

AFRRI SR71-9  
JULY 1971

**AFRRI**  
**SCIENTIFIC**  
**REPORT**

**ERYTHROPOIETIC STEM CELL RECOVERY  
IN IRRADIATED POLYCYTHEMIC DOGS**

AFRRI SR71-9

**ARMED FORCES RADIOBIOLOGY RESEARCH INSTITUTE**  
**Defense Nuclear Agency**  
**Bethesda, Maryland**

---

Approved for public release; distribution unlimited

All aspects of investigative programs involving the use of laboratory animals sponsored by DoD components are conducted according to the principles enunciated in the "Guide for Laboratory Animal Facilities and Care", prepared by the National Academy of Sciences - National Research Council.

July 1971

ERYTHROPOIETIC STEM CELL RECOVERY

IN IRRADIATED POLYCYTHEMIC DOGS

S. J. BAUM  
D. E. WYANT



S. J. BAUM

Chairman

Experimental Pathology Department



HUGH B. MITCHELL

Colonel, USAF, MC

Director

ARMED FORCES RADIOBIOLOGY RESEARCH INSTITUTE

Defense Nuclear Agency

Bethesda, Maryland

#### ACKNOWLEDGMENT

The technical assistance of J. L. Atkinson is greatly appreciated.

## TABLE OF CONTENTS

	Page
Foreword (Nontechnical summary) . . . . .	iii
Abstract . . . . .	v
I. Introduction . . . . .	1
II. Methods . . . . .	1
III. Results . . . . .	4
IV. Discussion . . . . .	6
References . . . . .	11

## LIST OF FIGURES

Figure 1. Hematocrits for polycythemic dogs subjected to 150 rads mixed gamma-neutron radiation . . . . .	5
Figure 2. Erythrocytic stem cell recovery in polycythemic dogs exposed to 150 rads mixed gamma-neutron radiation . . . . .	6
Figure 3. Erythropoiesis in normal and in polycythemic dogs exposed to 150 rads mixed gamma-neutron radiation . . . . .	7

## LIST OF TABLES

Table I. Radioiron Uptake in Polycythemic Dogs in Response to Administered Exogenous Erythropoietin . . . . .	3
Table II. Radioiron Uptake in Polycythemic Dogs in Response to Administered Exogenous Erythropoietin . . . . .	3

FOREWORD  
(Nontechnical summary)

Before a red cell moves into the circulation to assume its function as an oxygen carrier for tissue and cellular metabolism, it must go through several maturation stages in the bone marrow. The most primitive or multipotential stem cell is first differentiated into a cell which is specific for red cell productivity. During this committed stage this cell is sensitive to the hormone erythropoietin which initiates its capability to synthesize hemoglobin and therefore ultimately to produce mature red cells.

Since the earlier more primitive cells reproduce frequently, they are highly radiosensitive. However, in general, the erythropoietic system has the capability for cellular self-renewal and therefore it can repair itself after exposure to sublethal radiation. This system is controlled by a feedback mechanism. Sensitive cells in the kidney detect the intracellular partial oxygen pressure which depends upon the oxygen carried by the red cells. When the partial pressure is reduced, indicating a low level of oxygen carried by the red cells, erythropoietin is produced. This hormone stimulates the production of red cells from the committed stage.

In a previous study, the capability for postirradiation recovery of the red cell producing system was measured. It was found to recover in an oscillatory pattern during the early weeks after exposure.

The present experiment was designed to investigate the origin of this oscillatory recovery response. Dogs were hypertransfused with red cells from donor animals which inhibited new red cell formation by the erythropoietic system. The capability

of the stem cells to respond to measured quantities of erythropoietin, as indicated by  $^{59}\text{Fe}$  incorporation into newly formed cells, was used as an assessment of the erythrocytic stem cell compartment size in normal dogs as well as in animals subjected to a sublethal exposure of 150 rads of mixed gamma-neutron radiation. It was observed that the origin of the postirradiation oscillations in red cell recovery is within the stem cell compartment. It is proposed that, in the main, these oscillations are caused by differences between the differentiation rate of multipotential uncommitted stem cells and those committed for red cell production.

## ABSTRACT

The response of erythropoietic stem cells in postirradiated polycythemic dogs to 300 units of administered exogenous erythropoietin was measured. One week prior to irradiation the dogs were made polycythemic by transfused allogeneic erythrocytes. The dogs were subjected to 150 rads of mixed gamma-neutron radiation. On the day of irradiation or on 10 different days during the first 3 weeks postirradiation, erythropoietin was administered and the  $^{59}\text{Fe}$  incorporation in response to this stimulation was measured. Recovery of the erythropoietic stem cells occurred in an oscillatory manner. In general, this was ascribed to a possible slow rate of differentiation of erythropoietin responsive cells from multipotential stem cells and a more rapid rate of proliferation of the former cells into subsequent erythrocytic progeny. As the number of divisions resulting from each cell is limited, recovery in number of cells is halted or even decreased until more cells from the slower moving multipotential stem cell compartment are released. Contributions to this oscillatory recovery pattern by chalone or the competition of related blood cell lines for the common stem cells, however, have not been excluded.



## I. INTRODUCTION

Recently it was reported<sup>2</sup> that postirradiation erythropoietic recovery in dogs occurs in an oscillatory pattern. It was suggested that these oscillations were the result of cell population adjustments within the stem cell compartment and probably were not due to fluctuations in the stimulation for the release of cells to committed cell lines. This seems to be further supported by reports which indicate that erythropoietin levels apparently do not change in sublethally irradiated rats or dogs.<sup>9, 13, 14</sup>

In order to obtain more direct evidence for the origin of the postirradiation oscillatory erythropoietic recovery, an experiment was designed utilizing the polycythemic dog as the test animal. Since erythropoiesis is greatly reduced in this animal, the response of its erythropoietin responsive cells to a measured quantity of administered erythropoietin is a measure of its capability for erythropoiesis at the time of the hormone injection.

## II. METHODS

Healthy, purebred, AKC registrable male beagles, 1 to 2 years old, from the colony of the Armed Forces Radiobiology Research Institute (AFRRI) were used in this study. They were under a veterinarian's care for the prevention of parasite infestation and were immunized against distemper, hepatitis and rabies.

During the experiment the dogs were housed individually in stainless steel cages in temperature-controlled rooms. They were fed kibbled laboratory dog food supplemented once a week with high protein canned meat ration. Water was provided ad libitum.

A total of 102 dogs were utilized in this study; 18 were employed to determine the optimal concentration of erythropoietin\* necessary to stimulate erythropoiesis in unirradiated polycythemic dogs, and 84 were used in the main experiment. Of the latter group, 77 were subjected to 150 rads of mixed gamma-neutron radiation while 7 served as nonirradiated controls.

The absence of data on dogs in the literature made it necessary to determine experimentally the optimum concentration of erythropoietin to stimulate erythropoiesis in polycythemic dogs. This was particularly important in light of recent work by Byron<sup>5</sup> who demonstrated increasing fluctuation in erythropoietic responses when submaximal hormone doses were employed. In our hands, 6 units of erythropoietin stimulated maximal erythropoietic responses in polycythemic rats. On the basis of a fiftyfold plasma volume increase for dogs, the a priori estimate was approximately 300 units of erythropoietin.

Since sheep Erythropoietin A, Step 1, which can be used safely in rodents, was toxic when administered in larger concentrations to dogs, the more purified albeit more expensive Step 3 preparation was employed. However, only limited quantities of this preparation were available; therefore the titration studies were carefully conducted with a small number of animals.

Table I indicates that whereas 100 units of erythropoietin have no effect, the administration of 200 units induces a <sup>59</sup>Fe uptake of 59.5 percent and 300 units could well have been maximal in stimulating erythropoiesis. Additional tests as delineated

---

\* Erythropoietin, Step 3 (sheep), obtained from Connaught Medical Research Laboratories, Toronto, Canada

in Table II seem to confirm this. Apparently no further erythrocytic cell production is initiated with hormone doses above 300 units.

Table I. Radioiron Uptake in Polycythemic Dogs in Response to Administered Exogenous Erythropoietin

Number of dogs	Erythropoietin (units)	$^{59}\text{Fe}$ Uptake (percent of injected dose)
3	0 (saline)	$19.7 \pm 2.9^*$
3	100	$22.7 \pm 5.1$
3	200	$59.5 \pm 3.9$
3	300	$64.4 \pm 6.1$

\* Standard error

Table II. Radioiron Uptake in Polycythemic Dogs in Response to Administered Exogenous Erythropoietin

Number of dogs	Erythropoietin (units)	$^{59}\text{Fe}$ Uptake (percent of injected dose)
3	0 (saline)	$26.0 \pm 2.0^*$
1	300	61.5
7 <sup>†</sup>	300	$61.5 \pm 8.4$
1	500	56.2
1	700	49.2

\* Standard error

† Control dogs from the main experiment

The dogs were subjected to mixed gamma-neutron radiation from the AFRRI-TRIGA reactor. The absorbed dose (150 rads) is at the midline of the animal. The tissue kerma rate, free-in-air, was 20 rads/minute and the ratio of neutron kerma to gamma ray kerma, free-in-air, was 0.67. This ratio was not measured in tissue

where it was undoubtedly somewhat reduced. The effective gamma energy was between 1 and 2 MeV.

One week prior to irradiation, all dogs were made polycythemic by three transfusions, one every other day, of approximately 250 ml of packed allogeneic erythrocytes. To assure the maintenance of polycythemia, dogs administered erythropoietin beyond the 9th day postirradiation received a fourth transfusion of packed cells. On the day of irradiation or on postexposure days 1, 3, 5, 7, 9, 11, 12, 15, 18 or 21, groups consisting of seven different polycythemic dogs received intravenously 300 units of erythropoietin. A similar hormone dose was administered to seven unirradiated animals at the approximate midpoint of the experiment (day 12). Two days after the erythropoietin injection, the animals were injected via the left jugular vein with 1 ml of a sodium citrate-buffered  $\text{FeCl}_3$  solution containing  $10 \mu\text{Ci}$  of  $^{59}\text{Fe}$  in  $0.1 \mu\text{g}$  of total iron. A blood sample was obtained 7 days after the isotope injection and the  $^{59}\text{Fe}$  incorporation was determined. The methodology for the determination of the radioactivity and the radioiron uptake was described previously.<sup>2</sup> The hematocrit, measured by the standard microhematocrit method, was determined for each dog on the day of erythropoietin and  $^{59}\text{Fe}$  injection as well as on the day of blood sampling for the iron uptake determination.

### III. RESULTS

Figure 1 clearly indicates that the hematocrits of the dogs were significantly elevated throughout the 23 days of the present experiment and that all animals were polycythemic. As may be seen in Tables I and II, iron uptake and consequently erythropoiesis is greatly reduced in polycythemic dogs not receiving exogenous

erythropoietin. The  $^{59}\text{Fe}$  uptake in the seven control animals was 61.5 percent of the injected activity which was very close to most values obtained in unirradiated dogs receiving erythropoietin in quantities of at least 200 units.

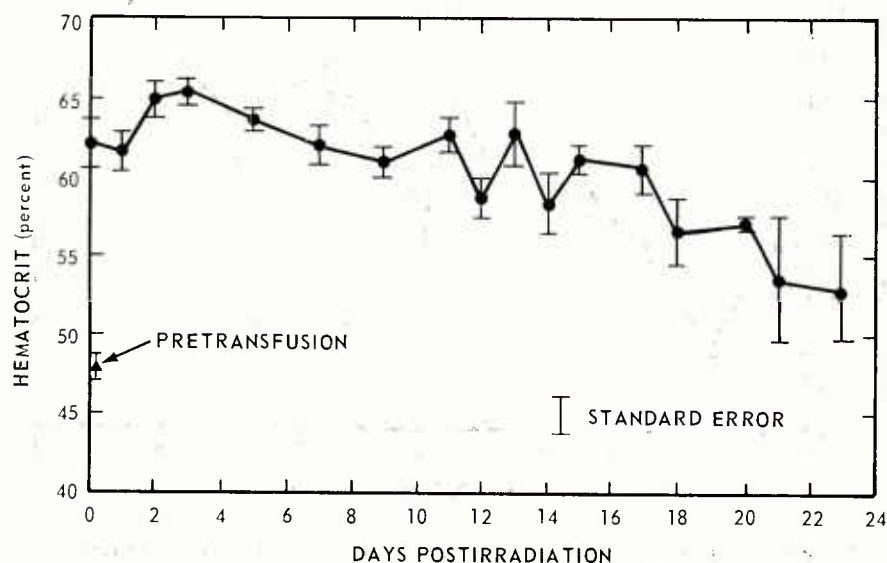


Figure 1. Hematocrits for polycythemic dogs subjected to 150 rads mixed gamma-neutron radiation

Iron incorporation in response to the administration of 300 units of erythropoietin immediately after irradiation (day 0) was reduced to approximately 17 percent of values obtained from unirradiated polycythemic dogs (Figure 2). This was followed by an apparent abortive rise 1 day later with about twice the uptake values. A second low value was measured on the 3rd day, followed by increases reaching approximately 50 percent of control values on day 7 postirradiation. No further increase is noted on the 9th day, followed by the third erythropoietic recovery to approximately 70 percent of control values on the 11th day. Thereafter, another depression is seen on the 12th day, a fourth recovery peak (approximately 76 percent) on the 15th day, one more

return to possible lower  $^{59}\text{Fe}$  uptake values on the 18th day and continued recovery beyond that time.

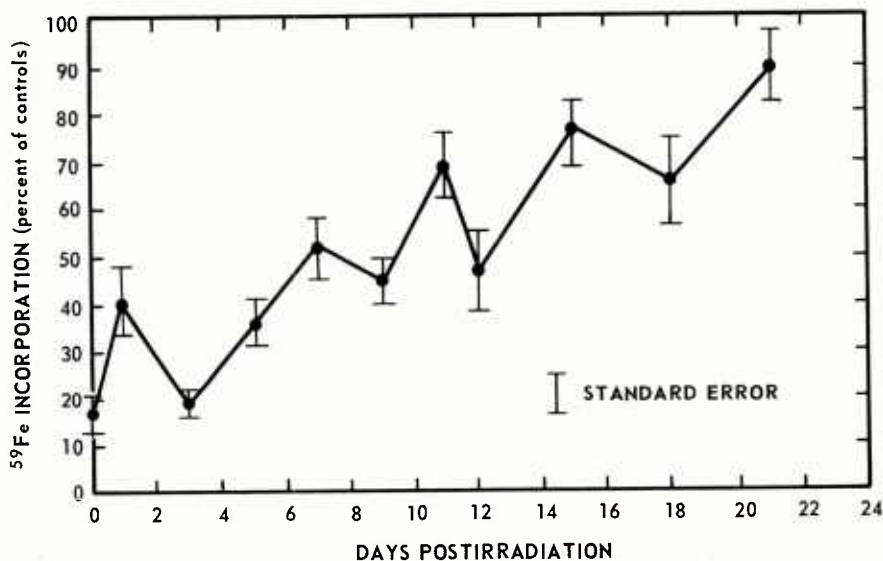


Figure 2. Erythrocytic stem cell recovery in polycythemic dogs exposed to 150 rads mixed gamma-neutron radiation

#### IV. DISCUSSION

Earlier reports<sup>6,7</sup> have demonstrated the validity of the assumption that the erythropoietic response in polycythemic animals to exogenous erythropoietin is a measure of their erythrocytic stem cell compartment size. This was further confirmed in a more recent experiment.<sup>11</sup> The data of the present study appear to establish that the origin of the postirradiation oscillatory erythropoietic recovery pattern in dogs is in the erythrocytic stem cell compartment.

It is of interest to compare the postirradiation recovery curve of the polycythemic animals in the present study with that of dogs with normal red cell mass published earlier.<sup>2</sup> First, it appears that the radiation effect upon the erythropoietic stem cells



as seen in the present study is much more severe when compared with that upon the total red cell precursor system seen previously (Figure 3). Iron uptake was reduced to 17 percent of control values in the dogs of the present study, while only to 84 percent in those of the previous study. Thereafter, it appears that recovery peaks for stem cells precede those for the total precursor system. The maxima for the first three consecutive peaks appear to occur about 3 to 4 days earlier in the polycythemic dogs. One might suggest the possibility that it takes approximately a 3- to 4-day period in dogs for released stem cells to convert to hemoglobin synthesizing cells. The higher iron incorporation values observed in nonpolycythemic irradiated dogs and reported in the previously published study<sup>2</sup> represent the capability of the precursor system for amplifying cellular production in animals where erythrocytic stem cells

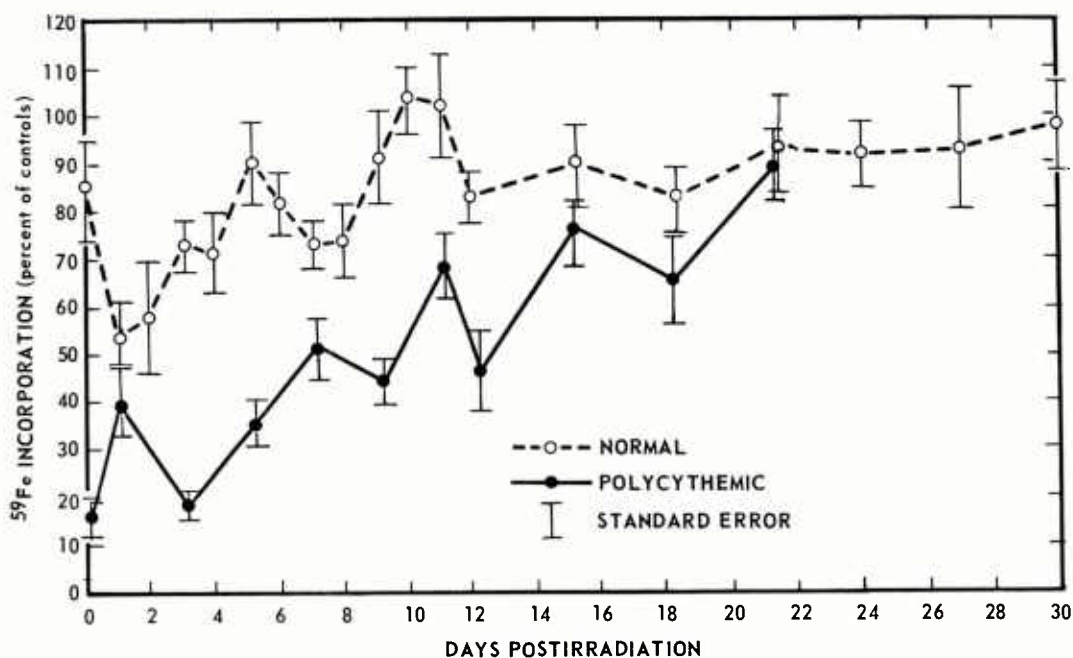


Figure 3. Erythropoiesis in normal and in polycythemic dogs exposed to 150 rads mixed gamma-neutron radiation

are released continuously due to stimulation by endogenous erythropoietin. It is assumed that the iron uptake values measured in the polycythemic dogs of the present experiment represent only the maximum number of erythropoietic stem cells capable of release in response to the administration of exogenous erythropoietin and their subsequent progeny.

Having ascertained that the origin of the postirradiation erythropoietic oscillations is within the bone marrow population, attempts to explain the pathophysiological basis are indicated. Morley and Stohlman<sup>10</sup> have presented evidence that normal erythropoiesis in dogs may occur in an oscillatory manner. These oscillations may be initiated by an inhibitor or chalone, the concentration of which controls stem cell compartment size.<sup>8,12</sup> However, particularly as the data of the present experiment indicate, the number of erythropoietic stem cells is drastically reduced after irradiation which in turn should have decreased the concentration of chalone. Oscillatory production of cells could possibly have occurred only if the inhibitions were initiated by the chalone concentration per stem cell.

Results of the present experiment appear not to support the contention by Bullough and Rytömaa<sup>4</sup> that chalone might be produced by circulating erythrocytes. In the postirradiated dog, erythropoiesis starts before a significant decline in mature erythrocytes is noted. This would be at a time when chalone concentration should still have been at a relatively high level if produced by erythrocytes. Furthermore, the concentration of peripheral erythrocytes was maintained artificially at an above normal level throughout this study.



Although chalone might control the normal turnover of stem cells, it is not entirely clear how or if they act during the early postirradiation days. Alternatively, the data of the present study suggest the following mechanisms. Within hours after irradiation, feedback stimulations from the now decimated committed erythropoietin responsive cell (ERC) population induce the release of cells from the multipotential stem cell compartment. The latter is of course extremely limited since the number of these cells was also reduced by radiation. Once released, the ERC's proliferate rapidly as indicated by the first rise (day 1) in the present study. However, there appears to be some constraint operating which permits these cells in polycythemic animals to multiply up to a certain number and not beyond.<sup>11</sup> Since differentiation from the multipotential stem cells to the ERC's apparently occurs at a slower pace<sup>3</sup> than the proliferation rate of the latter, further increase in size is halted. Indeed, if the final ERC's could only respond to erythropoietin within a relatively short period of time, this specific cell population in polycythemic animals would decrease before sufficient additional differentiation from the stem cells has occurred. Evidence for this was apparently obtained in a study using polycythemic mice.<sup>11</sup> In the normal nonpolycythemic animal, decreases in cellular populations would simply occur by the rapid release of ERC's into the erythrocytic cell lines as stimulated by endogenous erythropoietin and a slower rate of replacement from the multipotential stem cells. As more stem cells differentiate into ERC's, the next recovery cycle begins. In this way, differences in the rate of cell differentiation from the primitive multipotential stem cells to the committed ERC's could quite possibly have been responsible for the

oscillations in the stem cell compartment and consequently in red cell production observed in the present experiment.

However, this does not exclude possible contributions by chalone or the competition of related cell lines (i. e. , leukocytes) for the common stem cell. A so-called abortive rise in leukocytic response has been reported in the dog during the 2nd week postirradiation.<sup>1</sup> The unequal oscillations observed in the present study suggest greater complications as the postirradiation recovery time progresses than could be explained by any one single process.

## REFERENCES

1. Ainsworth, E. J. and Mitchell, F. A. Postirradiation leukocyte patterns in mice and dogs treated with endotoxin. *Radiation Res.* 33:325-336, 1968.
2. Baum, S. J. and Wyant, D. E. Hematopoietic recovery in irradiated dogs. *Radiation Res.* 44:531-544, 1970.
3. Bruce, W. R. and McCulloch, E. A. The effect of erythropoietic stimulation on the hemopoietic colony-forming cells of mice. *Blood* 23:216-232, 1964.
4. Bullough, W. S. and Rytömaa, T. Mitotic homeostasis. *Nature* 205:573-578, 1965.
5. Byron, J. W. Recovery of the erythropoietin-sensitive stem-cell population following total-body x-irradiation. In: *Effects of Radiation on Cellular Proliferation and Differentiation, Proceedings of a Symposium, Monaco, 1-5 April 1968*, pp. 173-185. Vienna, International Atomic Energy Agency, 1968.
6. Gurney, C. W. and Fried, W. The regulation of numbers of primitive hemopoietic cells. *Proc. Natl. Acad. Sci.* 54:1148-1153, 1965.
7. Jacobson, L. O., Goldwasser, E., Plzak, L. F. and Fried, W. Studies on erythropoiesis. IV. Reticulocyte response of hypophysectomized and polycythemic rodents to erythropoietin. *Proc. Soc. Exptl. Biol. Med.* 94:243-249, 1957.
8. Kirk, J., Orr, J. S. and Hope, C. S. A mathematical analysis of red blood cell and bone marrow stem cell control mechanisms. *Brit. J. Haematol.* 15:35-46, 1968.
9. Krantz, S. B. and Jacobson, L. O. *Erythropoietin and the Regulation of Erythropoiesis*. Chicago and London, The University of Chicago Press, 1970.
10. Morley, A. and Stohlman, F., Jr. Erythropoiesis in the dog: the periodic nature of the steady state. *Science* 165:1025-1027, 1969.
11. O'Grady, L. F. and Lewis, J. P. Proliferation of erythroid-committed cells in the absence of erythropoietin. *J. Lab. Clin. Med.* 76:445-450, 1970.
12. Orr, J. S., Kirk, J., Gray, K. G. and Anderson, J. R. A study of the interdependence of red cell and bone marrow stem cell populations. *Brit. J. Haematol.* 15:23-34, 1968.
13. Pesic, N., Radotic, M. and Hajdukovic, S. Erythropoietin production following gamma irradiation and hemorrhage in dogs. *Science* 143:49-50, 1964.

14. Stohlman, F., Jr. Observations on the physiology of erythropoietin and its role in the regulation of red cell production. *Ann. N. Y. Acad. Sci.* 77:710-724, 1959.

## DISTRIBUTION LIST

### AIR FORCE

The Surgeon General, U. S. Department of the Air Force, Washington, D. C. 20333 (1)  
Executive Officer, Director of Professional Services, Office of the Surgeon General, Hq. USAF (AFMSPA) T-8,  
Washington, D. C. 20333 (1)  
Headquarters, U. S. Air Force (AFMSPAB), Washington, D. C. 20333 (1)  
USAFSAM (SMBR), ATTN: Chief, Radiobiology Branch, Brooks AFB, Texas 78235 (1)  
Air Force Weapons Laboratory, ATTN: WLIL (1), ATTN: WLRB-2 (1), Kirtland AFB, New Mexico 87117 (2)  
Chief, Nuclear Medicine Department, P. O. Box 5088, USAF Hospital, Wright-Patterson AFB, Ohio 45433 (1)  
Office of the Command Surgeon (ADCSG), Hq. ADC, USAF, Ent AFB, Colorado 80912 (1)

### ARMY

The Surgeon General, U. S. Department of the Army, Washington, D. C. 20315 (1)  
Surgeon General, ATTN: MEDDH-N, U. S. Department of the Army, Washington, D. C. 20315 (1)  
USACDC CSSG, Doctrine Division, Fort Lee, Virginia 23801 (1)  
CG, USCONARC, ATTN: ATUTR-TNG (NBC), Fort Monroe, Virginia 23351 (1)  
Commanding Officer, U. S. Army Medical Research Laboratory, Fort Knox, Kentucky 40121 (1)  
Commanding Officer, USA Nuclear Medical Research Detachment, Europe, APO New York, N. Y. 09180 (2)  
Army Research Office, ATTN: Chief, Scientific Analysis Branch, Life Sciences Division, 3045 Columbia Pike,  
Arlington, Virginia 22204 (1)  
Division of Nuclear Medicine, Walter Reed Army Institute of Research, Walter Reed Army Medical Center  
Washington, D. C. 20012 (5)  
Commanding Officer, U. S. Army Environmental Hygiene Agency, ATTN: USAEHA-RP, Edgewood Arsenal, Mary-  
land 21010 (1)  
Commandant, U. S. Army Medical Field Service School, ATTN: MEDEW-ZNW, Fort Sam Houston, Texas 78234 (1)

### NAVY

Chief, Bureau of Medicine and Surgery, U. S. Navy Department, Washington, D. C. 20390 (1)  
Chief, Bureau of Medicine and Surgery, ATTN: Code 71, U. S. Navy Department, Washington, D. C. 20390 (1)  
Director, Biological Sciences Division, Office of Naval Research, Washington, D. C. 20360 (1)  
Commanding Officer, Naval Aerospace Medical Institute, NAMC, ATTN: Research Director, Pensacola, Florida  
32512 (3)  
Head, Animal Behavioral Sciences Branch, Naval Aerospace Medical Institute, Naval Aerospace Medical Center,  
ATTN: Dr. John S. Thach, Jr., Pensacola, Florida 32512 (1)  
Commanding Officer, U. S. Naval Hospital, ATTN: Director, REEL, NNMC, Bethesda, Maryland 20014 (1)  
Commanding Officer, Nuclear Weapons Training Center, Atlantic, Nuclear Warfare Department, Norfolk, Virginia  
23511 (1)  
Commanding Officer, Naval Submarine Medical Center, Naval Submarine Base, NL, ATTN: Medical Library,  
Groton, Connecticut 06340 (1)  
Commanding Officer, Naval Submarine Medical Center, Naval Submarine Base, NL, ATTN: Code 53, Nuclear Medi-  
cine Training Division, Groton, Connecticut 06340 (1)

### D. O. D.

Director, Defense Nuclear Agency, Washington, D. C. 20305 (1)  
Director, Defense Nuclear Agency, ATTN: DDST, Washington, D. C. 20305 (1)  
Director, Defense Nuclear Agency, ATTN: Chief, Medical Directorate, Washington, D. C. 20305 (4)  
Director, Defense Nuclear Agency, ATTN: Technical Library (APTL), Washington, D. C. 20305 (2)  
Commander, Field Command, Defense Nuclear Agency, ATTN: FC Technical Library, Kirtland AFB, New Mexico  
87117 (1)  
Director, Armed Forces Institute of Pathology, Washington, D. C. 20305 (1)  
Administrator, Defense Documentation Center, Cameron Station, Bldg. 5, Alexandria, Virginia 22314 (12)

### OTHER GOVERNMENT

U. S. Atomic Energy Commission, Headquarters Library, Reports Section, Mail Station G-17, Washington, D. C.  
20545 (1)  
U. S. Atomic Energy Commission, Division of Biology and Medicine, Washington, D. C. 20545 (1)  
U. S. Atomic Energy Commission, Bethesda Technical Library, 7920 Norfolk Avenue, Bethesda, Maryland 20014 (1)

OTHER GOVERNMENT (continued)

- National Aeronautics and Space Administration, ATTN: Lt. Col. Charles M. Barnes, USAF, DB-3, MSC, Houston, Texas 77058 (1)
- National Aeronautics and Space Administration, Manned Spacecraft Center, ATTN: Dr. B. D. Newsom, Mail Code DA, Houston, Texas 77058 (1)
- National Bureau of Standards, ATTN: Chief, Radiation Physics Division, Washington, D. C. 20234 (1)
- U. S. Public Health Service, Bureau of Radiological Health, Division of Biological Effects, 12720 Twinbrook Parkway, Rockville, Maryland 20852 (1)
- U. S. Public Health Service, Bureau of Radiological Health, Library, 12720 Twinbrook Parkway, Rockville, Maryland 20852 (1)
- U. S. Public Health Service, Northeastern Radiological Health Laboratory, 109 Holton Street, Winchester, Massachusetts 01890 (1)
- U. S. Public Health Service, Southeastern Radiological Health Laboratory, P. O. Box 61, Montgomery, Alabama 36101 (1)
- U. S. Public Health Service, Southwestern Radiological Health Laboratory, P. O. Box 15027, Las Vegas, Nevada 89114 (1)

OTHER

- Argonne National Laboratory, Library Services Department, Report Section Bldg. 203, RM-CE-125, 9700 South Cass Avenue, Argonne, Illinois 60440 (1)
- Dr. Donald G. Baker, Radiobiology Department, Zellerbach Saroni Tumor Institute, 1600 Divisadero Street, San Francisco, California 94115 (1)
- Dr. J. T. Brennan, Radiology Department, University of Pennsylvania, 3400 Spruce Street, Philadelphia, Pennsylvania 19104 (1)
- Brookhaven National Laboratory, Information Division, ATTN: Research Library, Upton, Long Island, New York 11973 (2)
- Dr. J. S. Burkle, Director of Nuclear Medicine, York Hospital, York, Pennsylvania 17403 (1)
- Director, Radiobiology Laboratory, University of California, Davis, California 95616 (1)
- University of California, Lawrence Radiation Laboratory, Library, Bldg. 50, Room 134, Berkeley, California 94720 (1)
- University of California, Lawrence Radiation Laboratory, Technical Information Division Library L-3, P. O. Box 808, Livermore, California 94551 (2)
- University of California, Laboratory of Nuclear Medicine and Radiation Biology, Library, 900 Veteran Avenue, Los Angeles, California 90024 (1)
- Cdr. William H. Chapman, USN (Ret.), Bio-Medical Division L-523, Lawrence Radiation Laboratory, University of California, P. O. Box 808, Livermore, California 94551 (1)
- Director, Collaborative Radiological Health Laboratory, Colorado State University, Fort Collins, Colorado 80521 (1)
- Dr. L. W. Davis, Radiology Department, University of Pennsylvania, 3400 Spruce Street, Philadelphia, Pennsylvania 19104 (1)
- Professor Merrill Eisenbud, New York University, Tuxedo, New York 10987 (1)
- Dr. T. C. Evans, Radiation Research Laboratory, College of Medicine, University of Iowa, Iowa City, Iowa 52240 (1)
- Dr. Arnold Feldman, Institute of Radiology, School of Medicine, Washington University, 510 South Kingshighway, St. Louis, Missouri 63110 (1)
- Mr. Orin Gelderloos, Division of Literature, University of Michigan, Dearborn Campus, Dearborn, Michigan 48124 (1)
- General Dynamics/Fort Worth, ATTN: Librarian, P. O. Box 748, Fort Worth, Texas 76101 (1)
- Gulf General Atomic Incorporated, ATTN: Library, P. O. Box 608, San Diego, California 92112 (1)
- IIT Research Institute, ATTN: Document Library, 10 West 35th Street, Chicago, Illinois 60616 (1)
- Dr. R. F. Kallman, Department of Radiology, Stanford University, Palo Alto, California 94305 (1)
- Dr. L. S. Kelly, Donner Laboratory, University of California at Berkeley, Berkeley, California 94720 (1)
- Los Alamos Scientific Laboratory, ATTN: Report Librarian, P. O. Box 1663, Los Alamos, New Mexico 87544 (1)
- Director, Nuclear Science Center, Louisiana State University, Baton Rouge, Louisiana 70803 (2)
- Lovelace Foundation for Medical Education and Research, Document Library, 5200 Gibson Blvd., S. E., Albuquerque, New Mexico 87108 (1)
- Dr. Ross A. McFarland, Guggenheim Professor of Aerospace Health and Safety, Harvard School of Public Health, 665 Huntington Avenue, Boston, Massachusetts 02115 (1)
- Dr. J. I. Marcum, Rand Corporation, 1700 Main Street, Santa Monica, California 90401 (1)
- Massachusetts Institute of Technology, M.I.T. Libraries, Technical Reports, Room 14 E-210, Cambridge, Massachusetts 02139 (1)



OTHER (continued)

- Dr. Charles W. Mays, Physics Group Leader, Radiobiology Division, University of Utah, Salt Lake City, Utah 84112 (1)
- Ohio State University, Nuclear Reactor Laboratory, 1298 Kinnear Road, Columbus, Ohio 43212 (1)
- Dr. Harvey M. Patt, Laboratory of Radiobiology, University of California, San Francisco Medical Center, San Francisco, California 94122 (1)
- Purdue University, Nuclear Engineering Library, Lafayette, Indiana 47907 (1)
- Dr. S. M. Reichard, Director, Division of Radiobiology, Medical College of Georgia, Augusta, Georgia 30902 (1)
- University of Rochester, Atomic Energy Project Library, P. O. Box 287, Station 3, Rochester, New York 14620 (1)
- Dr. H. H. Rossi, 630 West 168th Street, New York, N. Y. 10032 (1)
- Dr. Eugene L. Saenger, Director, Radioisotope Laboratory, Cincinnati General Hospital, Cincinnati, Ohio 45229 (1)
- Sandia Corporation Library, P. O. Box 5800, Albuquerque, New Mexico 87115 (1)
- Scientific Committee on the Effects of Atomic Radiation, ATTN: Library, United Nations Room 3267, United Nations Plaza, New York, N. Y. 10017 (1)
- Scope Publications, Franklin Station, P. O. Box 7407, Washington, D. C. 20004 (1)
- Dr. Arthur R. Tamplin, Biophysicist, Information Integration Group, University of California, Lawrence Radiation Laboratory, L-612, Livermore, California 94550 (1)
- Texas A. and M. University, Radiation Biology Laboratory, Texas Engineering Experiment Station, College Station, Texas 77840 (2)
- Texas Nuclear Corporation, ATTN: Director of Research, Box 9267 Allandale Station, Austin, Texas 78756 (1)
- Western Reserve University, Department of Radiology, Division of Radiation Biology, Cleveland, Ohio 44106 (1)
- Mr. Lionel Zamore, 601 Brightwater Court, Brooklyn, New York 11235 (1)

FOREIGN

- International Atomic Energy Agency, Kärntnerring 11, Vienna I, 1010, Austria (1)
- European Atomic Energy Community, C. E. E. A., Library, 51 rue Belliard, Brussels 4, Belgium (1)
- Dr. L. G. Lajtha, Paterson Laboratories, Christie Hospital and Holt Radium Institute, Manchester, England (1)
- Dr. L. F. Lamerton, Biophysics Department, Institute of Cancer Research, Surrey Branch, Belmont, Sutton, Surrey, England (1)
- National Lending Library for Science and Technology, Boston Spa, Yorkshire, England (1)
- Directorate of Medical and Health Services, FAF (Federal Armed Forces), Bonn, Ermekeilstrasse 27, West Germany (1)
- Abteilung für Strahlenbiologie im Institut für Biophysik der Universität Bonn, 53 Bonn-Venusberg, Annaberger Weg 15, Federal Republic of Germany (2)
- Prof. Dr. H. Langendorff, Direktor des Radiologischen Instituts der Universität, 78 Freiburg im Breisgau, Albertstrasse 23, Germany (1)
- Priv.-Doz. Dr. O. Messerschmidt, Radiologisches Institut der Universität, 78 Freiburg im Breisgau, Albertstrasse 23, Germany (1)
- Dr. Helmut Mitschrich, Akademie des Sanitäts- und Gesundheitswesens der Bundeswehr, Spezialstab ATV, 8 München, Schwere Reiterstrasse 4, Germany (2)
- Prof. Dr. F. Wachsmann, Gesellschaft für Strahlenforschung m.b.H., 8042 Neuherberg bei München, Institut für Strahlenschutz, Ingolstädter Landstrasse 1, München, Germany (1)
- Col. Joachim Emde, Direktor, Spezialstab ATV, ABC- und Selbstschutzschule, 8972 Sonthofen 2/Allgäu, Berghoferstrasse 17, West Germany (1)
- Dr. M. Feldman, Section of Cell Biology, The Weizmann Institute of Science, Rehovoth, Israel (1)
- Dr. G. W. Barendsen, Radiobiological Institute TNO, Rijswijk, Netherlands (1)
- Puerto Rico Nuclear Center, ATTN: Reading Room, College Station, Mayaguez, Puerto Rico 00708 (2)
- Dr. H. Cottier, Pathological Institut der Universität, Bern, Switzerland (1)