRACTOR NAME

Oak Ridge Associated Universities

BIN NUMBER	TASK NO.	REV. NO.	DATE PREPARED	CONTRACTOR NUMBER
		0	4-01-79	NEW

	FY 1979	FY 1980 PRESIDENT'S	FY 1980 REVISED	AUTHORIZED	FY 1981
20. STAFFING (in staff years)					
a. SCIENTIFIC	2.60		3.40		3.25
b. OTHER DIRECT	2.40		6.40		12.40
c. TOTAL DIRECT	5.00		9.80		15.65
21. OBLIGATIONS AND COSTS (in Thousands)					
a. TOTAL COSTS	200	0	325		462
b. TOTAL OBLIGATIONS	298	0	366		471
22. EQUIPMENT (in Thousands)					
a. EQUIPMENT COSTS	0		0		0
b. EQUIPMENT OBLIGATIONS					
23. OTHER COSTS (specify)					
aDirect Salaries & Ben.	105		172		262
bSupporting Services	37		60		83
cMaterials & Other Direct	25		39		41
dIndirect Expenses	33		54		76

24 OPTIONAL FIVE-YEAR PLAN (in Thousands) Constant BY dollars	BY +1	BY +2	BY +3	BY +4
a. TOTAL OPERATING COSTS				
b. TOTAL OPERATING OBLIGATIONS				
c. TOTAL EQUIPMENT COSTS				
d. TOTAL EQUIPMENT OBLIGATIONS				

25 MILESTONE SCHEDULE	PROPOSED SCHEDULE	AUTHORIZED SCHEDULE
Recruit, train and equip data collection team (3 persons).	May 1979	
Complete analysis of data availability at individual DOE sites.	October 1979	
Begin phased data collection at selected sites (possibly Bettis and KAPL).	October 1979	
Complete feasibility study of possible uniform DOE-wide record keeping system.	May 1980	
Complete training and equipping second field collection team.	October 1980	
Centralized data processing facility and staff fully operational (4 collection and processing teams).	June 1981	
Continual system of data processing and preparation of DOE site data bases for epidemiology analyses in place.	October 1981	

1114046

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No.	Date Prepared	Contractor Number
		0	4-01-79	NEW

Enter headings in accordance with Item 19.

19b. Publications:

New program activity.

19c. Purpose:

Modern epidemiologic studies must have data bases that are carefully collected, rigidly controlled and as uniform and error-free as possible so as to avoid biasing hypothesis testing and other epidemiologic analyses. Also as causal relations are sought by epidemiologic methods between such late effects as various cancers and low (occupational), chronic exposures to radiation and other industrial toxicants, extremely large study populations are needed to obtain biostatistical significance and reliability. To meet these needs, an as large as possible number of DOE workers under study much be achieved and the data for their work history files must be collected and managed under strict quality control for uniformity and completeness. This program provides the technical support to meet these goals. Specialists trained in data collection, data validation, quality control, and data processing obtain personnel and occupational data for past and current employees of DOE/DOE contractors at sites where employment and radiation exposure data are needed for the DOE Health and Mortality studies.

19f. Technical Progress:

FY 78

Program under study but not in place.

FY 79

An expert in business management, organization, task identification, assignments and performance evaluation of research associates, assistants, technicians and clerks was successfully recruited for day-to-day leadership of this program under the long-range guidance of our staff epidemiologist. Organization, recruitment and training was begun.

Visits to study raw data collection methods, training and operations were made to the Epidemiologic departments of Johns Hopkins University, University of North Carolina (UNC), and the Occupational Health Studies Group of UNC where the so-called "Rubber Workers Studies" are conducted.

1114047

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No.	Date Prepared	Contractor Number
		0	4-01-79	NEW

Enter headings in accordance with Item 19.

19f. Technical Progress (continued)

FY 79

A detailed analysis started as soon as possible in FY 79 was carried out to (1) contact personnel and record departments and other sources of epidemiologic data at all DOE sites, (2) survey the various methods used for record keeping there and determine status and the existence of all specific kinds of records needed, (3) assess the potential difficulties of data collection by off-site teams vs on-site permanent record clerks, and (4) from this detailed analysis of data availability, commonality of record keeping systems was determined and any needed changes to obtain universality of record keeping within all DOE establishments were identified. Costs of changes vs. basic data requirements will be evaluated and minimum recommendations formulated and passed forward for evaluation by DOE headquarters and field operational staffs, any overview committees then in place and program consultants.

A team consisting of three to four record clerks or data collection technicians was recruited, trained, equipped and organized as rapidly as possible to enable early field trial of data collection of, first, terminated employees; and then, current employees of two sites not previously involved in Health and Mortality studies. These sites chosen for feasibility study of this approach were identified because of long employment - 3,000 persons/yr/30 yrs.

The experience obtained from this feasibility study will be used in training the second team to alternate with the first team in the field. The plan is for the team to work at the centralized data processing facility to develop skills in transposing filmed raw data to standardized formats for computerization of the basic data of the employees of the plant visited while team B collects more data. Procedures will be developed to enable constant surveillance of the process, individual performance (accuracy and dependability) and rate of progress. Any missing data identified in this process will be researched in the field by the site-responsible team. It is currently planned that each team will initially have working with them at least one epidemiologic (pre-master) student in training (University of North Carolina) and one post-M.P.H. graduate student (University of North Carolina, Medical College of Georgia, Harvard, or other universities).

1114048

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No.	Date Prepared	Contractor Number
		0	4-01-79	NEW

Enter headings in accordance with Item 19.

19f. Technical Progress (continued)

Planned Progress in FY 80 and 81:

An overview committee (UNC) will be fully operational by the start of FY 80. All principal employees of the Study will have made several site visits to the University of North Carolina and cooperation firmly established.

Complete analysis of data availability at all DOE sites will have been completed. The first phases of the data collection program will have been completed (possibly at Bettis and KAPL) followed by an in-depth study of the problems and methodology. Refinement of the management and retrieval methods will be accomplished.

A fixed schedule will be established for data collection at all present and former DOE sites, realizing that retrieval methods will vary considerably at the various sites and at the disbanded sites. General guidelines will be established with specialized methods where needed. Retrieval procedures will be coordinated with ORO, other field offices and DOE epidemiologic centers.

Contractural agreements, review of Privacy Act, FOIA, state and federal regulations will be documented. Liaison with principal parties at Operations Offices and contractor sites will be established. Availability and accessibility of data will vary considerably at the different sites. It is anticipated that regional archives will be considered as a source of some data.

Data Collection Manager

He will visit, review and incorporate, where appropriate, collection methodology of other similar systems (i.e., SEER-Atlanta, NCI and National Death Index Office, Bethesda, National Cancer Registry). Site visits will be made.

Standardized retrieval processes for roster, medical, exposure, area/site monitoring, toxic substance and mortality data will be firmly established in early FY 80.

Constant monitoring of committee meetings of the subgroup of the Interagency Task Force on the Health Effects of Ionizing Radiation, the American Medical Record Association (AMRA), the Model State Vital Statistics Act and the Privacy Act Commission will be maintained by the Data Collection Manager. Each of these has a tremendous impact on epidemiology studies.

1114049

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No. 0	Date Prepared 4-01-79	Contractor Number NEW

Enter headings in accordance with Item 19.

19f. Technical Progress (continued)

FY 80-81 (Data Collection Manager)

Due to the unique problems involved with retrieval of data from disbanded DOE sites, one of the collection teams will be specially trained for this purpose.

An in-depth demographic study of all sites will be incorporated into the study. Selected area retired employees will be interviewed for archival data. Community and environmental analysis, worker distribution patterns, density of populations and vital statistics by counties will be documented since this is essential.

Since it is anticipated that difficulties will occur in regard to accessibility of state and county data at some sites, the Data Collection Manager or representative will be established and contact made as needed with various state health and vital statistics departments.

Liaison with National and Regional Social Security Administration Offices will be established through the Death Certificate Retrieval Office. Problems will be constantly monitored.

Nosological protocols will be firmly established and a preliminary trial program will be in operation.

The feasibility of a possible uniform DOE-wide record-keeping system will be made.

By mid-FY 80, the data from 50% of the active sites and 25% of the disbanded sites will have been reviewed. Collection teams will be working concurrently at several sites.

An overview to DOE management will provide a broad summary of accomplishments, milestones achieved, as well as projections and objectives of planned activities. Included will be an extensive Quality Control evaluation to ensure that errors are kept below a specified figure.

The design and timetable for a Central Data Processing Facility will be established.

Complete training and equipping of all of the collection teams will be completed by late FY 80.

1114050

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No. 0	Date Prepared 4-01-79	Contractor Number NEW

Enter headings in accordance with Item 19.

19f. Technical Progress (continued)

FY 80-81

Continuous monitoring of input will be maintained by the Data Collection Manager.

The in-house committee to be established in early FY 80 will be continuously evaluating record-keeping and data collection techniques for future studies. A formal recommendation will be made by mid-FY 81.

A completely automated information system will be in full operation by FY 81. The Centralized Data Processing Facility with staff will be fully operational (4 collection and processing teams). The main function of this facility then will be to maintain the flow of raw data and process it for the data files. Editing and verification will be automated to insure computerized input into consistent data. A strong security program for storage of critical data will be in place.

The Epidemiology teams which will have begun analyses of the data on a site-by-site basis will establish the priorities for special projects such as further data collection and data validation needed at sites where these studies have identified possible causal association of interest.

1114051

DOE Form 5120.1 (12-78)

DEPARTMENT OF ENERGY

FIELD WORK PACKAGE PROPOSAL/AGREEMENT

1. WP BIN NUMBER	2. REVISION NO.	3. CONTRACTOR NO.	4. DATE PREPARED
WP	0		3-24-80

5. WORK PACKAGE TITLE

HUMAN HEALTH EFFECTS FROM ENERGY GENERATION

6. BUDGET AND REPORTING CODE	7. CONTRACT NUMBER	8. PHASE	9. PROJECT NUMBER
HA 02 01 01 0	DE-AC05-76OR00033	B	

10. CONTRACT TERM	11. WORK PACKAGE TERM	12. Does this work package include any management services efforts?
Begin: 7/01/77 End: 6/30/82	Begin: 10-1-79 End: Open	☐ YES ☒ NO

13. HEADQUARTERS PROGRAM MANAGER:	16. HEADQUARTERS ORGANIZATION:	DOE ORGANIZATION CODE
14. OPERATIONS OFFICE/HQ WORK PACKAGE MANAGER:	17. OPERATIONS OFFICE:	DOE ORGANIZATION CODE
15. CONTRACTOR WORK PACKAGE MANAGER:	18. CONTRACTOR NAME:	CODE (See instructions)

19. WORK LOCATION (if different from contractor main office)

20. WORK PACKAGE DESCRIPTION (Approach, anticipated benefit in 200 words or less):

The purpose of this program is to determine epidemiologically (from work-history files which include demographic, radiation and chemical exposures, medical histories, and death certificates) whether or not atomic workers of AEC/DOE plant sites and research and development laboratories have experienced an increased incidence of and mortality from cancer and any other late effects. This program is carried out by four closely related task groups: Health and Mortality Study Group (Epidemiology); DOE/Death Certificate Retrieval Office; DOE/Data Processing Support Facility; and DOE/SSA Data Searches. Immediate scientific objectives include specific epidemiologic studies of the workers' health experience at the Oak Ridge plant sites (Y-12, X-10, K-25, Paducah and Portsmouth) and other workers involved in the uranium fuel cycle at DOE/contractor sites operated by Mallinckrodt, Monsanto, National Lead, DuPont, and Westinghouse corporations. Subsets of workers at these sites considered at risk from specific toxicants such as mercury, nickel, beryllium, etc. will be studied to assess the confounding influences of such exposure upon low-dose-rate occupational radiation exposure. In addition, an epidemiologic/medical study is being conducted of persons employed at 75 present or former DOE plant sites and civilians employed at 8 U. S. Navy submarine yards who have had "administrative" overexposures of more than 5 rem in any one year of employment.

The long-range goal of this program is to establish a National Roster of Radiation Workers as a gigantic data base that can be used to evaluate allegations of untoward injuries from occupations related to energy generation.

21. CONTRACT WORK PACKAGE MANAGER:	22. DOE WORK PACKAGE MANAGER:
(Signature) (Date)	(Signature) (Date)
23. ASSISTANT SECRETARY OR DESIGNEE	24. DESIGNATED HEADQUARTERS OFFICIAL
(Signature) (Date)	(Signature) (Date)

25. DETAIL ATTACHMENTS: (See instructions)

- ☐ a. Facility requirements
- ☐ b. Publications
- ☐ c. Purpose
- ☐ d. Background
- ☐ e. Approach
- ☐ f. Technical progress
- ☐ g. Future accomplishments
- ☐ h. Relationships to other projects
- ☐ i. Environmental assessment
- ☐ j. Explanation of milestones
- ☐ k. Other (Specify):

1114052

DOE Form 5120.1 (Page 2) (12-78)

WORK PACKAGE REQUIREMENTS FOR OPERATING/EQUIPMENT COSTS AND OBLIGATIONS

CONTRACTOR NAME	WP BIN NUMBER	REVISION NUMBER	CONTRACTOR NUMBER	DATE PREPARED
Oak Ridge Associated Universities	WP	0		3-24-80

	FY 80	FY 81 PRESIDENT'S	FY 81 REVISED	FY 81 AUTHORIZED	FY 82
26. STAFFING *(in staff years)*					
a. SCIENTIFIC	14.55		17.0		17.0
b. OTHER DIRECT	9.85		18.3		18.3
c. TOTAL DIRECT	24.4		35.3		35.3
27. OBLIGATIONS AND COSTS *(in Thousands)*					
a. TOTAL COSTS	1977.0		2655.0		2861.0
b. TOTAL OBLIGATIONS	2331.0		2717.0		2929.0
28. EQUIPMENT *(in Thousands)*					
a. EQUIPMENT COSTS	40		82		88
b. EQUIPMENT OBLIGATIONS	40		82		88
29. OTHER COSTS *(specify - show costs in Thousands)*					
a. Direct Sal. & Benefits	522		753		807
b. Materials & Other Direct	894		1161		1254
c. Supporting Services	307		410		441
d. Indirect Expenses	254		331		359
30. FIVE-YEAR PLAN *(in Thousands)* - constant BY $					
a. TOTAL OPERATING COSTS					
b. TOTAL OPERATING OBLIGATIONS					
c. TOTAL EQUIPMENT COSTS					
d. TOTAL EQUIPMENT OBLIGATIONS					

31. MILESTONE SCHEDULE	PROPOSED DOLLARS FY 80	FY 81	FY 82	PROPOSED SCHEDULE	AUTHORIZED SCHEDULE

1114053

DOE F 1325.2 (12-75)

U.S. DEPARTMENT OF ENERGY

FIELD TASK PROPOSAL/AGREEMENT

1. WP BIN NUMBER	2. TASK NO.	3. REV. NO.	4. PROJECT NO.	5. DATE PREPARED	6. CONTRACTOR NUMBER
		0		3-24-80	00 2493

7. TASK TITLE	8. WORK PACKAGE TITLE
Health and Mortality Study	HUMAN HEALTH EFFECTS FROM ENERGY GENERATION

9. BUDGET AND REPORTING CODE	10. TASK TERM Begin:	End:	11. CONTRACTOR NAME	12. CODE (see instructions)
HA 02 01 01 0	10-1-79	Open	Oak Ridge Associated Universities	ORU

13. CONTRACTOR TASK MANAGER (Name, FTS No.)	14. PRINCIPAL INVESTIGATORS
C. C. Lushbaugh FTS: 626-3090	C. C. Lushbaugh B. Dupree M. Hansard E. Frome

15. WORK LOCATION (See instructions): Name of facility, City, State, ZIP Code	16. Does this task include any management services efforts?
Oak Ridge Associated Universities P. O. Box 117 Oak Ridge, Tennessee 37830	☐ YES ☒ NO

17. TASK DESCRIPTION (Approach, relation to work package, in 200 words or less)

Epidemiologic studies are being conducted on populations of DOE (or DOE contractor) workers whose occupations involve potential exposure to internal and/or external radiation. These workers also have the potential of being exposured to uranium, uranium dust, and such toxic metals as lead, cadmium, and nickel, etc., in nuclear fuel production and enrichment and in the processing of radioactive material related to military applications. The principal aim of these studies is to assess long-term health effects of occupational exposure to low-level ionizing radiation and additive effects by confounding chemical stresses. Current studies concern mortality experience of workers at sites in Oak Ridge (Y-12 Tennessee Eastman Corporation, Y-12 Union Carbide, X-10, and K-25 plants), other current DOE facilities (Paducah, Portsmouth), disbanded Manhattan Engineering District (MED) sites (Mallinckrodt, Linde, Columbia University, Middlesex), and other selected sites (National Lead of Ohio, Mound, Savannah River, Argonne National Laboratory, Brookhaven National Laboratory, Idaho Test Site, and Nevada Test Site). In special cases where small populations of unique workers appear to suffer from a disease of interest (e.g. lung cancer, melanoma, etc) case control studies are done.

Statistical methods and data-management techniques are being developed through methodology research for improving the power of epidemiologic analysis of low-level stresses to large numbers of people. This biostatistical research also provides record-linkage algorithms and statistical data-editing procedures to facilitate handling problems generic to using large complex data sets in longitudinal cohort studies.

The long-range goal of this project is to be able to merge all occupational, rosters, radiation exposure records and other pertinent data from all MED/AEC/ERDA/DOE sites since 1942 into a National Atomic Energy Worker Roster to provide as many as possible person year rems for radiation risk assessment and a basis for a continuous health and safety survey for DOE workers.

18. CONTRACTOR TASK MANAGER

(Signature) 3-24-80 (Date)

19. DETAIL ATTACHMENTS: (See instructions)

☒ a. Facility Requirements
☒ b. Publications
☒ c. Purpose
☐ d. Background
☐ e. Approach
☒ f. Technical progress
☐ g. Future accomplishments
☐ h. Relationships to other projects
☐ i. Environmental assessment
☐ j. Explanation of milestones
☒ k. Other (specify): Capital Equipment Budget Explanation

1114054

DOE Form 3120.3 (Page 2) (12-78)

TASK REQUIREMENTS FOR OPERATING/EQUIPMENT COSTS AND OBLIGATIONS

CONTRACTOR NAME: Oak Ridge Associated Universities

BIN NUMBER	TASK NO.	REV. NO.	DATE PREPARED	CONTRACTOR NUMBER
		0	3-24-80	00 2493

	FY 80	FY 81 PRESIDENT'S	FY 81 REVISED	AUTHORIZED	FY 82
20. STAFFING (in staff years)					
a. SCIENTIFIC	8.0		10.0		10.0
b. OTHER DIRECT	3.0		4.0		4.0
c. TOTAL DIRECT	11.0		14.0		14.0
21. OBLIGATIONS AND COSTS (in Thousands)					
a. TOTAL COSTS	1,230		1,695		1,830
b. TOTAL OBLIGATIONS	1,451		1,736		1,874
22. EQUIPMENT (in Thousands)					
a. EQUIPMENT COSTS	40		82		88
b. EQUIPMENT OBLIGATIONS	40		82		88
23. OTHER COSTS (specify)					
a. Direct Sal. & Benefits	250		340		365
b. Mat. & Other Direct	690		954		1,033
c. Support Services	153		220		237
d. Indirect Expenses	137		181		195
24. OPTIONAL FIVE-YEAR PLAN (in Thousands) Constant BY dollars					
a. TOTAL OPERATING COSTS					
b. TOTAL OPERATING OBLIGATIONS					
c. TOTAL EQUIPMENT COSTS					
d. TOTAL EQUIPMENT OBLIGATIONS					

25. MILESTONE SCHEDULE	PROPOSED SCHEDULE	AUTHORIZED SCHEDULE
Preliminary mortality analysis of workers at: X-10	Sept. 1980	
K-25	Dec. 1980	
Mortality analysis: MCW	June 1980	
Y-12	May 1981	
X-10	Nov. 1981	
K-25	Dec. 1982	
Validate external radiation monitoring data for: Y-12	June 1980	
X-10	Aug. 1980	
Feasibility studies on evaluation of internal radiation exposures: Y-12, X-10	Sept. 1980	
Updated mortality analysis: TEC	Nov., 1980	
Y-12	April 1982	
X-10	Sept. 1982	
Feasibility of studying mortality:		
NLO	Feb. 1980	
MED sites (Linde, Columbia University, Middlesex)	Jan. 1981	
Mound	Sept. 1980	
Uranium enrichment facilities (Portsmouth, Paducah)	April 1981	
KAPL, Bettis	Dec. 1981	
TEC (female workers)	Jan. 1981	
Selected sites representative of all steps involved in the uranium fuel cycles	June 1982	

1114055

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No. 0	Date Prepared 3-24-80	Contractor Number 00 2493

Enter headings in accordance with Item 19.

19a. Facility Statement

The program, consisting of the Comprehensive Epidemiology Study (RPIS 2493, the Death Certificate Retrieval Office (RPIS 3034), the Data Processing Support Facility (RPIS 3401), and the DOE/Social Security Administration Data Searches, is housed in Oak Ridge in the "ORAU Tyrone Road Building." Of the 12,000 sq. ft. in this building, 2,300 sq. ft. were remodeled into office space and work areas in FY 79 and another 3,300 sq. ft. in FY 80. The anticipated FY 80 and 81 delivery of PSQ records reserved since 1965 for the use of the so-called "Mancuso Study" at the 40 or more DOE plant sites requires our development of 3,000 sq. ft. of additional secured storage space. In addition, the acquisition and installation of electronic data processing equipment in FY 80 and FY 81 to enable us to interface with the Computer Science Division CPUs at ORNL through a remote job entry station require an additional 2,000 sq. ft. for equipment and operators. On completion of this renovation in FY 80 and FY 81, this building will house a staff of 35 to 40 full- and part-time ORAU staff, university and student collaborators (UNC). Our group also uses temporary trailer offices and work facilities provided to the Epidemiology department staff at the University of North Carolina, Chapel Hill campus.

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No.	Date Prepared	Contractor Number
		0	3-24-80	00 2493

Enter headings in accordance with Item 19.

19b. Publications

FY 79

Armstrong, R. D. and Frome, E. L. *A remark on algorithm AS108.* Appl. Stat. 27: 378, 1978.

Armstrong, R. D. and Frome, E. L. *Least absolute value estimators for one-way and two-way tables.* Nav. Res. Logistics Quart. 26: 79-96, 1979. Work performed at the University of Texas, Austin.

Armstrong, R. D., Frome, E. L., and Kung, D. S. *A revised simplex algorithm for the absolute deviation curve fitting problem.* Commun. Stat. 8B: 175-190, 1979. Work performed at the University of Texas, Austin.

Armstrong, R. D., Frome, E. L., and Sklar, M. G. *Linear programming in exploratory data analysis.* Submitted to American Statistician.

Beck, W. L. and Holly, F. E. *Dosimetry studies for an industrial radiography accident* ^{192}Ir. In The Medical Basis for Radiation Accident Preparedness. Proceedings of a Symposium held in Oak Ridge, October 18-20, 1979, Elsevier/North-Holland, New York. In press.

Duffy, D., Beck, W. L., Gleason, G. I., and Wiggins, P. F. *Evaluation of dosimetry film by neutron activation and x-ray fluorescence.* J. Nucl. Sci. and Tech. 16: 89-94, 1979.

Dupree, E. A. and Meyer, M. B. *Role of risk factors in the complications of diabetes mellitus.* Am. J. Epidemiol. Work performed at the Johns Hopkins University. In press.

Frome, E. L. and Hudson, D. R. *A jackknife procedure for estimating standardized mortality ratios.* Proceedings of the Statistical Computing Section of the American Statistical Association, 1979, Washington, D. C. In press.

Frome, E. L. and Yakatan, G. J. *Statistical estimation of the pharmacokinetic parameters in the one-compartment open model.* Communications in Statist. Work performed at the University of Texas, Austin. In press.

Godbold, J. H., Jr. and Tompkins. E. A. *A long-term mortality study of workers occupationally exposed to metallic nickel at the Oak Ridge Gaseous Diffusion Plant.* J. Occup. Med. 21: 799-806, 1979.

Polednak, A. P. *Age changes in differential leukocyte count among female adults.* Hum. Biol. 50: 301-311, 1978. Work performed at Argonne National Laboratory, Argonne, Illinois.

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No.	Date Prepared	Contractor Number
		0	3-24-80	00 2493

Enter headings in accordance with Item 19.

19b. Publications (continued)

Polednak, A. P. *Fertility among women exposed to internal and external radiation.* J. Environ. Pathol. Toxicol. Work performed at Argonne National Laboratory, Argonne, Illinois. In press.

Polednak, A. P. *Long-term effects of radium exposure in female dial workers: liver disease and liver function.* Environ. Res. 18: 454-465, 1979. Work performed at Argonne National Laboratory, Argonne, Illinois.

Polednak, A. P. *Long-range studies of uranium workers and the Oak Ridge radiation-worker population.* In The Medical Basis for Radiation Accident Preparedness. Proceedings of a Symposium held in Oak Ridge, October 18-20, 1979, Elsevier/North-Holland, New York. In press.

Polednak, A. P., ed. The Longevity of Athletes. Springfield, Illinois: Charles C Thomas, 1979. Work performed at Argonne National Laboratory, Argonne, Illinois.

Polednak, A. P. *Thyroid tumors and thyroid function in women exposed to internal and external radiation.* J. Environ. Pathol. and Toxicol. Work performed at Argonne National Laboratory, Argonne, Illinois. In press.

Polednak, A. P. and Farnham, J. E. *Osteometry and autoradiography of long bones and skeletons of women exposed to radiation at 13-19 years of age.* Am. J. Phys. Anthropol. Work performed at Argonne National Laboratory, Argonne, Illinois. In press.

Polednak, A. P. and Frome, E. L. *Mortality among men employed between 1943 and 1947 at a uranium-processing plant.* Submitted to J. Occup. Med.

Polednak, A. P. and Frome, E. L. *Mortality among men employed between 1943 and 1947 at a uranium-processing plant.* In Proceedings of the 1979 DOE Statistical Symposium, Gatlinburg, TN, October 23-26, 1979. In press.

Polednak, A. P. and Janerich, D. T. *Sickle cell trait, birth characteristics, and complications of pregnancy: a case-control study.* Hum. Biol. Work performed at Argonne National Laboratory, Argonne, Illinois. In press.

Rundo, J., Polednak, A. P., Brues, A. M., Lucas, H. F., Jr., Patten, B. C., Rowland, R. E., and Stehney, A. F. *A study of radioactivity and health status of former thorium workers: Preliminary Report.* Environ. Res. 18: 94-100, 1979. Work performed at Argonne National Laboratory, Argonne, Illinois.

1114058

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No.	Date Prepared	Contractor Number
		0	3-24-80	00 2493

Enter headings in accordance with Item 19.

19b. Publications (continued)

FY 80

Frome, E. L. *Fisher's exact variance test for the poisson distribution.* Submitted to Applied Statistics.

Frome, E. L. and Khare, M. *Comments on Brodsky's statistical methods for evaluating epidemiological results.* Health Physics. In press.

Hansard, M. S. *DMMD's and epidemiology: a case study.* Submitted to Computers and Biomedical Research.

1114059

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No.	Date Prepared	Contractor Number
		0	3-24-80	00 2493

Enter headings in accordance with Item 19.

19c. Purpose

The purpose of this project is to evaluate the long-term health effects of occupational exposure to ionizing radiation. The objectives are to perform mortality studies on specific populations of DOE/DOE contractor employees occupationally exposed to radiation and to various chemicals or toxic agents and to analyze and to interpret these data. These results will lead to a significant increase in the scientific evidence for evaluating the health effects of occupational exposures to low levels of ionizing radiation. The results of these studies can be interpreted in the light of the findings of limited evidence from similar studies on occupational groups and the extensive data on Japanese atomic bomb survivors. In meeting these objectives, consideration of the effects of concomitant exposures to chemicals and other toxic agents will be evaluated. The latter work is needed both to assess the possible confounding effect of these other exposures in the analysis of radiation-exposure effects and to contribute to knowledge regarding the health effects of potentially toxic substances which may also be relevant to other energy technologies.

19f. Technical Progress

EPIDEMIOLOGIC STUDIES

1. *Y-12 Plant (Tennessee-Eastman Corporation, Oak Ridge)*

In FY 79 an analysis of mortality in workers employed at the Y-12 plant while it was operated by TEC during the period 1943-1947 was completed. Although 47 percent of the 38,000 workers were female, the analysis focused on white male workers only because the SSA method used to ascertain deaths is not efficient for women because of their multiple names changed due to marriage. This analysis was principally concerned with the 4,008 white males employed for more than one year in the plant where uranium isotopes were separated by an electromagnetic process. Many of these men worked in areas where levels of uranium dust were quite high in comparison to today's standards. The entire cohort of 18,869 white males was studied first. Copies of death certificates were obtained for over 95 percent of males declared dead in 1974 by the Social Security Administration. Using mortality rates for U. S. white males, the standard mortality rates (SMRs) for various causes were generally less than one. After corrections for unascertained deaths and missing death certificates, the SMR for lung cancer was 1.22. SMRs for various causes, including lung cancer, did not tend to be higher in 8,345 workers employed in areas where uranium dust was present or in 4,008 of these 8,345 workers employed for one year or longer at the plant. Logistic regression analysis techniques have been developed and used in these analyses. An increased number (of possible significance) of lung cancer deaths was found in a group of chemical workers hired at age greater than or equal to 45 years.

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No.	Date Prepared	Contractor Number
		0	3-24-80	00 2493

Enter headings in accordance with Item 19.

2. *Y-12 Plant (Union Carbide, Oak Ridge)*

A preliminary analysis of mortality among white males who were hired at Y-12 between 1947 and 1969 and who were monitored for external radiation exposure was completed. This group comprised 4,988 out of about 11,000 employees. Observed deaths prior to 1974 were not significantly greater than expected for all or various selected causes. The SMR for all cancers, lung cancer, bone cancer, and leukemia were less than 1.00. The SMR for brain cancer was high in value but not statistically significant (95 percent confidence interval; 0.79, 4.06). Cumulative occupational external radiation doses were low for this cohort. Film badge and uranium urinalysis data for Y-12 employees from about 1950 to present are now computerized. Oak Ridge Associated Universities (ORAU) obtained access to film badge data during FY 79 and anticipates access to uranium urinalysis data during FY 80. Checks on completeness and validity of these data continue through FY 80. Only 10 workers were ever exposed to greater than 5 rem in any one year. Preliminary data on cumulative occupational radiation (penetrating) exposure among white males, who worked only at Y-12 Carbide and no other Oak Ridge facility, have shown that among 6,550 white males monitored, only 2,030 have a career dose equivalent of $\geq$ 1 rem, and only 198 have a career total in excess of 5 rem. Although individual exposures were low, population exposures (person-rem) can be calculated in order to provide data relevant to assessment of risk of radiation-induced cancer. Various potential confounding factors have been identified and taken into account in these analyses.

The entire employee roster for Y-12 was resubmitted to SSA for identification of deaths in December 1979. A search for death certificates on individuals for whom no death certificates are on hand will be completed in FY 1980.

3. *Oak Ridge National Laboratory (Union Carbide)*

This facility (X-10) in operation since 1943 has been involved in the production of radioisotopes and in research on the recovery of uranium and plutonium from fission products. Of the Oak Ridge facilities under study, the potential for external radiation exposure was greatest at X-10.

An attempt to create a preliminary data analysis file was begun with data on about 20,000 workers. Film badge and in vivo exposure data were released to ORAU during FY 1979-1980.

The entire employee roster was resubmitted to SSA for death search in December 1979.

4. *Oak Ridge Gaseous Diffusion Plant (Union Carbide)*

About 40,000 persons have been employed at the Oak Ridge Gaseous Diffusion Plant (K-25) which began operation in 1945 and has been in continuous operation to the present. Many of these workers were monitored for external and internal radiation. The film badge

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No.	Date Prepared	Contractor Number
		0	3-24-80	00 2493

Enter headings in accordance with Item 19.

19f. Technical Progress (continued)

data were made available to ORAU during FY 79. Air sampling for uranium air concentrations and sampling for uranium alpha activity on surfaces have been examined (Schultz and Becher, 1963) for estimating potential employee exposures (as reflected by urinary excretion rate) using the surface contamination levels. Work-history data, specifically job classification and department codes, are also used in estimating exposure. External radiation exposure is not believed to be a major hazard at this facility since only one worker reportedly received greater than 5 rem whole-body exposure during any year of employment. Exposure groups are defined by use of data on uranium urinalysis (average values over specified time periods of employment and maximum and minimum values), along with work-history and uranium-air-concentration data. Inhalation of UF_6 is a potential hazard to the lung and kidney since UF_6 is regarded as a relatively "soluble" uranium compound; therefore, diseases of these organs are of particular interest in mortality studies.

Preliminary work leading to analyses of mortality will be ongoing through FY 80. The most recently completed search for decedents was conducted by SSA in late 1974. Another roster of K-25 employees was sent to SSA in December 1979, for identification of post-1973 deaths.

a. Study of Nickel Workers

An initial updated analysis of nickel workers was completed based on a 1974 death search. (JOM 21, 799-806, 1979).

b. Study of Welders at Union Carbide's Oak Ridge Facilities

A mortality study was conducted on 1,060 employees of Union Carbide, Nuclear Division, whose work history indicates that they were welders at X-10, Y-12, and/or K-25. The report is in progress.

5. *Mallinckrodt Chemical Works*

Mallinckrodt Chemical Works (MCW) was the earliest and one of the largest uranium-processing facilities in the U. S. During its operation from 1943 through 1966, MCW's Uranium Division employed about 3,700 workers at two sites located in St. Louis and Weldon Springs, Missouri. Workers were monitored for internal and external exposure to radiation.

Preliminary analysis of this population is under way. During FY 1979 information collected and computerized prior to ORAU's involvement in this project, was checked for completeness and validity using source documents on hand in Oak Ridge. This included work history, film badge, uranium urinalysis and breath radon data. The computerized film badge data were found to be inadequate, and they are being re-entered onto the computer from source documents. An analysis of mortality, with respect to external

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No.	Date Prepared	Contractor Number
		0	3-24-80	00 2493

Enter headings in accordance with Item 19.

19f. Technical Progress (continued)

radiation exposure and based on the results of a 1976 SSA death search, is scheduled to be completed by June 1980. Death certificates were obtained for over 95 percent of the individuals declared dead in this 1976 search.

Uranium dust exposures at this facility were often much higher than the maximum permissible concentration according to extensive dust studies. Study of the feasibility of correlating this air-sampling data with work-history and internal-radiation monitoring data on individual employees in order to investigate mortality was begun in FY 1980.

The entire employee roster was resubmitted to SSA for death search in December 1979. Search for death certificates on workers who have died since 1975 (the time of the last SSA death search for this population) is scheduled for FY 1980.

6. *Other Sites (Feasibility) Under Study*

Prior to starting an in-depth mortality study on a given occupational population, it is necessary to determine if information required to address the study hypothesis is available for this population. The decision will be based on information collected by the DOE Data Processing Support Facility. This information includes size of the population, evaluation of the types of records kept on employees, the completeness of information on each record type, and the effort required to transform this information into a format suitable for epidemiological analysis. The mission of each site as it relates to the HMS mission of conducting epidemiologic studies on DOE workers involved in all aspects of the uranium fuel cycles must also be considered when choosing sites for feasibility studies.

Sites were chosen for feasibility studies during FY 1980 for the following reasons:

a. Information was already available to HMS when ORAU took over the project. This includes NLO, Mound, Linde, Middlesex, Columbia University, and Paducah.

b. The sites have similar missions to those already under study by the HMS. This allows HMS to practice one of the tenets of epidemiology; namely, to investigate the consistency of results of studies on different populations with similar exposures analyzed by identical methods. NLO and Mound have missions similar to K-25, Paducah, Portsmouth, MCW, and Y-12, respectively.

c. The sites were active during the early days of the nuclear era and are no longer in operation. This provides for a long mortality follow-up on a closed worker population whose radiation exposures were more likely to have been greater than workers of recent times when exposure controls are more strict. Since most of these records are stored in federal records centers, access to them may be easier than access to records at current sites. These sites include Middlesex, Linde, and Columbia University.

1114063

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No.	Date Prepared	Contractor Number
		0	3-24-80	00 2493

Enter headings in accordance with Item 19.

19f. Technical Progress (continued)

d. Some sites involve an aspect of the uranium fuel cycle not presently included in studies already undertaken by HMS. This includes Bettis and Knolls Atomic Power Laboratory (KAPL), both of which are involved in the Naval Reactor Development Program.

e. A special study of persons who were occupationally exposed at any time during their AEC/ERDA/DOE or prime contractor employment to 5 rem or more in any one year was begun. All sites were "visited" through DOE field organization personnel and demographic and exposure data collected and collated. During FY 1979 and 80, data on about 2,300 such employees were obtained but the roster is still incomplete (random bits of information for ∿4% remain to be found).

In FY 1979 the Division of Naval Reactors (DNR) agreed to participate in this study and early in FY 1980 supplied names of 1,128 individuals from 12 sites.

In addition to the dates of the years in which these "administrative overexposures" occurred, the entire career accumulated exposures were obtained for all these workers (∿3,500). An SSA search was begun to determine vital status on the R & D and production site workers in late 1979. Preliminary data processing for an SSA search for DNR decedents was begun in early FY 1980.

7. *Integration of University of North Carolina Collaboration in Epidemiologic Analyses*

A major accomplishment of this year was the completion of a plan to strengthen our analytical capabilities through participation with a university epidemiologic staff. The selection criteria of 1) history of completion of major epidemiologic studies concerning occupational and environmental health problems, 2) availability of a professorial and professional research staff able to devote time to such studies now, and 3) a national reputation for vigorous participation in scientific debate of the issues our studies address; all, led us to choose the School of Public Health, University of North Carolina to collaborate with us. In early FY 1980 staff assignments and an ORAU/UNC subcontract for professional services was completed. A Research Planning Group merging both staffs was activated, monthly steering committee meetings held and collaborative studies gotten under way.

During FY 1979 a dosimetry assessment and research team was assembled containing three professional health physicists (one from ORAU and two from the University of North Carolina), two University of North Carolina (UNC) physics students, one postdoctoral student, and one master's student. A technician/clerk assists in collection and validation of dosimetry data.

The dosimetry research program has been divided into two major areas--external dosimetry and internal dosimetry. For external dosimetry, the major task is to collect and interpret reference materials including sample data, quality assurance reports, and other technical reports in order to assess the completeness and accuracy of the monitoring data. A "Dosimetry Assessment Fact Sheet" has been developed to insure uniformity and completeness in the study of each site's monitoring program. External dosimetry assessment studies are in progress for three populations (MCW, Y-12, and X-10).

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No.	Date Prepared	Contractor Number
		0	3-24-80	00 2493

Enter headings in accordance with Item 19.
19f. Technical Progress (continued)

Data-Management Systems

Computer methodology has been developed as a support function for HMS. As an off-shoot of this development, some computer science research topics such as management of large, research-oriented data sets have been pursued. Efforts have been directed toward the acquisition of adequate computer resources, which include equipment, personnel, and software systems. Remote computer terminals have been installed so that HMS software specialists can readily communicate with the computer resources at the Computer Sciences Division of Union Carbide. The integration of computer specialists into HMS has promoted development of software systems which meet the specialized needs of these epidemiologic studies.

A complete data-management plan is being developed, and initial emphasis has been placed on data editing, error correction, data security, and documentation. Partial editing of work-history data has been performed on the K-25, X-10, Y-12, TEC, and NLO cohorts; however, additional editing remains to be done. A closed-loop error-correction system has been initiated and applied to the TEC work-history data. Other manual and automatic procedures have been established to secure the HMS data and protect the privacy of individuals under study. Pseudo-identifiers have been assigned to the K-25, X-10, Y-12, Paducah, TEC, and NLO populations. Documentation has been stressed for both computerized data and source documents. A magnetic tape and disk file inventory system has been developed to document the location of data, the storage medium, access methods, and the individual fields within each file.

The overall goal of data management has been to integrate all data under one encompassing scheme so that systems developed for one population can readily be applied to others without reprogramming. To this end, a data-storage plan has evolved which balances usable resources, epidemiologic data-retrieval needs, and intrinsic data structure. Under this plan, the analysis of the TEC population has been carried to completion. Indications are that underlying data-management principles are workable, but only the major aspects of a complete system has been developed thus far.

Methods of Statistical Analysis

Description of a general data structure for statistical analysis has been developed, and specifications for creating master data-analysis files were completed in FY 1980. A master data-analysis file for each population will be created after record linkage has taken place and will not contain personal identifiers. Data transformation and selection procedures will then be used to create data analysis files appropriate to particular statistical procedures that are being considered. Methods for computing SMR's using the Monson analytic method have been completed. Procedures for generating multidimensional contingency tables have been developed and a computer program for logistic regression

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No.	Date Prepared	Contractor Number
		0	3-24-80	00 2493

Enter headings in accordance with Item 19.

19f. Technical Progress (continued)

analysis is under development. A logistical regression model is one approach that is being developed to deal with confounding factors that must be considered when evaluating the possible effects of internal and external radiation exposure. Several statistical packages are currently being used for statistical data analysis. These include SAS, TPL, and the BMDP series. Interfaces between these systems that allow optimal use of all available statistical software have been developed through cooperative efforts with the statisticians at Computer Sciences Division at ORNL.

Planned Progress FY 80 and FY 81

EPIDEMIOLOGIC STUDIES

1. *Y-12 Plant (Tennessee- Eastman Corporation, Oak Ridge)*

Continued follow-up of this cohort is planned to evaluate the long-term health effects of exposure to uranium. A second analysis of the TEC white male cohort using mortality data from the 1979 SSA search is in progress. The feasibility of studying female workers at TEC will be investigated during FY 1980. The large number of females employed by TEC provides a rare opportunity to consider study of a female worker population. Uranium urinalysis data on female workers are being edited and verified. The levels of exposure will be examined to see if they differ from the levels in male workers. The feasibility of further study will be based on these differences and on the results of the 1979 SSA search. An updated analysis of mortality on male employees is scheduled for completion by November 1980.

2. *Y-12 Plant (Union Carbide, Oak Ridge)*

The radiation dose assignment for all Y-12 workers will be completed in FY 1981. Confounding hazardous exposures to metals and other toxic substances will then be identified and employees characterized as to the complexity and duration of these exposures. With these data in hand, a definitive epidemiologic study will be designed, appropriate biostatistical analyses and testing procedures will be chosen. These developments will permit more extensive mortality analyses using Y-12 deaths reported by the 1979 SSA searches. These advanced analyses should be completed during FY 1981.

3. *Oak Ridge National Laboratory (Union Carbide)*

The search for death certificates based on the results of the 1979 SSA submission will be completed by the end of FY 80 to permit the updating of preliminary analysis of mortality (based on deaths through 1973). Evaluation of the extensive data on internal exposures started in January 1980 may have to continue into FY 81 before many of the

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No.	Date Prepared	Contractor Number
		0	3-24-80	00 2493

Enter headings in accordance with Item 19.

19f. Technical Progress (continued)

problems basic to making dose assignments are solved. However, external radiation exposure data of this cohort will be edited, corrected, and validated. In FY 1981 an epidemiologic study will be done to test the hypothesis that low-dose-rate occupational exposures at X-10 have had untoward late health effects.

4. *Oak Ridge Gaseous Diffusion Plant (Union Carbide)*

A preliminary mortality analysis of the K-25 population will be completed early in FY 81. In this population where radiation exposures have been extremely low, chemical exposures have been potentially more significant. Final analysis will be retarded by the need for industrial hygiene data which, because of the abundance, will require time-consuming procedures to condense, summarize, and assign to individual workers confounding toxic exposures.

5. *Mallinckrodt Chemical Works and Other Sites*

For MCW final analysis of the work experience and any resulting effects upon mortality rates and morbidity patterns will be completed in late FY 80 or early 81. This study will be used as a benchmark model for analyses in similar small cohorts of uranium workers at other DOE plants. The mortality experience of the 4,000 "$\geq$5 rem exposees" will be studied to determine in a preliminary way whether there may be any validity to the commonplace conjecture that the annual permissible occupational exposure guidelines have been overly permissive and therefore irresponsible. Frequency distribution studies of the career radiation doses of this nation-wide 30-year DOE occupational experience will be made to obtain an estimate of the man-rem involved in the high dosage subset of these workers. Depending on the results of this appraisal, the decision will be made whether or not this sample should be enlarged to include all other workers with comparable career exposures but who never exceeded the 5 rem/year constraint.

Data-Management Systems

New areas of system development in FY 1980 and 81 will be in record linkage, site interfacing and data entry. A complete record-linkage system will be designed and implemented to automatically match available identifiers between different types of records and provide for manual resolution of nonmatching identifiers. Specifically, this system will be used to link exposure data and medical data to work-history data for all cohorts under study.

This group will continue to use the shared resources of the Computer Sciences Division (CSD) of Union Carbide but will acquire additional interfacing and equipment to take advantage of that computing resource. A high-speed remote printer will be attached to the CSD computer to decrease the turn-around time for printed output. Terminals attached to a data concentrator will improve our terminal response. Additional on-line disk space will be acquired to increase data availability.

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No.	Date Prepared	Contractor Number
		0	3-24-80	00 2493

Enter headings in accordance with Item 19.

19f. Technical Progress (continued)

Statistical Analysis

A preliminary evaluation of the appropriateness of proportional hazards regression analysis will be made. If this method can be justified theoretically and is practical to implement, then it will be used to further study the health effects of radiation on nuclear workers. In this approach, survival time is the dependent variable; and covariates (e.g., age at hire, sex, duration of employment, etc.) are used in a regression model to evaluate the effects of radiation exposure on the longevity of nuclear workers. This approach can be used to deal with the competing risk problem by considering deaths due to causes other than the one of interest as censored observations. If the proportional hazards regression model is applicable to the HMS, then it should provide a sound methodology that addresses all the well-known statistical problems encountered in epidemiologic studies. Potential computational problems (that may limit the applicability of this method to large and/or complex data sets) will be identified and evaluated.

Planned Progress FY 82

A roster and records profile for all atomic workers ever employed in industries and laboratories related in any way to the uranium fuel cycle will be completed. In parallel, the data-management systems and statistical rules and procedures for construction of analytic files will be completed and functional. Hypotheses which concern potential health effects of working in this industry, generated by earlier analyses (FY 80 and 81) on small subsets of the data or specific geographically sited groups, will then be tested on large scale with this nationwide population comprised of large numbers of workers with the highly varied attributes of many other U. S. industrial populations.

It is anticipated that small high-risk population subsets will be searched for and identified in this industry as support for or against suggested protective measures and guidelines. Such case-control studies will provide hitherto unavailable analyses of many health-related problems.

A similarly large data base concerning a population of radiation workers with external radiation exposures in excess of that of the general population (and without uranium and other chemical exposures) will have been identified and characterized by career exposures. This population of irradiated persons should be sufficiently varied and large enough to allow "dose groups" to be constructed and dose-response models put to test. In addition, case-control studies should be possible for various mortality and morbidity endpoints using the extremely well documented medical histories available in the DOE occupational medicine clinics.

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No.	Date Prepared	Contractor Number
		0	3-24-80	00 2493

Enter headings in accordance with Item 19.

19f. Technical Progress (continued)

In FY 1982 the majority of data-management systems will be in place. A large portion of the workload will be devoted to maintaining existing systems and processing data from new sites using developed methodology. A new areas of investigation will seek to quantitate the association between job titles and hazardous exposures to various toxicants. This research is needed to provide an independent means of assessing risk in epidemiological analyses of populations in which exposure has not been measured or has been measured only on subsets of the population. The association between area exposure measurements, e.g., air sampling data, and bioassay measurements will also be investigated to increase the utility of bioassay data in epidemiological analyses of work populations. The system of computerization of death certificate verification will be completed which will provide uniformity within the master file of all AEC/DOE death certificates. Computerizing searches of state and national death indices will be completed.

1114069

January 27, 1981

1401 16th St. NW
Washington, D.C. 20036
(202) 483-1442

Mr. Wayne Range
Assistant to the Manager for Information
Department of Energy
Oak Ridge, TN.

Dear Sir:

Under the provisions of the Freedom of Information Act, 5 U.S.C. 522, I am requesting access to the records listed below by number and delineated specifically within the attached memorandum to Dr. C.C. Lushbaugh of ORAU. (Attachment A.)

As you know, the act permits you to reduce and waive fees when the release of the information is considered as "primarily benefiting the public." Since I am requesting this information as part of an on-going inquiry into the effects of radiation on man, and into the U.S. government's efforts to quantify those effects, and since these questions are still in debate within the scientific community and within the populace, I believe that this request fits that category and I therefore ask you to waive any fees.

If all or any part of this request is denied, please cite the specific exemption(s) which you think justifies your refusal to release the information, and inform me of the appeal procedures available to me under the law.

Information requested includes numbers:

2, 3, 4, 9, 11

I would appreciate your handling this request as quickly as possible and I look forward to hearing from you within 10 days, as the law stipulates.

Sincerely,

Howard L. Rosenberg
Staff Associate
Washington Merry Go Round

COPY

1114070

MEMO TO: C.C. Lus ugh

FROM: Howard L. Rosenberg
1401 16th St. NW
Washington, D.C. 20036
(202) 483-1442

January 27, 1981

ATTACHMENT A

RE: Information Request. Please provide the following documents and/or information regarding operations of the Medical and Health Sciences Division.

1) Articles published in the open literature re: studies of the Oak Ridge data compiled under the direction of University of Pittsburgh principal investigator T. Mancuso, including publications by Tomkins, Frome, et. al.

2) Reviews of your Oak Ridge study by NAS so-called "Salmon Committee."

3) Review of your Oak Ridge study by Office of Health and Environmental Research (intramural report) completed Nov. 21. (when and if it is available.)

4) Review of METBI/LETBI studies by DOE/AEC/ERDA which led, according to our conversation of yesterday, to the termination of the projects in 1974-1975. (Extramural program review.)

5) Membership list of the Human Use Committee jointly operated by ORAU and ORNL.

6) Protocols issued for LETBI/METBI studies, including those issued for review by Human Use Committee. (Therapy protocols)

7) Criteria for determining patients admitted for therapy at LETBI/METBI.

8) Sample of consent forms given to patients at the time of LETBI/METBI operations.

9) Copies of all "Financial plans" for ORAU Medical and Health Sciences Division for FY 57 through FY 75.

10) Any statistical analyses prepared of patients who received TBI at LETBI/METBI.

11) USAEC Report ORAU 112 1970

12) Proceedings of a panel on Total Body Irradiation in Humans at IAEA Vienna 1966.

13) Space Radiation Study Panel: Radiobiologic factors in manned space flight. July 1967.

14) Recent Progress in Asessment of Human Resistance to TBI--In Proceedings on Recovery from Nuclear War. Fort Monroe, Va. November 1967.

NASA 15) NASA TM-X 2440

16) Radiation Research 59:39 1974 Abstract on TBI.

17) Copies of photographs and diagrams (in reproducible form) available of LETBI/METBI facilities.

18) Form 189, also known as "work packages" for epidemiological studies of the Oak Ridge data from FY 1974 through current year.

19) Form 990 from your organization filed with the IRS for years 1965 through current year.

20)Your paper on the skin lesions of sheep caused by radiation.

Thank-you for your consideration.

FILED
INFO
81 JAN 27 PM 4:08

1114072

PS Form 3811, Jan. 1979

RETURN RECEIPT, REGISTERED, INSURED AND CERTIFIED MAIL

SENDER: Complete items 1, 2, and 3.
Add your address in the "RETURN TO" space on reverse.

1. The following service is requested (check one.)
   - ☐ Show to whom and date delivered ..... ¢
   - ☐ Show to whom, date and address of delivery ..... ¢
   - ☐ RESTRICTED DELIVERY
     Show to whom and date delivered ..... ¢
   - ☐ RESTRICTED DELIVERY.
     Show to whom, date, and address of delivery $ ____

   (CONSULT POSTMASTER FOR FEES)

2. ARTICLE ADDRESSED TO:
   Howard Rosenberg
   1401- 16th Street NW
   Washington, DC 20036

3. ARTICLE DESCRIPTION:

REGISTERED NO.	CERTIFIED NO.	INSURED NO.
	876756 3	

(Always obtain signature of addressee or agent)

I have received the article described above.
SIGNATURE ☐ Addressee ☐ Authorized agent

4. DATE OF DELIVERY
   2/6/81

5. ADDRESS (Complete only if requested)

6. UNABLE TO DELIVER BECAUSE:

CLERK'S INITIALS

POSTMARK

☆GPO : 1979 300-459

P15 8767563

RECEIPT FOR CERTIFIED MAIL

NO INSURANCE COVERAGE PROVIDED—
NOT FOR INTERNATIONAL MAIL
(See Reverse)

SENT TO
Howard Rosenberg

STREET AND NO.
1401-16th Street, NW

P.O., STATE AND ZIP CODE
Washington, DC 20036

POSTAGE				$
CONSULT POSTMASTER FOR FEES	CERTIFIED FEE			¢
	OPTIONAL SERVICES	SPECIAL DELIVERY		¢
		RESTRICTED DELIVERY		¢
		RETURN RECEIPT SERVICE	SHOW TO WHOM AND DATE DELIVERED	¢
			SHOW TO WHOM, DATE AND ADDRESS OF DELIVERY	¢
			SHOW TO WHOM AND DATE DELIVERED WITH RESTRICTED DELIVERY	¢
			SHOW TO WHOM, DATE AND ADDRESS OF DELIVERY WITH RESTRICTED DELIVERY	¢
TOTAL POSTAGE AND FEES				$
POSTMARK OR DATE				

PS Form 3800, Apr. 1976

1114073

February 2, 1981

Mr. Howard Rosenberg
Washington Merry Go Round
1401 16th Street, NW
Washington, D. C. 20036

Dear Mr. Rosenberg:

Please accept this letter in confirmation of your telephone conversation of today with William R. Bibb and James L. Foutch of ORO with regard to your Freedom of Information Act request of January 27, 1981, and as notification that your request has been determined to be appropriate for a fee waiver. Your request, therefore, has been deemed to be accepted for processing as of this date, as hereinafter modified.

As Mr. Foutch explained, items 2, 3 and 4 of your request are for documents that exist, if at all, at DOE-Headquarters in the offices of the Assistant Secretary for Environment. I am, therefore, by copy of this letter, referring these three items to the Headquarters' Freedom of Information Officer for referral to the appropriate Authorizing Official, who will respond to you directly.

As Dr. Bibb explained, the financial plans you requested in item 9 are probably not now in existence, having been disposed of under our normal records disposal program. Dr. Bibb suggested that he thought it would be possible to locate cost statements covering the activity of interest by year. You agreed that we should respond with "whatever [we] have" for the years and activity you described. This letter, therefore, confirms that item 9 of your request is modified to conform to this agreement.

CERTIFIED MAIL:
RETURN RECEIPT REQUESTED

1114074

PERSONNEL — FOIA 771

DOE F 1325.10
(7-79)

OFFICIAL FILE COPY

Your request for items 9 and 11 has now been forwarded to the Authorizing Official at ORO, who will respond within ten (10) working days.

Sincerely,

S/Wayne Range
Wayne Range
Freedom of Information Officer

CC-10:JLF

cc: Milton Jordan, HQ FOI
(w/cc of incoming request)

bcc: W. R. Bibb, Director, Research Div.
Dr. C. C. Lushbaugh, ORAU

CC-10:JLFoutch:cd:6-1204:2/2/81

CONCURRENCE
RTG. SYMBOL CC-10
INITIALS/SIG Foutch
DATE 2/2/81
RTG. SYMBOL M-4
INITIALS/SIG WR
Range
DATE 2/2/81
RTG. SYMBOL
INITIALS/SIG
DATE

1114075

Dr Brown to Mr. Bill
for info

MEMORANDUM OF CALL

TO: CC Lushbaugh

☐ YOU WERE CALLED BY— ☐ YOU WERE VISITED BY—

OF (Organization)

☐ PLEASE CALL → PHONE NO. CODE/EXT. _____ ☐ FTS

☐ WILL CALL AGAIN ☐ IS WAITING TO SEE YOU

☐ RETURNED YOUR CALL ☐ WISHES AN APPOINTMENT

MESSAGE

Per your request

Charlie Barnes

RECEIVED BY | DATE | TIME

NASA

63-109

STANDARD FORM 63 (Rev. 8-76)
Prescribed by GSA
FPMR (41 CFR) 101-11.6

☆U. S. GPO: 1977-0-246-145/6000

PERSONNEL

FOIA

1114076

1401 16th Street, N.W. Washington, D.C. 20036

March 26, 1980

RECEIVED

APR 11 2 49 PM '80

FOIA OFFICER
National Aeronautics and Space Administration
400 Maryland Ave., S.W.
Washington, D.C. 20546

Rec. 5/5/80

Dear Sir:

Under the provisions of the Freedom of Information Act, 5 U.S.C. 522, I am requesting access to all records, protocols, progress reports and final reports of a study of human radiation effects conducted under the auspices of your agency by Doctor Clarence C. Lushbaugh of the Oak Ridge Associated Universities. I have attached a xerox of an affadavit given by Dr. Lushbaugh in Las Vegas on May 16, 1977. He makes reference to the project during his testimony.

Specifically, I would like access to:

1) The contract proposal.
2) List of the contractors, subcontractors and principal investigators. (Including other agencies.)
3) The investigatory protocols.
4) All progress reports by prime and sub-contractors.
5) All peer reviews.
6) The final report of the contractors.
7) Any published findings.

As you know, the act permits you to reduce and waive fees when the release of the information is considered as "primarily benefiting the public." Since I am requesting this information as part of an on-going investigation into human experimentation, and since the findings of the investigators may indeed provide crucial information relating to the effects of radiation, and since a national debate is now underway concerning the safety of and impact of radiation exposure, I believe that this request fits that category and I therefore ask that you waive any fees.

-more-

10-F-80-44
Recd 3-31-80

1114077

If all or any part of this request is denied, please cite the specific exemption(s) which you think justifies your refusal to release the information, and inform me of the appeal procedures available to me under the law.

I would appreciate your handling this request as quickly as possible and I look forward to hearing from you within 10 days, as the law stipulates.

Sincerely,

Howard L. Rosenberg
1401 16th Street N.
Washington, D.C. 20036

1114078

AP4

April 29, 1980

Mr. Howard L. Rosenberg
1401 16th Street, N. W.
Washington, DC 20036

Dear Mr. Rosenberg:

This is in further response to your Freedom of Information Act request of March 26, 1980, and our interim acknowledgement of April 17, 1980.

The file on Defense Purchase Request T-88566 has been received from our Ft. Worth storage facilities, and the following comments and information are provided and listed in the order set forth in your letter:

(1) There was no contract proposal. The procurement action was simply a transfer of funds from NASA to Energy Research and Development Agency (ERDA) with an informal work statement. A copy of Purchase Request 9-323-080 and Exhibit "A", Statement of Work, Defense Purchase Request T-88566 and Mods through Amendment Number 8 are enclosed.

(2) There are no known contractors and subcontractors associated with T-88566. The Principal Investigators set forth in the order with ERDA were R. C. Ricks and C. C. Lushbaugh.

(3) The Procurement Office was not involved in investigatory protocol.

(4) The only report submitted was the final report by C. C. Lushbaugh and R. C. Ricks, entitled "Studies Relative to the Radiosensitivity of Man: Based on Retrospective Evaluations of Therapeutic and Accidental Total-Body Irradiation," a copy of which was furnished you by NASA Headquarters with their letter of April 9, 1980. This report was all inclusive and covered all aspects of the study performed.

(5) The file does not reflect any peer reviews.

(6) See (4) above.

1114079

(7) ERDA reported that several articles were published in the open scientific literature during this period. Copies of these articles are not available through NASA.

Fee for the enclosures is waived as the cost is less than $3.00.

?

Sincerely,
Original Signed By:
C. A. Biggs, Sr.

Charles A. Biggs
Chief, Public Services Branch
Office of Public Affairs

Cost more than this just to retrieve the records from the Ft. Worth records storage.

Enclosures

AP4/ILScott:jc:4/29/80:4241

MEMO ROUTE SLIP

Form ERDA-93 (1-75) ERDAM C. 40

☐ Note and return. ☐ For signature. ☐ For information.

TO (Name and unit)	INITIALS / DATE	REMARKS
Jim Foutch Office of Chief Counsel ORO		In response to the FOI request from Tony Capaccio, attached are three copies of all the health protection, industrial safety, OSHA and occupational medical appraisals performed from 1972 through 1979. (The three copies were handcarried to you on 11/28/79.)
TO (Name and unit)		
TO (Name and unit)		
FROM (Name and unit)		
William H. Travis Director, S&EC Div. ORO MS-334:RDS		
PHONE NO. 6-0855	DATE 11/29/79	

Jack Anderson Enterprises

PERSONNEL

FOIA 7282

USE OTHER SIDE FOR ADDITIONAL REMARKS

GPO : 1975 O—577-369

1114081

OFFICE OF CHIEF COUNSEL
ROUTING SLIP

	W. P. Snyder		J. J. Mercer
	J. C. Hall		M. A. McMurphy
1	J. L. Foutch		D. M. Stevens
	W. A. Schmidt		C. H. Seehorn, CRBRP/PO
	W. L. Brown		R. K. Shimabukuro, CRBRP/PO
	D. G. Darugh		P. R. Shlemon, CRBRP/PO
	J. J. Fowler	2	Mail and File Room
	P. M. Kannan		Law Library
	M. A. Lyle		Patent Group

REMARKS: Backup to FOIA response.

DATE: NOV 29 1979 LOG NO. 7282

Action Required

1114082

M-4

November 16, 1979

CC-10

Jack Anderson

Mr. Tony Capaccio
1401 16th Street, N.W.
Washington, D. C. 20036

Dear Mr. Capaccio:

This refers to the exchange of correspondence with Mr. Milton Jordan on your Freedom of Information Act request of October 30 concerning the Portsmouth Gaseous Diffusion Plant.

We have determined that the waiver of fees you requested is appropriate, and based on that determination have deemed that your request was considered to have been received for action on November 16, 1979. Your request is under consideration by Mr. W. R. McCauley, Jr., who is the FOI Authorizing Official for Oak Ridge Operations.

We will notify you promptly should it appear that we will be unable to respond within the 10 working days provided by Department regulations.

Sincerely,

S/ WAYNE RANGE

Wayne Range
Freedom of Information Officer

bcc: CC-10 Foutch, OCC
AD-44 Morrissey, Forrestal Bldg., GB-145, Headquarters

M-4:WRange:kd:60888:11-16-79

PERSONNEL - 1
FOIA
7075

1114083

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No. 0	Date Prepared 3-24-80	Contractor Number 00 2493

Enter headings in accordance with Item 19.

19k. Capital Equipment	FY 81	FY 82
Portable Computer Terminals To be used by personnel during non-working hours to gain access to CSD computer system.	5.0	2.5
CRT Data Terminals To be used by increased staff in the Health and Mortality Group.	3.0	1.5
Graphics Terminal and Printer To be used by biostatisticains in data analysis.	15.0	
Recordak Portable Microfilmers To be used to collect epidemiological data at various DOE sites.	3.0	1.5
Microfilm Reader/Printers To be used in data management in various offices.	3.0	1.5
Hardcopy Terminal with Dual Printer Heads To be used in epidemiological word processing.	3.8	
Disk Drive To be used for data storage.	35.0	35.0
Data Concentrator and Protocol Processor To be used to increase computer communication capability.	6.2	
Remote Job Entry Station To improve the efficiency of data handling for epidemiology.		40.0
Miscellaneous	8.0	6.0

1114084

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No.	Date Prepared	Contractor Number
		0	3-24-80	00 2493

Enter headings in accordance with Item 19.

19k. Budget Explanation

The total budget for the Health and Mortality Study increases by 38% from FY 1980 to FY 1981. While this is an increase, it is still consistent with the budget estimate submitted in our FY 1981 budget submission. The increase is also a reaction to the recent DOE guidelines calling for an expansion in the Health and Mortality Study effort to include all DOE and DOE workers involved in uranium fuel cycles.

The budget increases are primarily a result of increased staff in FY 1981 [one senior epidemiologist (M.D., Ph.D.), one epidemiologist (Ph.D.), and one data clerk] and an increase in data collection costs. The overall plan calls for data collection teams to be in the field during FY 1981. However, we intend, where possible, to subcontract data collection tasks to those contractors who are responsible for various sites and who have a well organized data collection system already in place. This approach will allow us to most effectively and efficiently increase the rate of data collection.

DOE F [illegible] 1239.2
(12-79)

U.S. DEPARTMENT OF ENERGY

FIELD TASK PROPOSAL/AGREEMENT

1. WP BIN NUMBER	2. TASK NO.	3. REV. NO.	4. PROJECT NO.	5. DATE PREPARED	6. CONTRACTOR NUMBER
		0		3-24-80	00 3034

7. TASK TITLE	8. WORK PACKAGE TITLE
Death Certificate Retrieval Office	HUMAN HEALTH EFFECTS FROM ENERGY GENERATION

9. BUDGET AND REPORTING CODE	10. TASK TERM Begin:	End:	11. CONTRACTOR NAME	12. CODE (see instructions)
HA 02 01 01 0	10-1-79	Open	Oak Ridge Associated Universities	ORE

13. CONTRACTOR TASK MANAGER (Name, FTS No.)	14. PRINCIPAL INVESTIGATORS
C. C. Lushbaugh 626-3090	Dr. C. C. Lushbaugh B. Dupree

15. WORK LOCATION (See instructions): Name of facility, City, State, ZIP Code	16. Does this task include any management services efforts?
Oak Ridge Associated Universities P. O. Box 117 Oak Ridge, Tennessee 37830	☐ YES ☒ NO

17. TASK DESCRIPTION (Approach, relation to work package, in 200 words or less)

The Death Certificate Retrieval Office (DCRO) supports Department of Energy sponsored epidemiologic studies by providing vital status follow-up of DOE/DOE-contractor workers. An important function which the DCRO performs is to act as a single point of contact with the Social Security Administration (SSA) which is one of the most complete sources of information concerning vital status in U. S. worker populations. The DCRO also uses a variety of methods such as searches of state death indices to determine vital status and to cross reference those results for validity.

After a worker has been identified as deceased, the DCRO conducts a search for a death certificate. When the death certificate is found. the DCRO verifies the certificate as the one sought. It is then reviewed by a nosologist for cause-of-death coding. The coded death certificates are then sent to the user requesting the vital status search. If a worker's status is undetermined, the DCRO attempts to determine the status via methods approved by epidemiologists conducting the study. Results from these searches are then reported to investigators to fulfill their request.

18. CONTRACTOR TASK MANAGER

(Signature) (Date)

19. DETAIL ATTACHMENTS: (See instructions)

- ☒ a. Facility Requirements
- ☐ b. Publications
- ☒ c. Purpose
- ☐ d. Background
- ☐ e. Approach
- ☒ f. Technical progress
- ☐ g. Future accomplishments
- ☐ h. Relationships to other projects
- ☐ i. Environmental assessment
- ☐ j. Explanation of milestones
- ☐ k. Other (specify):

1114086

DOE Form 3130.2 (Page 2) (12-78)

TASK REQUIREMENTS FOR OPERATING/EQUIPMENT COSTS AND OBLIGATIONS

CONTRACTOR NAME: Oak Ridge Associated Universities

BIN NUMBER	TASK NO.	REV. NO.	DATE PREPARED	CONTRACTOR NUMBER
		0	3-24-80	00 3034

	FY 80	FY 81 PRESIDENT'S	FY 81 REVISED	AUTHORIZED	FY 82
20. STAFFING (in staff years)					
a. SCIENTIFIC	1.0		1.0		1.0
b. OTHER DIRECT	2.3		2.3		2.3
c. TOTAL DIRECT	3.3		3.3		3.3
21. OBLIGATIONS AND COSTS (in Thousands)					
a. TOTAL COSTS	167		180		194
b. TOTAL OBLIGATIONS	186		184		199
22. EQUIPMENT (in Thousands)					
a. EQUIPMENT COSTS	0		0		0
b. EQUIPMENT OBLIGATIONS	0		0		0
23. OTHER COSTS (specify)					
a. Direct Sal. & Benefits	44		50		54
b. Mat. & Other Direct	64		67		71
c. Support Services	32		35		37
d. Indirect Expenses	27		28		32
24. OPTIONAL FIVE-YEAR PLAN (in Thousands) Constant BY dollars					
a. TOTAL OPERATING COSTS					
b. TOTAL OPERATING OBLIGATIONS					
c. TOTAL EQUIPMENT COSTS					
d. TOTAL EQUIPMENT OBLIGATIONS					

25. MILESTONE SCHEDULE	PROPOSED SCHEDULE	AUTHORIZED SCHEDULE
Scheduled SSA submissions:	April, Aug. & Dec.1980 April, Aug. & Dec.1981 April & Aug. 1982	
Report SSA search results to users:		
Dec 1979 search	March 1980	
April 1980 search	July 1980	
Aug. 1980 search	Nov. 1980	
Dec. 1980 search	March 1981	
April 1981 search	July 1981	
Aug. 1981 search	Nov. 1981	
Dec. 1981 search	March 1982	
April 1982 search	July 1982	
Death certificate searches based on SSA submissions from		
1976 Mallinckrodt	March 1980	
Jan. 1979 Y-12	June 1980	
TEC	April 1980	
Dec. 1979 X-10	Sept. 1980	
Mound	Dec. 1980	
K-25	March 1981	
Mallinckrodt	Dec. 1980	
April 1981 Y-12	Jan. 1982	
Develop computerized aids for death certificate searching	Feb. 1980	
Evaluate DCRO methods and report descriptive statistics to users.	Sept. 1981	

1114087

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No.	Date Prepared	Contractor Number
		0	3-24-80	00 3034

Enter headings in accordance with Item 19.

19a. Facility Statement

For increased efficiency and development of automated handling of computerized data this staff works as subgroups of the Epidemiology Group in the Tyrone Road Building.

19c. Purpose

The purpose of the Death Certificate Retrieval Office (DCRO) is to provide DOE-sponsored epidemiologic studies with skilled personnel who use sound methodology to conduct vital status follow-up. The DCRO provides an experienced and consistent approach to vital status follow-up for epidemiologic studies of diverse populations. Centralization of vital status follow-up benefits DOE-supported epidemiologic studies by reducing unnecessary duplication of effort. The DCRO is the single liaison with the Social Security Administration (SSA) and has set up methods for reporting and documenting results from use of SSA vital status information. The DCRO supplies DOE users with copies of death certificates for deceased individuals, verification that death certificate information agrees with that supplied by a user, and coding of cause of death. In addition, the DCRO staff works with users to conduct special follow-up studies.

19f. Technical Progress

Progress FY 79 and FY 80

The DCRO continued searching for death certificates using previous years' SSA information. The location of more than 95 percent of all deaths in the white male TEC population enabled epidemiological analysis of that cohort's mortality. Death certificates were coded for the TEC population by a nosologist using the Eighth Revision of ICDA.

In January 1979, mortality information was requested from SSA for 111,000 workers from the TEC, Y-12, Argonne, Oak Ridge Welders, Los Alamos, and Hanford populations. These results were received from SSA in August 1979 and were reported to all users. The delay in receiving results from the January 1979 SSA request was due to reorganization within SSA and a lapse in the DOE/SSA agency agreement to conduct mortality searches. A new agreement has been made and SSA will continue to be a prime source of mortality information. DCRO has begun looking for death certificates on those individuals SSA "declared dead" in the January 1979 search.

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No.	Date Prepared	Contractor Number
		0	3-24-80	00 3034

Enter headings in accordance with Item 19.

19f. Technical Progress (continued)

Thirteen state death indices* have been obtained and are in routine use in death certificate searches. Efforts are continuing to obtain additional state death indices. A special study was conducted to ascertain the completeness of SSA reporting using a subgroup chosen from all white male TEC employees (N = 720). Some 151 deaths were reported by the SSA in February 1974. Indices of all deaths recorded in Tennessee (1949-1974) and Kentucky (1963-1977) were available, and a search of these yielded an additional nine deaths occurring before 1974; four of these nine occurred in 1973, of which two were after mid-1973. Thus, at least 9 of 160 (5.6 percent) of pre-1974 deaths or 7 of 158 (4.4 percent) pre-med-1973 deaths were not ascertained by the SSA. Since most of the known deaths in this group (i.e., 83 of 145 deaths with certificates or 57.2 percent) occurred in Tennessee or Kentucky, it is unlikely that a large number of other deaths were missed.

Planned Progress FY 80 and FY 81

Efforts begun in FY 79 to develop computerized aids for follow-up and reporting will be completed in FY 80. The search for individuals "declared dead" in the January 1979 search is being conducted with the use of automated methods. Methodology for using the computerized state death indices and thereby avoiding clerical searches at state sites will be developed by mid 1980 and in place by 1981. Evaluation of SSA mortality information and search procedures and the ways they affect epidemiological mortality analyses will continue in 1980. SSA agreed to process a maximum of three searches a year, and DCRO staff have established a regular schedule of SSA submissions. In FY 80 (December 1979) the first of these scheduled searches was begun; it included over 82,000 names of workers from Mallinckrodt, Middlesex, 5-rem, Linde, LASL, NLO, SAM, Oak Ridge, and Savannah River populations. All SSA submissions and results feed into the DRCO system and work priorities on specific populations are set to accommodate individual users of the DCRO service.

Planned Progress FY 82

DCRO will continue to seek death certificates which have not been found for previous SSA searches. The majority of death certificates are readily found in areas surrounding DOE/DOE-contractor sites, but a few require lengthy searches of many states. New SSA submissions and resubmissions of populations formerly sent will be made on a scheduled basis. The DCRO will increase collaboration with all users to help them meet their objectives and deadlines. Continuing evaluation of search methodology will be made to improve efficiency and percent recovery. As more epidemiologic studies begin to evolve, studies of deaths in the 1980's, methods of death searches through obituaries, telephone service and business directories will come into broader use. DCRO will use the National Death Index and plans to develop the required operational interface and methodology to do so.

*see table.

1114089

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No.	Date Prepared	Contractor Number
		0	3-24-80	00 3034

Enter headings in accordance with Item 19.

19f. Technical Progress (continued)

*State Death Indices

1. Obtained and in place

Alabama	1908 - 1977
Arizona	1940 - 1977
California	1960 - 1977
Delaware	1939 - 1976
Florida	1940 - 1978
Kentucky	1963 - 1977
Louisiana	1975 - 1978
Maine	1960 - 1978
Montana	1954 - 1977
North Carolina	1975 - 1977
Ohio	1956 - 1977
Tennessee	1949 - 1977
Texas	1964 - 1977

2. Promised but not in place
   - Connecticut
   - Georgia
   - Hawaii
   - Mississippi
   - New Jersey
   - Utah
   - Louisiana (pre-1975)

3. Possible exchange with NCI

Kansas	1971 - 1977
Missouri	1960 - 1976
Nebraska	1954 - 1974
Wisconsin	1968 - 1976
Washington, D. C.	1971 - 1976

DOE F [illegible] (12-77)

U.S. DEPARTMENT OF ENERGY

FIELD TASK PROPOSAL/AGREEMENT

1. WP BIN NUMBER	2. TASK NO.	3. REV. NO.	4. PROJECT NO.	5. DATE PREPARED	6. CONTRACTOR NUMBER
		0		3-24-80	00 3401

7. TASK TITLE	8. WORK PACKAGE TITLE
DOE/Data Processing Support	HUMAN HEALTH EFFECTS FROM ENERGY GENERATION

9. BUDGET AND REPORTING CODE	10. TASK TERM Begin:	End:	11. CONTRACTOR NAME	12. CODE (see instructions)
HA 02 01 01 0	10-1-79	Open	Oak Ridge Associated Universities	ORH

13. CONTRACTOR TASK MANAGER (Name, FTS No.)	14. PRINCIPAL INVESTIGATORS
C. C. Lushbaugh 626-3090	C. C. Lushbaugh D. Robie

15. WORK LOCATION (See instructions): Name of facility, City, State, ZIP Code	16. Does this task include any management services efforts?
Oak Ridge Associated Universities P. O. Box 117 Oak Ridge, Tennessee 37830	☐ YES ☒ NO

17. TASK DESCRIPTION (Approach, relation to work package, in 200 words or less)

This program provides the technical support necessary for developing the data bases of workers at approximately 100 current and former DOE contractor sites for the Health and Mortality Study. These contractors include those engaged in all phases of the uranium fuel cycles, research and development, production, testing, and fabrication of nuclear weapons.

Specialists trained in data collection, data validation, quality control, and data processing, develop study files from personnel, medical, and occupational records on more than 800,000 DOE contract employees. Experts in health physics, industrial hygiene, and industrial management, will design and supervise abstracting and encoding procedures. Data collection teams are sent to contractor sites to transmit information to a centralized data-processing facility.

The data collection team, in cooperation with key DOE contractor and DOE Field Office Personnel, prepares the data for computerization. The computerized data can then be used for vital status searches, and biostatistical and epidemiological analysis. Epidemiologists, statisticians, health physicists, and computer scientists of the DOE Health and Mortality Study Program guide all aspects of data preparation with emphasis on quality control and data validation for final epidemiologic analysis and evaluation.

18. CONTRACTOR TASK MANAGER

(Signature) (Date)

19. DETAIL ATTACHMENTS: (See instructions)

☐ a. Facility Requirements
☐ b. Publications
☒ c. Purpose
☐ d. Background
☐ e. Approach
☒ f. Technical progress
☐ g. Future accomplishments
☐ h. Relationships to other projects
☐ i. Environmental assessment
☐ j. Explanation of milestones
☐ k. Other (specify):

1114091

DOE Form 5130.3 (Page 2) (12-78)

TASK REQUIREMENTS FOR OPERATING/EQUIPMENT COSTS AND OBLIGATIONS

CONTRACTOR NAME: Oak Ridge Associated Universities

BIN NUMBER	TASK NO.	REV. NO.	DATE PREPARED	CONTRACTOR NUMBER
		0	3-24-80	00 3401

20. STAFFING (in staff years)	FY 80	FY 81 PRESIDENT'S	FY 81 REVISED	AUTHORIZED	FY 82
a. SCIENTIFIC	2.8		3.0		3.0
b. OTHER DIRECT	3.7		11.0		11.0
c. TOTAL DIRECT	6.5		14.0		14.0
21. OBLIGATIONS AND COSTS (in Thousands)					
a. TOTAL COSTS	325		462		500
b. TOTAL OBLIGATIONS	389		473		512
22. EQUIPMENT (in Thousands)					
a. EQUIPMENT COSTS	0		0		0
b. EQUIPMENT OBLIGATIONS	0		0		0
23. OTHER COSTS (specify)					
a. Direct Sal. & Benefits	135		230		247
b. Mat. & Other Direct	79		70		76
c. Support Services	62		88		95
d. Indirect Expenses	49		74		82
24. OPTIONAL FIVE-YEAR PLAN (in Thousands) Constant BY dollars					
a. TOTAL OPERATING COSTS					
b. TOTAL OPERATING OBLIGATIONS					
c. TOTAL EQUIPMENT COSTS					
d. TOTAL EQUIPMENT OBLIGATIONS					

25. MILESTONE SCHEDULE	PROPOSED SCHEDULE	AUTHORIZED SCHEDULE
Recruit, train, and equip data collection and health physics team (two persons).	March 1980	
Prepare records profile of selected DOE sites (e.g., Bettis, KAPL, NLO, and Mound) and other uranium fuel cycle sites.	June 1980	
Prepare a records profile study of Portsmouth, Paducah, and other uranium fuel cycle sites.	April 1980	
Recruit, train, and equip the second field collection team.	Jan. 1981	
Conduct a feasibility study of establishing a uniform DOE-wide record keeping system.	June 1981	
Conduct a preliminary records availability review of remaining sites in the uranium fuel cycle and a records profile of all disbanded DOE sites.	Nov. 1981	
Centralized data-processing facility and staff fully operational (including three collection/processing teams).	Dec. 1981	
Establish a continual system data processing and preparation of DOE site bases for epidemiologic analysis.	Oct. 1982	

1114092

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No. 0	Date Prepared 3-24-80	Contractor Number 00 3401

Enter headings in accordance with Item 19.

19c. Purpose

Modern epidemiologic studies must have data bases that are carefully collected, rigidly controlled so as to be as uniform and error-free as possible to avoid biasing epidemiologic analyses. Large study populations are needed to obtain statistical significance and reliability to suggest causal relations between such late effects as cancer and low, chronic occupational exposures to radiation and other industrial toxicants. To meet these needs, the number of DOE workers under study must be as large as possible and the data for their work-history files must be collected and managed under strict quality control for uniformity and completeness. This program provides the technical support to meet these goals.

19f. Technical Progress

Progress FY 79 and FY 80

A manager for the data-collection group, hired in FY 79, experienced in research program administration and in personnel and business management, assumed responsiblity for the entire data-collection process. Responsibilities included recruiting, training, and directing the data-collection team of technical and clerical personnel. The technical members of the team are responsible for interpreting and evaluating medical and exposure data. They develop methods and procedures for computerizing the data to meet the demands of managing huge data bases. Many DOE sites were visited to determine feasibility of data collection and scheduled for data acquisition. Collection methodology of other epidemiology or related programs such as SEER-Atlanta, NCI and National Death Index Office, Bethesda, and National Cancer Registry were received. Clerical personnel performed actual data conversion, validation, etc. to encode the raw data for computerization prior to preparation of analysis files.

During this period of time, data feasibility studies were conducted at 12 DOE sites. Preliminary records reviews were completed at Bettis, Nevada Test Site, National Lead, and Mound Laboratory, in addition to the 3 Oak Ridge Plants. Five DOE operations offices were also visited to identify potential problems and needs for the data-collection teams in FY 80. A survey and follow-up visit of several Federal and DOE records collection centers was completed. These included the Federal Records Centers located in Bayonne, New Jersey and St. Louis, Missouri, and DOE records storage sites at the Environmental Monitoring Laboratory in Manhattan, and Oak Ridge Operations Office. A computerized record inventory was established to provide a comprehensive overview of historical AEC and DOE records. This detailed records profile system, started in FY 79, was designed to (1) contact personnel and record departments and other sources of epidemiologic data at selected DOE sites, (2) survey the various methods used for record keeping and determine status and existence of specific kinds of records needed, and (3) assess the potential difficulties of data collection by off-site teams vs on-site permanent record clerks. From this analysis, characteristics of record-keeping systems were determined

1114093

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No.	Date Prepared	Contractor Number
		0	3-24-80	00 3401

Enter headings in accordance with Item 19.
19f. Technical Progress (continued)

and plans were developed to standardize methods of record keeping within all DOE operations. A research planning committee, fully operational by the start of FY 80, reviewed all data-collection activities.

Planned Progress FY 80 and FY 81

Additional data collection team personnel are to be recruited, trained, and equipped as rapidly as possible so that field data collection can be expanded in FY 80 to include current sites of interest. Plans are made to study some terminated sites and current sites not previously involved in Health and Mortality Studies. These sites were chosen for feasibility study because of long employment--3,000 persons/year for 30 years. A formal arrangement has been established for obtaining civilian employee data from the Nevada Test Site.

A schedule will be established for data collection at all present and former DOE sites, particularly those involved in the uranium fuel cycle technology. Retrieval methods at various sites will be tailored according to accessibility of data. General guidelines will be established, and specialized methods will be developed as needed. Retrieval procedures will be coordinated with ORO, other field offices, and other DOE epidemiologic research projects.

Continuing the review begun in FY 79, all remaining regional archives and records centers will be reviewed and visited for additional data to determine the potential size of the National Roster of U. S. Atomic Workers. In early FY 80 an in-depth demographic study of selected sites will be completed. Selected area retired employees will be interviewed for archival data. Community and environmental analysis, worker-distribution patterns, density of populations and vital statistics by counties will be documented.

Planned Progress FY 82

The experience gained in FY 79, FY 80, and FY 81 will be used in training a second data-collection team to alternate with the first. The plan is for the two collection teams to work together--one at the centralized data-processing facility to develop skills in transposing filmed source data to standardized formats for computerization while the other team collects more data at a plant site. Procedures will be developed for quality control surveillance of the process, individual performance (accuracy and dependability) and rate of progress. Current planning has each team working with at least two epidemiologists in training (pre-master or doctoral student and one post-MPH graduate student from the University of North Carolina). Their progress will be supervised by the Research Planning Group as explained in that FTP. Complete training and equipping of all the collection teams will have been completed by late FY 81, and then will be operational in FY 82.

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No.	Date Prepared	Contractor Number
		0	3-24-80	00 3401

Enter headings in accordance with Item 19.

19f. Technical Progress (continued)

The Research Planning Group, established in FY 79, will continue to evaluate record-keeping and data-collection techniques in all studies.

A completely automated auditing system will be available to summarize the data acquisition accomplished by the Centralized Data Processing Facility staff to enhance the flow of source data and its processing for computerization. Automated procedures will be used to insure the quality of the data.

Complete record profiles of all active DOE sites will have been completed by mid FY 82. The data-collection program will have been completed at Bettis, KAPL, Mound, and NLO. Following these studies, an in-depth summarization of the problems and methodology of data retrieval, conversion, etc. will be completed. The management and collection methods will be refined based on our experience.

In FY 82 the computerized data from at least 50 percent of the active sites and 25 percent of the disbanded sites will have been reviewed. Most uranium fuel cycle sites will be included in this review. Collection teams will be working concurrently at several sites collecting and validating data.

By the beginning of FY 82 the Central Data-Processing Facility will be involved with updating the data previously obtained from active DOE plants and research sites and will have in place a national roster of persons who were previously or are presently atomic workers. It is expected that this National Roster of Atomic Workers will then comprise a large data base which can be used to test various epidemiologic hypotheses in the areas that concern the potential hazards of nuclear industry.

It is expected that through encrypting procedures to remove personal identifiers that the privacy of individuals in this data base will be protected from third parties so that procedures can be developed which allow large subsets of these data to be made available for additional independent analyses by recognized epidemiologists and biostatisticians with DOE, HEW, NIOSH, and other research groups.

By the end of FY 82 a DOE-wide system should be in place at all active sites to accomplish routinely an annual updating of the employment and exposure data in the National Radiation Workers Roster.

1114095

DOE F [illegible] 1330.2
(12-73)

U.S. DEPARTMENT OF ENERGY

FIELD TASK PROPOSAL/AGREEMENT

1. WP BIN NUMBER	2. TASK NO.	3. REV. NO.	4. PROJECT NO.	5. DATE PREPARED	6. CONTRACTOR NUMBER
		0		3-24-80	00 3489

7. TASK TITLE	8. WORK PACKAGE TITLE
DOE/Social Security Admn. Data Searches	HUMAN HEALTH EFFECTS FROM ENERGY GENERATION

9. BUDGET AND REPORTING CODE	10. TASK TERM Begin:	End:	11. CONTRACTOR NAME	12. CODE (see instructions)
HA 02 01 01 0	12-1-79	Open	Oak Ridge Associated Universities	ORU

13. CONTRACTOR TASK MANAGER (Name, FTS No.)	14. PRINCIPAL INVESTIGATORS
C. C. Lushbaugh 626-3090	C. C. Lushbaugh Elizabeth Dupree D. M. Robie

15. WORK LOCATION (See instructions): Name of facility, City, State, ZIP Code	16. Does this task include any management services efforts?
Oak Ridge Associated Universities P. O. Box 117 Oak Ridge, Tennessee 37830	☐ YES ☒ NO

17. TASK DESCRIPTION (Approach, relation to work package, in 200 words or less)

In late FY 77 the epidemiology group of ORAU Medical and Health Sciences Division was designated as the single DOE point of contact with Social Security Administration (SSA) and delegated the responsibility for initiating SSA data searches to determine the vital status of DOE atomic workers. Since then lists containing names with social security numbers submitted to DOE Death Certificate Retrieval Office (DCRO) by epidemiologists working on DOE prime contracts are transmitted by DCRO to SSA Office of Enumeration and Earnings Records according to interagency agreement. When the SSA data searches are completed, DCRO then conducts searches of state vital statistic departments for death certificates and validation of reported state of death, etc.

This FTP/A provides for administering the DOE/SSA interagency agreement and reimbursement of SSA for services to DOE. No additional staffing is required since this activity will be carried out by DCRO staff under RPIS 00 3034.

18. CONTRACTOR TASK MANAGER

(Signature) (Date)

19. DETAIL ATTACHMENTS: (See instructions)

☐ a. Facility Requirements	☒ d. Background	☒ g. Future accomplishments	☐ j. Explanation of milestones
☐ b. Publications	☐ e. Approach	☒ h. Relationships to other projects	☐ k. Other (specify):
☒ c. Purpose	☒ f. Technical progress	☐ i. Environmental assessment	

1114096

DOE Form 61363 (Page 3) (12-78)

TAS REQUIREMENTS FOR OPERATING/F IIPMENT COSTS AND OBLIGATIONS

CONTRACTOR NAME

Oak Ridge Associated Universities

BIN NUMBER	TASK NO.	REV. NO.	DATE PREPARED	CONTRACTOR NUMBER
		0	12-14-79	00 3489

20. STAFFING (in staff years)	FY 1980	FY 1981 PRESIDENT'S	FY 1981 REVISED	AUTHORIZED	FY 1982
a. SCIENTIFIC					
b. OTHER DIRECT					
c. TOTAL DIRECT	0	0			0
21 OBLIGATIONS AND COSTS (in Thousands)					
a. TOTAL COSTS	60	60			60
b. TOTAL OBLIGATIONS	78	60			60
22. EQUIPMENT (in Thousands)					
a. EQUIPMENT COSTS					
b. EQUIPMENT OBLIGATIONS					
23. OTHER COSTS (specify)					
aDirect Salaries & Ben.					
bSupporting Services	12	12			12
cMaterials & Other Direct	40	40			40
dIndirect Expenses	8	8			8

24 OPTIONAL FIVE-YEAR PLAN (in Thousands) Constant BY dollars	BY +1	BY +2	BY +3	BY +4
a. TOTAL OPERATING COSTS				
b. TOTAL OPERATING OBLIGATIONS				
c. TOTAL EQUIPMENT COSTS				
d. TOTAL EQUIPMENT OBLIGATIONS				

25 MILESTONE SCHEDULE	PROPOSED SCHEDULE	AUTHORIZED SCHEDULE
N/A		

1114097

FIELD TASK PROPOSAL/AGREEMENT
DETAIL ATTACHMENTS

Contractor Name				
Oak Ridge Associated Universities				
Bin Number	Task No.	Rev. No.	Date Prepared	Contractor Number
		0	3-24-80	00 3489

Enter headings in accordance with Item 19.

19c. Purpose

The purpose of this project is to administer the DOE/SSA interagency agreement under which all DOE-supported epidemiologic studies obtain reports from SSA as to the vital status of persons in their study populations. The costs incurred for these searches are reimbursed to SSA through this mechanism.

19d. Background

Formerly this activity was funded directly from OHER (ASEV). Communication difficulties often slowed reimbursements which were requested at such irregular intervals that they could not be anticipated and planned for. Since the DOE/Death Certificate Retrieval Office was the only customer and therefore constantly aware of all work in progress and all costs involved, the communication and payment tracks were simplified by this procedural change.

19f. Progress

The procedure was in place and operating in early FY 80.

19g. Future Accomplishments

In FY 81 and 82 the need for this service will continue at the present level.

19h. Relationships to Other Projects

This service function is integrated with the Death Certificate Retrieval Office and provides therefore basic support for the Health and Mortality Study (Oak Ridge), the Hanford Health and Mortality Study (Hanford Environmental Health Foundation and Battelle Pacific Northwest Laboratory) and the Plutonium Workers Study (Los Alamos Scientific Laboratory).

1114098

DO NOT REMOVE

Proceedings of the Symposium
held at Fort Monroe, Virginia
November 6-9, 1967 under auspices of
Advisory Committee on Civil Defense,
Advisory Committee on Emergency Planning,
Office of Civil Defense, and
Office of Emergency Planning

Postattack Recovery from Nuclear War

1114099

RECENT PROGRESS IN ASSESSMENT OF HUMAN RESISTANCE TO TOTAL-BODY IRRADIATION

C. C. Lushbaugh
Oak Ridge Institute of Nuclear Studies

Postattack recovery will depend largely upon man's ability to perform in high-radiation fields. His radiosensitivity will limit these operations because an amount of exposure must not be allowed that will lead to a high incidence of radiation sickness, or subsequent death from hematopoietic damage. Our knowledge of man's radioresistance is still quite meager. It is based on observations of accidental radiation exposures of normal men in situations where dose is a matter of retrospective conjecture; on observations of human effects after two atomic attacks where thousands of individual exposures and total-body doses are still being computed after 20 years of study (the Atomic Bomb Casualty Commission and Ichiban Programs); and on therapeutic and clinical observations of total-body irradiation of patients whose exposures were measured precisely, but whose high probability of becoming ill and dying had singled them out for radiation therapy. From such studies in the past, the lethal dose for man has been estimated as lying between 300 and 450 R. Confidence in this range is high, but any assumption of precision here is unwarranted. A recently completed retrospective study of more than 500 total-body-irradiated patients of different ages, sexes, and diseases, has attempted, by use of modern statistical techniques, to obtain more precise estimates of human dose/response relations. Probit regression analyses of these data pretending* that the necessary assumptions for this kind of data treatment were valid, have yielded estimates of the effective single doses required to cause various incidences of the untoward responses of acute radiation sickness and the hematopoietic damage. Conceptually such an approach avoids the clinically ambiguous impressions that 200 R will cause a man to vomit while 450 R will kill, and allows estimates of the probability of radiation-induced response while defining the limits of certainty.

---

* We pretend because we know the assumptions basic to the model can not be met.

1114100

The data in Table I show such estimates for loss of appetite, nausea, vomiting, and diarrhea in man. These data are not directly applicable to a population of normal healthy men, but since civil-defense-planners must not base their projections on the most resistant healthy status of man, they can use estimates such as these from sick patients that overstate the radiosensitivity of normal man.

All these data were derived from situations where the exposures were prompt, i.e., given in less than 2 hours. Dose protraction, however, promises to reduce the incidence of these effects in man, according to observations made in animals and in the accidentally exposed Marshallese natives where instead of the expected 60 percent incidence of vomiting, only 10 percent became sick.

Clinical evidence is abundant that dose fractionation diminishes the incidence of various responses to radiation exposure, but no estimate based on clinical data exists on the extent of this modification. It is assumed that, as with skin erythema or moist desquamation, the percent probability (P) of vomiting or death is related to the product of total dose and a fractional power function (x) of the number (N_f) of individual exposures: $P = \text{Dose} \cdot N_f^{(x)}$ We are now studying this problem retrospectively using about 1000 therapeutic case histories of fractionated total-body irradiation. In addition, we are making observations on whether dose protraction also diminishes clinical signs of radiation damage. The latter study involves the therapeutic trial of a newly constructed facility for total-body irradiation of patients with chronic blood dyscrasias. This facility has 10 cobalt-60 gamma-ray sources arranged in such a way that an isotropic-flux volume of 16 x 16 x 8 ft is produced and has an exposure rate of 1.5 R/hr. The patient is allowed to move at will about this room in which he lives for 3 to 5 days, or as long as may be needed to expose him to the dose his therapy requires. Three of the five patients studied to date in this facility previously received the same dose (70 rads) in another total-body irradiation facility where the dose rate is 60 times as rapid (1.5 R/min). All experienced severe acute gastrointestinal reactions with the more rapidly delivered dose, but were symptom free in the new facility (Table II). Depression of blood elements after exposure in the two facilities was compared; effects were less pronounced and less persistent after exposure at the low-exposure rate. These limited observations imply that the concept of equivalent residual dose is correctly applicable to man and that clinical data can be obtained that may allow tailoring of the appropriate constants to fit the concept directly to man's radioresistance.

Table III contains estimates of the population incidence of various symptoms of radiation sickness that might be expected if an infinitely large number of people were simultaneously exposed to a

1114101

single dose of 10 rads of total-body irradiation. The estimated incidences are all below 4 percent, a level that could easily be tolerated under austere conditions, and suggest that in extreme emergency situations man can work in much higher radiation fields such longer times than previously imagined. If total dose and exposure times of personnel are controlled, a balance can be achieved between the needs of the population to be rescued and a tolerable incidence of acute radiation sickness in the rescuers. Exposures of more than 30 R obtained at low rates over an entire day for several days up to a week will probably not cause even these low incidences of acute gastrointestinal symptoms. Since such exposures will, however, cause depressions in blood levels of important cells that can lead subsequently to infections and other diseases, the 30R/day/week exposure must be restricted to as small a number of heroic civil-defense volunteers as conditions permit.

1114102

TABLE I.

RECENT ESTIMATES OF EFFECTIVE DOSES (RADS)

FOR SOME HUMAN PRODROMAL RESPONSES *

Responses	ED_{10}	ED_{50}#
Anorexia	39^{+17}_{-20}	97^{+31}_{-26}
Nausea	51^{+17}_{-20}	139^{+72}_{-33}
Emesis	62^{+20}_{-20}	183^{+178}_{-53}
Diarrhea	87^{+46}_{-61}	238^{+122}_{-55}

* Space Radiation Study Panel Report (NAS/NRC).

\# ED_{50} = the "Effective Dose" that will probably cause 50% of the subjects under study to show a specific response that is defined with some temporal relation to the insult (here, total-body exposure to deeply penetrating gamma radiation for less than two hours).

1114103

TABLE II.

INITIAL EXPERIENCE WITH LOW-EXPOSURE-RATE TOTAL-BODY IRRADIATION FACILITY (1.5 R/HR)

No.	Patient Dx.*	Sex/Age	Total Residence Hr / Day	Total Exposure R/Hr	Average Fraction/Day %	Prodromal Symptoms
1	IT	M/61	116.0 (4.8)	150/100.0	86.2	0
2	CLL	M/75	73.1 (3.0)	100/66.7	91.2	0
3	CML	M/12	74.4 (3.1)	100/66.7	89.6	0
4	CML	F/45	78.7 (3.3)	100/66.7	84.6	#
5	LS	M/79	76.2 (3.2)	100/66.7	87.5	0

* IT = Ideopathic thrombocytopenia.
CLL = Chronic lymphatic leukemia.
CML = Chronic myeloid leukemia.
LS = Lymphosarcoma.

\# Nausea relieved by eating.

1114104

TABLE III.

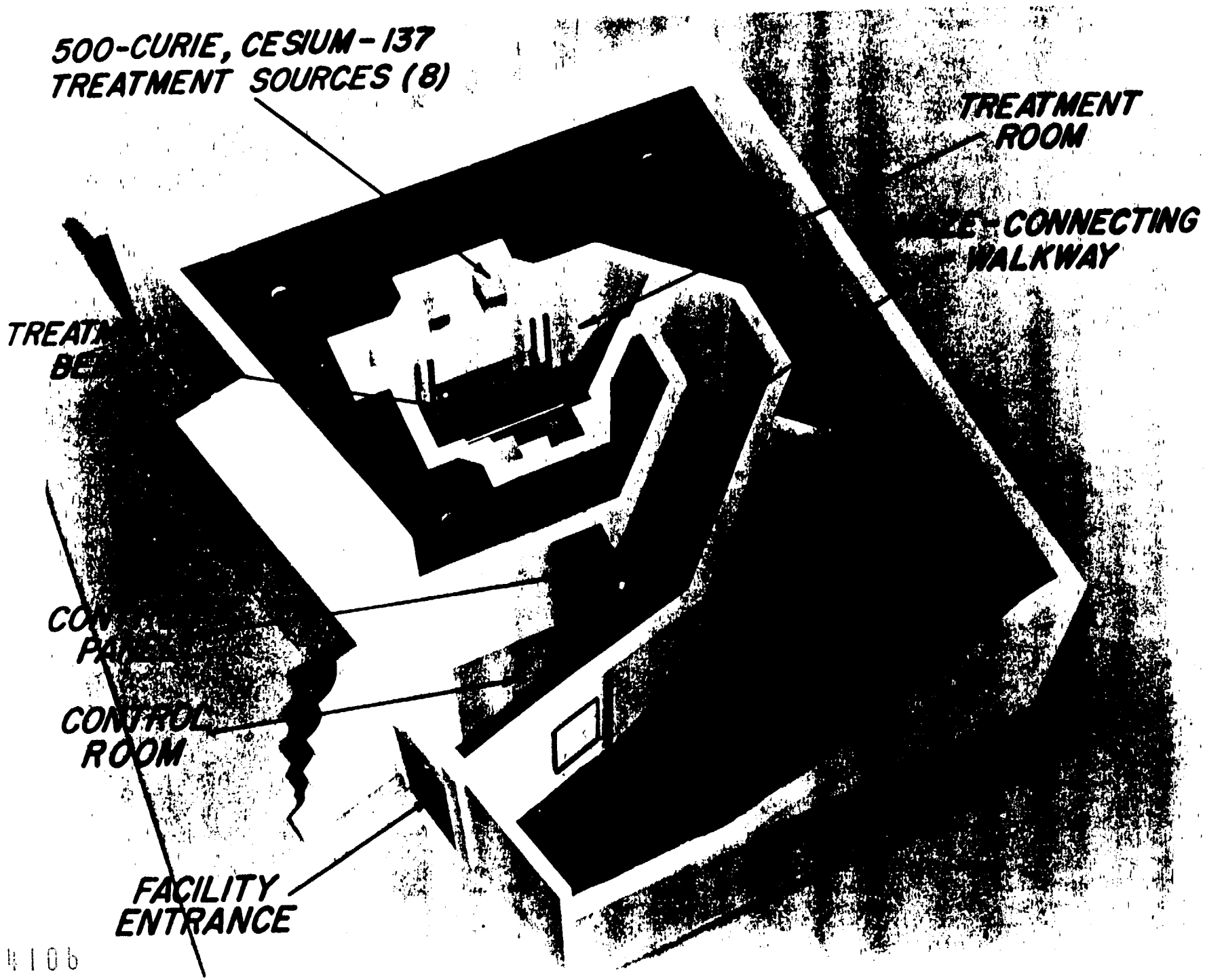
INCIDENCE OF RADIATION SICKNESS

Per thousand persons exposed to 10 rad whole-body radiation.

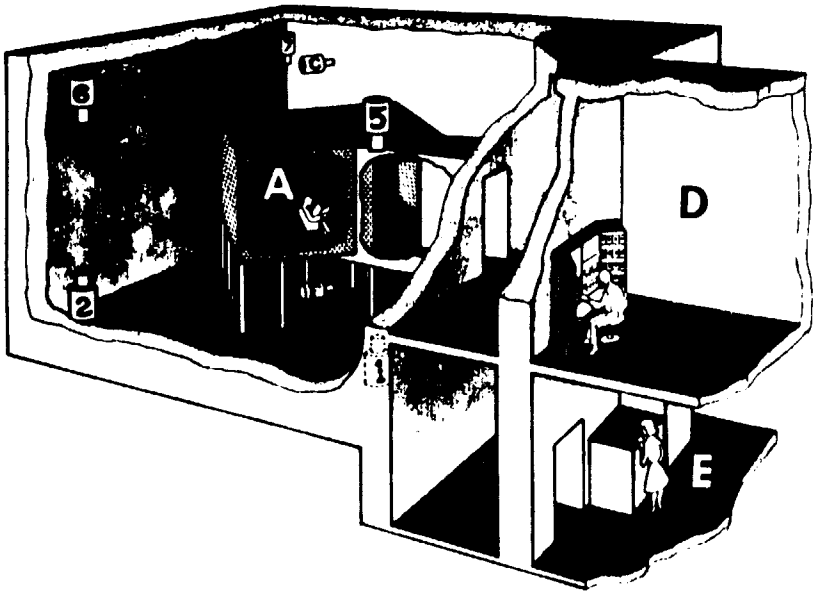
	DATA* FROM	
For	ORAU	Others
Anorexia	5	40
Nausea	4	15
Vomiting	3	11
Diarrhea	12	2

* Obtained from therapeutic studies on patients at the Medical Division, Oak Ridge Associated Universities (ORAU), and 50 other U. S. hospitals (Others).

1114105


500-CURIE, CESIUM-137
TREATMENT SOURCES (8)
TREATMENT
ROOM
-CONNECTING
WALKWAY
TREAT
BE
CON
PA
CONTROL
ROOM
FACILITY
ENTRANCE

1114106



1114107

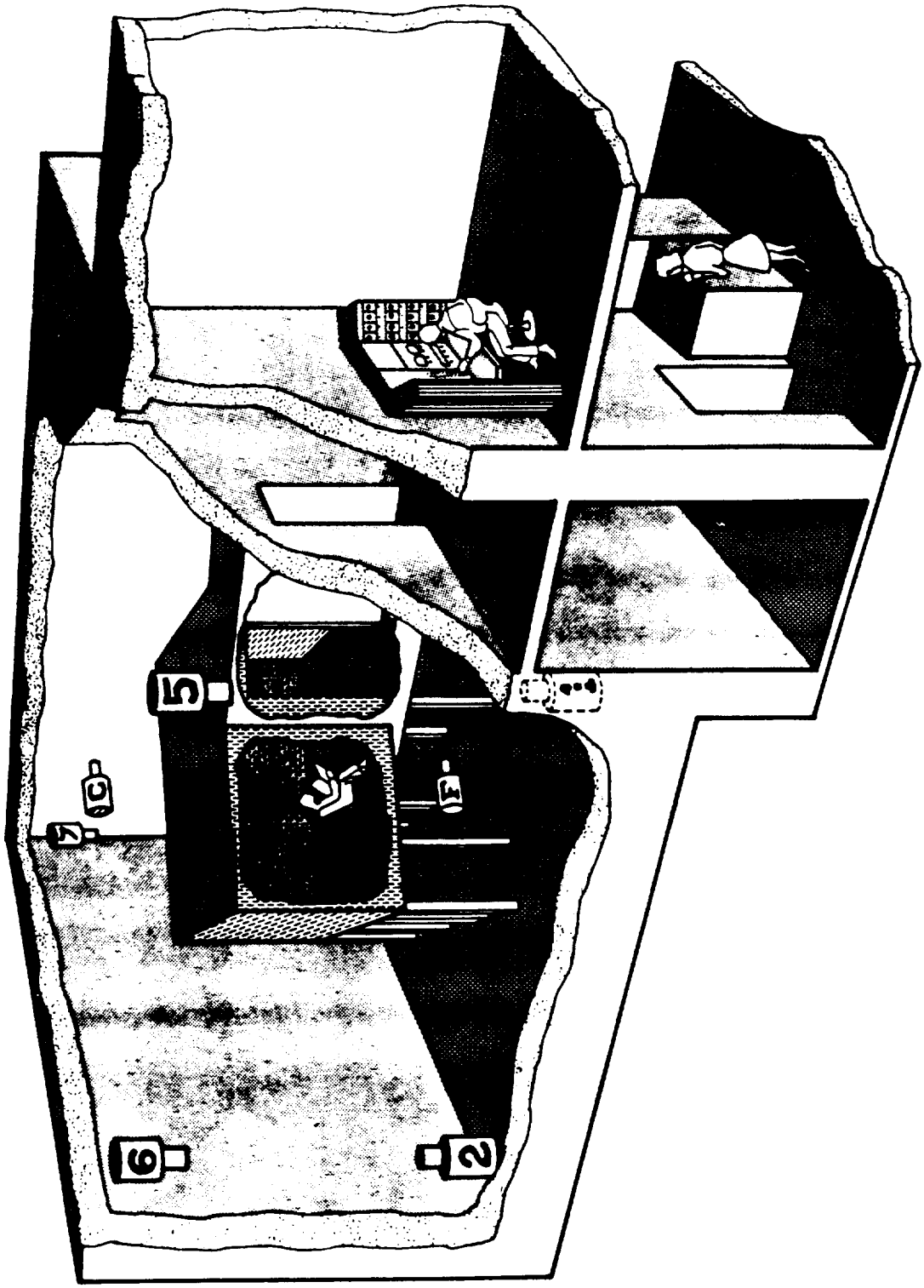
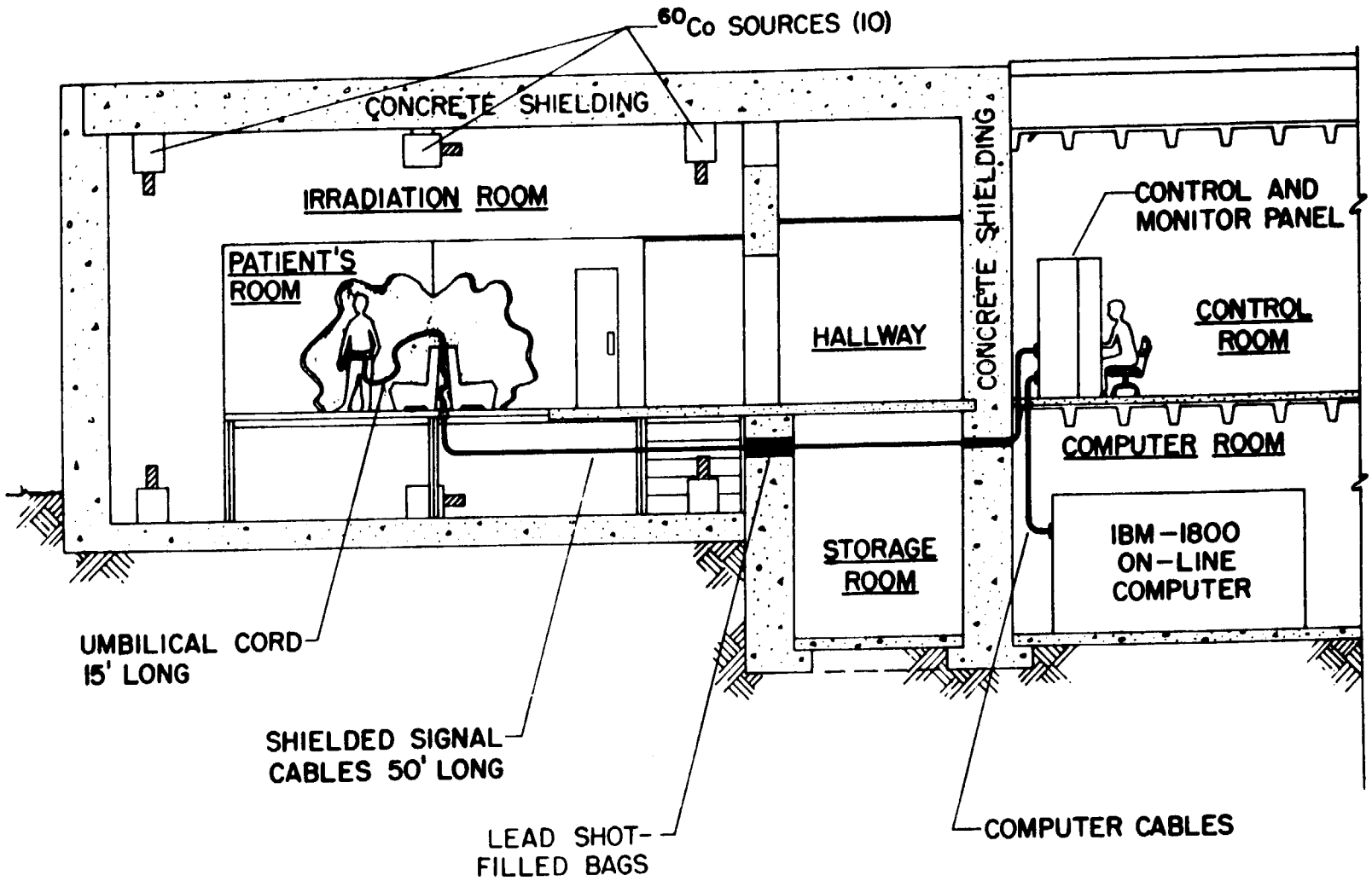
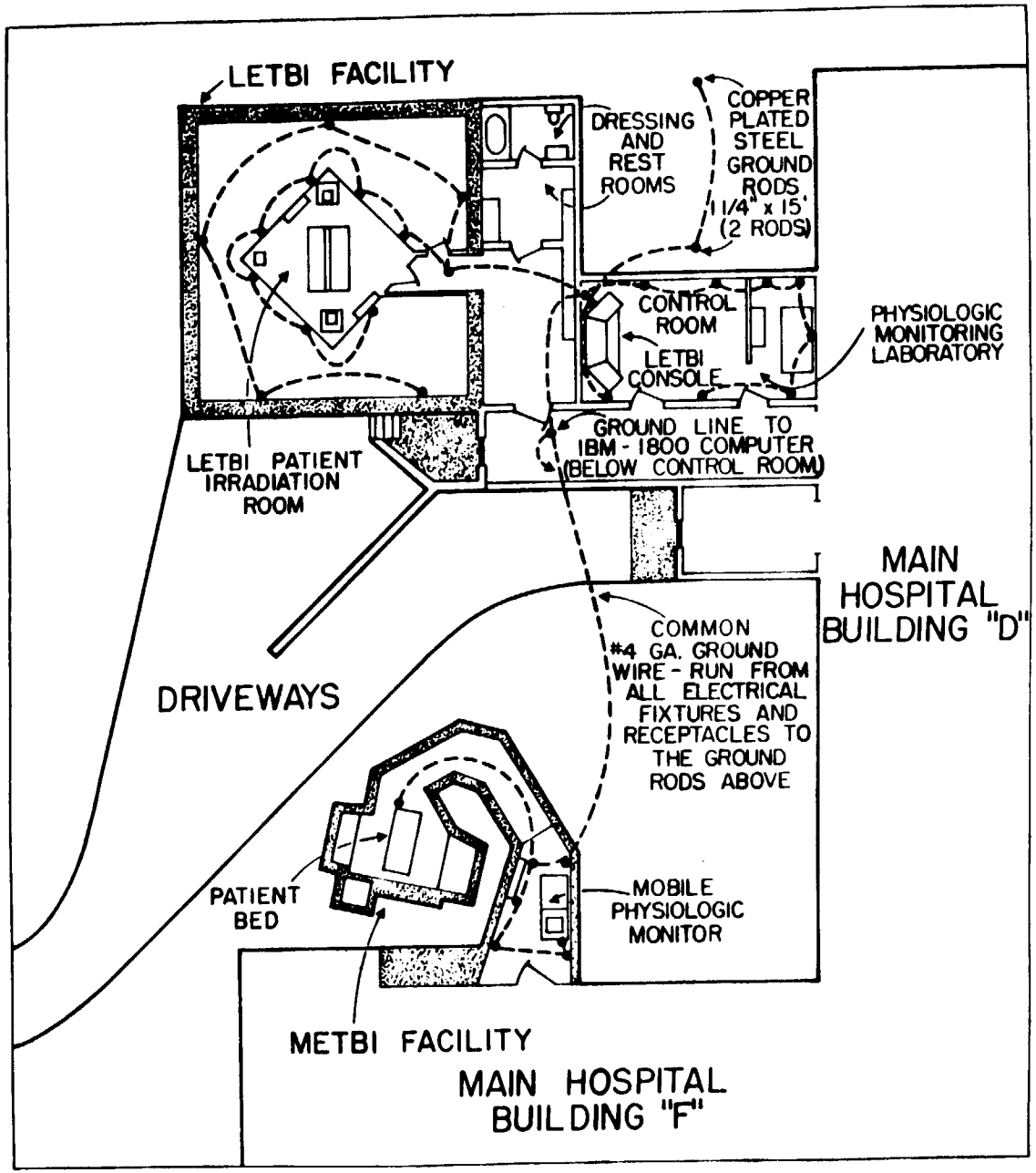


Fig. 16


^{60}Co SOURCES (10)
CONCRETE SHIELDING
IRRADIATION ROOM
PATIENT'S ROOM
HALLWAY
CONCRETE SHIELDING
CONTROL AND MONITOR PANEL
CONTROL ROOM
COMPUTER ROOM
STORAGE ROOM
IBM-1800 ON-LINE COMPUTER
UMBILICAL CORD 15' LONG
SHIELDED SIGNAL CABLES 50' LONG
LEAD SHOT-FILLED BAGS
COMPUTER CABLES

1114109


LETBI FACILITY
DRESSING AND REST ROOMS
COPPER PLATED STEEL GROUND RODS 1 1/4" x 15' (2 RODS)
CONTROL ROOM
LETBI CONSOLE
PHYSIOLOGIC MONITORING LABORATORY
GROUND LINE TO IBM - 1800 COMPUTER (BELOW CONTROL ROOM)
LETBI PATIENT IRRADIATION ROOM
MAIN HOSPITAL BUILDING "D"
COMMON #4 GA. GROUND WIRE - RUN FROM ALL ELECTRICAL FIXTURES AND RECEPTACLES TO THE GROUND RODS ABOVE
DRIVEWAYS
PATIENT BED
MOBILE PHYSIOLOGIC MONITOR
METBI FACILITY
MAIN HOSPITAL BUILDING "F"

1114110

P15 767565

RECEIPT FOR CERTIFIED MAIL

NO INSURANCE COVERAGE PROVIDED—
NOT FOR INTERNATIONAL MAIL
(See Reverse)

SENT TO
Howard L. Rosenberg
STREET AND NO.
1401-16th St., NW
P.O., STATE AND ZIP CODE
Wash., D.C. 20036

POSTAGE				$
CONSULT POSTMASTER FOR FEES	CERTIFIED FEE			¢
	OPTIONAL SERVICES	SPECIAL DELIVERY		¢
		RESTRICTED DELIVERY		¢
		RETURN RECEIPT SERVICE	SHOW TO WHOM AND DATE DELIVERED	¢
			SHOW TO WHOM, DATE AND ADDRESS OF DELIVERY	¢
			SHOW TO WHOM AND DATE DELIVERED WITH RESTRICTED DELIVERY	¢
			SHOW TO WHOM, DATE AND ADDRESS OF DELIVERY WITH RESTRICTED DELIVERY	¢
TOTAL POSTAGE AND FEES				$
POSTMARK OR DATE				

PS Form 3800, Apr. 1976

SENDER: Complete items 1, 2, and 3.
Add your address in the "RETURN TO" space on reverse.

1. The following service is requested (check one)
- ☐ Show to whom and date delivered ..... ¢
- ☐ Show to whom, date and address of delivery ..... ¢
- ☐ RESTRICTED DELIVERY
  Show to whom and date delivered ..... ¢
- ☐ RESTRICTED DELIVERY.
  Show to whom, date, and address of delivery. $ ____

(CONSULT POSTMASTER FOR FEES)

2. ARTICLE ADDRESSED TO:
Howard L. Rosenberg
Washington Merry-go-Round
1401-16th Street NW
Washington DC 20036

3. ARTICLE DESCRIPTION:

REGISTERED NO.	CERTIFIED NO.	INSURED NO.
	767565	

(Always obtain signature of addressee or agent)

I have received the article described above.
SIGNATURE ☐ Addressee ☐ Authorized agent

4. DATE OF DELIVERY
2/6

POSTMARK

5. ADDRESS (Complete only if requested)

6. UNABLE TO DELIVER BECAUSE:

CLERK'S INITIALS

☆GPO : 1979-300-450

RETURN RECEIPT, REGISTERED, INSURED AND CERTIFIED MAIL

FEB 6 1981

Mr. Howard L. Rosenberg
Washington Merry Go Round
1401 16th Street, NW
Washington, D. C. 20036

Dear Mr. Rosenberg:

Please accept this letter in response to your Freedom of Information Act request of January 27, 1981, deemed to have been received as of February 2, 1981, as explained in Mr. Range's letter to you of the latter date. As Mr. Range's letter explained, ORO's response is limited to item 9, as modified, and item 11.

Enclosed in response to item 9 is a listing, by year from 1957 through 1975, of funds provided by DOE's predecessor agencies, the Atomic Energy Commission and the Energy Research and Development Administration, to the Medical and Health Sciences Division of Oak Ridge Associated Universities. The amounts for years 1962 through 1975 were extracted from DOE sources; the entries for 1957 through 1961 were obtained from ORAU records because existing DOE records do not cover that period.

Enclosed in response to item 11 is a December 1970 publication, numbered ORAU-112. It is furnished you without deletions.

Transmittal of the enclosure completes ORO's response to your request. Inasmuch as the cost of reproducing the documents did not exceed DOE's de minimus amount, there is no charge associated with our response.

Sincerely,
ORIGINAL SIGNED BY
H. S. OSTER, JR

H. S. Oster, Jr.
Acting Assistant Manager
for Administration
Authorizing Official

CC-10:JLF

Enclosures: As stated

CERTIFIED MAIL:
RETURN RECEIPT REQUESTED

PERSONNEL-1

DOE F 1325.10
(7-79)

OFFICIAL FILE COPY

FOIA 783

bcc: Wayne Range, PIO
W. R. Bibb, Dir., Research Div.
Dr. C. C. Lushbaugh, ORAU

CC-10:JLFoutch:cd:6-1204:2/5/81

CONCURRENCE	
RTG. SYMBOL	CC-10
INITIALS/SIG.	Foutch
DATE	2/5/81
RTG. SYMBOL	AD-40
INITIALS/SIG.	Oster
DATE	2/5/81
RTG. SYMBOL	
INITIALS/SIG.	
DATE	
RTG. SYMBOL	
INITIALS/SIG.	
DATE	
RTG. SYMBOL	
INITIALS/SIG.	
DATE	
RTG. SYMBOL	
INITIALS/SIG.	
DATE	
RTG. SYMBOL	
INITIALS/SIG.	
DATE	
RTG. SYMBOL	
INITIALS/SIG.	
DATE	

1114113

2/6/81

DOE FUNDS PROVIDED FOR THE MEDICAL AND HEALTH SCIENCES DIVISION, ORAU, UNDER DOE CONTRACT NO. DE-AC05-76OR00242

Financial plans for years 1957 through 1975 are not available. Funds indicated below were extracted or derived from various budget and financial resources ($ in thousands).

	$		$
1975	1,170	1965	1,323
1974	1,827	1964	1,548
1973	1,800	1963	1,377
1972	1,819	1962	1,254
1971	1,836	1961	977
1970	1,869	1960	885
1969	1,777	1959	835
1968	1,799	1958	668
1967	1,592	1957	639
1966	1,490		

1114114

FOIA

ORAU-112

HEMATOLOGIC AND THERAPEUTIC EFFECTS OF TOTAL-BODY IRRADIATION (50 R TO 100 R) IN PATIENTS WITH MALIGNANT LYMPHOMA, CHRONIC LYMPHOCYTIC AND GRANULOCYTIC LEUKEMIAS, AND POLYCYTHEMIA VERA

December 1970

Medical Division
Oak Ridge Associated Universities, Incorporated
Oak Ridge, Tennessee

UNITED STATES ATOMIC ENERGY COMMISSION · DIVISION OF TECHNICAL INFORMATION

1114115

ORAU-112
BIOLOGY AND MEDICINE
(TID-4500)

HEMATOLOGIC AND THERAPEUTIC EFFECTS OF TOTAL-BODY IRRADIATION (50 R–100 R) IN PATIENTS WITH MALIGNANT LYMPHOMA, CHRONIC LYMPHOCYTIC AND GRANULOCYTIC LEUKEMIAS, AND POLYCYTHEMIA VERA*

G. A. Andrews, F. V. Comas, C. L. Edwards, R. M. Kniseley,
C. C. Lushbaugh, and Helen Vodopick

* *From the Medical Division, Oak Ridge Associated Universities, under contract with the U. S. Atomic Energy Commission.*

1114116

CONTENTS

Page

Hematologic and Therapeutic Effects of Total-Body Irradiation (50 R-100 R) in Patients with Malignant Lymphoma, Chronic Lymphocytic and Granulocytic Leukemias, and Polycythemia Vera 1

Introduction 1
Materials and Methods 3
Laboratory Methods 7
The Radiation Facility and Dosimetry 7

Observations 8

Chronic Lymphocytic Leukemia 8
Malignant Lymphoma 12
Hodgkin's Disease 17
Chronic Granulocytic Leukemia 18
Polycythemia Rubra Vera and Primary Thrombocythemia. 23
Changes in Uric Acid 27

Discussion 28

Lymphocytes 30
Granulocytes 31
Platelets 32

Summary 32

Acknowledgements 33

References 34

Appendices 36

1114117

Hematologic and Therapeutic Effects of Total-Body Irradiation (50 R - 100 R) in Patients with Malignant Lymphoma, Chronic Lymphocytic and Granulocytic Leukemias, and Polycythemia Vera*

G. A. Andrews, F. V. Comas, C. L. Edwards, R. M. Kniseley, C. C. Lushbaugh, and Helen Vodopick

Introduction

Since 1957 the staff of the Medical Division of Oak Ridge Associated Universities has been studying the hematologic and clinical courses of patients receiving total-body irradiation. In an early experiment the radiation therapy was done in connection with attempts to graft bone marrow (1). We also have studied intensively the hematologic courses of victims of accidental exposure to radiation (2-7). The present report covers the therapeutic and hematologic results of a ten-year study — 1959 through 1968 — of single exposures of 50 R and 100 R given at approximately 1.5 R/min in a specially designed facility for total-body radiation therapy. Some of the data from this series have been published previously in brief form (8).

This study was initiated with two principal objectives; the first was to seek information that might lead to improved radiation therapy for disseminated malignant disease, especially leukemia and lymphoma, by determining the best criteria for selection of patients, radiation dose, and dose rate. For many years radiotherapists have been able to control progression of certain hematologic disorders by giving "spray X-irradiation" and have obtained similar effects using internally administered radiation, in particular phosphorus-32 (9). Fractionation and dose protraction quite logically have been used to reduce the incidence of undesirable side effects and are believed also to decrease the damage to normal tissues more than to malignant ones. However, differences in fractionation, energy of the beams, and uniformity of exposures to different parts of the body make it difficult to evaluate and compare the effects of various radiation-exposure patterns used in such therapy.

The second objective was to acquire radiobiologic information. The radiobiologic aspects of total-body irradiation on man have been studied clinically

---

* From the Medical Division, Oak Ridge Associated Universities, under contract with the U. S. Atomic Energy Commission.

1114118

since Walsh (10) first described radiation sickness in 1897. The dose-response relationships, however, are still poorly known and present estimates are based largely on conjectures and extrapolations from animal experiments, or from experience with accident victims, atom bomb casualties, and patients treated by irradiation. Because patients in the past ordinarily have been treated with divided doses, it has been difficult to compare biologic effects in the many clinical series with each other, or with the effects seen after radiation accidents.

We decided to obtain baseline data by giving individual doses of 50 or 100 R and then observing the patients long enough to evaluate effects. These single doses of radiation, somewhat higher than individual doses in a fractionated regimen, would provide a response that could be measured with a clear temporal relation to the date of irradiation. In contrast, an effect gradually induced by two or more variably spaced small doses would be more difficult to analyze and compare among groups of patients. Single exposures also would permit us to compare the hematologic responses with those of accident victims who usually receive single rapid exposures. Careful definitions of the effects of 50 R and 100 R, as attempted in this paper, are a necessary basis for later evaluating the effect of fractionation.

It was not our plan to evaluate the long-range effectiveness of these relatively large individual doses of total-body irradiation as a repetitive and sole therapy. This would have required establishing a total treatment plan with this technique, which we were not prepared to do. The larger doses provide a less continuous control, a possible disadvantage emphasized by Osgood. We wanted to be able to add or substitute other forms of treatment when specific clinical considerations seemed to indicate them. One should not infer from this study that we expected these individual or infrequently given exposures to produce better clinical results than fractionated total-body or portal irradiation. At present we feel that some pattern of fractionated exposure, such as that of R. E. Johnson (11), probably offers a preferable approach for total-body radiotherapy. The data reported here, by defining the range of clinical and hematologic effects that single exposures of 50 and 100 R can be expected to produce in these diseases, should provide a yardstick for comparisons in future total-body irradiation trials using different exposure patterns.

Such information, even though obtained in the abnormal conditions of disease, is helpful for assessing levels of accidental gamma and neutron irradiation injury and guiding therapeutic efforts. During the course of the study the urgent need arose for information on hematologic effects in man, since the National Aeronautics and Space Administration was faced with potentially high levels of radiation exposures in space exploration. The principal answers we sought were the pattern of responses for leukocytes, red blood cells, and platelets in chronic lymphocytic leukemia, lymphoma, chronic granulocytic leukemia, and polycythemia rubra vera. What differences occurred in response to 50-R and 100-R exposures? Did normal blood cells differ in radiosensitivity from their counterparts in proliferative disorders? For example, do platelets have a different radiosensitivity in chronic lymphocytic leukemia or lymphoma compared with polycythemia rubra vera? Or, do "normal" lymphocytes of polycythemia rubra vera have the same sensitivity as lymphocytes of chronic lymphocytic leukemia? We also wanted to observe

1114119

the degree and length of clinical improvement as manifested by relief of general symptoms, and regression of masses, lymph nodes, liver, and spleen. In addition, we wanted to determine the incidence and analyze the nature of the unpleasant symptoms of acute radiation exposure which are included in another study (12).

This report completes one phase of our total-body irradiation study program. In brief this study will: 1) provide baselines for the study of fractionation effects, 2) be simpler to analyze than more complex regimens, 3) provide information relevant to radiation injury in "normal" humans. It will not: 1) demonstrate that 50 or 100 R is better than the currently accepted fractionation modes, or 2) analyze the long-range therapeutic effectiveness of these doses.

Materials and Methods

Patients - A total of 89 treatments were given. This report covers information on 29 exposures to 50 R, and 55 to 100 R. The remaining five were dropped from the protocols because of an urgent need for additional or different therapy before the study was finished, or because of the patient's inability to meet the appointments for follow-up outpatient visits during the study period. The number exposed and their disease categories are listed in Table 1, along with the abbreviations used in the text.

All patients with these diseases admitted to the Medical Division hospital during this period were considered for this therapeutic program. The diagnoses were established by clinical history, physical examination, and microscopic study of surgical biopsies, bone marrow, and peripheral blood samples. The urgency for treatment was assessed, and those patients whose condition required some other kind of therapy, or no therapy at all, were omitted. If the clinical status was changing rapidly and we anticipated that other additional treatment might be needed during the postirradiation observation period, these patients were also excluded. If no clearly superior therapy was available for a particular patient and the total-body radiation treatment was regarded as an acceptable way of management, the patient was offered this form of treatment, following an explanation of the research protocol. Informed consent was obtained in accordance with ethical practice to protect the rights of the individual as a research subject. We recognize some bias in the selection of one of the two doses. In a concern for the patient's safety early in the study we evaluated only the results of 50-R exposures before using the higher dose. Later, some of the patients selected for the 100-R exposure were those with more pronounced symptoms, or in lymphoma, had tumor masses that were judged to need the more vigorous treatment. On reviewing histories and clinical status,* however, we believe that these biases are not sufficiently great to prevent us from comparing a 50-R group with a 100-R group. Other forms of treatment for the disease were discontinued before the irradiation, except that

* Summaries of clinical histories and status changes of the individual patients have been collated and included in the Appendix of this report.

1114120

in a few patients who required it, maintenance steroid therapy was kept up (see Tables D and E in Appendix). Of the patients with chronic lymphocytic leukemia, blood transfusions were given during the six-week posttreatment period (Table 2) to three exposed to 50 R and four patients exposed to 100 R. No other treatments were given during this time.

Table 1

Patients Exposed to Total-Body Radiation in Each of the Disease Categories

	50 R			100 R		
	1st R_x	2nd R_x	Total R_x	1st R_x	2nd R_x	Total
Chronic Lymphocytic Leukemia (CLL)	12	3	15	16	4	20
Malignant Lymphoma	5	0	5	17	5	22
Hodgkin's Disease	1	0	1	1	0	1
Chronic Granulocytic Leukemia (CGL)	6	2	8	4	0	4
Polycythemia Rubra Vera (PRV)	0	0	0	7*	1	8
Total			29			55

*One patient had primary hemorrhagic thrombocythemia rather than PRV.

Hodgkin's disease was originally included in the study but was eliminated early because we believed that a larger dose is needed to control the malignant process than we could safely give to the whole body at one time. The most effective modern therapy for this disease is irradiation of lymphatic tissues, sometimes involving large fields, but allowing some hematopoietic tissue to remain unirradiated. The lesions of this disease are generally less radiosensitive and less intimately involved in hematopoietic tissue than those that can be helped by total-body irradiation.

Study Protocol - A uniform study protocol was devised to collect laboratory data on specified days during the six-week study period (Table 3). The six-week period of data collection was adopted as the most reasonable compromise between clinical research objectives and patient's needs; a longer period would

1 1 1 4 1 2 1

Table 2

The Requirement for Blood Transfusions in Patients with Chronic Lymphocytic Leukemia Before and After Radiotherapy with 50 R and 100 R TBI

		Transfusions during 6 weeks pretreatment		Transfusions during 6 weeks posttreatment	
Radiation Dose	No. Patients	No. Patients	No. Trans.	No. Patients	No. Trans.
50 R	13	3	18	3	15
100 R	8	3	15	4	31

have been clinically more desirable, and most of the patients continued under our care and had further observations. Because of the enormous spread of initial blood values, all results were normalized by using the immediate pretreatment values for each patient as 100%. In most instances, this value consisted of the average of day minus three and day zero (pretreatment) counts; in a few only day zero values were available. Table 4 gives the ranges and geometric means of the pretreatment data from which the normalized curves were derived.

Table 3

Protocol for Blood and Bone-Marrow Sampling Times Used in 50 R and 100 R TBI Study for All Patients

Radiation Day	-7	-3	0	+1	+2	+3	+4	+7	+14	+21	+28	+35	+42
Bone Marrow		x					x				x		
WBC, RBC, Platelets Blood Film, Hgb., Hct.	x	x	x	x	x		x	x	x	x	x	x	x
Uric Acid		x	x	x			x	x	x	x	x		

1114122

Table 4

Range of Pretreatment Blood Values Among Patients in Each Category

(Average of Day -3 and Day 0)

Diagnostic Group	No. of Exposures	Leukocytes $mm^3 \times 10^3$			Absolute Lymphocytes/$mm^3 \times 10^3$			Platelets/$mm^3 \times 10^3$			Hemoglobin gm/100 ml		
		Range		Geom. Mean	Range		Geom. Mean	Range		Geom. Mean	Range		Geom. Mean
		High	Low		High	Low		High	Low		High	Low	
Polycythemia Vera 100 R	8	41.6	10.0	25.3	4.2	1.2	2.1	1,619	289	806.1	15.9	11.6	13.6
Chronic Lymphocytic Leukemia - 50 R	15	304.0	9.8	83.5	294.9	9.4	76.9	337	40	131.9	16.8	8.3	12.5
Chronic Lymphocytic Leukemia - 100 R	20	396.2	6.2	69.8	388.6	4.3	61.4	412	13	113.1	14.8	6.9	11.4
Chronic Granulocytic Leukemia - 50 R	8	463.9	52.1	114.5	9.8	1.1	3.5	1,061	211	446.5	14.2	9.0	11.3
Chronic Granulocytic Leukemia - 100 R	4	246.3	103.8	148.5	4.2	0.9	2.1	1,326	392	707.5	12.0	9.0	10.4
Malignant Lymphoma 50 R	5	14.2	6.5	9.6	9.9	1.6	4.5	238	50	134.1	16.2	9.7	13.5
Malignant Lymphoma 100 R	22	28.3	2.3	7.7	26.9	1.1	3.4	444	45	205.0	15.8	8.5	12.4
Hodgkins - 50 R	1			10.0			2.9			310			11.0
Hodgkins - 100 R	2	11.5	9.0		10.3	2.0		521.2	481.2		10.2	8.2	

1114123

Bone-marrow aspirations were performed according to the protocol described; we have decided not to present the findings in the present report.

Laboratory Methods

The hematologic studies were performed on venous blood samples using well established laboratory methods. The hemoglobin value was determined by the cyanmethemoglobin method and hematocrit percent by the Wintrobe method. Leukocytes and erythrocytes were counted electronically. Platelets were enumerated by the method of Brecher and Cronkite using phase microscopy (13). When platelet counts were low, dilutions of 1:20 were used rather than 1:100. The number of small squares counted in the chamber was increased to 10, 25, or 50 until more than 100 platelets were counted, or all platelets in 50 squares counted. In determining absolute lymphocyte values for patients with PRV, we performed differential counts on 400 leukocytes for greater statistical confidence.

The Radiation Facility and Dosimetry

The irradiation room, designated the medium-exposure-rate total-body irradiator (METBI), was completed in 1959; it is an eight-foot cube, concrete shielded, with a 385-curie source of cesium-137 in each of the eight corners. A maze connects the treatment room to its control room where a nurse or operator is in visual contact with the patient by a series of mirrors. The patient lies on an aluminum bed suspended in the center of a homogenous 2 x 2 x 6 foot radiation field. The beams from the eight sources are shaped so that the exposure rate is uniform to within ± 5% within the treatment volume. The exposure rate can be varied by a series of attenuating filters and values from 0.64 to 1.52 R/min have been used; but most treatments were given at 1.50 R/min. This facility has been described in detail by Brucer (14) and a detailed description of the radiation field has been published (15).

We made two independent dosimetry studies to determine the dose received by patients. We filled three compartmentalized phantoms with Fricke chemical dosimeter and determined spectrophotometrically the average dose to each of the 13 compartments. In addition, we measured the midplane isodose lines by an ionization probe; details are given by Hayes et al (16). In the second study,* with a tissue-equivalent plastic phantom containing an implanted skeleton and density-adjusted lung spaces, we measured the dose to various organs using LiF thermoluminescent dosimeters in the volumes representative of these organs. Except for the bone marrow, the average rad response of the dosimeters in an organ was defined as the average organ dose. We calculated the marrow dose as a weighted average since this tissue, located at variable depths beneath the

---

* W. L. Beck and T. R. Stokes performed the thermoluminescent dosimetric measurements as part of our continuing total-body irradiation program.

1114124

Table 5

Variations in Average Dose to Body Compartments According to Body Size

Compartment	Average Compartment Dose in Rads Per 100 R		
	Adult*	Adolescent*	Child*
Head	78	81	79
Neck	76	83	84
Chest	63	66	70
Abdomen	66	69	71
Pelvis	65	70	71
Arms	76	78	75
Thighs	75	78	82
Legs	86	88	87
Feet	76	78	81
Whole Body	70	74	75

*Hayes Water Phantoms

surface, is not placed uniformly in a single, well defined site. The assumed marrow distribution used for the dose estimates was that suggested by R. E. Ellis (17) for a normal man. It is well known that its volume and location varies widely in patients with the diseases studied here.

The average tissue dose to the total torso of a standardized normal adult was estimated by each of the dosimetry studies to be 65 rads/100-R exposure by the compartmentalized phantom study and 68 rads/100 R by the heterogeneous phantom. The minimal bone-marrow dose occurs in the pelvic region and is only 53 rads/100 R. Variations in dose due to difference in body size and configuration are shown in Table 5. Table 6 lists the absorbed dose in various organs.

OBSERVATIONS

Chronic Lymphocytic Leukemia

During the first six weeks after therapy in 35 patient treatments with either 50 R or 100 R, palpable lymph nodes shrank in 20 and remained unchanged in 12.

1114125

Table 6

Anatomical Organ Doses in Cesium-137 Total-Body Irradiation Facility

Organ	Total Organ Dose (Rads/100 R)		
	Average	Ranges	
Bone Marrow	64	53-86	(137)*
Cerebellum	77	74-81	(9)
Cerebrum	75	70-79	(21)
Heart	66	58-70	(16)
Intestines	67	54-76	(107)
Kidneys	66	62-70	(6)
Lenses of Eyes	87	85-90	(2)
Liver	67	61-78	(42)
Lungs	67	58-77	(185)
Skin (above sternum)	73	72-75	(2)
Skin (front waist)	74	72-75	(2)
Spleen	69	64-73	(7)
Stomach	64	59-69	(34)
Thyroid	76	75-77	(2)

*Figures in parentheses indicate the number of bodily locations where dose was measured with LiF dosimeters.

Of the palpable spleens, ten were smaller after treatment, seven remained unchanged, but palpable, and seven enlarged during the same interval. There was no clear pattern of change in liver size.

Twelve patients gained weight, 13 lost, and eight had no change. (The others are unrecorded.) The general feeling of well-being improved to some degree in 21, remained unchanged in 12, and decreased in two. We could not demonstrate with any of these clinical responses that the effect of 100 R was greater than that of 50 R, although the small numbers of patients is a deterrent to comparisons.

1114126

Figure 1 shows the WBC responses of individual patients to 50 R and Fig. 2 those to 100 R. Radiosensitivity differed considerably from patient to patient. In both groups of patients (50- and 100-R exposures) there was a subgroup of "resistant" patients whose response was significantly less pronounced. There was no trend of climbing toward pretreatment values by day 42 in either dose or sensitivity subgroup.

Figure 3 shows the changes in mean blood lymphocyte numbers following 50-R and 100-R exposures in the resistant and sensitive patients. We saw no statistically significant differences in the degree of lymphocyte depression caused by these two doses. Although the most rapid fall occurred in the first week, a nadir was not reached until three or four weeks after exposure.

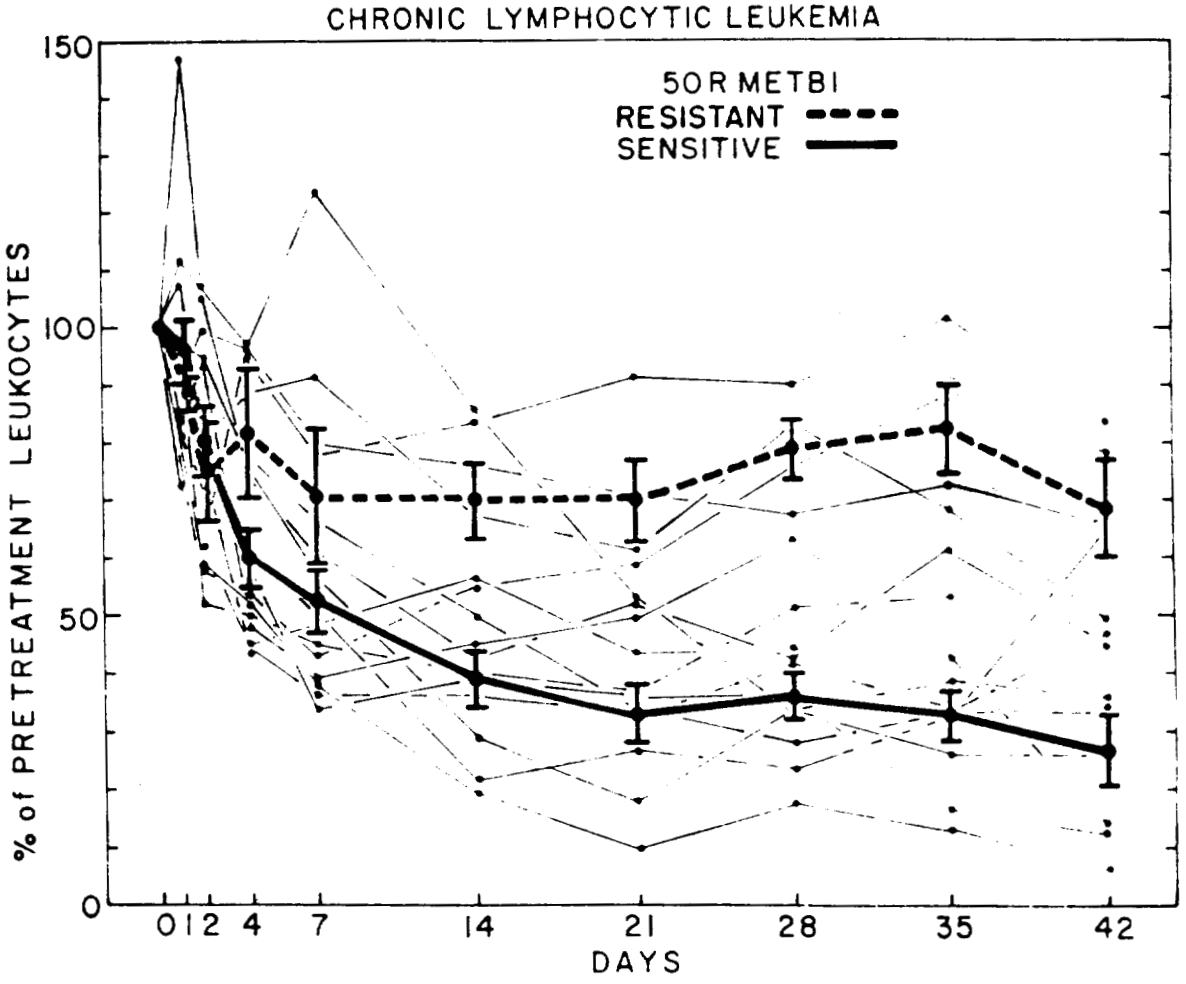


Fig. 1. Changes in the white blood levels in 15 patients with chronic lymphocytic leukemia after 50 R. The leukocyte counts have been normalized to the individual patient's pretreatment values. Two geometric means with their standard errors are shown; one (solid line) is that for the leukocyte levels in the 11 more responsive patients and the other (dotted line) is that for the four patients whose course seems more resistant. The two computed means (after seven days) are statistically different at the 95% confidence level.

1114127

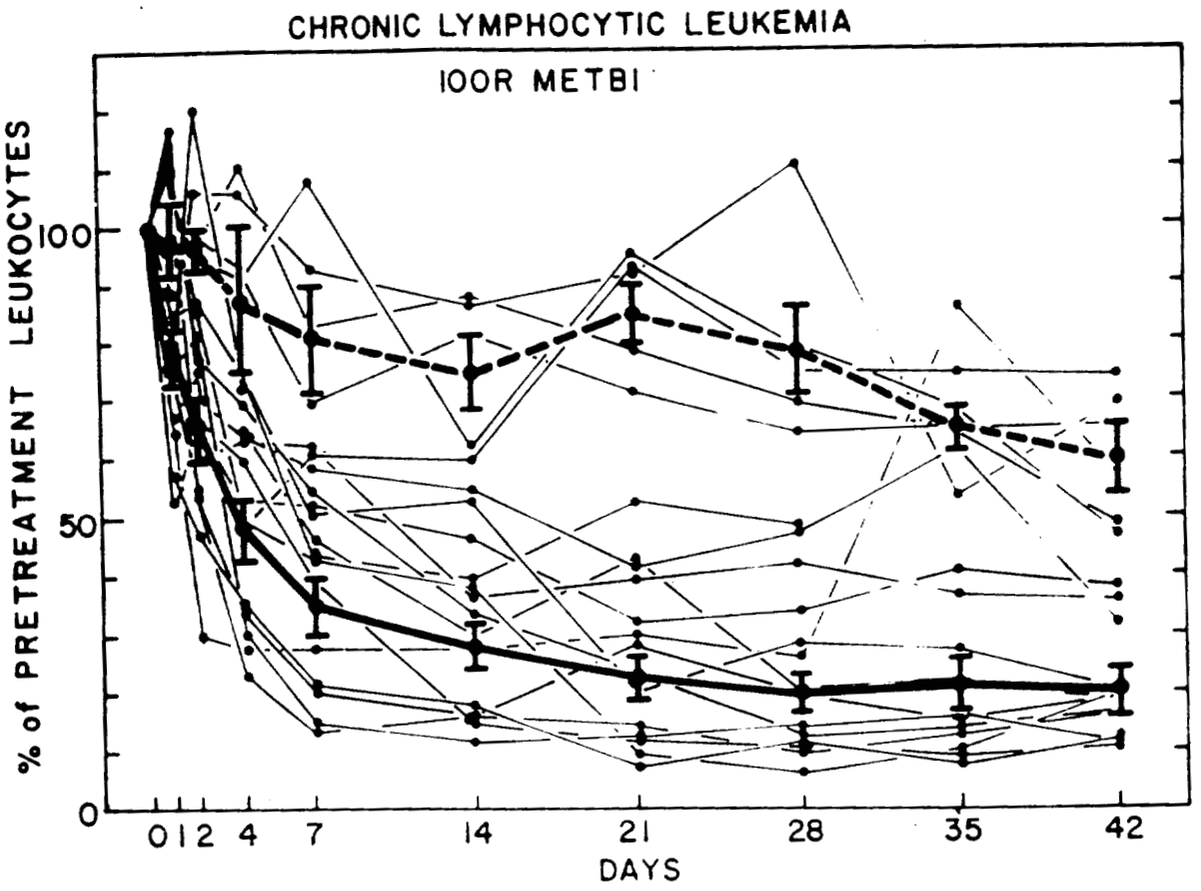


Fig. 2. Changes in the white blood counts (shown in Fig. 1) of 19 patients with chronic lymphocytic leukemia after 100 R. As in Fig. 1, the two geometric means are those for the 14 "sensitive" and five "resistant" patients and are significantly different at the 95% level from the second day onward.

The response of leukemic lymphocytes to 100 R was unrelated to the level of the pretreatment leukocyte counts, nor did it correlate with lymphocyte size, notching of nuclei, or tendency to smudge. The degree of marrow infiltration as judged by histologic examination of marrow aspirated did not tell us why some patients had "radioresistant" lymphocytes. Furthermore, we found no correlation between the lymphocyte response and the clinical response or length of "remission"; eight patients required no other treatment for seven and a half or more months, while nine patients needed additional treatment for leukemia shortly after the study period, less than three months from the irradiation.

While the leukemic lymphocytes responded similarly to 50 R and 100 R, the effect of these two doses on the platelet levels differed strikingly as shown in Figs. 4 and 5. These graphs show also that the responses of patients given 50 R vary more than those of patients given 100 R, suggesting that recovery may be manifested more variably with the lower dose. A trend toward recovery

1114128

is definitely established during the fifth and sixth weeks after exposure. As can be seen in Fig. 6, the recovery in numbers of circulating platelets after 50 R occurs earlier and more rapidly on the average than after 100 R. The standard errors of these geometric means are also larger with the lower dose indicating the greater variability of the response to the lower dose.

Hemoglobin values remained stable in the 10 patients not anemic before treatment; those that were anemic usually had no rise in their hemoglobin levels or became more anemic during the six weeks following irradiation. In a few patients who had been requiring transfusions before treatment, the 100-R exposure increased the number of transfusions needed while 50 R did not (see Table 2).

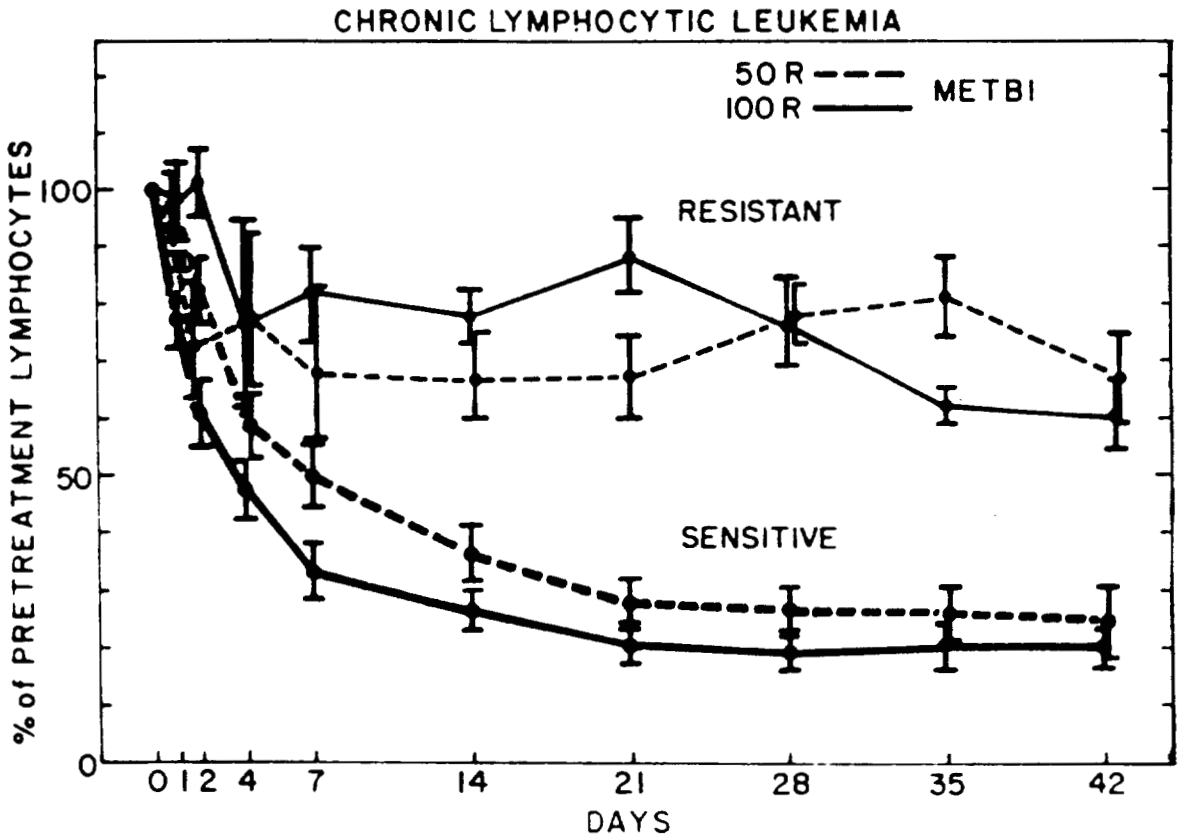


Fig. 3. Changes in the geometric-mean blood lymphocyte values (shown as normalized percentages of pretreatment differential lymphocyte counts) for the patients with chronic lymphocytic leukemia whose changes in white blood cell values are shown in Figs. 1 and 2. There is no statistical difference between the computed mean changes after 50-R and 100-R exposures in either the "sensitive" or "resistant" groups but the statistically valid difference between the mean responses of the two groups is obvious.

Malignant Lymphoma

This group of 20 patients included five who were given 50 R, two of whom subsequently received 100-R treatments. Of the 17 patients who received 100 R,

1114129

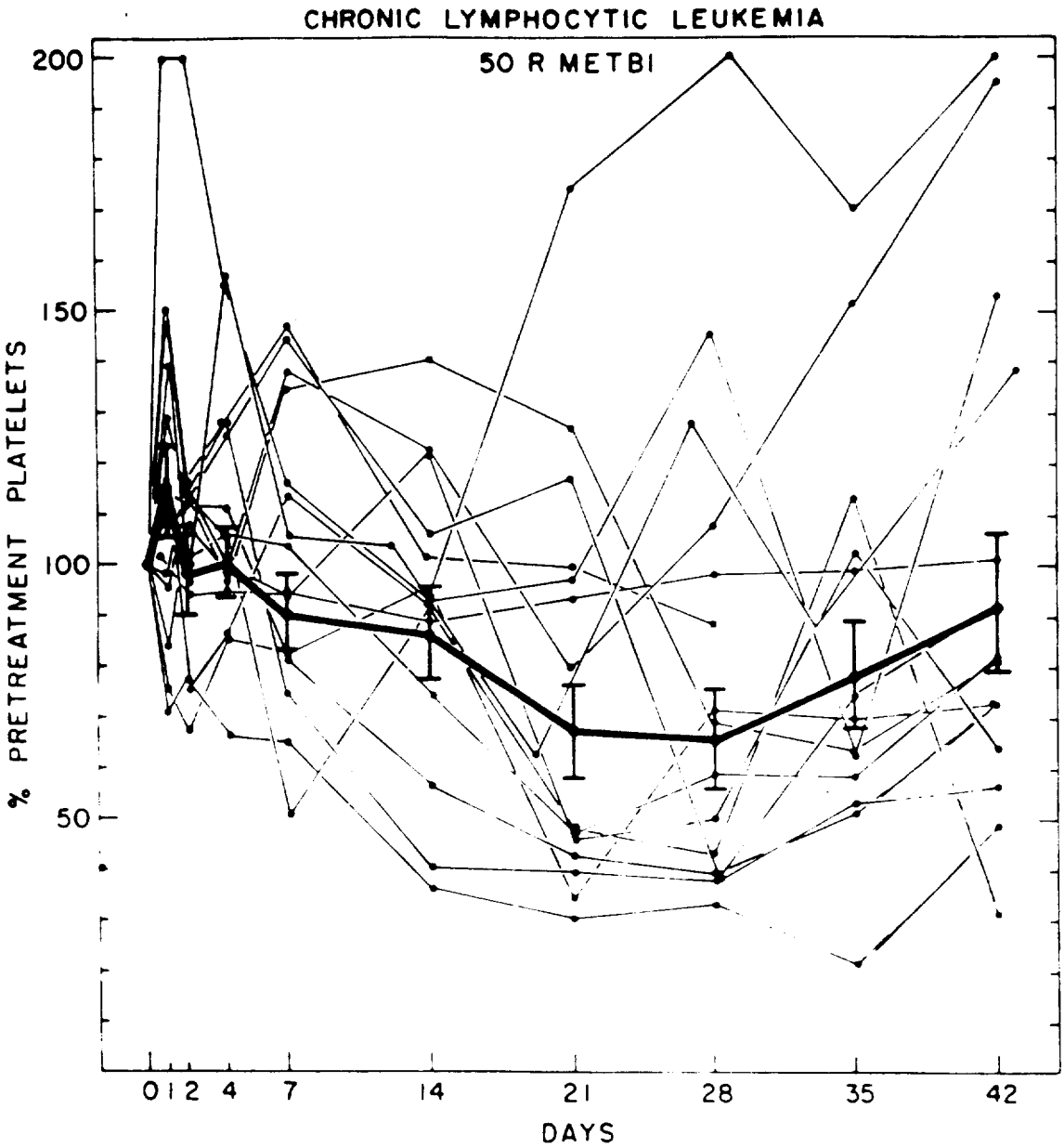


Fig. 4. Changes in the individual and geometric mean percent of pretreatment platelet levels in 15 patients with chronic lymphocytic leukemia after 50 R.

five were given a second 100-R treatment. There were 27 exposures in all.

During the first six weeks after treatment there was no clear difference in clinical responses between the 50-R and 100-R groups. In the 27 treatments, 23 of the 27 patients showed at least some degree of shrinkage of lymph nodes; 17 responded moderately or substantially, while in three the nodes remained unchanged and in one they enlarged after therapy. In the eight patients with palpable spleens, only two spleens definitely regressed, while five others

1114130

remained large and one was questionably changed. Nine palpable livers regressed while eight remained unchanged or enlarged. There was no consistent pattern of change in body weight. The subjective general feeling of well-being remained poor or unchanged in 17 patients, while 10 expressed some degree of improvement.

Most of these patients had at least a few atypical lymphocytes in the blood, and we were unable to separate definitely those that should be considered as having a "leukemic" stage of lymphosarcoma, except for two who had larger numbers of abnormal cells. These two patients described in a later paragraph responded

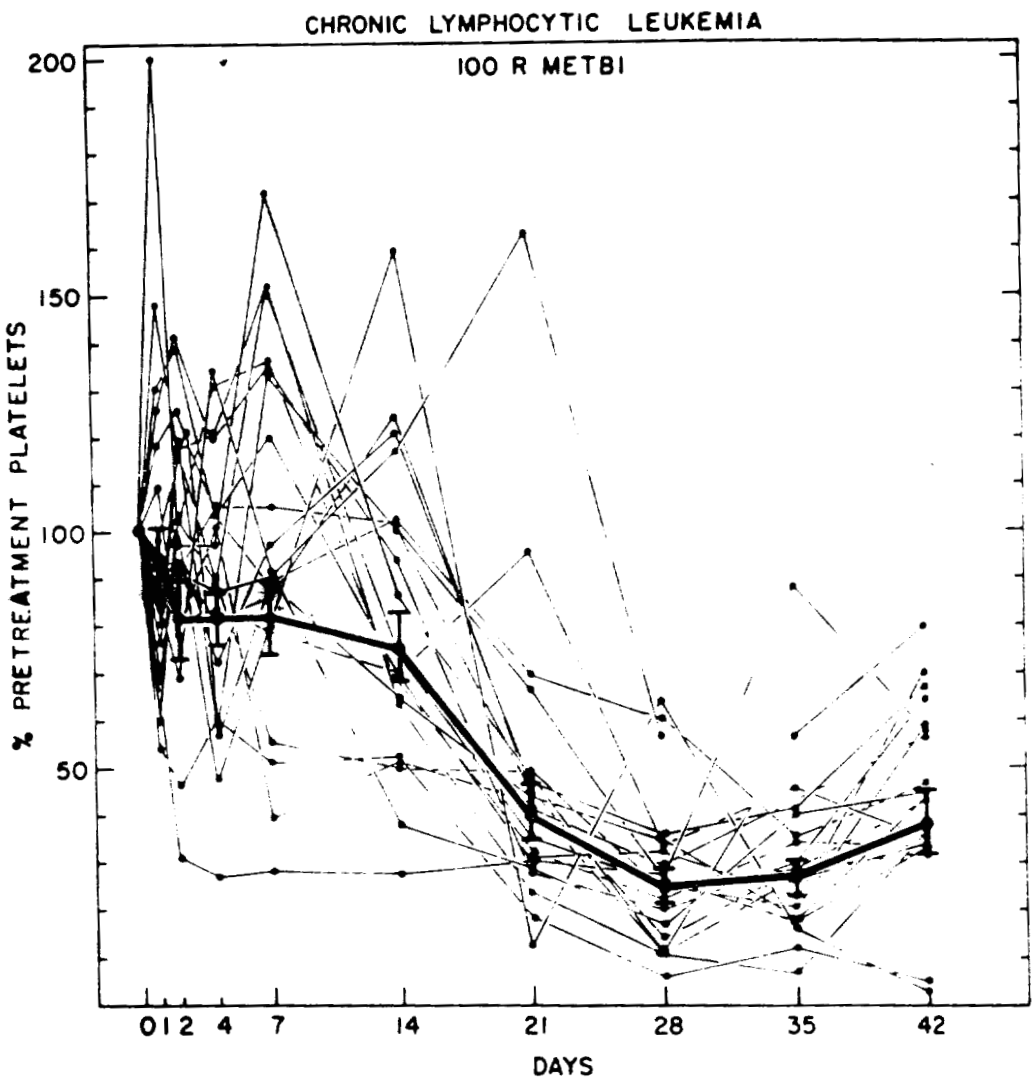


Fig. 5. Changes in the individual and geometric mean percent of pretreatment platelet levels in 20 patients with chronic lymphocytic leukemia after 100 R. Comparison of the geometric means and their standard errors in this figure and in Fig. 4 shows that the degree of response in the two dosage groups differs significantly from 21 days on. Five individual patients who received 50 R, however, reacted as the 100-R group, while three in the 100-R group responded similarly to the 50-R patients.

1114131

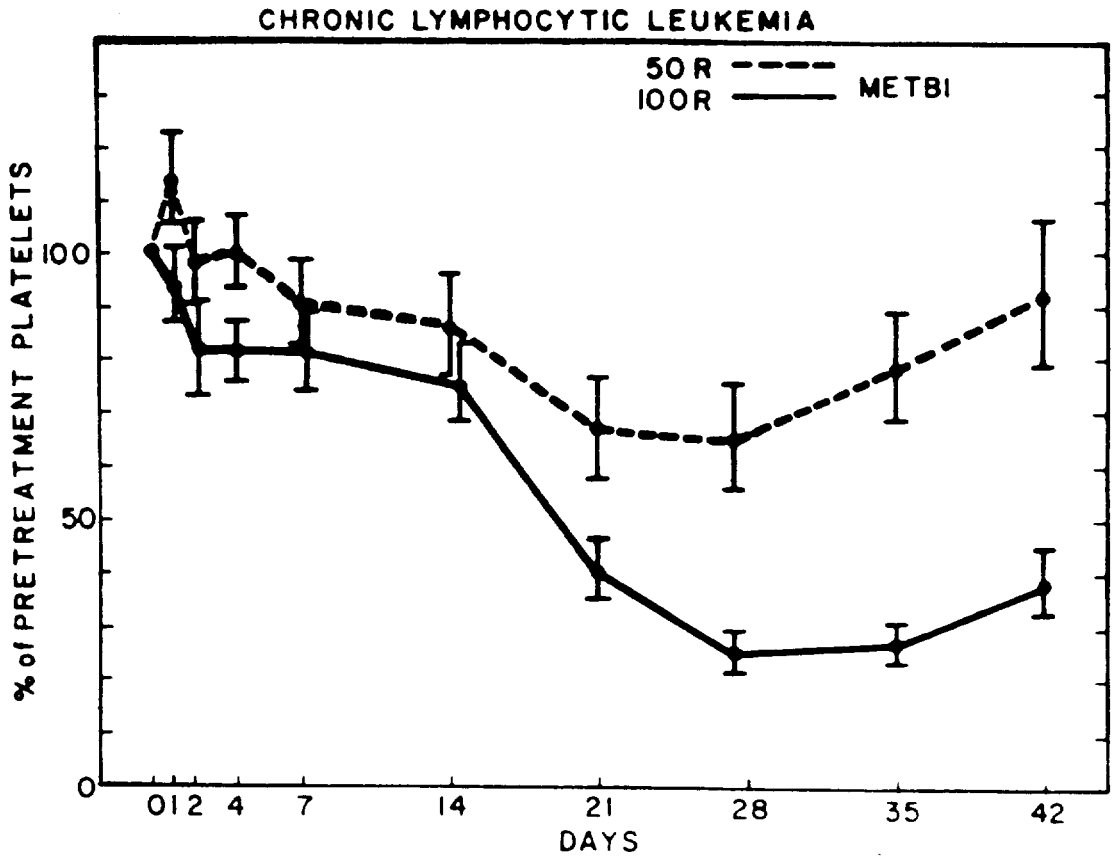


Fig. 6. Comparison of the geometric means for blood platelet levels in patients with chronic lymphocytic leukemia after 50 and 100 R. The curves become statistically different only after 21 days.

quite differently from the rest of the group. All the others had pretreatment leukocyte counts of less than 15,000/mm^3; the numbers of lymphoid cells were less than 11,000/mm^3. The subsequent decrease in lymphocytes was not great (the lowest value was about 50% of pretreatment level, reached at seven days). In the majority of the patients (11/17) lymphocyte levels began to recover from this decrease by 14 days; this was unlike the response in CLL. In Fig. 7 the geometric means for the leukocytes of the main groups of patients with malignant lymphoma who received 100 R are plotted, along with one standard error of the mean. The changes in total leukocytes after 100 R in patients with malignant lymphoma have been graphed in Fig. 7 for comparison with later graphs in this study and with those of other investigators who have not differentiated the hematologic response of the various white blood cell types. In Fig. 8 the sequential changes in lymphocyte counts in individual patients can be seen varying widely.

By contrast, in the two "leukemic" patients with high numbers of abnormal lymphoid cells in the blood before irradiation (16,000 and 26,000/mm^3) these cells decreased profoundly and rapidly after 100 R. Their course differed

1114132

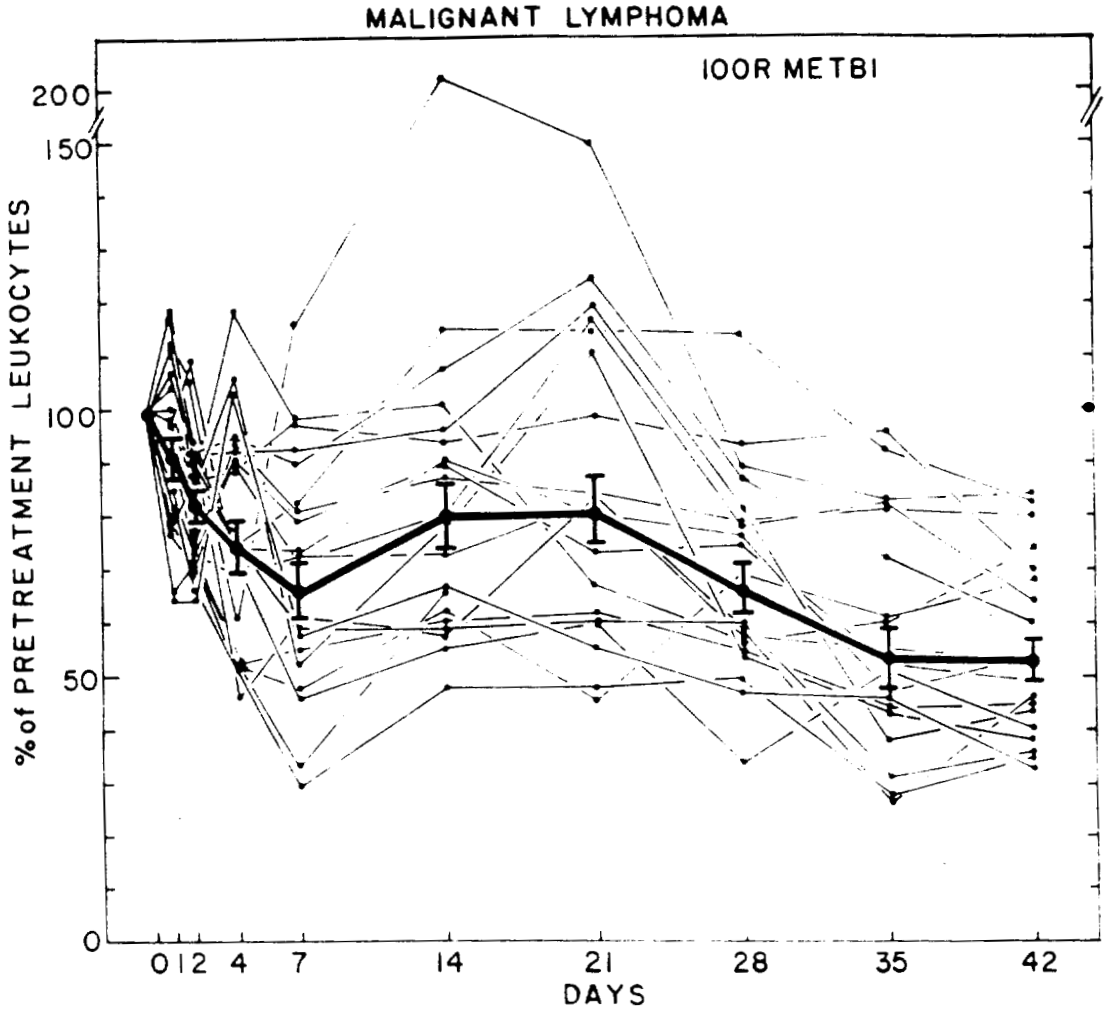


Fig. 7. Changes in blood leukocyte values in 20 patients with malignant lymphoma after 100 R. The actual WBC counts have been normalized to individual pretreatment levels and the geometric mean and its standard error computed on this basis.

considerably from that of the other members of the lymphoma group and resembled more closely the extreme responders of the chronic lymphocytic leukemia groups. (See Figs. 1-3).

The platelet values for the 50-R group dropped only slightly on the average and varied widely from patient to patient. In the 100-R group, the platelets responded more consistently; a steep drop appeared during the third and fourth weeks and reached a nadir of 27% of the pretreatment values. This curve resembles quite closely that of the patients with chronic lymphocytic leukemia given the same dose (Fig. 4). All showed a trend toward recovery during the fifth and sixth weeks (Figs. 4 and 10). Hemoglobin values did not change significantly during the six weeks after irradiation with either 50 R or 100 R.

1114133

Hodgkin's Disease

Only three patients with Hodgkin's disease were treated. One patient who received 50 R early in her disease failed to respond and was quickly transferred to more conventional therapeutic regimens. The second patient, who received 100 R, showed similarly no benefit, and the third one failed to return after two weeks for further follow-up studies. The platelet and lymphocyte responses for the 50-R and 100-R exposure behaved as in patients with other types of lymphomas.

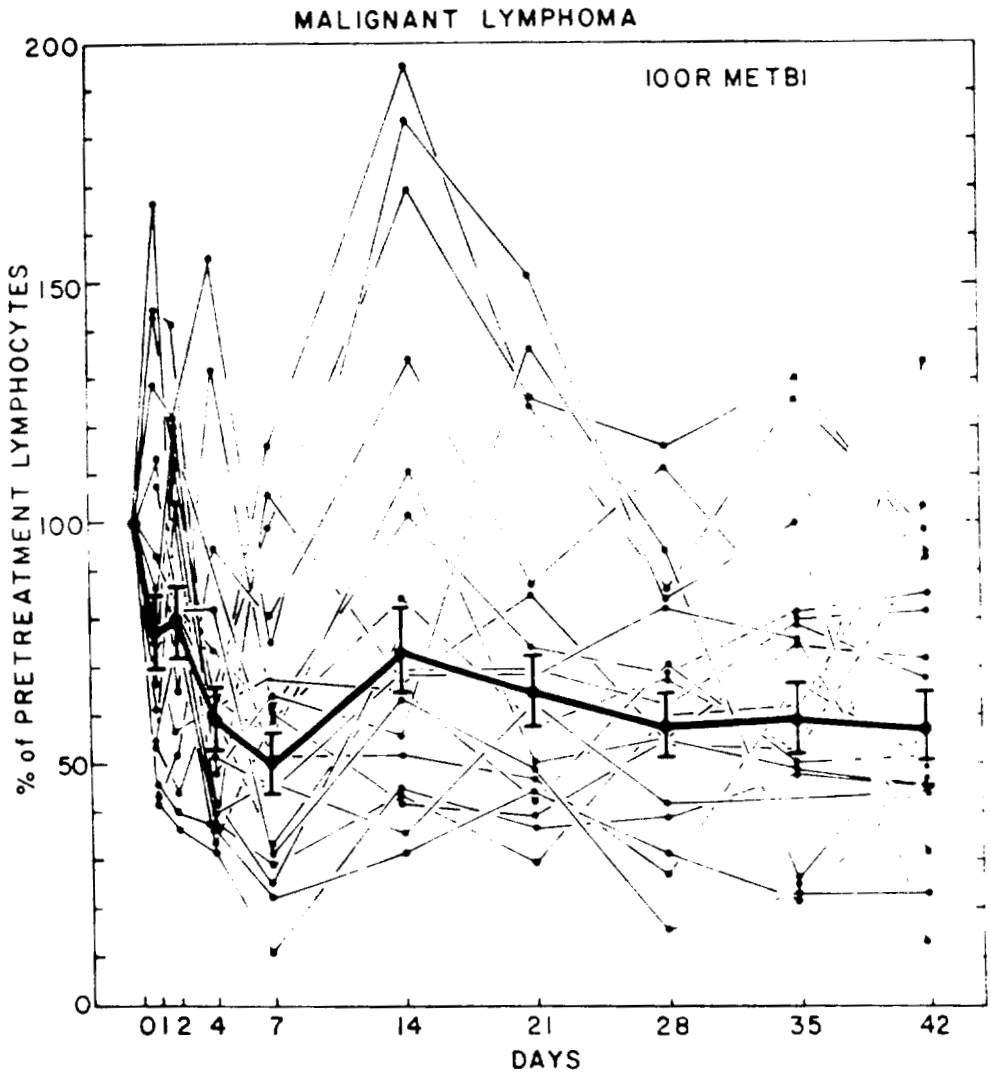


Fig. 8. The changes in Fig. 7 are shown here as changes in lymphocyte levels computed from individual absolute lymphocyte counts before and after exposure. These extremely variable responses of individual patients reduce to a geometric mean not statistically different from that of the "resistant" type of response in lymphocyte levels of patients with chronic lymphocytic leukemia treated with either 50 or 100 R (see Fig. 3). In several of these patients total-body irradiation obviously resulted in lymphocytosis in relation to pretreatment levels.

1114134

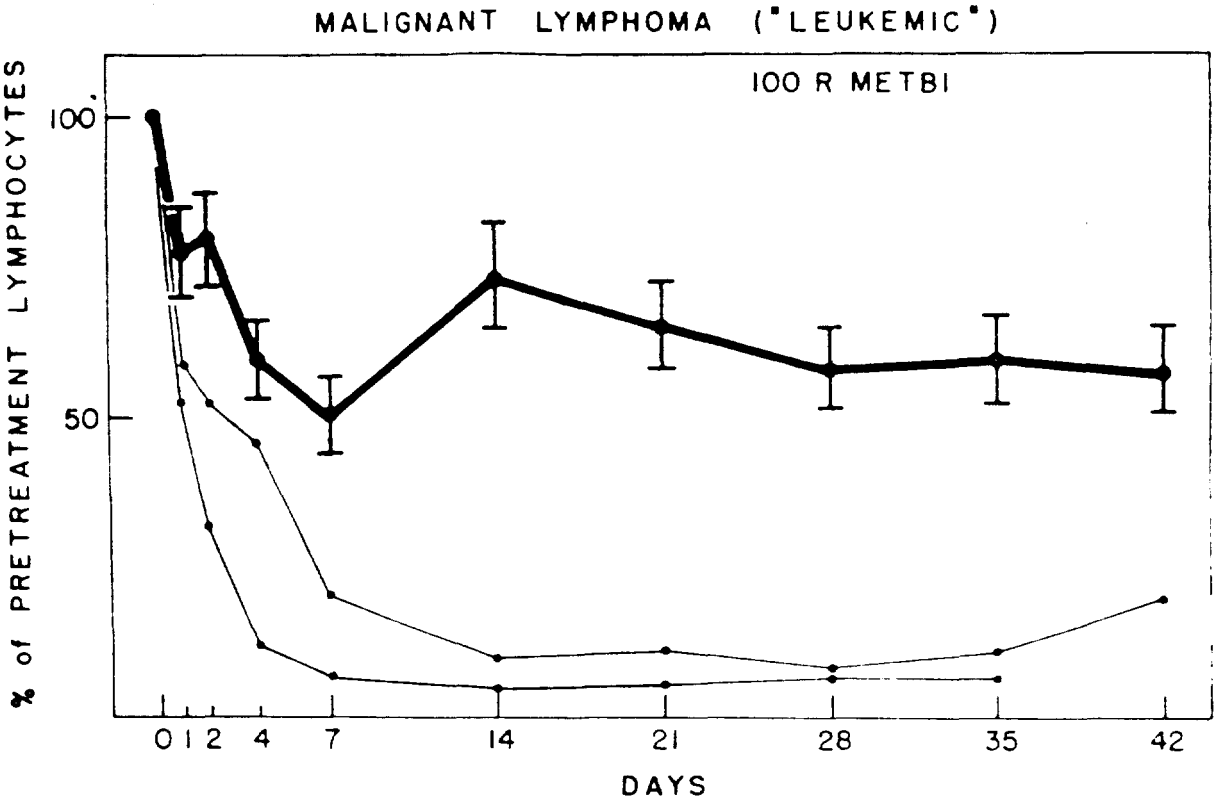


Fig. 9. The lymphocyte response curves of two patients with "leukemic" malignant lymphoma were so atypical in comparison with those of the 20 other patients with this disease (Fig. 7) that they are shown here separately along with the geometric mean of the other 20 patients. These two individual lymphocyte response curves fit within the 95% confidence limits of the "sensitive" type of lymphocyte response curves shown for chronic lymphocytic leukemia in Fig. 3.

Chronic Granulocytic Leukemia

This group included eight patients exposed to 50 R and four exposed to 100 R. Their spleens remained palpable and unchanged in size in eight, became slightly smaller in one, and distinctly smaller in one. In the other two, the spleen was not palpable before or after treatment. A definite decrease in liver size was recorded in only one patient. The general feeling of well-being was improved in eight patients but unchanged in three and poorer in one.

All patients had high initial leukocyte counts consisting predominantly of mature granulocytes. Nongranulocytic elements were so few that the curves shown in Figs. 11 and 12 can be considered as representing chiefly changes in granulocytic numbers. The numbers of leukocytes began a decrease promptly after these doses and the degree of fall indicated a greater radiation sensitivity than we see in normal granulocytes (see Fig. 7). Further, this depression usually persisted longer than would a similar degree of depression produced in normal persons by a higher dose as in radiation accidents. After 50 R the decline

1114135

in values began promptly, the mean dropping to 55% on day seven, 48% by day 14, then staying in this range for the six-week period of observation (Fig. 11). The response of the four patients given 100 R (see Fig. 12) was similar to that of the 50-R group, but the degree of depression was greater: 35% on day 7, 21% on day 14. By day 21, three of the four patients had granulocyte levels below 20% of pretreatment levels; one patient showed a transient partial recovery pattern. This suppression persisted throughout the 42-day period at the end of which there was still a trend toward even lower levels.

The platelets in CGL before treatment were either in the normal range or elevated; in a few instances they were at levels over 1,000,000/mm^3. After 50-R exposures, the platelet counts rose to a mean level of 136% by day 14 before declining to a nadir of 82% on day 28. The means then returned toward the pre-

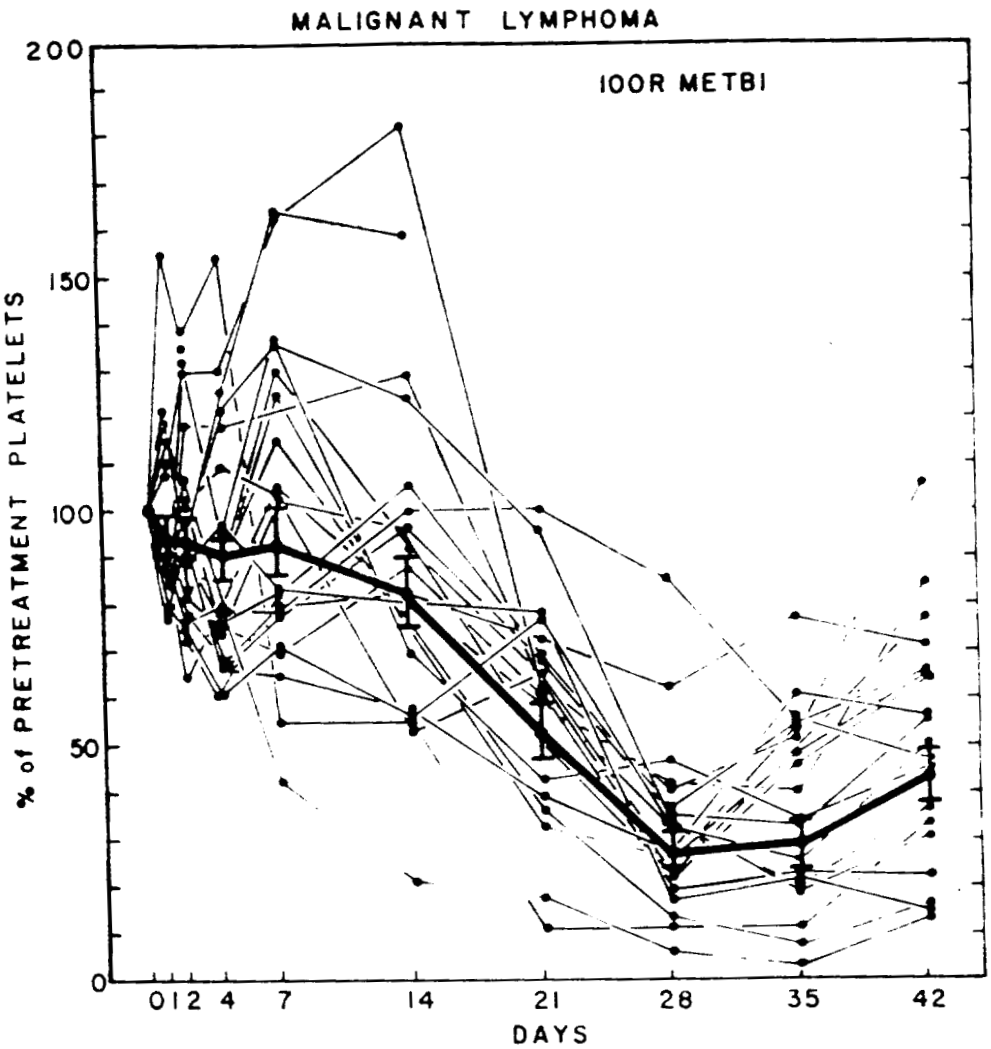


Fig. 10. Platelet response curves in patients with malignant lymphoma exposed to 100 R. The heavy solid line represents the geometric means and their standard errors. The curve closely resembles that in Fig. 6 of chronic lymphocytic leukemia after 100 R.

1114136

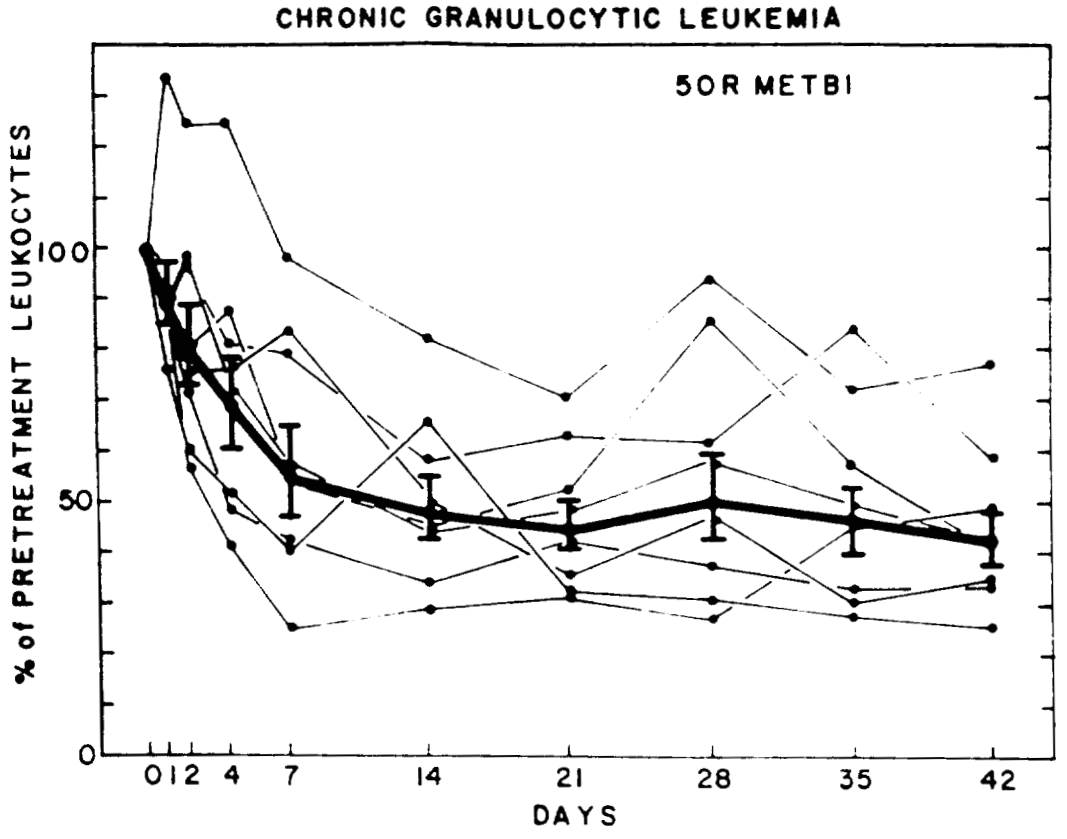


Fig. 11. Changes in blood leukocyte values, expressed in terms of individual pretreatment WBC counts, of eight patients with chronic granulocytic leukemia exposed to 50 R. The dark solid line represents the geometric means and their standard errors.

treatment range during the fifth and six weeks (Fig. 13), but the values ranged widely (53% to 191% of pretreatment values).

The platelets of the group exposed to 100 R also rose during the first two weeks but much less conspicuously (Fig. 14). The subsequent depression followed the usual temporal pattern and reached a nadir of 48% on day 42. This progressive decrease which persisted beyond 42 days is presently being observed also in our ongoing studies with fractionated and low-dose-rate exposures. A comparison of mean responses for platelets and leukocytes after 50 R and 100 R is made in Fig. 15.

The percent response (relative to pretreatment values) of the leukemic granulocyte appears from this graph (Fig. 15) to be about a factor of two greater than that of the platelets. The comparison here shows that in the occasional patients where injury to the platelet system is to be avoided because of borderline thrombocytopenia, a 50-R exposure would offer some therapeutic effect on granulocyte numbers while sparing platelet numbers.

Mean hemoglobin values were not significantly altered during this period of study. Figure 16 shows the hemoglobin values for the patients who received 100 R.

1114137

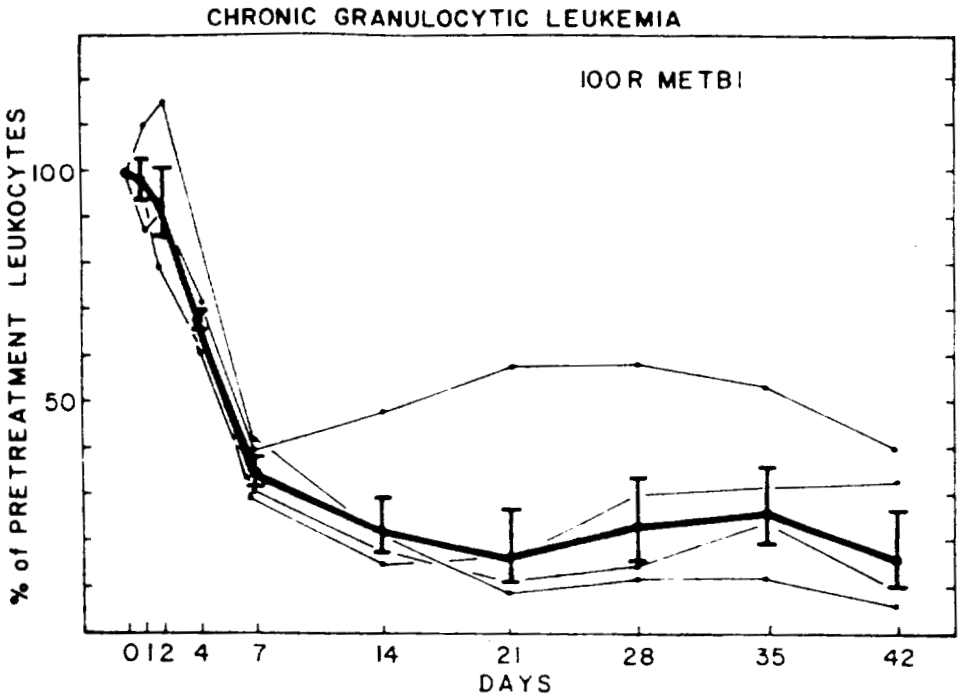


Fig. 12. Changes in blood leukocyte values, expressed in terms of individual pretreatment WBC counts, of four patients with chronic granulocytic leukemia exposed to 100 R. The dark solid line represents the geometric means and their standard errors.

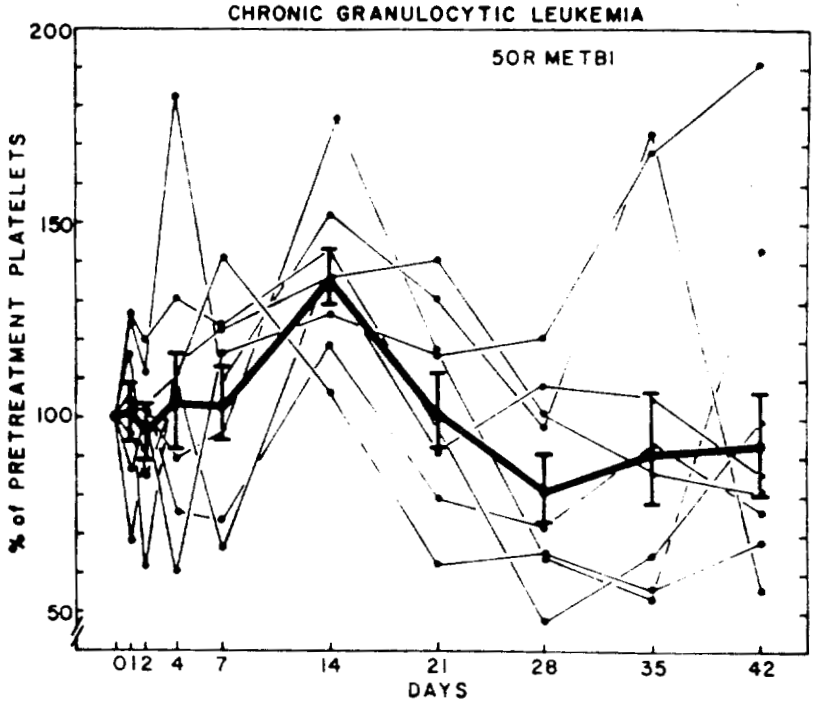


Fig. 13. Changes in platelet values expressed in terms of individual pretreatment platelet counts of eight patients with chronic granulocytic leukemia exposed to 50 R. The dark solid line represents the geometric means and their standard errors.

1114138

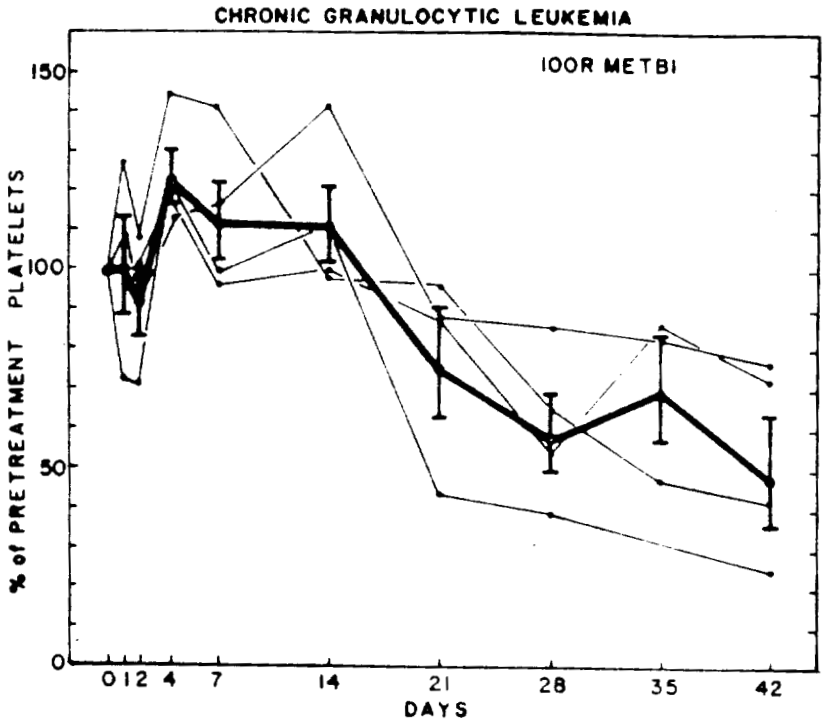


Fig. 14. Changes in platelet values, expressed in terms of individual pretreatment platelet counts, of four patients with chronic granulocytic leukemia exposed to 100 R. The dark solid line represents the geometric means and their standard errors.

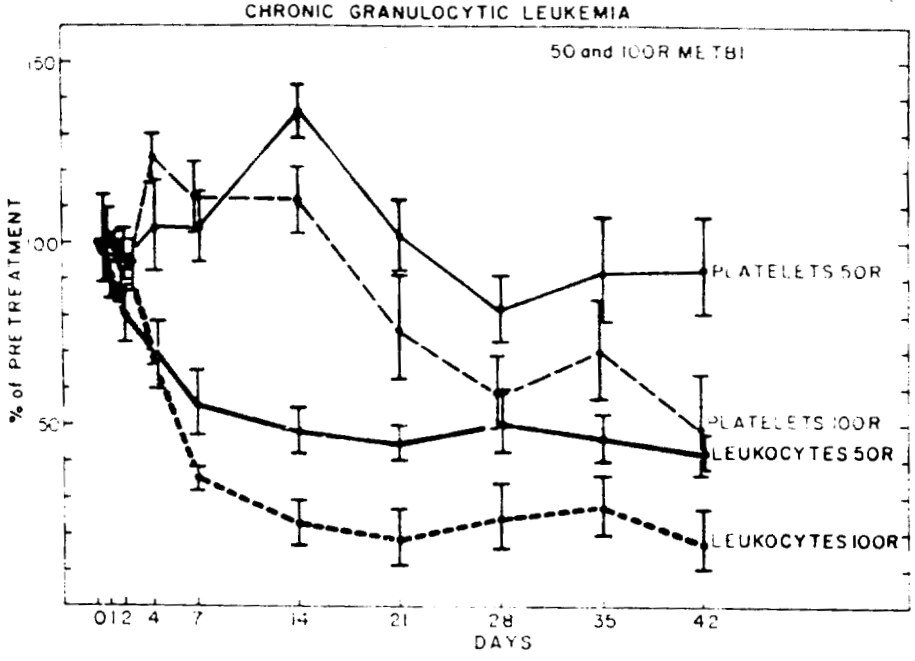


Fig. 15. Comparison of the geometric means of the leukocyte and platelet values in chronic granulocytic leukemia exposed to 50 and 100 R, shown in Figs. 13 and 14, showing the greater sensitivity of the leukocytes of these patients. In comparison with the curves for platelets (Fig. 6) in chronic lymphocytic leukemia, changes after 50 and 100 R occur earlier and are more extreme.

1114139

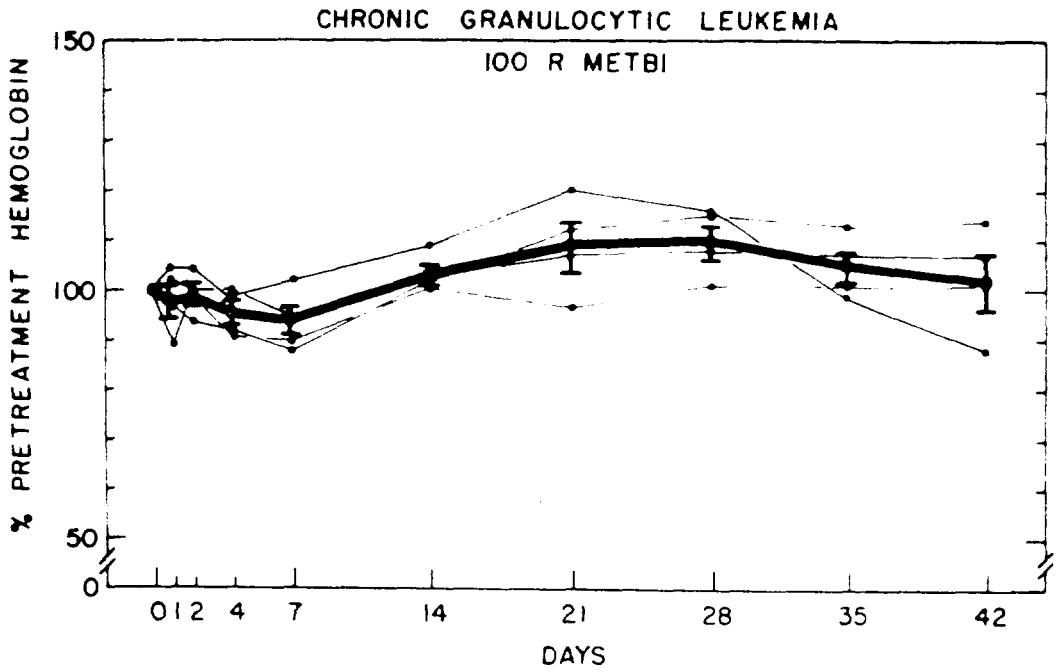


Fig. 16. Changes in blood hemoglobin values in four patients with chronic granulocytic leukemia exposed to 100 R showing a slight improvement relative to initial hemoglobin levels.

Polycythemia Rubra Vera and Primary Thrombocythemia

This group included eight patient-exposures to 100 R. Six patients had polycythemia rubra vera (PRV); one received two separate treatments (seven treatments); the seventh patient had primary thrombocythemia. In five patients there was an improvement in general feeling of well-being; in three there was no change. Of the large spleens, the size decreased in three, increased in one, and remained unchanged in two. The effects on liver size were slight and variable. In six patients a significant gain in weight was recorded.

All the PRV patients had initial leukocyte counts above 10,000/mm^3. These ranged up to 41,000/mm^3 pretreatment. As is shown in Fig. 17, leukocyte values began to drop after one week and reached their nadir at the six-week point, considerably later than has been observed in normals or in patients with most other diseases. As with platelet values (see below), the return of the leukocyte level toward normal was slow and was prolonged up to six months. The changes in absolute lymphocyte values in relation to pretreatment levels after 100 R (Fig. 18) were more like those after 100-R accident cases. Typically no return to normal was seen during the 42-day observation period.

Except for one patient with a normal platelet count, all had pronounced elevated platelet counts ranging from 575,000 to 1,600,000/mm^3 before treatment. The qualitative platelet responses to 100 R were similar to those of accidentally irradiated normal persons and of patients without leukemic diseases in that a nadir was reached at about 30 days (Fig. 19), but characteristically the fall in

1114140

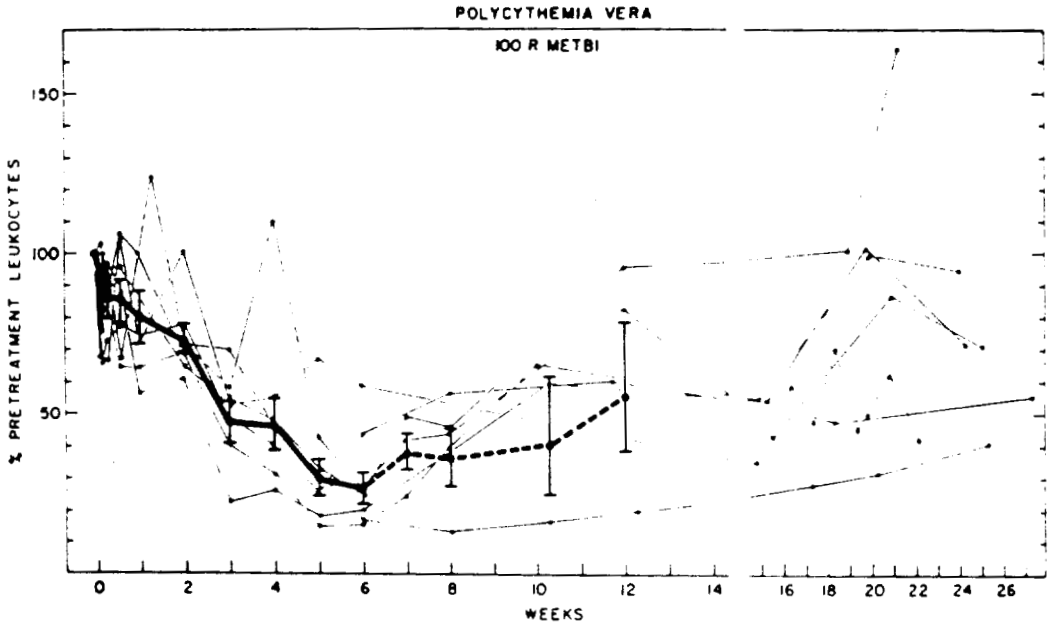


Fig. 17. Changes in blood leukocyte levels in eight patients with polycythemia rubra vera after 100 R. The solid heavy line is the geometric mean of these values through the usual 42-day postirradiation study period; the dotted line extends this mean through less regularly obtained data points over six months.

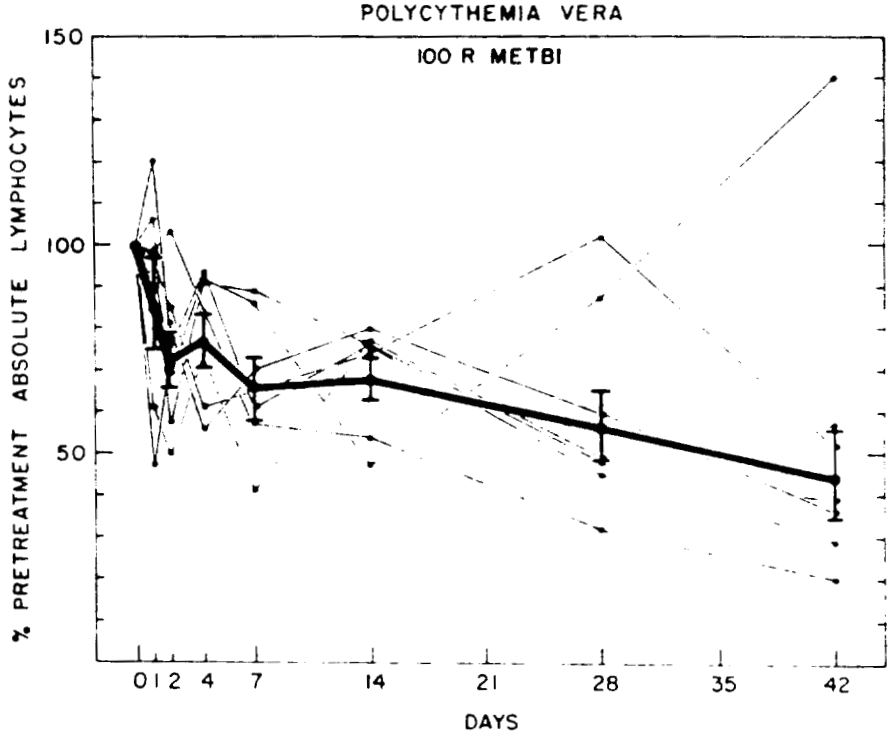


Fig. 18. Changes in blood lymphocyte values in seven patients with polycythemia rubra vera exposed to 100-R total-body irradiation. To improve statistics, 400 leukocytes were counted at each data point. One patient whose baseline values were believed to be unreliable is excluded from this figure.

111441

count either did not begin for two weeks or was slight until that time. The return toward normal, however, was much delayed and did not reach pretreatment levels for many months. This temporal pattern differs distinctly from the response of accident victims where a return to normal (or even a rebound elevation) occurs within six weeks. It appears that some homeostatic mechanism tends to prevent platelet values from returning to abnormal pretreatment values. Figure 19 shows the platelet response during the usual six-week study period and for the following six months.

Hemoglobin values for this group were not significantly elevated at the time of treatment; excessively high platelet and leukocyte values dominated their blood picture. Evaluation of changes in red cell numbers and morphology was complicated by pretreatment phlebotomies, stage of disease, and previous marrow-depressing treatments with ^{32}P or drugs (only two of the six were new, untreated cases). Hemoglobin and hematocrit values changed little after treatment (Figs. 20, 21) with 100 R. We believe, however, that this dose suppressed the rise that usually would have occurred with therapy. The mean corpuscular hemoglobin concentration before treatment was invariably low, due to phlebotomies and intestinal bleeding. It did not change in the postirradiation period (Fig. 22).

There was a 12% decrease in numbers of RBC and 12% increase in mean corpuscular volume that offset one another so that little or no change was seen in hematocrit values. Blood volume studies, however, were not done. Generally the mean corpuscular hemoglobin concentration did not change significantly

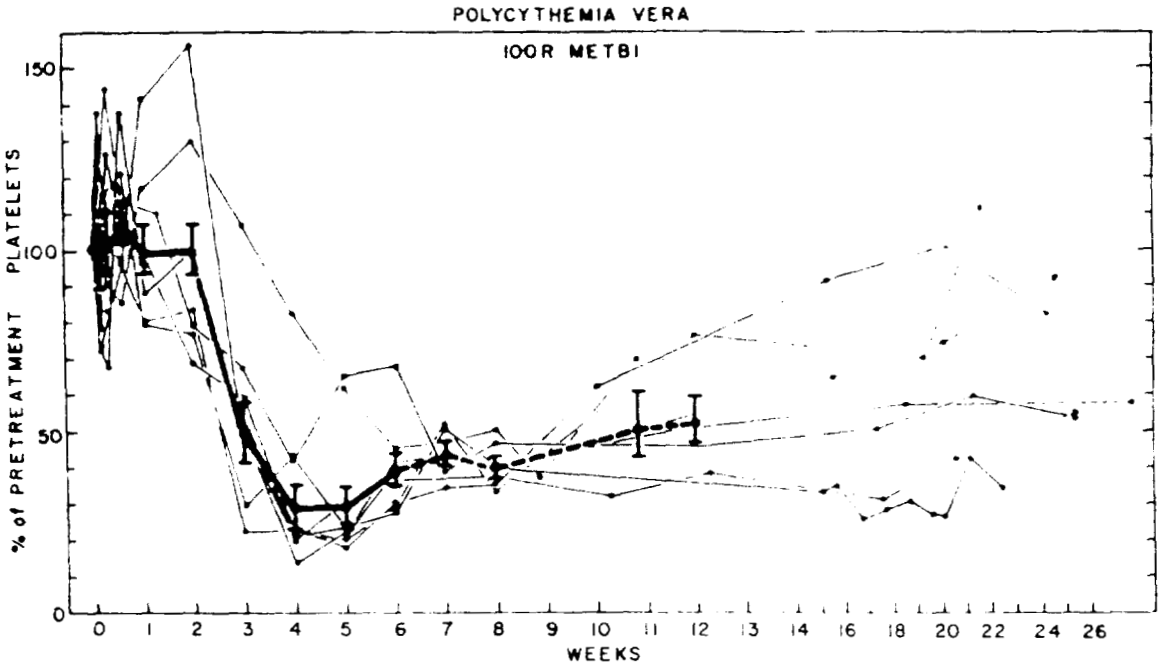


Fig. 19. Changes in blood platelet levels in eight patients with polycythemia rubra vera exposed to 100 R. Geometric mean is shown on a solid heavy line for 42 days of the protocol and as a broken line after that time when data points were less rigidly obtained.

1114142

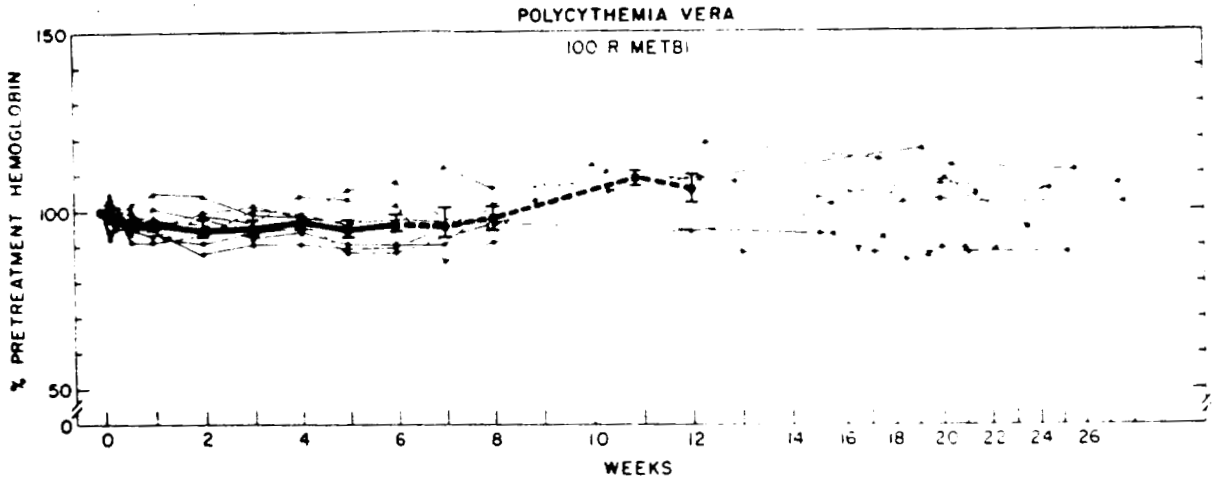


Fig. 20. Changes in hemoglobin values of eight patients with polycythemia rubra vera over the six months after 100-R exposure.

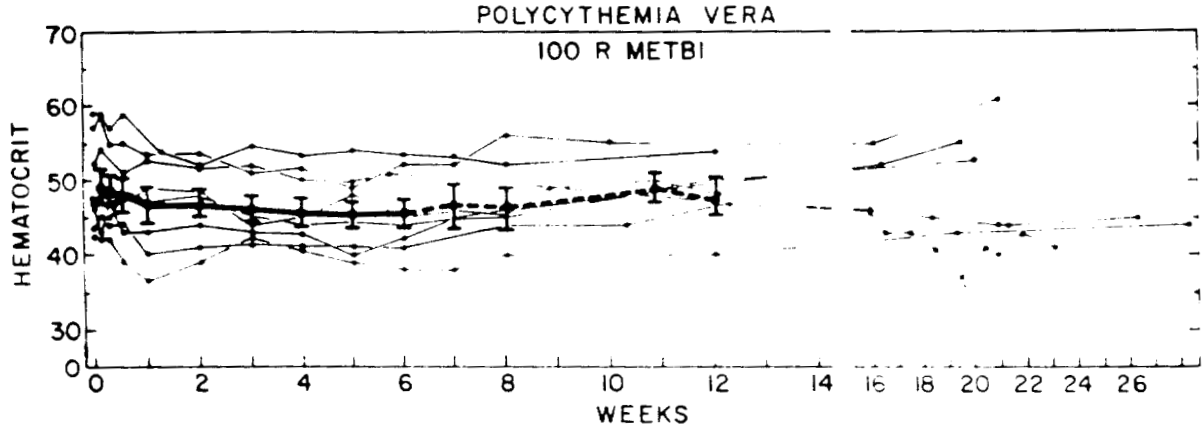


Fig. 21. Changes in hematocrit values (not normalized) of eight patients with polycythemia rubra vera over the six months after 100-R exposure.

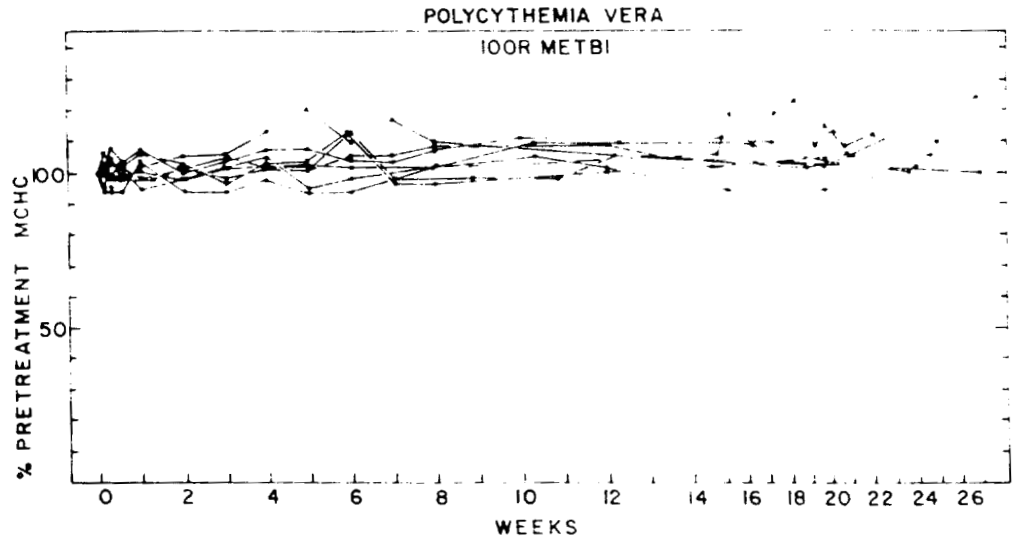


Fig. 22. Changes in mean corpuscular hemoglobin concentration of eight patients with polycythemia rubra vera over the six months after 100-R exposure.

1114143

but in some individuals it rose 10 to 20% (Figs. 22 and 23).* Detailed red cell values in one patient are shown for a 26-week period (Fig. 23). The principal clinical problem in this patient was her excessively high platelet count which ranged above 1,000,000/mm^3 and was believed to be a factor in intestinal hemorrhage and its associated iron loss.

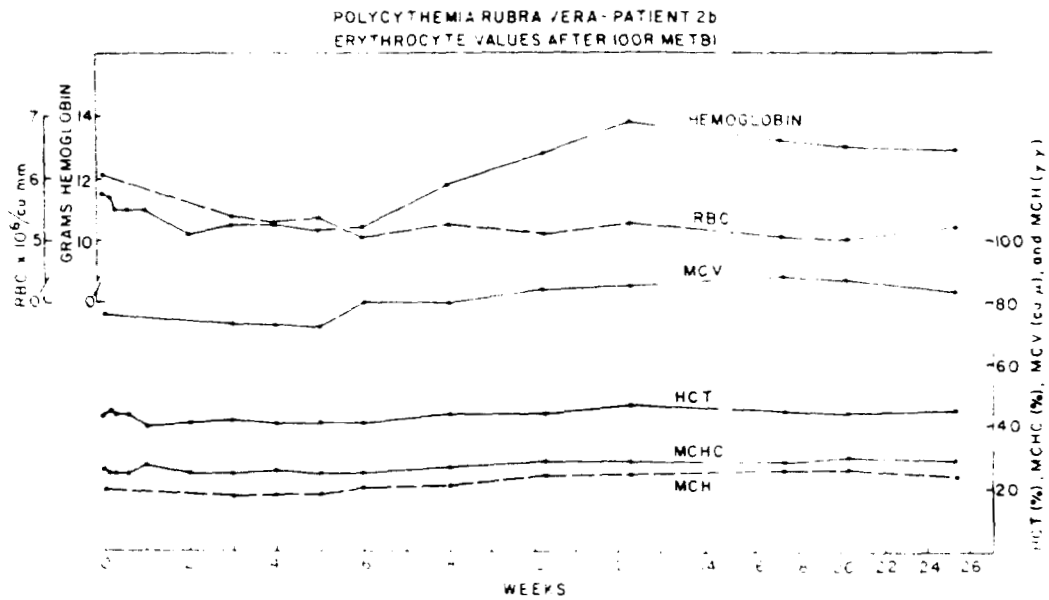


Fig. 23. Changes in actual values of blood erythrocyte parameters in one patient with polycythemia rubra vera treated with an exposure of 100 R.

Changes in Uric Acid

In all disease categories and both dose groups, we examined serum uric acid levels. After exposure, the levels changed, as might be expected from previous observations, but in this series of patients the changes were, in general, small, inconsistent, and of little clinical value. In some patients an early increase and subsequent decrease were sufficiently large to be accepted as indicative of the tissue destruction caused by the radiation exposure.

In 100-R treated lymphosarcoma and CLL, there were increased average levels on postirradiation days through four or seven (Table 7). Among the patients given 50-R exposure the CGL group showed elevated uric acids on only the second day

---

* In a study of RBC size distribution after low-dose-rate total-body irradiation (to be reported elsewhere; see ORAU Medical Division Research Reports 1968, 1969), we have found by electronic measurements of red cell size that irradiation produces changes in cell volume that are not demonstrated by measurements of hemoglobin, hematocrit, and cell numbers/cm^3. We are finding that the erythron returns to normal within 120 days in this study only if iron stores have not been depleted by phlebotomy or hemorrhage.

1114144

Table 7

STATISTICAL SIGNIFICANCE OF OBSERVED MEAN SERUM URIC ACID LEVELS AFTER TBI

Disease Category	TBI (R)	Days 1	2	4	7	14	21	28
Lymphosarcoma	50	0 (5)*	0 (5)	0 (4)	0 (5)	0 (5)	0 (4)	0 (4)
	100	0 (15)	+ + (16)	+ + (17)	0 (17)	0 (17)	0 (15)	0 (11)
Polycythemia	100	0 (7)	0 (5)	0 (7)	0 (7)	0 (7)	0 (7)	- (6)
Chronic Granulocytic Leukemia	50	0 (7)	+ (7)	0 (7)	0 (7)	0 (7)	0 (7)	0 (7)
	100	0 (3)	0 (2)	0 (3)	0 (4)	0 (4)	0 (2)	- (3)
Chronic Lymphocytic Leukemia	50	0 (15)	0 (14)	0 (14)	+ (15)	0 (15)	0 (14)	0 (13)
	100	0 (14)	+ + (13)	+ + (15)	+ (14)	0 (15)	0 (15)	0 (13)
All Disease	50 or 100	0 (66)	+ + (61)	+ + (68)	0 (69)	0 (69)	0 (64)	- (57)
Uric Acid mg/100 ml		pre-treatment						
	$\bar{X}$	5.82	6.18	6.48	6.38	6.04	5.67	5.38
	± S.D.	1.75	1.73	1.82	2.02	1.98	1.75	1.60	1.71

*Figures in parentheses indicate the number of patients in each group.

0 — No statistically significant change from pretreatment levels.

+ — Increase $P \leq 0.05 - 0.01$; + + $P < 0.001$

— Decrease $P < 0.05 - 0.01$

and the CLL group on only the seventh day. In other disease categories and exposure groups no statistically significant early changes were found in the mean values from day to day, although some individual patients, even in these groups, showed alterations that possibly reflected increased cellular destruction. On day 28 following 100 R a decrease was seen in some disease categories and in the averaged data for all, but was not found in individual groups after 50 R.

These observations are compatible with the view that change in uric acid level is a dose-related response that is modified by at least three factors: the amount of radiosensitive tissue present at exposure, the degree of radiosensitivity, and the rate of uric acid production in relation to renal excretory capacity. Appraisal of radiation-induced perturbations in this metabolic system might be better elucidated from study of total urinary uric acid and other protein-related excretory products rather than serum levels.

DISCUSSION

This large amount of hematologic data suffers from the usual variabilities of most clinical investigations — wide range in laboratory values, many of them unexplained, and the lack of a true control population. The information derived, however, is clinically useful and meaningful for radiation biology. The differences

1114145

in response in different clinical disorders are of special interest and give some insight into the relative dependence of these disease processes on cellular survival and replication. In this discussion "sensitivity" is used to mean simply a response in cell numbers after irradiation; it is not meant to imply any specific mechanism for altered numbers.

Most of the rapid major alterations in blood values during the six-week post-treatment period were the result of irradiation. To be valid, this statement requires us to assume that all peripheral blood cell values would have remained stationary if no treatment had been given. This steady state was not always present. In fact, therapy was often indicated because certain cellular systems were changing, but the rate of change was usually slow in comparison with that induced by irradiation. Patients with chronic leukemia, polycythemia, or lymphoma were in reasonably good condition and the changes in hematologic status that would have occurred in the absence of treatment during the observation period could be predicted with some certainty. For example, most of the patients with chronic leukemia were becoming worse only gradually; white cell levels and symptoms were increasing slowly. Some with lymphocytic leukemia had falling red cell values that required transfusions. Patients with polycythemia were in need of treatment to alleviate symptoms and to lower hazardous elevations in platelet values; two had phlebotomies shortly before irradiation. A rise in red cell values might have been expected had no therapy been given.

Problems of interpreting the quantitative nature of radiation-induced hematologic response have recently been reexamined by Bergner with theoretical and stochastic mathematical models (18). He points out that all curves of blood cell counts are a composite of the effect of radiation damage and its repair, and variations introduced by data that is poor in reliability and numbers. From his theoretical viewpoint he demonstrates that an increase in dose augments the speed of "the response process" as well as the maximum response itself. He feels, however, that large numbers of patients and observations do little for quantitation of the hematologic response and that biologic variation in patients and its many causes force the development of a qualitative rather than a quantitative theory. In attempting this task he shows that the onset of repair processes and their continuance cause the "spread" of the hematologic response data to increase with time. Since larger doses more effectively suppress repair processes and thus tend to reduce one contributing cause to variability, especially later in the course of response, one would expect that larger doses would give more uniform responses. This effect is seen in most of our data but not in all of it. Bergner's analysis of the patients with chronic lymphocytic leukemia, where maximum response of lymphocytes to 50 and 100 R was the same, revealed unexpectedly that greater variability in response (evidence for greater reparative efforts) occurred with the 100-R dose rather than with the 50 R. Since this greater reparative effort after 100 R resulted in a response curve similar to that of 50 R, these observations suggest together that the expected additional cell-damaging response to 100 R was offset by the reparative processes stimulated by the 100 R, thus providing another basis for considering the 100-R dose in this disease unnecessary as well as undesirable. Further analyses, based on Bergner's "Theory of Quantitative Radiation-Response Time-Data," or on other such analytical models, are needed in radiobiology.

1114146

When examined from a cytokinetic viewpoint the mechanisms of the changes in blood cell values produced by the irradiation are, of course, complex. This problem has been well discussed by Mathé (19) and Bond et al (20). Presumably radiation-induced death of circulating cells cannot account for much of the total effect of the exposure. Alterations in patterns of tissue sequestration and release of abnormal numbers of cells may have a significant effect upon peripheral blood cell values. The basis for most of the reduction in the cells of the blood, however, is undoubtedly interference with cell proliferation brought about most likely by a radiation-induced decrease in stem cells. Therefore, it may be necessary to relate the patterns of radiation effects to a balance between cell production, release, "normal" life span or turnover rate for each cell type as it occurs in the various disease states, and cellular radiosensitivity. Table 8 lists the geometric means of the minimum blood values reached during the six-week study period in the various diseases studied after the 50-R and 100-R doses.

The patterns of hematologic response to irradiation are influenced by the dose and also by the altered cytokinetic state in each disease. We have attempted, as yet, only preliminary interpretation of our results in the light of these factors.

Lymphocytes

Patients with polycythemia rubra vera provided data on the response of presumably normal lymphocytes to 100 R. An early drop occurred by day two to 76% of pretreatment levels and a gradual decline continued to 53% at the end of the 42-day study period, so that we do not know the precise time when the lowest lymphocyte values were reached but this curve was most like that of normal men accidentally irradiated.

Table 8

Minimum Geometric Mean Values During 6 Weeks after TBI
Expressed as Percent of Pretreatment Level

	50 R	100 R
Total WBC		
CLL	34.8 (26.5 good response) (65.3 poor response)	29.7 (19.7 good response) (59.5 poor response)
Malignant Lymphoma	61.[illegible]	5[illegible].1
CGL	44.4	17.3
PRV	-	26.7
Lymphocytes		
CLL	31.9 (23.7 good response) (66.9 poor response)	26.7 (19.3 good response) (60.6 poor response)
Malignant Lymphoma	59.3	50.0
CGL	49.4	48.5
PRV	-	44.4
Platelets		
CLL	65.0	25.2
Malignant Lymphoma	70.9	27.3
CGL	81.5	45.5
PRV	-	25.6

1114147

Perhaps the most striking observation related to radiation sensitivity of lymphocytes is their response in chronic lymphocytic leukemia to 50 R and 100 R. The two curves are not significantly different. The two series were not entirely comparable and the stage of illness may limit the interpretation of this fact. Our data suggest, however, that if the clinical objectives can be equated with reduction of only the lymphocyte count, the lower dose may be preferable since 50 R appears to reduce lymphocyte numbers adequately with less depression of platelets. Lymphocytes in chronic lymphocytic leukemia are certainly most sensitive to 50 R, and using the lymphocyte response data of the patients with PRV (Fig. 18) as a substitute for our lack of normal control data we can say that those with leukemia are almost three times as sensitive. A comparison with the lymphocyte counts of the Marshallese normals on Rongerik Island (Group III) who were estimated to have been exposed to 78 R (21) also shows that lymphocytes of normal people are less sensitive than those patients with lymphocytic leukemia.

Schrek (22) has reported that some patients with chronic lymphocytic leukemia have radioresistant lymphocytes. In our study (Figs. 1, 2, 3) several of the patients given 50 R or 100 R showed a significantly decreased response, in contrast with the common pattern of a drop to 50% or less of initial values in four or seven days. We have been unable to discern any clear-cut clinical or hematologic correlations with this nonresponsiveness. In some of these patients the resistance of the lymphocytes is actually greater (compare Fig. 3 with Fig. 18) than that of those in PRV (considered to be "normal").

On the other hand, two cases of "leukemic" lymphosarcoma showed inordinately sensitive lymphocytes with an early precipitous drop to 10% of the pretreatment values (Fig. 9). The remainder of the patients with malignant lymphoma had depressions of the mean lymphocyte values that were less than the response in polycythemia and must be considered more resistant than normal. We wondered whether the numbers of circulating lymphosarcoma cells in the peripheral blood of these patients before treatment might be related to radiosensitivity, but when the values were graphed after sorting the patients into two groups (those with lymphocyte counts above 4,000/mm^3, and those with counts less than this level) no differences in response could be detected. We found no clear relation between height of the initial lymphocyte count in CLL and the subsequent percentage fall with therapy. There is a slight suggestion that when the initial counts are low a somewhat exaggerated response may be anticipated. In general, however, from a clinical viewpoint, one cannot prescribe the amount of treatment needed on the basis of the height of the initial count.

Granulocytes

Granulocytes in chronic granulocytic leukemia begin to drop promptly and appear to be more sensitive to radiation than in other patients and in normal man. Mean values after 50 R can be superimposed on the responses of lymphocytes in lymphocytic leukemia even though we are comparing different cell types. However, the degree of change in granulocytic leukemia is related to the initial

1114148

white cell level, a relation that does not exist for lymphocytic leukemia*. As noted earlier, leukocyte values were elevated in patients with polycythemia rubra vera before treatment, in some instances to a moderately pronounced degree. The drop after 100 R was less precipitous in PRV than in patients with chronic granulocytic leukemia, with a mild decrease during the first two weeks continuing to a nadir on day 42 in contrast to the response expected in normal persons. This depression from pretreatment values persisted for a number of months, although the pattern of climb toward pretreatment values varied considerably.

Platelets

Platelets usually reach their lowest level between the 21st and 35th days. In every group, responses to 100 R were significantly greater than to 50 R, and there was little overlap; 50 R produced little change in the patients with lymphoma, lymphocytic leukemia, and with chronic granulocytic leukemia. Individual variations were rather pronounced. Patients with polycythemia rubra vera who usually have moderate or high platelet values were not rebounding toward normal by the end of the six-week study period but had leveled off, remaining for many weeks or months at values considerably below the pretreatment ones (Fig. 16). This desirable effect from the point of view of therapy perhaps indicates that a new cellular steady state has been achieved either through the establishment of normal homeostatic mechanisms or depletion of stem cells to limiting levels of cell production.

SUMMARY

Eighty-nine treatments of total-body irradiation were given in single exposures of 50 R and 100 R at 1.5 R/min to patients with lymphoma, chronic leukemia, or polycythemia rubra vera. The clinical and hematologic responses during a 42-day study period were analyzed according to disease and dose; not unexpectedly the therapeutic responses varied. In lymphoproliferative disorders measurable clinical benefit did not depend solely on the radiation dose; the majority showed some shrinkage of enlarged lymph nodes, liver, or spleen, but the larger dose was not proportionally more effective in all cellular systems. Many required additional therapy within three months but this was not surprising in view of our use of only a single exposure. In granulocytic leukemia, improvement occurred in more than half of the patients. For polycythemia, the most clinically beneficial response appeared to be a decline of the dangerously elevated platelet counts to more normal levels that were maintained for many weeks or months.

The hematologic responses to 100 R usually but not invariably exceeded those to 50 R. A notable exception was the lymphocyte response of CLL in which the mean values of the responses of two groups were statistically the same. In general the abnormal proliferating blood elements did not return to pretreatment

---

* This analysis is to be the subject of a separate report by J. Yuhas (ORNL), C. C. Lushbaugh, and T. Stokes (ORAU).

1114149

values in the same time sequence that is seen in recovery of normal cell lines in the acute radiation syndrome, suggesting that homeostatic mechanisms have been reestablished to hold the values within normal ranges. For example, elevated platelets in polycythemia rubra vera were depressed by the treatment but did not return toward normal by day 42, in contrast to events in lymphocytic leukemia where initial platelet levels are usually normal or low and recovery of platelet values is usually well under way by day 42.

The detailed graphs of blood cell values, together with their geometric means for each disease and exposure group form a useful reference for radiobiologic comparison with patterns in normal persons accidentally exposed, and relate the radiosensitivity of the various blood cell lines in the diseases studied.

The graphs also show the most probable or predictable response of the average patient with these diseases for 42 days after 50-R and 100-R exposure, providing a temporal course for comparing the relative effectiveness of similar total exposures of radiation given in small daily fractions at high or low dose rates. Such a comparative study of dose-rate effects upon therapeutic effectiveness is in progress.

Acknowledgements

This study represents a group effort of the clinical staff of the Medical Division with nurses, technologists, and physicians too numerous to mention. Special recognition should be given to Mary Smyser for accumulating and plotting the data, and to the Medical Illustrators, Cathy Stubbs and Jane Kimbro. The hematology technologists, Martha Clevenger, Joyce Hewins, Kathryn Lore, Shirley Colyer, and Mary Thomas performed with great care the innumerable procedures that form the backbone of the study. Dr. David White (present address: Centerville Clinic, Route 1, Fredericktown, Pa. 15333) with skill and dedication performed most of the follow-up clinical evaluations.

1114150

References

1. G. A. Andrews, B. W. Sitterson, A. L. Kretchmar, and R. Tanida, Studies of Total-Body Irradiation and Attempted Marrow Transplantation in Acute Leukemia, Acta Haemat. (Basel) 26: 129-153 (1961).

2. M. Brucer, The Acute Radiation Syndrome, A Medical Report on the Y-12 Accident, June 16, 1958, USAEC Report ORINS-25, April, 1959.

3. G. A. Andrews, B. W. Sitterson, A. L. Kretchmar, and M. Brucer, Accidental Radiation Excursion in the Oak Ridge Y-12 Plant. IV. Preliminary Report on Clinical and Laboratory Effects in the Irradiated Employees. Health Physics 2: 134-138 (1959).

4. G. A. Andrews, B. W. Sitterson, A. L. Kretchmar, and M. Brucer, Criticality Accident at the Y-12 Plant, in Diagnosis and Treatment of Acute Radiation Injury. Geneva. World Health Organization. New York. International Documents Service, 1961, pp. 27-48.

5. G. A. Andrews, Criticality Accidents in Vinca, Yugoslavia and Oak Ridge, Tennessee. Comparison of Radiation Injuries and Results of Therapy, JAMA, 179: 191-197 (1962).

6. T. M. Fliedner, G. A. Andrews, E. P. Cronkite, and V. P. Bond, Early and Late Cytologic Effects of Whole Body Irradiation on Human Marrow, Blood, 23: 471-487 (1964).

7. T. M. Fliedner, E. P. Cronkite, V. P. Bond, and G. A. Andrews, Mitotic Activity and Cytology of Human Bone Marrow After Accidental Exposure to Ionizing Radiation, in Proc. 7th Congress Europ. Soc. Hemat., London 1959, Part II, 1960, pp. 458-467.

8. G. A. Andrews, C. C. Lushbaugh, R. M. Kniseley, D. A. White, and B. I. Friedman, Haematological Effects of Whole-Body Irradiation in the Human Being, in IAEA Panel Effects of Ionizing Radiations on the Haematopoietic Tissue, International Atomic Energy Agency, Vienna, 1967, pp. 75-83.

9. E. E. Osgood, Treatment of Chronic Leukemias, J. Nucl. Med., 5: 139-153 (1964).

10. D. Walsh, Deep Tissue Traumatism From Roentgen Ray Exposure, Brit. Med. J., 2: 272 (1897).

11. R. E. Johnson, Evaluation of Fractionated Total-Body Irradiation in Patients with Leukemia and Disseminated Lymphomas. Radiology 86: 1085-1089 (1966).

1114151

12. W. H. Langham (Ed.), Radiobiological Factors in Manned Space Flight, National Academy of Sciences, Washington, 1967, pp. 76-90.

13. G. Brecher and E. P. Cronkite, Morphology and Enumeration of Human Blood Platelets, J. Appl. Physiol., 3: 365-377 (1950).

14. M. Brucer, A Total-Body Irradiator. Int. J. Appl. Radiat., 10: 99-105 (1961).

15. A. C. Morris, Jr., Measurements in a Total-Body Irradiation Facility, Int. J. Appl. Radiat., 11: 108-113 (1961).

16. R. L. Hayes, T. H. Oddie, and M. Brucer, Dose Comparison of Two Total-Body Irradiation Facilities, Int. J. Appl. Radiat., 15: 313-318 (1964).

17. R. E. Ellis, The Distribution of Active Bone Marrow in the Adult, Phys. Med. Biol., 5: 255-258 (1961).

18. P.-E. E. Bergner, Theory of Quantitative Radiation-Response Time-Data, USAEC Report ORAU-109, 1969.

19. Georges Mathé, Total Body Irradiation Injury: A Review of the Disorders of the Blood and Hematopoietic Tissues and Their Therapy, in Nuclear Hematology, E. Szirmai (Ed.), Academic Press Inc., New York, 1965, pp. 275-338.

20. V. P. Bond, T. M. Fliedner, and J. O. Archambeau, Mammalian Radiation Lethality, Academic Press Inc., New York, 1965.

21. V. P. Bond, E. P. Cronkite, R. S. Farr, and H. H. Hechter, Hematologic Observations, in Some Effects of Ionizing Radiation on Human Beings. A Report on the Marshallese and Americans Exposed to Radiation from Fallout and a Discussion of Radiation Injury in the Human Being, E. P. Cronkite, V. P. Bond, and C. L. Dunham (Eds.), USAEC Report TID-5358, July, 1956, pp. 43-63.

22. R. Schrek, S. L. Leithold, I. A. Friedman, and W. R. Best, Clinical Evaluation of an In Vitro Test for Radiosensitivity of Leukemic Lymphocytes, Blood, 20: 432-442 (1962).

1114152

TABLE V APPENDIX

RESPONSE TO 100 R METBI - POLYCYTHEMIA

Pt. No.	Sex	Age at R_x	Interval D_x to TBI R_x	Previous R_x (approx. amt.)	Interval from last R_x to TBI	Spleen Change in Size	Systemic Symptoms + = Improvement	Pruritis + = Improvement	Subsequent Major Forms of R_x	Interval from TBI to next R_x	Follow-up Interval (3)
1	F	62	3 mo.	Phlebot. 6 x	1 mo.	N	NC	NC	Phlebotomy	2 yr. 4 mo.	4 yr. 6 mo.
2 a	F	73	1 mo.	None	-	- 2	NC	N	^{32}P 5 mc METBI 100 R Busulfan	3 mo. 23 mo. 3 yr.	4 yr.
2 b	F	75	3 yr.	METBI 100 R ^{32}P x 1	20 mo.	- 1	+ 1	N	Busulfan	13 mo.	2 yr.
3	F	64	$7\frac{1}{2}$ yr.	^{32}P x 1 Myleran Phleb. 25 x	$2\frac{1}{2}$ mo.	NC	+ 1	+ 1	Phlebotomy	7 mo.	4 yr.
4	M	55	15 yr	Phleb. 50 x ^{32}P 7 x	6 mo. 6 mo.	NC	N	N	Phlebotomy	$4\frac{1}{2}$ mo.	4 yr.
5	M	68	6 yr. 7 mo	Phleb. 15 x ^{32}P 7 x	17 mo.	NC	+ 2	+ 2	None	-	D 1 yr. 7 mo.
6 (1)	M	59	1 mo.	None	-	-	+ 2	+ 2	LETBI 100 R LETBI 250 R	23 mo.	2 yr.
7 (2)	M	60	4 mo.	^{32}P 2 x	3 mo.	N	N	N	LETBI 150 R 2 x	15 mo.	2 yr.

(1) Splenectomy 4 yrs. earlier after abdominal trauma
(2) Primary thrombocythemia
(3) All patients alive at latest follow-up except patient 5; none with leukemia

Change in Size:
NC = No change - abnormal before and after treatment
N = Normal or absent before and after
+ 1 or + 2 = Larger
- 1 or - 2 = Smaller

Systemic Symptoms:
NC = No change - abnormal before and after treatment
N = Normal or absent before and after
+ = Improvement
- = Worse

1114153

TABLE B APPENDIX

RESPONSE TO 50 R CHRONIC GRANULOCYTIC LEUKEMIA

Pt. No.	Sex	Age at R_x	Interval D_x to TBI R_x	Previous R_x	Interval from last R_x to TBI	Change in Size		Systemic Symptoms + = Improvement	Subsequent Major Forms of R_x	Interval from TBI to Later R_x	Follow-up Interval
						Spleen	Liver				
1	M	67	3 days	None	-	NC	NC	+ 2	Ext. rad. to spleen Busulfan Splenectomy Hydrocortisone Prednisone Hydrocortisone	$2\frac{1}{2}$ mo. $5\frac{1}{2}$ mo. 14 mo. 14 mo. $14\frac{1}{2}$ mo. 15 mo.	D 15 mo.
2	M	48	3 days	None	-	- 2	- 1	+ 2	Ext. rad. to spleen Busulfan 6-MP	$2\frac{1}{2}$ mo. 6 mo. 2 yr. 1 mo.	D 2 yr. 3 mo.
3 a	F	52	5 days	None	-	- 1	- 1	+ 1	Busulfan METBI 50 R	1 yr. 4 yr. 4 mo.	D 6 yr. 7 mo.
3 b	F	57	4 yr. 4 mo.	METBI (50 R) Myleran	$8\frac{1}{2}$ mo.	NC	NC	NC	Ext. rad. to spleen Ext. rad. to liver 6-MP Prednisone Cyclophosphamide Methotrexate Hydrocortisone	9 mo. 18 mo. 23 mo. 23 mo. 2 yr., 3 mo. 2 yr., $3\frac{1}{2}$ mo. 2 yr., $3\frac{1}{2}$ mo.	D 2 yr. $3\frac{1}{2}$ mo.
4 a	F	60	34 days	None	-	N	N	+ 1	Busulfan METBI 50 R	3 mo. 3 yr.	D 5 yr. 7 mo.
4 b	F	63	3 yr. $1\frac{1}{2}$ mo.	METBI (50 R) Myleran	13 mo.	NC	NC	NC	Ext. rad. to spleen Ext. rad. to liver METBI 100 R (See Table C, Case 2) Busulfan Prednisone 6-MP Hydrocortisone	2 mo. 9 mo. 11 mo. 13 mo. 2 yr. 5 mo. 2 yr. 5 mo. 2 yr. 7 mo.	D 2 yr. 7 mo.

1114154

TABLE B APPENDIX - Continued

Pt. No.	Sex	Age at R_x	Interval D_x to TBI R_x	Previous R_x	Interval from last R_x to TBI	Change in Size		Systemic Symptoms + Improvement	Subsequent Major Forms of R_x	Interval from TBI to Later R_x	Follow-up Interval
						Spleen	Liver				
5	M	59	1 yr. 9½ mo.	None	-	NC	NC	N	Ext. rad. to spleen Busulfan 6-MP Prednisone Hydrocortisone	2 yr. 10 mo. 3 yr. 8 mo. 3 yr. 10 mo. 3 yr. 10 mo. 3 yr. 10½ mo.	D 3 yr. 10½ mo.
6	F	53	1 mo.	None	-	NC	NC	+ 2	Ext. rad. to spleen (x 2) Ext. rad. to liver Ext. rad. to spleen (x 2) Hydrocortisone Prednisone 6-MP Prednisone	1½ mo. & 21 mo. 3 yr. 3 yr. 5 mo. & 4 yr. 3 mo. 4 yr. 9 mo. 4 yr. 9 mo. 4 yr. 10 mo. 4 yr. 10 mo.	D 4 yr. 10 mo.

1114155

TABLE C APPENDIX

RESPONSE TO 100 R CHRONIC GRANULOCYTIC LEUKEMIA

Pt. No.	Sex	Age at R_x	Interval R_x to TBI R_x	Previous R_x	Interval from last R_x to TBI	Change in Size Spleen	Change in Size Liver	Systemic Symptoms + = Improvement	Subsequent Major Forms of R_x	Interval from TBI to Later R_x	Follow-up Interval
1	F	64	4 yr	METBI 50 R (See Table B, Case 4) Myleran METBI 50 R (See Table B, Case 4) Ext. rad. to spleen Ext. rad. to liver	2½ mo.	NC	NC	+ 1	Busulfan Prednisone 6-MP Hydrocortisone	2 mo. 18 mo. 18 mo. 19 mo.	D 19½ mo.
2	M	53	16 mo.	Cytoxan Ext. rad. to liver Ext. rad. to spleen Ext. rad. to spine Ext. rad. to spleen x 2	2½ mo.	NC	NC	+ 1	Ext. rad. to rt. ilium Alkeran Ext. rad. to spleen 6-MP	4½ mo. 5 mo. 16 mo. 17½ mo.	D 17½ mo.
3	M	44	4 yr., 10 mo.	Ext. rad. to spleen x 8 Ext. rad. to liver Ext. rad. to spleen	6 mo.	NC	NC	- 2 (1)	Ext. rad. to spine	24 days	D 50 days
4	F	46	20 mo.	Ext. rad. to liver Ext. rad. to spleen LETBI 100 R	3 mo.	N	N	+ 2	METBI 100 R (divided dose)	5 mo.	A 13½ mo.

(1) Paraplegia - terminal blastic state

Organ Size:
NC No change - abnormal before and after treatment
N Normal or absent before and after
- 1 or - 2 = Smaller
+ 1 or + 2 = Larger

1114156

TABLE D APPENDIX

RESPONSE TO 50 R CHRONIC LYMPHOCYTIC LEUKEMIA

Pt. No.	Sex	Age at R_x	Interval D_x to TBI R_x	Previous R_x	Interval from last R_x to TBI	Change in Size			Systemic Symptoms + = Improvement	Subsequent Major Forms of R_x	Interval from TBI to Later R_x	Follow-up Interval
						Spleen	Liver	Lymph Nodes				
1 a	M	67	3 yr., 8 mo.	^{32}P x 4	$6\frac{1}{2}$ mo.	- 2	N	- 2	+ 2	Chlorambucil Prednisone Ext. rad. to spleen ^{32}P x 2 METBI 50 R	$6\frac{1}{2}$ mo. $6\frac{1}{2}$ mo. 10 mo. 2 yr., 4 mo. & 3 yr., 2 mo. 4 yr., 7 mo.	A 9 yr., 3 mo.
1 b	M	72	8 yr., 3 mo.	^{32}P x 4 METBI 50 R Chlorambucil Prednisone Ext. rad. to spleen ^{32}P x 2	17 mo.	- 1	NC	NC	+ 1	Prednisone	5 mo.	A 4 yr., 9 mo.
2 a	M	51	23 mo.	None	-	N	N	NC	N	Prednisone Ext. rad. to neck x 2 Chlorambucil ^{32}P x 4 Prednisone ^{32}P Ext. rad. to axilla Ext. rad. to axilla and groin METBI 50 R	9 days 14 days & 27 days 5 mo., 12 mo., 14 mo., 16 mo. & 21 mo. 22 mo. 23 mo. 2 yr., 1 mo. 2 yr., 2 mo. 2 yr., 9 mo.	D 6 yr., 4 mo.

1114157

TABLE D APPENDIX - continued

2 b	M	54	4 yr., 8 mo.	Prednisone Ext. rad. to neck x 2 Chlorambucil ^{32}P x 5 Prednisone Ext. rad. to axilla Ext. rad. to axilla and groin	7 mo.	+ 1	- 1	NC	+ 2	Chlorambucil Prednisone Ext. rad. to cervical nodes	3 mo., 3 mo. 3 yr., 5 mo.	D 3 yr., 8 mo.
3	M	71	3 days	None	-	NC	N	N	UD (1)	None	-	D 4 yr., 5 mo.
4	M	52	$1\frac{1}{2}$ mo.	None	-	NC	N	N	N	^{32}P x 3 Prednisone METBI 100 R Hydrocortisone Prednisone METBI 100 R (See Table E, Case 4) Hydrocortisone	$4\frac{1}{2}$ mo., $5\frac{1}{2}$ mo., 17 mo. 22 mo. 2 yr. 2 yr., 2 mo. 2 yr., 4 mo. 3 yr., $4\frac{1}{2}$ mo. 3 yr., 5 mo.	D 4 yr., 2 mo.
5	F	67	3 yr., 1 mo.	Prednisone Splenectomy Chlorambucil	11 mo.	- (absent)	- 2	- 2	+ 1 UD (2)	Prednisone Dexamethasone	14 d. $2\frac{1}{2}$ mo.	D $2\frac{1}{2}$ mo.
6	M	70	28 days	Ext. rad. to lymph nodes Chlorambucil	6 mo.	+ 1	- 1	NC	+ 1	Prednisone Hydrocortisone	$1\frac{1}{2}$ mo. 4 mo.	D $4\frac{1}{2}$ mo.
7	M	55	$6\frac{1}{2}$ mo.	^{32}P x 2	6 mo.	N	N	- 2	+ 1	^{32}P	6 mo.	D 7 yr., 4 mo.

1114158

TABLE D APPENDIX - continued

Pt. No.	Sex	Age at R_x	Interval D_x to TBI R_x	Previous R_x	Interval from last R_x to TBI	Change in Size			Systemic Symptoms + = Improvement	Subsequent Major Forms of R_x	Interval from TBI to Later R_x	Follow-up Interval
						Spleen	Liver	Lymph Nodes				
8 a	M	68	3 days	None	-	+ 1	+ 1	- 1	NC	Prednisone METBI 50 R	5 mo. 3 yr., 5 mo.	D 6 yr., 7 mo.
8 b	M	71	3 yr., 5 mo.	METBI 50 R Prednisone	23 mo.	+ 1	+ 1	- 1	+ 1	Chlorambucil	15 mo.	D 3 yr., 2 mo.
9	M	74	$5\frac{1}{2}$ mo.	Prednisone ^{32}P x 2	3 mo. (3)	N	N	- 2	+ 2	Prednisone Hydrocortisone	Cont. (3) 11 mo.	D 11 mo.
10	M	82	14 days	None	-	NC	NC	- 1	UD (4)	^{32}P	2 mo.	D 1 yr., 2 mo.
11	M	63	14 days	Prednisone Hydrocortisone	(3) 7 days	- 2	UD	- 2	NC	Prednisone Hydrocortisone Ext. rad. to spleen	(3) Continuous 28 days 1 mo.	D 3 mo.
12	M	79	$23\frac{1}{2}$ mo.	METBI 100 R (See Table F, Case 15) Prednisone	- 18 days	- 1	NC	NC	+ 1	Prednisone Hydrocortisone Ext. rad. to spine Hydrocortisone Prednisone 6-MP Hydrocortisone	12 days $2\frac{1}{2}$ mo. 3 mo. 5 mo. $5\frac{1}{2}$ mo. 7 mo. $7\frac{1}{2}$ mo.	D $7\frac{1}{2}$ mo.

(1) Hospitalized for acute meningitis days 25 - 54
(2) Hospitalized with hemolytic anemia days 14 - 44
(3) On Prednisone during and after treatment
(4) Hospitalized with pneumonia days 35 - 45

1114159

TABLE E APPENDIX

RESPONSE TO 100 R CHRONIC LYMPHOCYTIC LEUKEMIA

Pt. No.	Sex	Age at R_x	Interval D_x to TBI R_x	Previous R_x	Interval from last R_x to TBI	Change in Size			Systemic Symptoms + = Improvement	Subsequent Major Forms of R_x	Interval From TBI to Later R_x	Follow-up Interval
						Spleen	Liver	Lymph Nodes				
1	F	40	2 mo.	Ext. rad. to spleen	11 days	NC	+ 1	- 2	N	Ext. rad. to abdomen ^{32}P Prednisone Ext. rad. to neck & chest Ext. rad. to pelvis Ext. rad. to neck & rt. axilla Dexamethasone	3 mo. 4½ mo. 7 mo. 15 mo. 2 yr., 6 mo. 2 yr., 10 mo. 5 yr.	D 5 yr., 9 mo.
2	M	49	2 yr., 1 mo.	TEM Ext. rad. to rt. axilla Ext. rad. to naso-pharynx Chlorambucil Ext. rad. to lt. axilla	12 mo.	NC	+ 1	NC	UD (1)	Prednisone ^{32}P	2 mo. 4 mo.	D 3 mo.
3	F	49	3 days	Ext. rad. to neck and abd., axill. & ing. nodes	- 12 mo.	NC	NC	NC	NC	Prednisone Ext. rad. to liver Hydrocortisone	1½ mo. 2 mo. 4 mo.	D 4 mo.
4 a	M	54	2 yr., 2 mo.	METBI 50 R (See Table D, Case 4) ^{32}P x 3 Prednisone	1½ mo. (2)	- 1	- 2	- 2	NC	Hydrocortisone Prednisone METBI 100 R	2 mo. (2) 16½ mo.	D 21 mo.
4 b	M	55	3 yr., 6 mo.	METBI 50 R (See Table D, Case 4) ^{32}P x 3 Prednisone METBI 100 R Hydrocortisone	3 days	+ 1	+ 1	NC	+ 1	Hydrocortisone Prednisone	11 days 1½ mo.	D 4½ mo.
5	M	88	4 yr.	Chlorambucil	1 mo.	N	N	+ 2	- 2	^{32}P	1½ mo.	D 1 yr., 1½ mo.

1114160

TABLE E APPENDIX - continued

Pt. No.	Sex	Age at R_x	Interval D_x to TBI R_x	Previous R_x	Interval from last R_x to TBI	Change in Size			Systemic Symptoms + = Improvement	Subsequent Major Forms of R_x	Interval From TBI to Later R_x	Follow-up Interval
						Spleen	Liver	Lymph Nodes				
6	M	57	6 days	None	-	+ 1	+ 1	NC	+ 1	32p Ext. rad. to neck Prednisone Hydrocortisone	$3\frac{1}{2}$ mo. 7 mo. 9 mo. 2 yr., 5 mo.	D 3 yr., 5 mo.
7	F	54	13 days	None	-	+ 1 ?	N	- 1	N	Chlorambucil Prednisone Dexamethasone Hydrocortisone Cortisone Acetate Splenenectomy	$2\frac{1}{2}$ mo. 4 mo. 2 yr., 2 mo. 3 yr., $4\frac{1}{2}$ mo. 3 yr., $4\frac{1}{2}$ mo. 3 yr., $4\frac{1}{2}$ mo.	A 4 yr., 9 mo.
8 a	M	61	7 days	None	-	- 1	NC	NC	+ 2	METBI 100 R	22 mo.	D 2 yr., 2 mo.
8 b	M	63	22 mo.	METBI 100 R	22 mo.	- 1	NC	- 1	+ 1	Prednisone	$2\frac{1}{2}$ mo.	D $4\frac{1}{2}$ mo.
9	F	82	1 mo.	None	-	N	N	N	NC	None	-	A 4 yr., $4\frac{1}{2}$ mo.
10 a	M	74	3 days	None	-	N	N	- 1	N	METBI 100 R	18 mo.	D 3 yr., 9 mo.
10 b	M	75	18 mo.	METBI 100 R	18 mo.	N	N	- 1	+ 1	Ext. rad. to lt. ear LETBI 100 R LETBI 100 R Prednisone	8 mo. 16 mo. 21 mo. 2 yr.	D 2 yr., 3 mo.

1114161

TABLE E APPENDIX - continued

11	M	69	10 days	None	-	- 2	- 2	- 1	+ 1	Prednisone Hydrocortisone	9 mo. 3 yr., 4 mo.	A 4 yr., 1 mo.
12	M	76	1 mo.	Chlorambucil	18 days	NC	NC	NC	+ 1	Prednisone Hydrocortisone	2 mo. 4 mo.	D 4 mo.
13 a	M	61	14 mo.	Prednisone ^{131}I x 3 (3) ^{32}P x 3	$3\frac{1}{2}$ mo.	+ 1	+ 1	NC	+ 1	Ext. rad. to abd. Prednisone METBI 100 R	$2\frac{1}{2}$ mo. $8\frac{1}{2}$ mo. 12 mo.	D 3 yr., 8 mo.
13 b	M	62	2 yr., 2 mo.	METBI 100 R Ext. rad. to abd. Prednisone	1 mo.	N	NC	- 1	+ 1	Ext. rad. to ing. nodes Prednisone Cyclophosphamide Ext. rad. to lt. eye	9 mo. 15 mo. 21 mo. 2 yr., 4 mo.	D 2 yr., 8 mo.
14	M	71	18 days	None	-	- 1	- 1	UD	UD (4)	Prednisone Hydrocortisone	43 days $2\frac{1}{2}$ mo.	D $2\frac{1}{2}$ mo.
15	M	77	3 days	None	-	- 1	NC	NC	+ 1	Prednisone METBI 50 R (See Table D, Case 12) Hydrocortisone Ext. rad. to spine 6-MP	$7\frac{1}{2}$ mo. $23\frac{1}{2}$ mo. 2 yr., 2 mo. 2 yr., $3\frac{1}{2}$ mo. 2 yr., $6\frac{1}{2}$ mo.	D 2 yr., 7 mo.
16	M	55	4 days	None	-	- 1	- 1	- 2	+ 2	Prednisone	8 mo.	A 3 yr., 1 mo.

(1) Hospitalized 3 weeks post R_x for thrombocytopenia
(2) On Prednisone during and after treatment
(3) Toxic adenoma of thyroid
(4) At 6 weeks post R_x admitted for transfusions and Prednisone

1114162

TABLE F APPENDIX

RESPONSE TO 50 R METBI - LYMPHOSARCOMA

Pt. No.	Sex	Age at R_x	Interval D_x to TBI R_x	Previous R_x	Interval from last R_x to TBI	Change in Size			Systemic Symptoms + = Improvement	Subsequent Major Forms of R_x	Interval From TBI to Later R_x	Follow-up Interval
						Spleen	Liver	Lymph Nodes				
1	F	37	12 days	None	-	NC	- 1	NC	+ 1	METBI 100 R (See Table G, Case 3 a)	3 mo.	D 4 yr.
										Splenectomy	13 mo.	
										METBI 100 R (See Table G, Case 3 b)	16 mo.	
										Ext. rad. to pelvic and abdominal nodes	21½ mo.	
										Prednisone	2 yr.	
										Nitrogen mustard	3 yr.	
										Ext. rad. to axillae	3 yr., 3 mo.	
										Vinblastine	3 yr., 6 mo.	
										Ext. rad. to lower abdominal mass	3 yr., 11 mo.	
										Hydrocortisone	3 yr., 11½ mo.	
2	M	42	19 days	None	-	?	?	- 1	N	Ext. rad. to ing. and iliac nodes	2 yr., 7 mo.	D 3 yr., 5 mo.
										METBI 100 R (See Table G, Case 13)	3 yr., 1 mo.	
										Ext. rad. to abd.	3 yr., 1½ mo.	
										Nitrogen mustard	3 yr., 2½ mo.	
										Chlorambucil	3 yr., 4 mo.	
										Prednisone	3 yr., 4½ mo.	
										Ext. rad. to mediastinum	3 yr., 5 mo.	

1114163

TABLE F APPENDIX - continued

3	M	46	2 yr., 3 mo.	Ext. rad. to neck & axilla ^{32}P x 3	5 mo.	+ 1	N	- 1	NC	Chlorambucil Prednisone	5 mo. 7 mo.	D 3 yr., $2\frac{1}{2}$ mo.
4	M	72	17 days	None	-	N	- 1	- 1	NC	^{32}P x 3 Chlorambucil	2 mo. $13\frac{1}{2}$ mo.	A 4 yr., 10 mo.
5	M	45	10 mo.	Nitrogen mustard Ext. rad. to spleen Thio-Tepa	$8\frac{1}{2}$ mo. ?	+ 1	+ 1	+ 1	+ 1	Prednisone	2 mo.	A 2 yr., 1 mo.

1114164

TABLE G APPENDIX

RESPONSE TO 100 R METBI LYMPHOSARCOMA

Pt. No.	Sex	Age at R_x	Interval D_x to TBI R_x	Previous R_x	Interval from last R_x to TBI	Change in Size				Systemic Symptoms + = Improvement	Subsequent Major Forms of R_x	Interval from TBI to Later R_x	Follow-up Interval
						Spleen	Liver	Lymph Nodes	Abd. Mass				
1 a	F	49	2 mo.	Ext. rad. to left inguinal nodes	1 mo.	N	- 1	- 2	0	N	Ext. rad. to submandibular nodes 32P METBI 100 R	10 min. 11 mo. 21 mo.	D 4 yr., 9 mo.
1 b	F	51	23 mo.	Ext. rad. to left inguinal nodes METBI 100 R Ext. rad. to submandibular nodes 32P	$10\frac{1}{2}$ mo.	N	N	- 2	- 1	+ 1	Ext. rad. to abdomen Nitrogen mustard Ext. rad. to spine Ext. rad. to rt. inguinal nodes Ext. rad. to rt. cerv. nodes Prednisone Ext. rad. to rt. thigh Ext. rad. to left pelvis 32P Hydrocortisone	2 mo. 5 mo. $5\frac{1}{2}$ mo. 14 mo. 14 mo. 17 mo. 20 mo. 2 yr., 3 mo. 2 yr., 9 mo. 2 yr., 11 mo.	D 2 yr., 11 mo.
2	F	48	16 yr.	Ext. rad. to right cerv. nodes Ext. rad. to nasopharynx Ext. rad. to left cervical nodes Ext. rad. to abd. Ext. rad. to right breast and axilla Nitrogen mustard	16 yr. 11 mo. 2 mo.	N	2	- 2	NC	(1)	None	-	D $2\frac{1}{2}$ mo.
3 a	F	38	$3\frac{1}{2}$ mo.	METBI 50 R (See Table F, Case 1)	3 mo.	+ 1	NC	- 2	0	N	Splenectomy METBI 100 R	10 mo. 13 mo.	D 3 yr., 8 mo.

1114165

TABLE G APPENDIX - continued

3 b	F	39	1 yr., $4\frac{1}{2}$ mo.	METBI 50 R (See Table F, Case 1) METBI 100 R Splenectomy	3 mo.	-	NC	- 1	0	NC	Ext. rad. to pelvic and abd. nodes Prednisone Nitrogen mustard Ext. rad. to axillae Vinblastine Ext. rad. to abd. mass Hydrocortisone	$5\frac{1}{2}$ mo. $7\frac{1}{2}$ mo. $19\frac{1}{2}$ mo. 23 mo. 2 yr., 2 mo. 2 yr., 7 mo. 2 yr. $7\frac{1}{2}$ mo.	D 2 yr., $7\frac{1}{2}$ mo.
4	M	80	1 mo.	None	-	N	NC	- 1	0	- 1 (2)	Ext. rad. to mediastinum ^{198}Au to right pleural cavity Ext. rad. to mediastinum	$1\frac{1}{2}$ mo. 2 mo. $2\frac{1}{2}$ mo.	D $6\frac{1}{2}$ mo.
5 a	F	60	9 mo.	Ext. rad. to cheeks	$8\frac{1}{2}$ mo.	N	N	- 2	0	+ 1	METBI 100 R	12 mo.	D 4 yr., $2\frac{1}{2}$ mo.
5 b	F	61	21 mo.	Ext. rad. to cheeks METBI 100 R	12 mo.	N	N	- 2	0	+ 1	Ext. rad. to rt. inguinal nodes Ext. rad. to rt. cervical nodes Ext. rad. to lt. femur & iliac nodes	3 mo. 13 mo. 2 yr., 7 mo.	D 3 yr., $2\frac{1}{2}$ mo.
6	F	68	8 yr.	^{32}P x 1 Triethylenemelamine Ext. rad. to neck Ext. rad. to rt. axill. and inguinal nodes Ext. rad. to upper chest Ext. rad. to mediastinum	2 mo.	+ 1	NC	- 2	0	- 1 (3)	Ext. rad. to lt. axilla Ext. rad. to abd. mass Hydrocortisone	13 mo. 2 yr., 2 mo. 2 yr., 10 mo.	D 2 yr., 10 mo.
7 a	M	76	$1\frac{1}{2}$ mo.	None	-	N	- 1	- 1	0	N	^{32}P METBI 100 R	10 mo. $18\frac{1}{2}$ mo.	D $22\frac{1}{2}$ mo.

TABLE G APPENDIX - continued

Pt. No.	Sex	Age at R_x	Interval D_x to TBI R_x	Previous R_x	Interval from last R_x to TBI	Change in Size				Systemic Symptoms + = Improvement	Subsequent Major Forms of R_x	Interval from TBI to Later R_x	Follow-up Interval
						Spleen	Liver	Lymph Nodes	Abd. Mass				
7 b	M	78	20 mo.	^{32}P METBI 100 R	18½ mo.	UD	UD	- 2	- 1	N	Ext. rad. to abd. mass Nitrogen mustard Hydrocortisone	3½ mo. 4 mo. 4 mo.	D 4 mo.
8	M	49	10 days	None	-	N	+ 1	- 1	0	N	Ext. rad. to neck, axill. & ing. nodes Ext. rad. to rt. cervical nodes ^{32}P Prednisone Ext. rad. to iliac and inguinal nodes Ext. rad. to left axilla Ext. rad. to cheek Ext. rad. to spine Ext. rad. to spine Ext. rad. to thorax Ext. rad. to lt. cheek Cyclophosphamide	2 mo. 9½ mo. 13½ mo. 15 mo. 17 mo. 17½ mo. 3 yr., 2 mo. 4 yr., 9 mo. 5 yr., 5½ mo. 5 yr., 7 mo. 5 yr., 8 mo. 5 yr., 8½ mo.	A 5 yr., 10 mo.
9	M	87	53 days	None	-	N	N	NC (4)	0	NC	Ext. rad. to both ing. & iliac nodes Ext. rad. to neck nodes	28 d. 5½ mo.	D 6 mo.
10 a	F	55	1 mo.	None	-	N	+ 2	1 (5)	0	+ 1	Ext. rad. to rt. clavicle Ext. rad. to lt. axilla	2 mo. 2½ mo.	D 4 yr., 9 mo.

111467

TABLE G APPENDIX - continued

											Ext. rad. to rt. & lt. axillae Ext. rad. to neck METBI 100 R	10 mo. 10½ mo. 1 yr., 5 mo.	
10 b	F	57	1 yr., 6 mo.	METBI 100 R Ext. rad. x 4	6½ mo.	N	N	- 2	0	UD (6)	Prednisone Ext. rad. to neck Chlorambucil Ext. rad. to lt. chest Ext. rad. to rt. chest Ext. rad. to abdomen Hydrocortisone Cyclophosphamide	6 mo. 19½ mo. 20½ mo. 2 yr., 4 mo. 2 yr., 5 mo. 3 yr., 1 mo. 3 yr., 2 mo. 3 yr., 2½ mo.	D 3 yr., 4 mo.
11	F	55	3 mo.	None	-	N	N	- 2	0	NC	32p	6½ mo.	A 5 yr., 2 mo.
12	M	72	5 days	None	-	N	- 2	- 1	0	+ 1	32p Ext. rad. to rt. iliac & ing. nodes Ext. rad. to abdomen Dexamethasone Prednisone Hydrocortisone	2½ mo. 4½ mo. 9½ mo. 12 mo. 18½ mo. 20 mo.	D 21 mo.
13	M	45	4 yr., 1 mo.	METBI 50 R (See Table F, Case 2) Ext. rad. to ing. & iliac nodes	- 5½ mo.	N	N	NC	NC (7)	NC	Ext. rad. to abdomen Nitrogen mustard Chlorambucil Prednisone Ext. rad. to mediastinum	16 d 2 mo. 3 mo. 3½ mo. 4 mo.	D 4 mo.

1114168

TABLE G APPENDIX - continued

Pt. No.	Sex	Age at R_x	Interval D_x to TBI R_x	Previous R_x	Interval from last R_x to TBI	Change in Size				Systemic Symptoms + = Improvement	Subsequent Major Forms of R_x	Interval from TBI to Later R_x	Follow-up Interval
						Spleen	Liver	Lymph Nodes	Abd. Mass				
14	M	78	$1\frac{1}{2}$ mo.	None	-	N	- 1	- 1	0	+ 1	Ext. rad. to sacrum Prednisone	8 mo. 20 mo.	D 21 mo
15	M	78	3 mo.	None	-	- 1	- 1	- 1	0	+ 1	LETBI 100 R Chlorambucil Prednisone Cyclophosphamide Hydrocortisone	15 mo. 22 mo. 23 mo. 2 yr., $3\frac{1}{2}$ mo. 2 yr., 4 mo.	D 2 yr., 4 mo.
16	M	76	4 yr., 1 mo.	Ext. rad. to neck & both axillae Nitrogen mustard Ext. rad. to neck, both axillae, and mediastinum Ext. rad. to abdomen x 3 Local rad. sq. Ca cheek Methylprednisolone Triethylenemelamine Prednisone	(8)	N	NC	- 1	0	UD (8)	Prednisone Ext. rad. to keratoses Cortisone Acetate	(8) $1\frac{1}{2}$ mo. $5\frac{1}{2}$ mo.	D $5\frac{1}{2}$ mo
17	M	68	4 mo.	None	-	- 1	NC	- 2	0	+ 1	Cyclophosphamide Ext. rad. to sq. Ca face Ext. rad. to met. Ca pelvis	9 mo. 10 mo. 2 yr., 9 mo.	A 2 yr., 9 mo.

(1) In terminal condition at time of R_x
(2) In hospital with bilateral pleural effusion days 31-81 post R_x
(3) In hospital with pneumonia days 21-66 post R_x
(4) No regression at day 14. External radiation at day 28
(5) Maximum regression at 4 weeks, enlarging again by 6 weeks
(6) In another hospital with herpes zoster at 6 weeks
(7) External radiation to abdomen on day 16. No change at day 42
(8) On Prednisone during and after treatment

1114169

TABLE II APPENDIX

RESPONSE TO METBI - HODGKIN'S

Pt. No.	Sex	Age at R_x	Dose	Interval D_x to TBI R_x	Previous R_x	Interval from last R_x to TBI	Change in Size			Systemic Symptoms + - Improvement	Subsequent Major Forms of R_x	Interval From TBI to Later R_x	Follow-up Interval
							Spleen	Liver	Lymph Nodes				
1	F	21	50 R	1 mo.	None	-	N	N	- 1	N	Ext. rad. to supraclavicular and mediastinal nodes	1½ mo.	A 8 yr., 10 mo.
											Nitrogen mustard	17 mo.	
											Ext. rad. to axillae	2 yr., 2½ mo.	
											Ext. rad. to clavicular nodes	3 yr., 1 mo.	
											Ext. rad. to axillae	3 yr., 9 mo.	
											Nitrogen mustard	5 yr., 1 mo.	
											Ext. rad. to mediastinum	5 yr., 3 mo.	
											Ext. rad. to spine	5 yr., 8 mo.	
											Uracil Mustard	5 yr., 9 mo.	
											Ext. rad. to breast mass	7 yr., 1 mo.	
											Ext. rad. to abd. mass	7 yr., 7 mo.	
											Vinblastine	7 yr., 11 mo.	
											Ext. rad. to left neck	8 yr., 3 mo.	
											Cytoxan in right chest cavity	8 yr., 5 mo.	
											Ext. rad. to right chest	8 yr., 5 mo.	
											Ext. rad. to right iliac nodes	8 yr., 6 mo.	
2	F	65	100 R	14 d.	None	-	N	N	- 1 (1)	NC (1)	None	-	D 14 d.

1114170

TABLE II APPENDIX - continued

Pt. No.	Sex	Age at R_x	Dose	Interval D_x to TBI R_x	Previous R_x	Interval from last R_x to TBI	Change in Size			Systemic Symptoms + Improvement	Subsequent Major Forms of R_x	Interval From TBI to Later R_x	Follow-up Interval
							Spleen	Liver	Lymph Nodes				
3	F	20	100 R	21 d.	None	-	N	N	- 1	NC	Nitrogen mustard	$1\frac{1}{2}$ mo.	D 2 yr., $3\frac{1}{2}$ mo.
											Prednisone	2 mo.	
											Ext. rad. to supraclav. nodes and mediastinum	$2\frac{1}{2}$ mo.	
											Ext. rad. to mediastinum & left axilla	$7\frac{1}{2}$ mo.	
											Ext. rad. to lt. neck	$7\frac{1}{2}$ mo.	
											Ext. rad. to rt. axill. & supraclav. nodes	$12\frac{1}{2}$ mo.	
											Nitrogen Mustard	14 mo.	
											Vinblastine	17 mo.	
											Ext. rad. to abdominal mass	2 yr.	
											Ext. rad. to left axilla & mediastinum	2 yr.	
											Uracil Mustard	$2\frac{1}{2}$ yr.	

(1) Last seen at 2 weeks after R_x

TABLE J APPENDIX

GEOMETRIC MEANS (% PRETREATMENT)

Values of the Computed Geometric Means Used in the Hematologic Figures of this Report

Day

Disease	R	Blood Value	1	2	4	7	14	21	28	35	42	49	56	62	76	84	No. Pts.	Fig. No.
CLL	50	WBC (all)	94.3	79.0	65.2	56.5	45.6	39.8	44.3	41.6	34.8						15	
		WBC (good response)	96.0	80.5	60.2	52.2	39.0	32.5	35.9	32.4	26.5						11	1
		WBC (poor response)	89.8	74.9	81.2	70.5	69.8	69.7	79.1	82.3	68.3						4	1
		Absolute Lymphs (all)	94.3	79.4	63.1	54.4	42.9	34.6	36.2	34.6	31.9						15	
		Abs. Lymphs (good response)	96.9	81.7	58.4	50.0	36.5	27.2	26.6	25.4	23.7						11	3
		Abs. Lymphs (poor response)	87.7	73.5	78.1	68.4	67.2	66.9	78.1	81.0	66.9						4	3
		Platelets	114.1	97.9	100.4	90.5	86.3	67.0	65.0	78.2	92.0						15	4,6
	100	WBC (all)	86.1	74.3	58.4	46.3	38.1	35.0	29.7	32.6	30.7						20	
		WBC (good response)	78.1	65.4	48.4	35.2	28.1	22.4	19.7	21.2	21.0						14	2
		WBC (poor response)	97.7	96.2	87.0	81.4	74.9	85.2	78.4	65.1	59.5						5	2
		Abs. Lymphs (all)	82.2	69.3	54.2	42.3	34.9	30.0	28.2	27.7	26.7						19	
		Abs. Lymphs (good response)	77.2	60.6	47.3	33.3	26.2	20.4	19.3	20.3	19.5						14	3
		Abs. Lymphs (poor response)	97.9	101.3	77.3	82.6	78.0	88.5	76.3	62.3	60.6						5	3
		Platelets	94.0	81.6	81.6	81.6	75.4	40.5	25.2	26.8	38.4						20	5,6

1114172

TABLE J APPENDIX - continued

Disease	R	Blood Value	Day 1	2	4	7	14	21	28	35	42	49	56	62	76	84	No. Pts.	Fig. No.
Lymph-oma	50	WBC	86.56	93.9	86.78	77.07	67.58	70.21	64.55	68.55	61.75						5	
		Absolute Lymphs	92.8	81.1	76.8	69.7	59.3	72.2	72.1	77.4	69.4						5	
		Platelets	97.7	102.3	104.8	105.6	131.6	85.6	70.9	87.1	92.6						5	
	100	WBC	91.1	81.7	74.5	66.1	80.1	81.1	66.5	53.5	53.1						20	7
		Absolute Lymphs	77.7	79.9	59.2	50.0	73.4	65.1	57.9	59.5	57.6						20	8
		Platelets	95.2	94.0	88.7	97.2	82.4	52.7	27.3	28.6	42.8						22	10
CGL	50	Hgb	99.6	98.9	95.7	95.1	96.9	101.0	101.4	102.4	105.2						8	
		Absolute Lymphocytes	68.6	59.0	64.3	52.4	49.4	58.4	77.3	57.9	76.8						8	
		WBC	90.81	80.47	68.91	55.38	48.58	45.25	50.66	46.58	43.09						8	11, 15
		Platelets	101.9	96.6	104.0	103.7	136.5	101.7	81.5	91.8	92.9						8	13, 15
	100	Hgb	97.7	99.2	95.5	93.7	103.3	108.7	109.8	104.8	102.0						4	16
		Absolute Lymphocytes	99.3	111.7	82.9	80.7	48.5	73.8	65.6	58.8	63.8						4	
		WBC	98.7	93.6	68.5	35.2	22.8	17.8	23.9	26.9	17.3						1	12, 15
		Platelets	100.6	91.8	123.7	111.8	111.5	75.6	58.7	69.9	48.5						4	14, 15
PRV	100	Hgb	99.1	95.2	96.1	96.0	95.6	95.8	97.0	95.1	96.5	96.7	98.7	102.4	109.0	106.1	8	20
		Hct*	19.2	48.7	47.9	46.5	46.9	46.5	45.8	45.3	45.5	46.5	46.7	49.0	49.1	47.6	8	21
		MCHC	99.4	99.8	99.5	101.1	100.3	100.9	104.0	102.9	104.7	103.9	104.3	98.1	105.8	105.1	8	22
		WBC		85.1	85.0	80.1	73.4	47.1	46.2	29.7	26.7	38.0	35.8	-	40.0	55.6	7	17
		Absolute Lymphs		72.4	77.2	65.1	68.1	-	56.4	-	44.4						7	18
		Platelets	98.2	101.9	107.3	100.0	95.5	49.1	28.6	29.2	39.4	43.9	40.3		50.9	52.1	8	19

* Absolute values rather than percent pretreatment.

1114173