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Human Radiation Experiments

Associated with the U.S. Department of Energy and Its Predecessors

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U.S. Department of Energy
Assistant Secretary for Environment, Safety, and Health
July 1995

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U.S. Department of Energy
Assistant Secretary for Environment, Safety, and Health
Washington, D.C. 20585
July 1995

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The Secretary of Energy

Hazel R. O'Leary

Assistant Secretary for Environment, Safety, and Health

Tara O'Toole, M.D., M.P.H.

The Office of Human Radiation Experiments

Ellyn Weiss, Special Counsel and Director

Archives and Research

William G. LeFurgy, Deputy Director
Elly Melamed, Project Coordinator
Roger Anders, Chief Historian

Ann Brower
Alyson Burgess
Tom Fisher
Karoline Gourley
David Harrell
Jean Mansavage
Prita Pillai
Cindy Shindledecker
Michael Yuffee

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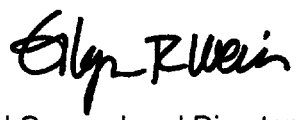
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Foreword

In February 1995, the Department of Energy's (DOE) Office of Human Radiation Experiments published *Human Radiation Experiments: The Department of Energy Roadmap to the Story and the Records ("The DOE Roadmap")*. The *Roadmap* summarized work undertaken at the direction of Secretary of Energy Hazel R. O'Leary to find, declassify, and make publicly available DOE records related to human experimentation. This effort was also a part of Secretary O'Leary's larger openness initiative, which commited the Department to conduct business as openly as possible as well as to provide information needed to assess past agency activities.

This volume is a supplement to the *Roadmap*, as well as a continuation of the Secretary's openness initiative. Along with methodological and historical descriptions, topical discussions, and records series descriptions, the *Roadmap* included summaries of approximately 150 human radiation experiments associated with DOE and its predecessors. Those summaries are included here, along with summaries of over 275 additional studies that have since been identified, documented, and confirmed. Taken together, these summaries describe a wide range of activities from the early 1940s through the early 1970s. The intent is to be as inclusive as possible in identifying human radiation research projects associated with the Department and its predecessors.

Many people have contributed to this volume, including those listed on the facing page and a number of the people acknowledged previously in the *Roadmap*. Particular credit is due Dr. Darrell Fisher, Ph.D., for his research skills and to the staff of the Lawrence Berkeley Laboratory Archives and Records Management Office, who provided special research services. Elly Melamed, Cindy Shindledecker, Alyson Burgess and Daphne Zweifel provided the outstanding organizational and document management skills that made this publication possible. It has been a privilege and pleasure to work with everyone connected with this important project.



Ellyn R. Weiss, Special Counsel and Director
Office of Human Radiation Experiments
U.S. Department of Energy
July 1995

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Introduction

Background

THIS DOCUMENT CONTAINS a listing, description, and selected references for documented human radiation experiments sponsored, supported, or performed by the U.S. Department of Energy (DOE) or its predecessors, including the U.S. Energy Research and Development Administration (ERDA), the U.S. Atomic Energy Commission (AEC), the Manhattan Engineer District (MED), and the Office of Scientific Research and Development (OSRD). The list represents work completed by DOE's Office of Human Radiation Experiments (OHRE) through June 1995.

The experiment list is available on the Internet via a Home Page on the World Wide Web (http://www.ohre.doe.gov). The Home Page also includes the full text of *Human Radiation Experiments: The Department of Energy Roadmap to the Story and the Records* (DOE/EH-0445), published in February 1995, to which this publication is a supplement .

This list includes experiments released at Secretary O'Leary's June 1994 press conference, as well as additional studies identified during the 12 months that followed. Cross-references are provided for experiments originally released at the press conference; for experiments released as part of *The DOE Roadmap*; and for experiments published in the 1986 congressional report entitled *American Nuclear Guinea Pigs: Three Decades of Radiation Experiments on U.S. Citizens.* An appendix of radiation terms is also provided.

Basic guidance for identifying experiments is contained in Executive Order 12891, issued January 15, 1994, and in a January 19, 1994 White House memorandum entitled "Retrieval and Inventory of Records of Human Radiation Experiments." These authorities define human radiation experiments as:

> Experiments on individuals involving intentional exposure to ionizing radiation. This category does not include common and routine clinical practices, such as established diagnosis and treatment methods, involving incidental exposures to ionizing radiation;

and

> Experiments involving intentional environmental releases of radiation that (A) were designed to test human health effects of ionizing radiation; or (B) were designed to test the extent of human exposure to ionizing radiation.

For more information about environmental releases, please see *The DOE Roadmap.*

Criteria for Listing Experiments

SEVERAL ADDITIONAL CRITERIA were used in compiling the list. First, clear evidence that an experiment took place was required. Given the fragmented and highly disparate nature of the documentation, this was often a challenge. Many documents refer to proposed studies, and in other cases documents provide inconclusive leads that require further research. The experiments listed below have been confirmed through research in primary and secondary sources.

Second, the list is limited to experiments conducted or supported by DOE, its predecessor agencies, or agency contractors. Starting in the late 1940s, hundreds of hospitals and other institutions did work with scores of radionuclides and radioactively labeled compounds. Much of this work involved human radiation experiments. Apart from distributing licenses and isotopes, DOE and its predecessors had no active role in most of these experiments. The agency did, however, operate its own cancer hospitals and other research facilities where human subjects were used in radiation research. Moreover, the agency contracted with universities and other institutions for human radiation research. Such experiments are included.

The third consideration for inclusion on the list was evidence that an experiment involved exposure of human subjects to radiation. Studies involving only human tissue samples were not included. Research involving various drugs, hormones, minerals, or other substances also was not included unless radiation was involved.

In judging whether a procedure was a "common and routine clinical practice," a human radiation experiment included any of the following situations where radiation was administered:

- without realistic expectation of a benefit to the subject;
- to test or determine the potential usefulness of a treatment for other individuals;
- to healthy human subjects; and
- to an individual to calibrate radiation detection instruments.

Several types of procedures did not fall within the scope of human radiation experiments. These included procedures where

- workers occupationally exposed to radiation were measured for potential internal or external radiation exposure by routine dosimetry, bioassay, or whole-body counting methods;
- workers were assayed after accidental internal or external radiation exposures;
- individuals were treated with chelating agents for removal of accidental or occupational internal contamination;
- patients were measured for internal radioactivity as part of a legitimate medical, diagnostic or therapeutic process; and
- preexisting internal deposition of radionuclides were assessed, measured, or studied in body fluids, excreta, blood, cells, or tissue samples.

Basic Categories of Human Radiation Experiments

THERE ARE SEVERAL common and recurring categories of human radiation experiments:

Tracer studies involved use of radioisotopes as tools to learn more about the properties of other biological compounds, transport pathways, and processes in the body. Tracer studies also involved using isotopes as labeling agents where a drug was labeled with a radioactive isotope, including studies conducted to gain knowledge of the effect of radiation upon humans.

All *radionuclide metabolism studies* in human subjects were considered as human radiation experiments. These tests involved the study or analysis of radioisotope uptake, retention, and excretion, and were done to learn more about the specific behavior of elements in the body.

Biological effects of radiation were often determined during *dose response studies.*

Radionuclides were used in *diagnostic studies* to research human physiological conditions, or to calibrate radiation detectors or imaging systems.

Finally, *experimental treatments for disease,* cancer perhaps the most prominent, involved the use of various radiations and radioactive materials. Over time, many of these therapies moved from the experimental stage to the routine. The point at which they ceased to be experimental may be difficult to draw with precision. The reviewers have used their best judgment in listing those treatments that appear to have been experimental at the time they were administered. Particularly in the case of the AEC cancer hospitals, the choice has been to be inclusive in listing these treatments.

The Process of Identifying Experiments

SEVERAL STEPS were involved in locating and reviewing documentary evidence related to human radiation experiments. To start, OHRE staff and other personnel searched records with information of potential value. This selective search covered records in work spaces, offices, Federal Records Centers, the U.S. National Archives, and other archival repositories.

When documents were found that might contain information related to human radiation experiments, the documents were copied and provenanced. Provenancing involves noting the location of the original document (site, series, box, and folder). The copies were sent to OHRE through a document processing facility, the Coordination and Information Center (CIC). The CIC numbered and indexed the documents, optically scanned them, and produced copies for distribution to DOE public reading rooms and other interested parties. Copies of the documents were also provided to the Advisory Committee on Human Radiation Experiments, which President Clinton established in 1994 to review all human radiation studies sponsored or supported by the Federal government from 1944 to 1974.

About 218,000 document pages are included in this collection. In addition to basic document indexes, sophisticated full-text searching capabilities and full access to the document images are available through the Internet World Wide Web Home Page noted on page 1.

Many varieties of documents reference experiments. These include reports from laboratories or contract correspondence between researchers and agency officials, researcher notes, medical files, experiment protocols and proposals, and research bibliographies. References usually contain fragmentary information, and considerable research in primary and secondary sources is often necessary to verify and describe a specific experiment. This research involved gathering all documents related to a particular experiment and comparing the information with published journal literature. Much of the information on human radiation experiments was published in the open scientific literature.

Summarizing and Listing Experiments

THE EXPERIMENT SUMMARIES provide a concise description of what occurred based on the information that could be found. The focus has been on learning when and where the experiment took place; type and dosage of radiation used; how radiation was administered; why the experiment was conducted; numbers and types of subjects involved; experimental results; and funding sources for the experiment. Each experiment summary is followed by a reference section which lists citations to information sources. In addition, case files have been prepared with information concerning each experiment listed.

Challenges

IN PREPARING THIS LIST, and in continuing the work to find experiments, a variety of challenges have been encountered. One issue relates to subject populations. With some exceptions, little evidence exists about how researchers chose experimental subjects or what factors went into such decisions. More details are often available about the composition of subject populations, but information in this area is hardly complete.

Another obstacle is dating: references to experiment dates are often incomplete, as some studies were conducted over several years. In many cases, the date given in the experiment summary is an estimated date based on available information.

The use of informed consent—or any degree of consent at all—is also very difficult to document for many experiments dating before the standard requirements issued by the National Institutes of Health in 1974. Contemporaneous professional literature typically does not provide much detail about consent issues, nor do contracts, progress reports, or other information sources.

In addition, it can be difficult to determine the role of the Federal government in some experiments. Studies occurring at AEC research hospitals or other agency facilities have an obvious connection to the Government. Yet experiments done in private hospitals often do not. The AEC provided grants, contracts, and other forms of direct support for human radiation experiments, and examples are included in the list. Funding status, however, is not always clear. To the extent it is available, funding information is included in the experiment summaries.

About This List

THIS LIST IS ARRANGED BY LOCATION and incorporates studies previously published in *The DOE Roadmap*. These studies are listed first for each location and have retained numbers original assigned to them in *The DOE Roadmap*. In some cases the descriptions have been revised based on new information, and this is indicated at the end of the summary. In addition to the studies previously published in *The DOE Roadmap,* more than 275 additional studies have been summarized.

The notation ❋ ❋ ❋ indicates where the newly published summaries begin for each location.

Human radiation experiments took place at a number of DOE sites and laboratories and at the three AEC cancer research hospitals. These include Argonne National Laboratory in Illinois, Brookhaven National Laboratory in New York, Hanford sites in Washington State, Idaho sites in Idaho, Lawrence Berkeley Laboratory and Lawrence Livermore National Laboratory in California, Los Alamos National Laboratory in New Mexico, Oak Ridge sites in Tennessee, and the University of Chicago's Argonne Cancer Research Hospital in Illinois. The primary focus for the DOE search has been these sites and closely related facilities, which are listed under separate headings. For more information about these DOE sites and the history of their involvement in human radiation experiments, see *The DOE Roadmap.*

The list also includes some experiments conducted at universities and private hospitals that were supported by DOE and its predecessors. These are listed under the heading *Other* (OT). Please note that this search has been primarily for experiments that took place prior to 1974, the year in which broadly applicable guidelines for the protection of human research subjects were adopted.

In producing this list, a number of summaries were prepared that did not appear to meet the criteria for final inclusion, i.e., they did not appear to be funded by DOE or its predecessors, or there was no definitive documentation indicating that they actually took place. Although they have not been included in this publication, the documentation and summaries have been retained by OHRE, provided to the Advisory Committee on Human Radiation Experiments, and are available for review.

Finally, while this list represents our best effort to identify human subject research performed or sponsored by the Department and its predecessors up to 1974, the passage of time and the state of the agency's historical records preclude any claim of absolute completeness. A wealth of valuable data has been uncovered and is presented here. As indicated above, the experiment list and all primary source documents are available on the Internet. ❑

List of Experiments

Plutonium Injection

PI-1. Plutonium Injection Studies

DURING 1945 TO 1947, 18 persons were injected with amounts of plutonium at the Manhattan Engineer District Hospital in Oak Ridge, Tennessee, (1 patient), at Strong Memorial Hospital in Rochester, New York (11 patients), at Billings Hospital of the University of Chicago (3 patients), and at the University Hospital of the University of California in San Francisco (3 patients). Excreta were obtained from patients and sent to Los Alamos for plutonium analysis. These data were used to establish mathematical equations describing plutonium excretion rates.

This research was funded by the Manhattan Engineer District; follow-up studies were supported by the U.S. Atomic Energy Commission and the U.S. Energy Research and Development Administration. (This experiment was referenced in the Markey report and included in *The DOE Roadmap* of February 1995.)

References

Durbin, P.W. *Plutonium in Man: A Twenty-Five Year Review.* Berkeley: Lawrence Radiation Laboratory, UCRL-20850, 1971.

Durbin, P.W. "Plutonium in Man: A New Look at the Old Data." Section 7, Chapter 2 in *Radiobiology of Plutonium,* edited by B.J. Stover and W.S. Jee, pp. 469–530. Salt Lake City: The J.W. Press, 1972.

Langham, W.H., H. Bassett, P.S. Harris, and R.E. Carter. *Distribution and Excretion of Plutonium Administered Intravenously to Man.* Los Alamos: Los Alamos Scientific Laboratory, LA-1151. Republished in *Health Physics.* Vol. 38, 1980, pp. 1,031–1,060.

Stannard, J.N. *Radioactivity and Health: A History.* Office of Scientific and Technical Information. 1988, pp. 350–355. ❑

Argonne National Laboratory

ANL-1. Radium as an Experimental Therapy for Treating Mental Disorders at Elgin State Hospital in Elgin, Illinois

PATIENTS IN A state mental hospital were injected with radium as an experimental therapy for mental disorders. The experiment appears to have been conducted at the Elgin State Hospital, in Elgin, Illinois, between 1931 and 1933. Documents indicate that 70 to 450 micrograms of radium-226 (Ra^{226}) were injected. This experiment occurred prior to the establishment of the Argonne National Laboratory and the U.S. Atomic Energy Commission. Argonne National Laboratory later collected records and attempted to locate the subjects. Researchers believed that if the patients could be located and body content measurements made in the 1950s, a valid retention curve for radium in humans over several decades could be constructed. Argonne National Laboratory made all later measurements.

The records contain information regarding radium content of the located subjects, medical information relating to the subjects' admission to the hospital, periodic medical examination results, and causes of death and death certificates for deceased subjects. (Previously described in #31 on the original list of 48 experiments released by DOE in June 1994; included in *The DOE Roadmap* of February 1995, and since revised)

References

Looney, W.B., R.J. Hasterlik, and A.M. Brues. "A Clinical Investigation of the Chronic Effects of Radium Salt Administered Therapeutically." *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine.* Vol. 73, 1955, pp. 1,006–1,037.

Miller, C.E., R.J. Hasterlik, and A.J. Finkel. *The Argonne Radium Studies: Summary of Fundamental Data.* Chicago: Argonne National Laboratory and Argonne Cancer Research Hospital. ANL-7531 and ACRH-106.

Norris, Speckman, and Gustafson. "Studies of the Metabolism of Radium in Man." *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine.* Vol. 73, 1955, p. 785.

Rowland, R.E., A.F. Stehney, and H.F. Lucas. "Dose-Response Relationship for Radium-Induced Bone Sarcomas." *Health Physics.* Vol. 44 (Suppl. 1), 1983, pp. 15–31.

Schlundt, H., J.T. Nerancy, and J.P. Morris, "Detection and Estimation of Radium in Living Persons. IV. Retention of Soluble Radium Salts Administered Intravenously," *American Journal of Roentgenology and Radium Therapy.* Vol. 30, 1933, pp. 515–522. ❑

ANL-2. Effect of Phosphorus-32 on Hemoglobin Metabolism in Polycythemia Rubra Vera

THIS STUDY was conducted by the Health Division of the Metallurgical Laboratory at the University of Chicago at the University Hospital's Hematology Clinic (six patients) and at the University of Minnesota (one patient). Five patients were administered 15 to 40 microcuries of phosphorus-32 (P^{32}), and two patients were injected with undetermined amounts of P^{32} in a study of the metabolism of hemoglobin in man. These experiments took place between October 1944 and June 1945. (Previously described in #10 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

References

Schwartz, S., E.J. Katz, L.M. Porter, L.O. Jacobson, and C.J. Watson. *Studies of the Hemolytic Effect of Radiation.* Chicago: Metallurgical Laboratory, CH-3760, July 10, 1946. National Archives and Records Administration, Record Group 326, U.S. Atomic Energy Commission, MED/AEC, Metallurgical Laboratory/Argonne National Laboratory, Classified Correspondence Files, Box 23X, 2 of 4, Folder 651. ❑

ANL-3. Plutonium Ingestion Study

IN MAY 1946, six male employees of the Metallurgical Laboratory of the Manhattan Engineer District in Chicago drank a water solution containing about 0.18 nanocurie of plutonium-239 (Pu^{239}). The purpose of this study was to investigate the gastrointestinal absorption and fecal excretion rate of ingested plutonium. Researchers also hoped to use the results to improve the interpretation of previously collected data on persons occupationally exposed to plutonium. Participation in this experiment was voluntary, and the amounts of plutonium ingested were sufficiently low to be barely detectable in urine and feces with instrumentation available in 1946. At least two of the subjects were still alive in 1994. (Previously described in #7 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

References

Russell, E.R. *Monthly Summary for Biochemical Survey Section.* U.S. Department of Energy: Chicago Operations Office, Center for Human Radiobiology, Plutonium Documents, June 20, 1946. ❑

ANL-4. Arsenic-76 Biodistribution and Excretion Studies

THIS STUDY WAS CONDUCTED by the Argonne National Laboratory in 1947 in Chicago. Twelve hospital patients were injected intravenously with arsenic-76 (As^{76}), administered as potassium arsenite, to study the uptake, retention, distribution, and excretion of arsenic. The subjects included five males and seven females, all between the ages of 18 and 67 years and hospitalized with leukemia, Hodgkin's disease, polycythemia rubra vera, melanocarcinoma, and carcinoma of the parotid. Amounts of As^{76} administered were 0.5 to 15.4 millicuries.

This study showed that As^{76} rapidly distributed throughout the body, failed to localize in tumors or lymphatic tissue, and was rapidly excreted in urine and via the intestinal tract. The study was supported by the U.S. Atomic Energy Commission. The therapeutic administration of As^{76} trioxide was attempted in 1948 on 19 patients with tumors of the hematopoietic system. This therapy resulted in no significant remission of disease. (Previously described in #11 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

References

Jacob, L.O., M.H. Block, E.K. Marks, E. Skirmont, and E. Simmons. *Clinical Studies on the Treatment of Leukemia, Hodgkin's Disease, and Related Diseases with Various Doses of Radioarsenic.* Chicago: Argonne National Laboratory, Biology and Medical Divisions, ANL-4227, November 1, 1948, pp. 14–15.

Neal, W.B., L.O. Jacobson, H. Ducoff, and T. Kelly. *Arsenic-76 Preliminary Studies Progress Report.* Chicago: Argonne National Laboratory, Biology Division, CH-3830, June 1, 1947, pp. 1–16. National Archives and Records Administration, Record Group 326, U.S. Atomic Energy Commission, MED/AEC, Metallurgical Laboratory/Argonne National Laboratory, Classified Correspondence Files, Box 23, Box 3 of 5, Folder 699. ❑

ANL-5. Whole-Body Counter Calibration with Sodium-24

THIS STUDY WAS CONDUCTED at Argonne National Laboratory, in the early 1950s, to test and calibrate a sodium iodide scintillation counter. Three individuals ingested a few microcuries of sodium-24 (Na^{24}) and the sodium iodide scintillation counter apparatus was used to determine the gamma-ray activity of Na^{24} in the subjects. The three subjects were Argonne employees. (Included in *The DOE Roadmap* of February 1995)

References

Marinelli, L.D., C.E. Miller, P.F. Gustafson, and R.E. Rowland. "The Quantitative Determination of Gamma-Ray Emitting Elements in Living Persons." *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine.* Vol. 73, No. 4, April 1955, pp. 661–666. ❑

ANL-6. Uptake of Tritiated Thymidine by Human Tumor

IN 1962, A STUDY was conducted on the uptake of thymidine labeled with tritium (H^3) by human tumors. This study was a cooperative effort between the Departments of Pathology and Surgery, Northwestern University Medical Hospital, Chicago, and Argonne National Laboratory. Four male patients between the ages of 54 and 69 years old were included in the study. Three were in the terminal stages of various forms of cancer.

All subjects were injected with 10 microcuries of H^3-labeled thymidine prior to their previously scheduled surgery. Samples consisting of tumor and normal abdominal tissues were removed during surgery and later were analyzed for H^3. Samples were also collected during the autopsies of the terminal subjects.

The results showed similar growth in both cancerous and noncancerous cells, a finding that was in agreement with previous animal studies. This project was partly funded by the U.S. Atomic Energy Commission. (Previously described in #9 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

References

Baserga, R., G.C. Henegar, W.E. Kisieleski, and H. Lisco. "Uptake of Tritiated Thymidine by Human Tumors *In Vivo*." *Laboratory Investigation.* Vol. 11, No. 5, May 1962, pp. 360–364. ❑

❋ ❋ ❋

ANL-7. Hematological Effects of Total-Body X-Ray Irradiation

DURING 1943 AND 1944, researchers at the Manhattan Engineer District's (MED) Metallurgical Laboratory, at the University of Chicago conducted studies of blood changes in patients after total-body irradiation (TBI) at Billings Hospital, University of Chicago, and in volunteer laboratory staff members. A total of 14 subjects ranging in age from 23 to 75 years participated, and were divided into three groups as follows: (Group I) 8 patients (both male and female) with incurable neoplasms; (Group II) 3 male and female patients with generalized, chronic illnesses; and (Group III) 3 normal male volunteers. Subjects were exposed to fields of x-ray radiation at various levels.

Group I subjects each received a single exposure of 27, 60, or 120 roentgens. Group II subjects each received multiple exposures up to a total of 100, 300, or 500 roentgens. Group III subjects each were exposed to a total of 21 roentgens over a period of 3 days. Study subjects were exposed to total-body radiation at

various exposure levels specifically to better measure radiation-induced changes in circulating blood at different dose levels and intervals post-exposure. This information was needed to improve the scientific basis for radiation protection of MED workers.

These studies showed that the most consistent effect of total-body irradiation in Groups I and II was the reduction of white blood cells that are formed in lymphoid tissue. No effect was observed in Group III. This latter finding suggested that the existing radiation protection limit for occupational exposure of 0.1 roentgen per working day was protective against directly detectable radiation injury, and that routine monitoring of the blood components would not be a practical method for assessing usual occupational radiation exposures. This work was supported by the Manhattan Engineer District. (This experiment was referenced in the Markey report.)

References

Nickson, J.J. "Blood Changes in Human Beings Following Total-Body Irradiation." Chapter in *Industrial Medicine on the Plutonium Project*, edited by R.S. Stone, New York: McGraw-Hill, 1951, pp. 308–337. ❑

ANL-8. Studies on the Biochemical Effects of Total-Body X-Rays in Humans

STUDIES WERE CONDUCTED between 1943 and 1946 at the Manhattan Engineer District's (MED) Metallurgical Laboratory at the University of Chicago on the effects of radiation, process chemicals, and toxic metals in man. The purpose of these studies was to identify biochemical indicators of tissue damage after excessive exposures. Some of the data used in these studies were obtained by observing the effects of radiation in patients treated for cancer (solid tumors) with external x-rays or with internally administered phosphorus-32 (for polycythemia vera). These were standard procedures for cancer therapy at the time. However, a separate group of four healthy, volunteer Metallurgical Laboratory employees was administered total-body x-rays (30 roentgens at the skin surface) to evaluate various blood changes and other observable biochemical responses.

One of the four subjects received 15 daily exposures of 2 roentgens of radiation from x-rays, while the three others each received 3 daily exposures of 10 roentgens. Adenosine triphosphate (a normal compound in the body that is active in glucose metabolism and energy production) levels were then evaluated in samples of white cells from each subject.

Inconsistent changes in white blood-cell phosphorus were observed among the four subjects after total-body x-ray radiation. The study also included review of various biochemical and tissue-function changes in Manhattan Project workers exposed to different types of radiation and toxic metals during the course of their employment at sites including: Los Alamos, the Metallurgical Laboratory, Iowa State University, Ames, Oak Ridge, and Washington University in St. Louis.

It was concluded that white blood-cell chemistry was an important factor in assessing the radiation sensitivity of workers to radiation, and that a test for urinary excretion of uranium was the best method for determining worker exposures to uranium. This work was supported by the Manhattan Engineer District.

References

Schwartz, S. "Biochemical Studies Relating to the Effects of Radiation and Metals." *U.S. Atomic Energy Commission Report AECD-2198*, Technical Information Division, Oak Ridge, Tennessee, July 1, 1947, p. 18. ❑

ANL-9. Studies of the Metabolism of Arsenic-76

STUDIES WERE CONDUCTED between 1946 and 1948 at Argonne National Laboratory on the tissue localization, metabolism, and excretion of arsenic-76 (As^{76}) in animal and human subjects. The purpose of these studies was to provide a basis for calculating the radiation dose to a particular tissue or organ in preparation for the clinical use of As^{76}.

Two hospital patients (one with Hodgkin's disease and one with lymphatic leukemia) were administered 2.7 or 3.0 millicuries of As^{76} as sodium arsenite by intravenous injection. Measurements were then made of the amounts of As^{76} excreted in urine and feces for 7 days post-injection.

Large differences were observed in the rates of excretion of As^{76} by human subjects when compared to rates in laboratory animals, suggesting a species-dependent biological retention. Arsenic levels in circulating blood were also determined. A third human subject (a moribund 65-year-old female with carcinoma of the parotid) was given 500 microcuries As^{76} by intravenous injection 20 hours before death in anticipation of post-mortem tissue studies. The distribution of As^{76} in liver, kidneys, spleen, and 17 other organs and tissues was determined at time of death. This work was supported by the U.S. Atomic Energy Commission.

References

Ducoff, H.S., W.B. Neal, R.L. Straube, L.O. Jacobson, and A.M. Brues. "Biological Studies with Arsenic-76. II. Excretion and Tissue Localization." In *Proceedings of the Society for Experimental Biology and Medicine*. Vol. 69, October–December 1948, pp. 548–554.

Straube, R.L., W.B. Neal, Jr., T. Kelly, and H.S. Ducoff. "Biological Studies with Arsenic-76 I. Preparation of Arsenic-76 by Pile Irradiation of Cacodylic Acid." In *Proceedings of the Society for Experimental Biology and Medicine*. Vol. 69, October–December 1948, pp. 270–272. ❑

ANL-10. Effects of Single-Dose X-Rays to the Nail Fold Area

IN 1947, RESEARCHERS in the Health Division of the University of Chicago exposed hands of subjects to x-rays in order to identify and examine changes that may occur in the skin of people occupationally exposed to radiation. Fifteen subjects participated in this study. Fourteen subjects were hospitalized cancer patients who were receiving x-ray therapy to parts of their body other than their hands. The other subject was a member of the hospital staff who occasionally prepared radiation materials for patient treatment.

The 14 patients received between 200 and 600 rads of radiation from x-rays to the cuticle of the left fourth finger. The staff member was exposed to radiation from a radium plaque placed on the skin. Skin biopsies were obtained before the treatment and for up to 2 weeks after, and were examined microscopically for radiation-induced changes.

The results indicated that some patients showed temporary reddening of the skin and enlarged or broken blood vessels. No permanent changes to the skin occurred at or below the 600-rad dose level. This study was funded by the U.S. Atomic Energy Commission. (This experiment was referenced in the Markey report.)

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ANL-11. Studies on the Therapeutic Potential of Arsenic-76

BETWEEN 1948 AND 1953, studies were conducted at the Departments of Medicine and Surgery at the University of Chicago and Argonne National Laboratory on the value of arsenic-76 (As^{76}) as an internally administered radiotherapeutic agent. The purpose of these studies was to determine the effects of As^{76} on the hematopoietic (blood-forming) tissues of 24 hospital patients with leukemia, and on the potential effectiveness of As^{76} as a treatment for several different malignant tumors in an additional 19 patients.

Arsenic-76 (17 to 90 millicuries) was administered intravenously to 24 patients with tumors of the hematopoietic tissues, 2 with polycythemia vera, and 1 with a metastatic carcinoma of the stomach. Arsenic-76 was found to be about as effective as any of the commonly used therapy agents; remissions were induced in some cases of leukemia, multiple myeloma, and metastatic carcinoma.

In a follow-up study, the researchers studied the biological effects of As^{76} on normal hematopoietic tissues, such as the liver, spleen, and bone marrow. Tissue biopsies were obtained before and after administration of As^{76} from 19 patients with leukemia, polycythemia vera, and multiple myeloma. The amounts of As^{76} administered ranged from 12 to 88 millicuries. Patients received one to four As^{76} injections. Normal tissue biopsies were evaluated for signs of cellular destruction after As^{76} injection.

Results of these studies showed that As^{76} occasionally produced cellular damage and de-

creased cellularity, but there was little evidence of cytolysis or inhibition of cellular proliferation. Results were similar to those observed earlier with nitrogen mustard chemotherapy. This work was supported by the American Cancer Society, the U.S. Public Health Service, and the U.S. Atomic Energy Commission.

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ANL-12. Elimination of Intravenous Carbon-14–Labeled Sodium Bicarbonate

IN THE EARLY **1950S,** conducted in the Division of Biological and Medical Research, Argonne National Laboratory compared human excretion rates of injected carbon-14 (C^{14})–labeled sodium bicarbonate to rates observed in animals. The purpose was to provide a basis for computation of permissible human doses of this isotopic compound.

Ten microcuries of C^{14}-bicarbonate in isotonic solution were injected into an unspecified number of healthy volunteers. Expired CO_2 was collected during the following 3 hours with the subjects at rest, and measured for C^{14} activity. Ninety-five percent of the radioactivity exhaled as CO_2 was eliminated during this period. These results were then compared with isotope excretion data from other species.

It was concluded that a hypothetical intravenous injection of 20 to 40 millicuries of C^{14}-bicarbonate or the inhalation of a comparable amount of $C^{14}O_2$ would be required to give a 70-kilogram man a total radiation dose of 1 roentgen equivalent over his entire life span. The research was supported by the U.S. Atomic Energy Commission.

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ANL-13. Study of Dextran Metabolism Using Carbon-14

IN THE EARLY **1950S,** scientists at Argonne National Laboratory administered carbon-14 (C^{14})–labeled dextran to an unreported number of subjects to determine its metabolic fate. After administration, the patients' urine, feces, and exhaled breath were monitored for tracer C^{14} and $C^{14}O_2$. The available literature suggested that an isotonic solution containing 6 microcuries per gram was used. The amounts administered are unknown.

The results indicated that human dextran metabolism was similar to dextran metabolism measured in rats and dogs. About 50 percent of the administered dextran was excreted unchanged during the first 3 days, while a large part of that remaining in the animals oxidized into CO_2 over a longer period of time. After administration, neither dextran nor any of its metabolic products was excreted by way of the intestinal tract. This work was supported by the U.S. Atomic Energy Commission.

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ANL-14. Whole-Body Counter Calibration and Evaluation of Techniques Using Potassium-42

A SERIES OF STUDIES was conducted at the Argonne National Laboratory in the 1950s and 1960s to calibrate a whole-body counting apparatus, and to evaluate whole-body counting techniques. In 1955, potassium-42 (K^{42}) was administered orally (or possibly by intravenous injection) to as many as 75 subjects, and whole-body radioactivity measurements were made. Urine samples were also collected and analyzed for K^{42} content at various times after administration. The amounts administered varied for each group of subjects, but some are known to have received 0.54, 2.0, or 5.0 microcuries. Some of the subjects received multiple doses. Twelve of the subjects have been identified as Argonne employees. Other employees also participated in similar but unreported experiments.

In the mid-1960s, Argonne scientists collaborated with workers at the Department of Medicine of Loyola University Stritch School of Medicine in Hines, Illinois, and with others at the Bionucleonics Department of Purdue University in Lafayette, Indiana, in investigations of the precision of whole-body potassium assays made at Argonne and Purdue University. In this study, 44 healthy subjects participated in whole-body counting studies before and after oral or intravenous administrations of an unreported amounts of K^{42}. Because measurements of the latter were not made until 2 to 5 days (4 to 10 half-lives) after administration and "relatively high count rates" were reported, the amounts administered may have been very substantial. In other collaborative studies with researchers at Loyola University, 250 microcuries were administered. These investigations were supported by the U.S. Public Health Service and by the U.S. Atomic Energy Commission.

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ANL-15. Whole-Body Counter Calibration Using Hospital Patients Administered Cesium-132

BETWEEN 1955 AND 1964, measurements of radionuclides in subjects from natural sources and from fallout from atmospheric weapons testing were made at Argonne National Laboratory using the whole-body counter. The whole-body counter was calibrated for potassium measurements by administering known amounts of potassium-42 (K^{42}) to subjects, both Laboratory employees and hospital patients. The whole-body counter was also calibrated for cesium by administering known amounts of cesium-132 (Cs^{132}) to a separate group of hospital patients. The number of subjects and the amounts administered for calibration purposes were not stated. These subjects showered, dressed in activity-free garments, and were then counted for 50-minute measurements. The calibration factors were used over a period of several years to determine trends in fallout uptake. This work was supported by the U.S. Atomic Energy Commission.

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ANL-16. Absorption and Dissolution of Atmospheric and Inhaled Radon

IN 1956, nine Argonne National Laboratory employees participated in experiments to study the natural levels of radium in subjects by measuring radon gas exhalation. In order to improve the accuracy of radium estimates, scientists at Argonne National Laboratory sought ways to distinguish between radon produced in the body and radon absorbed by the body from the environment. This required two new experiments: one to measure the amount of atmospheric radon absorbed through the skin, the other to estimate the amount of atmospheric radon that is dissolved in the body.

In the first experiment, two subjects were immersed for several hours in an atmosphere containing elevated levels of radon gas. During the period of exposure, they breathed from a radon-free air supply. The purpose of this experiment was to measure the amount of exhaled radon that might result from the absorption of environmental radon through the skin. One subject was exposed for several hours in a room in which the radon concentration was in the range of 120 to 144 picocuries of radon per liter of air. The same subject was later exposed for several hours while enclosed to the neck in a bag containing 180 picocuries of radon per liter of air. A second subject was exposed for several hours while enclosed to the neck in a bag containing 310 to 340 picocuries of radon per liter air.

In a second experiment, eight subjects, including one who participated in the first experiment, were exposed for either 8 or 72 hours in a room where the radon gas was maintained at elevated levels in the range of 48 to 107 picocuries of radon per liter of air. The subjects' radon exhalation rates were measured at the end of the exposure period in order to provide baseline information for the interpretation of radon exhalation data from subjects exposed to environmental radon.

The goal of both experiments was to provide a measure of the natural radium content of subjects based on the exhalation of radon internally generated from the decay of natural radium. These experiments were funded by the U.S. Atomic Energy Commission.

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ANL-17. Studies of the Use of Tritium and Carbon-14–Labeled Bile Acids in Metabolic Studies

IN THE EARLY 1970s, investigators at Argonne National Laboratory participated in experiments to study the role of bile acids in gallstone formation. These experiments were conducted through various phases at the Mayo Clinic, in Rochester, Minnesota. The work was part of an effort to determine whether bile acids labeled with tritium (H^3) were useful in human metabolic studies and also to determine whether compounds labeled with stable isotopes could be used in the place of radioactively labeled compounds.

Two healthy subjects were injected intravenously with 46 microcuries of chenodeoxycholic acid (a bile acid) labeled with H^3 and 10 microcuries of chenodeoxycholic acid labeled with carbon-14 (C^{14}). This series of experiments was conducted to determine the metabolic fate and excretion routes of various labeled bile acids. In another series, bile acids labeled with carbon-13 (C^{13}) and C^{14} were administered orally to an unknown number of fasting patients. Bile and serum samples were obtained for the evaluation of bile acid content. The purpose was to validate the use of C^{13}-labeled bile acids in the measurement against conventional methods based on C^{14}-labeled acids; to validate bile acid kinetic measurements based on serum sampling; and to establish procedures for the simultaneous measurement of all bile acids. The estimated radiation doses to subjects were 2.8 millirems from H^3 and 21.0 millirems from C^{14}-committed effective dose equivalent to the whole body.

Both experiments indicated that radioactively labeled as well as stable isotope-labeled bile acids are suitable for kinetic studies of bile acids in humans. Methods using stable isotope labels were intended to increase patient comfort, eliminate the need for hospitalization, and

eliminate the use of radioactive tracers for the measurement of bile acid kinetics. The U.S. Atomic Energy Commission, U.S. Energy Research Development Administration, the National Institutes of Health, and the U.S. Public Health Service funded these experiments in conjunction with the Eli Lilly Research Foundation, Eli Lilly and Co., and Mead Johnson and Co.

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Brookhaven National Laboratory

BNL-1. Effectiveness of Iodine-131 in Diagnosing and Treating Graves' Disease and Metastatic Carcinoma of the Thyroid

IN 1950, BROOKHAVEN National Laboratory conducted a study on the use of iodine-131 (I^{131}) to treat patients with metastatic carcinoma of the thyroid or with Graves' disease. Patients for the study were sent to Brookhaven from Memorial Hospital in New York City.

In the study, a therapeutic dose of 4 to 360 millicuries of I^{131} was given to the patients; the exact dose depended in part on the number of metastases and on previous radiation treatment. Graves' disease patients who were unsuitable for surgical therapy were treated with I^{131} in doses of 6 to 20 millicuries. The patients were monitored for hematological damage. Metabolic studies were also conducted, including study of the effects of radiation dose on renal tubular function. Twelve patients participated in the study, ranging in age from 15 to 63 years. Of the 12 patients, 8 were female. The study was conducted in conjunction with the Memorial Hospital and was funded by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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BNL-2. Boron Neutron Capture Therapy

BROOKHAVEN NATIONAL LABORATORY conducted boron neutron capture therapy (BNCT) on 45 patients from 1951 to 1961. The patients all were suffering from aggressive and otherwise untreatable types of brain tumors, such as glioblastoma multiforme or malignant glioma; all had received conventional radiation treatments. The purpose of BNCT was to attack more precisely the tumors with radiation, destroying the tumor cells. The patients were injected with a discrete amount of boron that was intended to deposit in the tumor. The tumors were then bombarded with a beam of neutrons that was directed to the boron and thus aimed at destroying the tumor.

The results of this therapy were unsuccessful. Patients who were treated with BNCT generally lived only as long as those patients, with the same types of brain tumors, who were treated with conventional radiation therapies. This work was funded by the U.S. Atomic Energy Commission. Currently, advances in technology that deliver higher concentrations of boron to tumor tissues for potentially improved therapy have brought about the return of BNCT. As a result, Brookhaven is currently involved in BNCT research and clinical trials. (BNCT was referenced in the Markey report; this summary was included in *The DOE Roadmap* of February 1995, and since revised.)

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BNL-3. Iodine-131 Used to Measure Thyroid Function in Young Children with Nephrotic Syndrome

SCIENTISTS AT BROOKHAVEN National Laboratory conducted a series of experiments using a group of young children suffering from nephrotic syndrome (kidney disease). In 1951, eight of these children, ages 2 to 6 years, with renal functions varying from 14 to 225 percent of normal and with varying degrees of edema or lack thereof, were studied after administration of iodine-131 (I^{131}).

A uniform ability by the thyroid gland to extract radioactive iodine from the blood was noted. The maximum uptake by the gland varied from 30 to 60 percent of the administered doses, which ranged from 3 to 5 microcuries. These data were evaluated against comparable data obtained in normal children. The scientists concluded that there is no impairment of the thyroid gland in its ability to take up iodine in young children with the nephrotic syndrome. (Included in *The DOE Roadmap* of February 1995)

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BNL-4. Radioactive Chlorine, Bromine, and Sodium in Extracellular Fluids

FROM 1952 TO 1953, the total volume of extracellular fluids in 15 subjects was studied at Brookhaven National Laboratory. Five chronically ill hospital patients were injected with chlorine-38 (Cl^{38}) and sodium-24 (Na^{24}). Ten other patients were injected with Cl^{38} and bromine-82 (Br^{82}). Total radiation doses were planned so that the weekly dose limit of 0.3 rad would not be exceeded. Blood samples were drawn at various times after injection and the radioactivity measured. During the course of this experiment, urine, red blood cells, pleural fluid, gastrointestinal fluid, and spinal fluid were also measured for Cl^{38} and Br^{82}. The subjects were considered to be "normal" for purposes of this study. The U.S. Atomic Energy Commission funded this study. (Previously described in #3 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

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BNL-5. Measurement of the Turnover Rate of Sodium in Nephrotic Children Using Sodium-24

BROOKHAVEN NATIONAL LABORATORY conducted an experiment in 1954 on children suffering from nephrotic syndrome to study the rates of exchange of sodium in edema fluid, in ascitic fluid, and in the plasma. Sodium-24 (Na^{24}) as sodium chloride was injected intravenously and the plasma Na^{24} disappearance curve was analyzed and compared to the Na^{24} appearance curves in the two fluids. It was found that in both fluids the ratio of (a) the rate of change of the Na^{24} concentration to (b) the difference between the Na^{24} concentration in the plasma and that in the fluids, increased with time during the first few hours after injection. (Included in *The DOE Roadmap* of February 1995)

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BNL-6. Degradation Rate of Iodine-131–Labeled Normal Albumin Using the Whole-Body Gamma Spectrometer

IN 1954, Brookhaven National Laboratory conducted metabolic studies in humans with iodine-131 (I^{131})-tagged serum albumin. In prior studies, plasma protein fractions labeled with I^{131} had been administered to normal subjects and to patients. A gamma spectrometer was constructed to determine transfer rates of locally injected I^{131} serum albumin and other substances tagged with gamma-emitting isotopes.

In this study, the biological half-time of I^{131}-labeled human albumin was determined by two methods. The first method was the calculation from serum and urine samples following injection of 59 microcuries of I^{131}. The second method used the whole-body gamma spectrometer to measure the amount of labeled albumin present in the body at stated intervals following injection of 6.6 microcuries of I^{131}. Plasma-specific activity and urinary excretion were followed up to 60 days after injection. The rate of disappearance of the labeled albumin was measured in two patients. The first was a

49-year-old woman with chronic cystic mastitis; the second was a 40-year-old woman who had previously had a mastectomy. This research was supported by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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BNL-7. Studies on the Metabolism of Plasma Proteins in the Nephrotic Syndrome

THIS STUDY WAS conducted at Brookhaven National Laboratory from 1955 to 1956. The subjects were six children in various phases of the nephrotic syndrome using iodine-131 (I^{131}), including one child who had recovered from the illness, and nine normal subjects, consisting of eight men and one woman, all between the ages of 21 and 29 years. These subjects were given intravenous tracer doses of radioiodinated human plasma albumin and radioiodinated human gamma globulin. Three of the children were then given intravenous injections of radioiodinated human iron-binding globulin. The amount of activity administered was not to exceed 1.5 microcuries I^{131} per kilogram of body weight.

The disappearance of specific radioiodinated plasma protein from circulation and its cumulative appearance in the urine were studied; the urinary excretion of nonprotein radioiodine was also investigated. This study was supported by grants from the National Institutes of Health, the U.S. Public Health Service, the Muscular Dystrophy Association of America, the Playtex Park Research Institute, and the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995, and since revised)

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BNL-8. Metabolism Studies with Acetate Labeled with Carbon-14

IN 1957 AND 1958, scientists at Brookhaven National Laboratory conducted studies to investigate carbon acetate metabolism. Forty to 200 microcuries of 1-C^{14}–labeled acetate or 2-C^{14}–labeled acetate were intravenously injected into subjects, including diabetics who had fasted and were denied insulin on the day of the experiment. Some of the subjects were cancer patients (nondiabetics); and others were patients with severe diabetes. More than 13 studies were conducted using various treatment combinations involving diet, fasting, insulin, or prednisone. The total number of subjects was about 20, both men and women, ranging in age from 12 to 60 years.

After medical staff administered the intravenous trace dose of C^{14}-labeled acetate, metabolism products such as triglycerides, cholesterol, ketone bodies, glucose, pyruvic and alpha-ketoglutaric acids, and carbon dioxide were isolated from the blood, urine, and breath, and analyzed for C^{14} content. The study was supported by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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BNL-9. Metabolic Studies with Manganese-54

In 1957, Brookhaven National Laboratory conducted human metabolic studies with the isotope manganese-54 (Mn^{54}). This study was the first to use Mn^{54} in human subjects. Manganese had been assumed to participate indirectly in hematopoiesis (blood formation). Two or more patients were injected with Mn^{54} and followed to determine count-rate at the body surface, blood radioactivity, and excretion rates. Blood taken from one of the patients 66 days after injection contained almost the entire radioactivity in the red cell fraction. This research was supported by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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BNL-10. Magnesium Metabolism Studies in Humans with Magnesium-28

In 1959, Brookhaven National Laboratory used magnesium-28 (Mg^{28}) to study the *in vivo* distribution and retention of magnesium in humans. Ten adults, 3 men and 7 women, were studied at the metabolic wards of the Brookhaven Medical Research Center Hospital. All but one of the men suffered from hypertension.

Nine of the subjects received intravenous injections of the isotope; two were studied after oral administration of Mg^{28}. The intravenous dosages, which ranged from 20 to 104 microcuries, were slowly administered to prevent toxic symptoms. Excretion rates were analyzed by measuring Mg^{28} in urine and stool specimens. This study was conducted with support from the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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BNL-11. Whole-Body Counting Technique Used to Study Turnover of Globulins Labeled with Iodine-131

In 1959, Brookhaven National Laboratory conducted studies on the turnover of beta- and gamma globulins labeled with iodine-131 (I^{131}).

The investigators used both the conventional method of blood and urine sampling and a new technique that used the whole-body gamma spectrometer. The new device allowed scientists to measure the retention of labeled globulins over long periods of time following administration of low levels of isotopes, particularly internally deposited gamma emitters.

One patient participated in these studies; he was placed in the whole-body counter 34 times. The subject was a multiple myeloma patient who was injected with the I^{131}-labeled globulins on three occasions. The amount of iodine activity in the labeled globulins ranged from 17.0 to 50.16 microcuries. The study was supported by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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BNL-12. A Study of Metabolic Pathways of Carbohydrate Formation Using Carbon-14

STUDIES WERE carried out at Brookhaven National Laboratory to study the metabolic pathways by which subjects in various metabolic states form glucose. In this study, the subjects were three men with bronchogenic carcinoma, three male diabetics, and one 13-year-old female diabetic. On the day of the experiment, the subjects were denied food and insulin and then were injected with C^{14}-acetate. Carcinoma patients received 200 microcuries; diabetic patients received from 40 to 100 microcuries as a single 1- to 2-minute injection. Breath samples were collected and analyzed. Some of these patients participated in multiple studies.

In a related study, two moderately diabetic subjects fasted and were orally administered 0.5 to 1.0 gram of C^{14}-labeled ethanol per kilogram of body weight. The blood and urinary glucose were isolated. The results indicated that in one patient about 1 percent as much C^{14} was present in total-body glucose as had been excreted as CO_2 after 2.5 hours. In the other patient about 2 percent as much was present. Both patients had excreted about 25 percent of the total administered C^{14} by the end of 24 hours. This research was partly supported by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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BNL-13. Analysis of Blood Glucose Following Intravenous Injection of Carbon-14

IN 1959, at Brookhaven National Laboratory, diabetic and nondiabetic patients were given intravenous injections of 40 to 150 microcuries of lactate or pyruvate labeled with carbon-14 (C^{14}). The injections were followed by serial analysis of blood glucose for C^{14} content. Subsequently, glycogen was injected in an attempt to estimate relative glycogen labeling. Seven diabetic and three nondiabetic subjects were used in this study. The effects of insulin, tolbutamide, and glucose load were also studied in the same patients. This study was funded by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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BNL-14. The Metabolism and Fate of Tritiated Thymidine in Humans

THIS STUDY WAS CONDUCTED in 1959, at Brookhaven National Laboratory as part of an investigation of H^3-thymidine as a label for DNA of proliferating cells *in vivo* and *in vitro* systems. In this study, H^3-thymidine metabolism was studied in selected patients following intravenous injection. All patients were beyond reproductive age and were judged to have short life expectancies.

In two control patients with normal hematopoietic (blood-formation), thymidine labeled with tritium (H^3) rapidly cleared the plasma and distributed in a volume as large as total-body water within a few minutes after injection. Two of the subjects selected for this initial investigation were patients with brain tumors, judged to have short life expectancies, and to be in hematopoietic equilibrium at the time of study. This research was supported by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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BNL-15. Study of Carbon-14–Labeled Ascorbic Acid Metabolism

A RESEARCH COLLABORATION in the early 1970s between Brookhaven National Laboratory and Verwoerd Hospital in Pretoria, South Africa, resulted in a study of ascorbic acid (vitamin C) labeled with carbon-14 (C^{14}) metabolism in Bantu tribesmen with a disease called hemosiderosis. This disease is similar to scurvy and is common among the South African Bantu. It involves excessive iron accumulation and failure to utilize ascorbic acid. This research was conducted to determine the metabolism of ascorbic acid.

Four adult Bantu men who had been diagnosed with hemosiderosis and scurvy participated in this study. Ascorbic acid labeled with carbon-14 was given orally, after which blood samples, urine samples, and respiratory CO_2 samples were collected and analyzed. The results indicated that most of the C^{14} was excreted primarily by respiration and secondarily in the urine. This work was jointly supported by the U.S. Atomic Energy Commission and the South African Atomic Energy Board. (Included in *The DOE Roadmap* of February 1995)

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BNL-16. Dose–Response Relationships Between Iodine-131 Administrations and Hematopoietic Effects

IN APPROXIMATELY 1951, physicians in the Medical Department of Brookhaven National Laboratory conducted a study to examine the relationship between the level of exposure to radiation from internally administered iodine-131 (I^{131}) and the extent of radiation-induced effect to the hematopoietic (blood-cell–forming) system in exposed subjects. The scientists sought to determine a reliable indicator of I^{131} radiation-induced effect; the most accurate method of estimating the radiation dose delivered to tissue relative to the amount of I^{131} administered; and the predictability of a prior tracer study of the radiation dose

delivered to the hematopoietic system by administration of a large amount of I^{131}.

Study subjects were 33 patients with various metabolic rates associated with myxedema (a condition associated with a low thyroid activity), hypothyroid (slight depression of thyroid function), euthyroid (normal thyroid function), and hyperthyroid (overactivity of the thyroid). Some subjects had a history of prior I^{131} administrations in tracer or therapeutic amounts.

Subjects received tracer amounts of I^{131}, followed a few weeks later in at least 18 cases by the administration of a therapeutic amount of I^{131}, for total amounts of between 52 and 247 millicuries. All doses were administered orally. Blood and urine specimens were collected at intervals and analyzed for radioactivity. Differential white cell counts were obtained for at least 30 days after each I^{131} administration to monitor changes in the lymphocyte and neutrophil counts over time relative to pre-treatment.

The results suggested a that there was a reasonably good correlation between therapeutic amounts of I^{131} and the hematopoietic system response, and that the magnitude of the radiation dose to the hematopoietic system from any given amount is influenced by a variety of factors, primarily the individual's metabolism of iodine.

The lymphocyte count was found to be the most sensitive and reliable measure of the magnitude of the radiation effect induced by exposure to I^{131}. The fall in the lymphocyte count following administration of large amounts of I^{131} correlates well with the microcuries administered, but poorly with the integrated blood concentration of I^{131} together with a factor representing the integrated amount of I^{131} remaining in the body. This study was supported by the U.S. Atomic Energy Commission.

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BNL-17. Estimation of Body Water Volume and Potassium in Children Using Tritium and Potassium-42 as a Tracer

BETWEEN 1951 AND 1956, researchers in the Medical Department of Brookhaven National Laboratory conducted a physiological study to evaluate the use of water labeled with tritium (H^3; tritiated water) in estimating total-body water and exchangeable potassium compared with an established antipyrine-based methodology. Study subjects included nine children ranging in age from 3 to 8 years, who were hospitalized in, or had been recently discharged from, the nephrotic unit at Brookhaven National Laboratory. All had protein in their urine, but eight were free of edema (swelling due to presence of abnormally large amounts of fluid in the spaces between cells of body tissues).

Three microcuries of potassium-42 (K^{42}) per kilogram of body weight, 75 microcuries of H^3, and 400 milligrams of antipyrine in 10 milliliters of saline were administered simultaneously to each subject by intravenous infusion over a period of 1 hour. Blood samples for body water estimations were obtained from each subject at 2, 3, and 4 hours after infusion and continued at intervals up to 14 days. Urine samples also were obtained for H^3 analysis. The data were used to examine the biological clearance of H^3, H^3 kinetics, and body water mixing, and to calculate and compare estimates of total-body water and exchangeable potassium based on H^3 and antipyrine indications.

The results indicated that H^3 equilibrium was completed in all subjects within 30 to 40 minutes of H^3 infusion. Total body water volumes estimated using H^3 were almost identical to those obtained using antipyrine. Estimates of exchangeable potassium obtained by either method ranged between 1.5 to 1.8 grams per liter per kilogram of body weight. This study was funded by the U.S. Atomic Energy Commission.

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BNL-18. Cerebrospinal Fluid Studies Using Chlorine-38, Potassium-42, and Iodine-131

BETWEEN 1952 AND 1953, physicians in the Department of Surgery at Harvard University, the Department of Neurosurgery at Massachusetts General Hospital, and the Division of Medicine of Brookhaven National Laboratory collaborated on a study to examine the formation and cycling of cerebrospinal fluid. The two study subjects had histories of cerebrospinal fluid blockage as a result of spinal tumors. The blockages responded to surgical treatment in both cases. Potassium-42 (K^{42}) and chlorine-38 (Cl^{38}) were selected as dual tracers for intracellular and extracellular ions. Human serum albumin labeled with iodine-131 (I^{131}) as a tracer was used in one patient to determine the volume of subarachnoid space.

Following the injections of the tracers, the researchers monitored the activity of the cerebrospinal fluid in the lateral ventricles and the lumbar subarachnoid space by assaying the radioactivity levels of the plasma for 5 hours. The investigators concluded that the amount of cerebrospinal fluid created daily is small and that fluid creation is not the sole responsibility of the choroid plexus, as was previously hypothesized. This study was supported by the National Institutes of Health, the U.S. Public Health Service, and the Associated Universities, Inc., and the U.S. Atomic Energy Commission.

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BNL-19. Study of Manganese Metabolism Using Manganese-56 as a Tracer

IN THE MID-1950s, researchers in the Medical Department of Brookhaven National Laboratory conducted a study to describe and determine the kinetics of the turnover of manganese-56 (Mn^{56}) in tissue, and to better understand the transport mechanisms directly from the bloodstream. Study subjects were 14 patients—7 males and 7 females—between 40 and 71 years of age. Of these, six had Parkinson's disease, three had metastatic cancer, two were hypertensive, one had heart disease, one had diabetes, and one had rheumatoid arthritis.

Between 15 and 20 microcuries of Mn^{56}, as the sulfate in saline solution, with 3.6 micrograms of stable Mn^{56}, were administered to each subject by intravenous injection following overnight fasting. Venous blood samples were obtained in quick succession after the administration, with the interval between samples increasing to 5 minutes. The samples were promptly assayed and weighed.

The study concluded that Mn^{56} dispersed rapidly throughout the body, with the most rapid uptake occurring in the liver. From these data, the scientists concluded that mitochondrial uptake of manganese was the primary cause of the extensive retention and rapid tissue uptake. This study was supported by the U.S. Atomic Energy Commission.

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BNL-20. Experimental Systemic Therapy of Bone Tumors Using Gallium-72

BETWEEN 1954 AND 1958, the Medical Department of Brookhaven National Laboratory studied the effectiveness of gallium-72 (Ga^{72}) in therapy of bone cancers. Twenty-one patients were treated with Ga^{72} for advanced bone malignancies. Most of the patients had diffuse bone metastases secondary to breast or prostate cancer; the remainder had primary bone malignancies.

All had exhausted conventional therapy before admission to Brookhaven National Laboratory Research Hospital.

The patients were intravenously injected with 1 microcurie of Ga^{72}, in the form of gallium citrate, per kilogram of body weight. Complete blood and platelet counts were analyzed for damage to cells in the circulating blood and blood-forming tissues. Total-body doses of 75 rads or less were delivered, but the hematologic findings were similar to the effects seen with the administration of 150 to 200 rads of external x- or gamma radiation. The enhanced effect of the internal radiation exposure (compared to other patients receiving the same dose external to the body) was attributed to the localization of Ga^{72} in the bone.

The research also found that the effect of large doses of radiation on the bone marrow appeared to be cumulative to a point beyond which regeneration was not possible. It was also found that a total white count below 1,000 and a platelet count below 25,000 could be tolerated for weeks without infection or gross bleeding and with ultimate recovery. This study was supported by the U.S. Atomic Energy Commission.

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BNL-21. Investigation of Carbohydrate Formation Using Carbon-14–Labeled Acetate

BETWEEN 1956 AND 1957, the pathway of carbohydrate formation was investigated using carbon-14 (C^{14}) by researchers at the Medical Department of Brookhaven National Laboratory. The study was conducted in two parts to include both diabetic and nondiabetic subjects.

In the first part, four patients hospitalized with various types of cancer were selected as the nondiabetic subjects. They included three males, aged 40 to 60 years, and one 63-year-old female. Subjects fasted 15 to 24 hours before being administered between 190 and 500 microcuries of C^{14}-labeled sodium acetate by intravenous injection. Blood samples were obtained approximately 2 hours later and the blood sugar (glucose) was isolated and analyzed for the distribution of fatty acid carbons in the ring of the blood glucose.

In the second part, the diabetic group was composed of three females ages 11, 34, and 38 years, and two males ages 55 and 59 years. After fasting, they were administered 80 to 100 microcuries of C^{14}-labeled acetate solution by intravenous injection. Similar analyses were performed to assess carbohydrate formation.

This study confirmed earlier findings and showed no differences in the formation of carbohydrates by normal and diabetic subjects. This work was supported by the U.S. Atomic Energy Commission.

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BNL-22. Studies on the Retention of Vitamin B_{12} Using Cobalt-60 and Cobalt-58 Tracers

FROM 1957 TO 1967, researchers at the Medical Research Center of Brookhaven National Laboratory conducted studies on the rate of loss of vitamin B_{12} using cobalt-58 (Co^{58}) and cobalt-60 (Co^{60}) as tracers. The purpose of these studies was to evaluate the biological retention half-time of vitamin B_{12} and to demonstrate its rate of loss from the body after administration of large amounts of the vitamin.

Ten clinic and hospital patients (males and females) with a variety of diagnosed blood diseases participated as study subjects. Each subject also received either an intravenous or an intramuscular injection of 0.3 to 3.0 microcuries of Co^{60}-labeled vitamin B_{12}. Two subjects received intramuscular injections of 2 to 5 microcuries of Co^{58}-labeled hydroxocobalamin, a chemical analog of vitamin B_{12}. The first injection occurred in 1957. Six of the 10 subjects received nonradioactive cyanocobalamin or hydroxocobalamin therapy at varying intervals after the injection to their respective metabolism. Whole-body counting of patients administered radiocobalt-labeled vitamin B_{12} began in early 1963 and continued through 1968.

This study showed that there is no single biological half-time for vitamin B_{12} in man; rather, the biological half-time changes continuously over time. The study also showed that large dosages (500 to 1,000 micrograms) of vitamin B_{12} or hydroxocobalamin caused a decrease in biological retention half-time, while small dosages of vitamin B_{12} (100 micrograms) had no detectable effect on rate of loss. This work was supported by the U.S. Atomic Energy Commission.

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BNL-23. Use of Iodine-124 for Scanning Brain Tumors

THE APPLICABILITY OF iodine-124 as an imaging agent and tracer for certain proteins was investigated in a collaborative study between Brookhaven National Laboratory, the School of Medicine at Wake Forest University in North Carolina, and Massachusetts General Hospital. The study, which took place between 1958 and 1962, involved a combination of laboratory and clinical studies aimed at identifying the physiochemical properties and functions of serum proteins in cancer. The objective was to demonstrate that human fractionated globulin could be labeled with iodine-124 (I^{124}), and that such a preparation could be concentrated in sufficient amounts in brain tumor tissue to be detected by positron scanning.

The study group consisted of three patients with brain tumors that had been scanned previously with either radioactive copper or arsenic. Gamma globulin labeled with I^{124} was injected and multiple scans were conducted to determine how effectively the labeled protein concentrated in tumors. A typical level of administered activity was 260 microcuries of I^{124}. Up to five scans were performed on each patient.

The experiment showed that I^{124} could be used as an imaging agent for positron scanning, but the limited number of cases precluded any meaningful comparison with I^{131}. The research was funded by the American Cancer Society and the U.S. Atomic Energy Commission.

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BNL-24. Studies of the Proliferation of Leukemic and Multiple Myeloma Cells Using Tritiated Thymidine

BETWEEN 1959 AND 1961, researchers at the Medical Research Center of Brookhaven National Laboratory conducted a series of studies to better understand the growth characteristics of normal and malignant (leukemia and multiple myeloma) cells. Thymidine labeled with tritium (H^3) was used as a tracer of the biological process involved.

In one study, three patients with confirmed diagnoses of multiple myeloma participated as study

subjects. There were two males and one female, ages 60, 69, and 44 years, respectively. Tritiated thymidine was administered to each subject in single intravenous injections. One subject received a second injection after an interval of 45 minutes. Bone marrow samples were obtained by aspiration from each subject 30 to 60 minutes after the injections. The samples were fixed and processed for examination by autoradiography. It was found that approximately 60 minutes after injection only about 3 percent of the myeloma cells were labeled. The generation time of the label ranged from 2 to 6 days.

The study of leukemic cells involved four subjects with various types of myelogenous leukemia. The subjects were two males and two females, aged 62, 65, 60, and 73 years, respectively. Tritiated thymidine was administered to each subject in a single intravenous injection. Samples of blood and one sample of bone marrow were obtained from each subject at intervals up to 24 hours after injection. The bone marrow samples were fixed and processed for examination by autoradiography.

This study showed that the average generation time for normal neutrophil precursors was approximately 48 hours. The researchers concluded that the study results did not support the general concept of acute leukemia as a disorder of rapid proliferation. This research was supported by the U.S. Atomic Energy Commission.

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BNL-25. Study of the Role of Sodium in Hypertension Using Sodium-22

BETWEEN 1959 AND 1961, researchers at the Medical Research Center of Brookhaven National Laboratory studied the role of sodium in hypertension (high blood pressure). Subjects in the study were nine hypertensive patients, including seven males aged 48 to 66 years and two females aged 42 and 56 years; and nine normotensive (normal blood pressure) patients, including three males aged 39, 56, and 60 years, and six females aged 17 to 52 years. Some subjects were hospitalized for treatment of underlying diseases at the time of the study.

Between 2.6 and 7 microcuries of sodium-22 (Na^{22}) were administered orally with a low-sodium diet to each subject. Using a whole-body counter, the total-body retention of Na^{22} was measured in each subject at 1- to 3-day intervals for 6 to 11 months following administration.

Comparisons of the values obtained indicated that the biological retention half-time of Na^{22} was significantly longer in hypertensive subjects than in normotensive subjects, and that hypertensives may have a larger sodium pool than normotensives. This work was supported by the U.S. Atomic Energy Commission.

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BNL-26. Study of Iron Absorption and Loss by Whole-Body Counting Using Iron-59

DURING THE LATE 1950s AND EARLY 1960s, scientists at the Medical Research Center of Brookhaven National Laboratory, possibly in collaboration with researchers at Mount Sinai Hospital, New York, conducted a series of studies to better understand and to develop improved methods for evaluating iron metabolism in patients. Study subjects included patients with normal iron metabolism and/or patients under treatment for iron metabolism disorders due to underlying diseases. Some subjects participated in more than one study. Iron-59 (Fe^{59}) as ferrous citrate was administered to the subjects as a tracer of the biological processes of interest. Whole-body counting was also explored as a technique for determining the amount of iron retained in the body at different intervals after its intake.

Between 1959 and 1961, researchers at the Medical Research Center of Brookhaven National Laboratory conducted two related studies to determine and evaluate iron absorption, turnover, and loss as measured by whole-body counting using Fe^{59} tracer. Fifty female patients participated as study subjects in one of the two studies, including 14 with polycythemia vera (malignant overproduction of red cells), 6 with longstanding menorrhagia (excessive menstrual bleeding), 4 with aplastic anemia, 10 with various chronic nonmalignant conditions, and 16 patients whose iron metabolism was normal. Approximately 40 of these subjects also participated in a follow-up study.

In both studies, 1 to 10 microcuries of Fe^{59} as ferrous citrate were administered orally to each subject, followed by a drink of water. No food was given for 1 hour. Several 2- to 10-minute body counts were obtained for each subject over the 8- to 10-hour period following the ingestion of Fe^{59} to determine body Fe^{59} content. Whole-body counts were also obtained at intervals over periods up to several months to measure Fe^{59} retention and subsequent loss. These studies demonstrated the benefits of using Fe^{59} with whole-body counting in studying iron metabolism. This research was supported by the U.S. Atomic Energy Commission.

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BNL-27. Plasma Binding Capacity for Vitamin B_{12} Using Cobalt-57 Tracer

DURING THE EARLY 1960s, researchers at Brookhaven National Laboratory and the Long Island Jewish Hospital in New York conducted studies on the plasma binding capacity for vitamin B_{12} (cyancobalamin) using cobalt-57 (Co^{57}) as an isotope label. Subjects included four hospitalized patients with normal serum vitamin B_{12} levels, and four patients with known pernicious anemia in remission who were receiving routine monthly therapeutic injections of vitamin B_{12}. Three subjects received an intravenous injection and five subjects received an intramuscular injection of 2.5 to 5.0 microcuries of Co^{57}-labeled vitamin B_{12}. Blood samples were drawn at various intervals over a 48-hour period and the Co^{57} activity was measured in the separated plasma. Total plasma vitamin B_{12} volume was calculated.

These studies provided new information about the plasma binding capacity for vitamin B_{12}, and

demonstrated the presence of protein carriers involved in vitamin B_{12} transport in plasma. This work was supported by the U.S. Atomic Energy Commission.

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BNL-28. A Short-Term Comparison of Calcium and Strontium Metabolism Using Calcium-47 and Strontium-85

DURING THE EARLY 1960s, scientists at Brookhaven National Laboratory compared the behavior of strontium and calcium using calcium-47 (Ca^{47}) and strontium-85 (Sr^{85}). Study subjects were six patients (four females and two males) between the ages of 30 and 73 years, with different clinical conditions reflecting various degrees of skeletal involvements.

Subjects were administered 20 microcuries of Ca^{47} and 5 microcuries of Sr^{85} intravenously in the form of their chloride salts. Blood samples were collected at 4, 12, and 24 hours and on days 2, 3, 4, 5, 7, and 10 after injection. Twenty-four hour urine and stool samples were collected from each patient for 10 days after administration of the isotope. The concentrations of Ca^{47} and Sr^{85} were measured in the excreta and blood samples. Body retention was determined by whole-body counting daily for the first 10 days, then every second day for the next 20 days.

This study showed no differences between the rates at which the skeleton absorbs Ca^{47} and Sr^{85} during the first 10-day period. However, differences between the rates developed subsequently, and Ca^{47} and Sr^{85} metabolism over the long term could not be predicted from data obtained within 10 days of administration. This work was supported by the U.S. Atomic Energy Commission.

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BNL-29. Study of Tryptophan Metabolism Using Carbon-14

IN THE EARLY 1960s, researchers at Brookhaven National Laboratory examined the effects on tryptophan metabolism in humans of the administration of tryptophan-2 labeled with carbon-14 (C^{14}) with and without unlabeled tryptophan carrier. Loading studies were conducted to allow the detection of abnormal metabolism which might not have been detected otherwise. Study subjects were six volunteer patients ranging in age from 45 to 72 years; three males (two whites and one black) and three females. They were hospitalized on the metabolic ward with achondroplasia with osteoarthritis (one subject), alcoholism with gallstones (one subject), multiple myeloma (three subjects), and breast cancer (one subject).

Under controlled dietary and drug conditions, each patient was administered 17 to 78 milligrams of DL-tryptophan-2 with 96 to 157 microcuries of C^{14} as a tracer. All doses were administered orally except for one intravenous injection of DL-tryptophan-2-C^{14}.

Samples of expired air, urine collected for four consecutive 24-hour periods (one before and three after administration), and blood were obtained from each patient. These samples were then analyzed for C^{14} activity from labeled carbon dioxide ($C^{14}O_2$) and tryptophan metabolites relative to standard (control) values. About 19 to 36 percent of the total C^{14} administered was excreted in the urine, with or without the loading dose of unlabeled tryptophan. This study was supported in part by the American Cancer Society, the National Cancer Institute, and the U.S. Atomic Energy Commission.

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BNL-30. Use of Iodine-131 and Tritium Tracers in Studies of Vasopressin Metabolism

IN 1960, researchers at the Medical Research Center of Brookhaven National Laboratory studied the usefulness of iodine-131 (I^{131}) and tritium (H^3) as radioactive labels on vasopressin in studies of vasopressin metabolism in humans under various physiological and clinical conditions. Vasopressin, which was isolated from beef pituitary glands, is an antidiuretic hormone.

Five ambulatory hospital patients were selected for this study. They included patients with both normal and elevated blood pressures. Two subjects were given arginine vasopressin (AGV) labeled with I^{131} (approximately 0.8 microcurie); another subject was given AGV labeled with tritium (6.25 or 12.5 microcuries); the remaining two subjects were given labeled forms of AGV. Blood samples were drawn at intervals up to 3 hours after injection and the levels of I^{131} and H^3 in the plasma were measured. The results showed that I^{131} and tritium were effective labels for studying vasopressin metabolism under various conditions. This work was supported by the U.S. Atomic Energy Commission.

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BNL-31. Metabolism of Carbon-14–Labeled Acetate in Diabetics

IN 1960, a study was conducted at the Medical Research Center of Brookhaven National Laboratory to learn more about the metabolism of acetate in diabetics. Four subjects—two with juvenile-type diabetes in severe ketoacidosis (a condition resulting from severe insulin deficiency) and two with stable adult-type diabetes and mild ketosis—were included in the study.

None of the patients received insulin within 24 hours of the experiment and none received long-acting insulin within 72 hours. The stable diabetic subjects received 30 milligrams of prednisone 3 and 9 hours prior to injection of acetate. Subjects then received 50 to 100 microcuries of sodium acetate labeled with carbon-14 (C^{14}) by intravenous injection.

Blood samples were collected at later time intervals for analyses for C^{14}-ketone bodies and C^{14}-glucose (blood sugar). Urine samples were collected at 2 and 6 hours for analysis for C^{14} in ketone bodies and glucose. The breath of the stable diabetics was sampled at intervals for C^{14}-labeled carbon dioxide. This study showed that ketone bodies in diabetes are not part of the metabolic process that converts acetate to carbon dioxide. The study was funded by the U.S. Atomic Energy Commission.

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BNL-32. Study of Vitamin B_{12} Metabolism Using Cobalt-58 and Cobalt-60

IN 1960 AND 1961, researchers at the Medical Research Center of Brookhaven National Laboratory studied the metabolism of vitamin B_{12} after administration by different routes, to determine the effect of the administration route. Four hospital patients with illnesses unrelated to vitamin B_{12} metabolism participated as subjects.

Two patients were given double tracers of 2 microcuries of cobalt-60 (Co^{60})–labeled vitamin B_{12} administered by intravenous injection, followed 3, 4, and 7 days later by oral administrations of 3.56 microcuries of cobalt-58 (Co^{58})–labeled vitamin B_{12}. Cobalt-58 and Co^{60} radioactivity retained by these subjects was measured at intervals for up to 60 days.

Two other subjects first were given 20 microcuries per 0.21 micrograms of Co^{58}-labeled vitamin B_{12} orally followed after 30 and 42 days, respectively, by intravenous administration of 15 microcuries per 0.20 micrograms of Co^{58}-labeled vitamin B_{12}. Plasma radioactivity levels were measured for another 35 and 48 days, respec-

tively. Whole-body turnover rates of ingested and injected vitamin B_{12} were measured over 250 days.

The results indicated there was little difference between the excretion rates of orally and intravenously administered vitamin B_{12}. The research was supported by the U.S. Atomic Energy Commission.

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BNL-33. Studies of Strontium Metabolism Using Calcium-47 and Strontium-85

BETWEEN 1960 AND 1962, researchers at the Medical Research Center of Brookhaven National Laboratory conducted a series of studies to characterize the short- and long-term metabolism of strontium in the human body and to compare it with that of calcium. Strontium-85 (Sr^{85}) and calcium-47 (Ca^{47}) were used as tracers of the biological processes involved in subjects with either bone disease or normal calcium balances.

Long-term biological turnover of Sr^{85} was studied among 10 subjects; 6 males ranging in age from 54 to 73 years, and 4 females, ages 57 to 73 years. All 10 subjects were ambulatory patients in good physical condition, but had primary diagnosis of nonmetastatic cancer with 10 to 13 years survival after surgery for: cancer of the breast (2 subjects) or thyroid (1 subject); thyroid cancer, status unspecified (1 subject); pseudomyxoma peritonei (mucuslike material in the abdominal cavity) with diabetes (1 subject); hypopituitarism secondary to a pituitary tumor (1 subject); Paget's disease of bone (1 subject); and osteoporosis, alone or with osteoarthritis (3 subjects). Of these, eight subjects had associated skeletal disease, but six had normal calcium balances and possibly served as comparison subjects.

Single intravenous injections of 10 to 14 microcuries of Sr^{85} were administered to eight subjects. Forty microcuries Sr^{85} were administered orally to each of the other two subjects. Urine and feces were collected for 24-hour periods for 20 to 48 days after the Sr^{85} administrations and were analyzed for Sr^{85}. Urinary excretion of calcium was measured daily for each subject. Whole-body retention of Sr^{85} was measured weekly in the whole-body counter. Based on 100 to 320 days of observation, the biological retention half-time of strontium was estimated to be 843 days. Data were insufficient to distinguish between two mathematical models developed to describe the life-time biological turnover of Sr^{85} in humans.

In a related study, the same researchers examined the effects of prolonged daily ingestion of stable strontium on the long-term turnover of strontium fixed in bone. Four female patients participated as subjects, including three who participated in the long-term Sr^{85} turnover study (above). Ten microcuries of Sr^{85} were administered intravenously to each subject. From 130 to 240 days after Sr^{85} administration, the subjects were given daily dietary supplements of 1,100 grams of calcium gluconate (two subjects) or 570 grams strontium lactate (two subjects).

The Sr^{85} turnover rates determined for this period were found not to be statistically different from the pre-Sr^{85} administration, suggesting that the exchange of bone-fixed strontium is not influenced directly by the amount of stable strontium or calcium available for exchange.

Subsequently, the research team conducted a further study to compare the short-term kinetics of Ca^{47} and Sr^{85} in humans. Six patients—two males aged 30 and 56 years, respectively, and four females between the ages of 53 and 73 years (none of whom was included in the long-term kinetic studies)— participated as subjects.

Of these, three had multiple myeloma, and the three others had essential hypertension, scleroderma, and chylous ascites (serous fluid in the abdominal cavity, "dropsy"), respectively. Their degrees of disease-related skeletal involvement ranged from "normal" (one subject) to "extensive" (one subject).

A moderately alkaline saline solution of 2 microcuries of high-specific-activity Ca^{47} chloride and 5 microcuries of Sr^{85} chloride tracers was administered by intravenous injection. Blood samples were collected at 4, 12, and 24 hours, and on days 2, 3, 5, 7, and 10 after administration of the radionuclides. Daily urine and stool samples were collected from each patient during the same period. Plasma, urine, and stool samples were measured for radioactivity. Whole-body retention of Sr^{85} was measured by gamma spectrometry, daily for the first 10 days, and twice weekly for the next 20 days.

The results indicated that similarities observed between strontium and calcium metabolism in the short term (10 days) are not predictive of their kinetics in the long term. This work was supported by the U.S. Atomic Energy Commission.

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BNL-34. Study of the Metabolism of Cesium-137

BETWEEN 1960 AND 1962, researchers in the Metabolic Section of the Veterans Administration Hospital, Hines, Illinois, and the Medical Research Center of Brookhaven National Laboratory collaborated on a study of cesium-137 (Cs^{137}) metabolism in humans. A total of 15 hospitalized patients participated in the study.

Eleven of the 15 subjects reportedly had good nutrition, normal kidney function, and healthy gastrointestinal tracts. Nine of the subjects were males, ages 45 to 66 years, 7 of whom had malignant diseases including Hodgkin's disease (2 subjects); lung cancer (3 subjects); multiple myeloma (1 subject) and lymphoma (1 subject); and 2 had chronic lung diseases. The other six subjects were females, ages 48 to 66 years, with cancers of the colon (two subjects), breast (two subjects), or uterus (one subject), or Hodgkin's disease (one subject).

Single administrations of between 10 and 50 microcuries of Cs^{137} chloride were given by intravenous injection to eight subjects, and orally to the other seven subjects. Cesium-137 activity was measured in samples of blood, urine, and feces obtained from 11 of the subjects at intervals over periods ranging from 9 up to 160 days after the Cs^{137} administration. Five subjects also had whole-body counts about three times a month. The distribution of Cs^{137} was also studied in tissues obtained from five of the subjects after their deaths from their disease which occurred 3 to 165 days after the Cs^{137} administration.

The investigators found that Cs^{137} taken orally was rapidly and almost completely absorbed into the bloodstream where it was cleared quickly and deposited preferentially in muscle. The major route of excretion was found to be through the kidney into the urine. Estimation of the biological half-time for cesium by analysis of excreta (two subjects) was found to be 50 and 60 days, respectively. Estimates of biological retention half-time by whole-body counting ranged from 54 to 114 days with an average of 75 days. This research was supported by the U.S. Atomic Energy Commission.

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BNL-35. Study of Tryptophan Conversion to O-Aminophenol Using Carbon-14

A STUDY IN 1961 by researchers at Brookhaven National Laboratory determined that tryptophan (an essential amino acid), was metabolized to o-aminophenol, a urinary product of tryptophan. This process was shown using carbon-14 (C^{14}) as a tracer.

Thirty-nine milligrams of DL-tryptophan-7a-C^{14} containing 51 microcuries of C^{14} were administered orally to one female patient with multiple myeloma. Expired carbon dioxide (CO_2) and urinary output were collected for the next 12 to 24 hours, respectively. Of the administered C^{14}, 5 percent was found to have been excreted as expired $C^{14}O_2$ in 12 hours, and 14 percent was excreted in the urine in 24 hours. The metabolite o-aminophenol-2-C^{14} was identified in the urine. The study was supported by the U.S. Atomic Energy Commission.

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BNL-36. Total-Body Water and Hematologic Studies in the Pacific Islanders Using Chromium-51 and Tritium

BETWEEN 1961 AND 1966, a medical team from Brookhaven National Laboratory conducted a series of studies on persons, both natives and others, living in the Marshall Islands. These islands and some of the population were contaminated with radioactive fallout as the result of an unexpected distribution of fallout from a nuclear test on Bikini Atoll in 1954.

In 1961, five Marshallese and five Americans were administered chromium-51 (Cr^{51})–labeled red cells by intravenous injection to determine their blood volumes. In 1962, eight unexposed Rongelap Island natives and seven Americans participated in an identical procedure. Another group of 25 subjects may have undergone the same study during the period 1961 to 1962.

In 1963, 21 Marshallese islanders were administered Cr^{51} and 1 milliliter of water labeled with tritium (H^3) to determine red cell mass, blood volume, lean body mass, and total-body water. Similar body-water and lean-body-mass studies were conducted on residents of Enewetok Atoll in 1965 and 1966.

These studies showed that there was a slight tendency for the Marshallese to be anemic. It was determined that the anemia was characteristic of the Pacific island study population and not the result of exposure to fallout radiation. This work was supported by the U.S. Atomic Energy Commission.

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BNL-37. Study of Iron Metabolism in Humans with Aregenerative Anemia Using Iron-59 and Chromium-51

IN APPROXIMATELY 1962, researchers at the Medical Research Center of Brookhaven National Laboratory conducted a study to better understand the effect of anemia (low red blood-cell count) on iron metabolism in humans. This study involved four male and three female patients, ranging in age from 5 to 68 years, who had aregenerative anemia (reduced capacity to replace red blood cells), and two normal sub-

jects. Subsequently, the Brookhaven researchers collaborated with medical scientists at the Karolinska Hospital in Stockholm, Sweden, to increase the size of the study group. Twenty anemia patients and 37 others of unspecified health status participated in the collaborative Swedish-American study.

Subjects initially were orally administered 250 micrograms of iron as ferrous sulfate or gluconate together with 0.5 to 5.0 microcuries of iron-59 (Fe^{59}) as a tracer to evaluate iron absorption and excretion. At Brookhaven, red blood-cell mass was measured in patients using a standard test involving administration of chromium-51 (Cr^{51}). On completion of the absorption study, all patients received 1 to 10 microcuries of Fe^{59} as ferrous citrate by intravenous injection for other evaluations.

From the results of these studies, it was concluded that anemia has an effect on iron absorption; however, the relationship was not well defined. The initial study was supported solely by the U.S. Atomic Energy Commission. The second study in this series was supported jointly by the Swedish Nutritional Foundation, the O. and E. Ericsson Foundation, and the U.S. Atomic Energy Commission.

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BNL-38. Metabolism of Zinc-65

IN 1962 AND 1963, researchers in the Metabolic Section of the Veterans Administration Hospital, Hines, Illinois, and the Medical Research Center of Brookhaven National Laboratory, investigated the metabolism of zinc-65 (Zn^{65}). A total of 19 hospitalized patients participated as study subjects, including 4 males ranging in age from 56 to 73 years and 4 females ranging in age from 45 to 60 years. Subjects had been diagnosed with cancer of the breast (three female subjects); lung (two subjects) or larynx (one subject); rheumatoid arthritis (one subject); or chronic pulmonary disease. These subjects were well-nourished, had normal kidney function and disease-free gastrointestinal tracts, and received 10 to 12 milligrams of stable zinc in their daily diet.

Tracer amounts (20 to 53 microcuries) of Zn^{65} as chloride were administered to each subject in single intravenous injections. Serial blood samples were obtained with declining frequency after the first day following the Zn^{65} administration throughout the study period. Zinc-65 activity in these samples and in 24-hour urine samples and all fecal samples was determined throughout the study. Retention of Zn^{65} was estimated in two subjects by whole-body counting.

Eleven subjects participated in the tissue distribution phase of this study. These subjects, including seven males ranging in age from 56 to 90 years and four females ranging in age from 32 to 67 years, had advanced malignant diseases of various types, including: bronchogenic cancer (three subjects); cancers of the colon (two subjects), breast (one subject), pancreas with ascites (one subject); Hodgkin's disease (one subject); fibrosarcoma with bone involvement; and hepatoma (liver tumor) (one subject). Each subject received 100 microcuries of Zn^{65} with 0.001 to 2.0 milligrams of stable zinc chloride in a single intravenous injection. Samples of blood, urine, feces, and solid tissues were obtained for radioassay at autopsy, 1 to 71 days after the Zn^{65} administration.

The study found that Zn^{65} levels in blood decreased rapidly while concentrations in whole blood (most notably red blood cells) remained high. Zinc-65 uptake was found to be highest in the liver, spleen, and kidney, followed by glandular organs, such as the pancreas and prostate gland. This work was supported by the National Cancer Institute and the U.S. Atomic Energy Commission.

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BNL-39. Study of Fatty Acid Synthesis Using Tritium and Carbon-14–Labeled Glucose and Lactic Acid

BETWEEN 1962 AND 1964, investigators at the Medical Research Center of Brookhaven National Laboratory and the Department of Physiology, University of Cincinnati School of Medicine, collaboratively conducted a study to examine the relative efficiency of glucose and lactic acid as sources of hydrogen in fatty acid synthesis, using tritium (H^3) and carbon-14 (C^{14}) as tracers. Study subjects included lean diabetics, obese mild diabetics, and obese nondiabetics who had fasted overnight.

Subjects received H^3-labeled and C^{14}-labeled glucose or similarly labeled lactic acid by intravenous injection. Blood samples were drawn at various intervals after the injection, and the H^3 and C^{14} activity in the plasma triglycerides (fatty acids) and plasma water and the concentration of plasma triglycerides were determined.

The study showed that triglyceride fatty acid synthesis did not depend solely on glucose; the availability of other hydrogen sources, such as the oxidation of lactic acid, was even more important. This study was supported by the U.S. Atomic Energy Commission.

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BNL-40. Study of the Metabolism of a Bladder Carcinogen Using Carbon-14

IN APPROXIMATELY 1963, Brookhaven National Laboratory researchers conducted a study of the metabolism of 3-hydroxyanthranilic acid using carbon-14 (C^{14}) as a tracer. Three-hydroxyanthranilic acid is a metabolite of tryptophan that at the time of the study had been confirmed as a bladder carcinogen in mice, and had been observed in abnormally high levels in patients with bladder cancer.

Fourteen milligrams of carboxyl-labeled 3-hydroxyanthranilic acid containing 51 microcuries of C^{14} were administered orally to a 51-year-old female subject with achondroplasia (abnormal conversion of cartilage into bone).

Twenty-four-hour collections of expired carbon dioxide and urine, and blood samples drawn at 0, 0.5, 2, 4, 8, 12, and 24 hours after the administration, were analyzed for C^{14} activity. Within 6 hours, 40 percent of the administered activity appeared in expired air as $C^{14}O_2$; 35 percent and another significant amount of activity were found in the urine and circulating blood, respectively, within 24 hours. This study was supported by the U.S. Atomic Energy Commission and in part by the American Cancer Society, the National Cancer Society, and the National Cancer Institute.

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BNL-41. Study of Metabolism of Lactate and Pyruvate with Diabetes Using Carbon-14 Tracer

IN 1963, RESEARCHERS at the Medical Research Center of Brookhaven National Laboratory conducted a series of 17 studies of the effects of diabetes, insulin, tolbutamide (an anti-diabetic medication), and glucose on the metabolism of carbon-14 (C^{14})–labeled lactic and pyruvatic acids. The study subjects included four patients (two males and two females, ages 32 to 60 years) with diabetes of varied severity. Two

other subjects, females ages 32 and 37 years, were nondiabetics.

All subjects were administered 50 microcuries of C^{14}-labeled lactate or C^{14}-labeled pyruvate in 10 to 25 milliliters of normal saline by intravenous injection. Insulin in an amount proportional to body weight was either injected 5 to 10 minutes before intravenous injection of the C^{14}-labeled lactate or pyruvate, or infused 30 to 45 minutes prior to, and 45 to 60 minutes after injection of the labeled compound. Twenty-five grams of glucose were injected 20 minutes before injection of the C^{14}-labeled compound. Tolbutamide was administered 15 to 20 minutes before the labeled compound.

Breath samples were collected 15, 30, 45, 60, 90, 120, 180, and 240 minutes after injection of the labeled compounds and measurements were made of carbon dioxide exhaled by the subjects. Blood samples were also obtained to measure the concentration of C^{14}-labeled lactate and pyruvate in the blood.

This study showed that the insulin does not promote the utilization of lactic acid compared to its effect on the utilization of glucose. This work was funded by the U.S. Atomic Energy Commission.

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BNL-42. A Study of Calcium Metabolism in Parathyroid Deficiency Using Tracer Calcium-47

IN 1963, RESEARCHERS in the Medical Research Center of Brookhaven National Laboratory investigated the effects of parathyroid hormone deficiency on calcium metabolism. Calcium-47 (Ca^{47}) was used as tracer in the study of calcium metabolism in a 64-year-old female patient with hypoparathyroidism (decreased function of the parathyroid glands) following an operation for a goiter (disease of the thyroid gland) approximately 6 years previous. Hypoparathyroidism is associated with low levels of parathyroid hormone and is characterized by low levels of calcium in the blood and neurologic disorders.

The control group consisted of two males, 79 and 80 years old, with normal calcium metabolism.

The patient and normal control subjects were fed a normal diet with controlled levels of calcium and phosphorus for 10 days prior to receiving the Ca^{47} tracer. Each subject in the study received 20 microcuries of Ca^{47} administered intravenously as calcium chloride. The levels of Ca^{47} were measured daily in the blood, urine, and feces for 10 days. Retention of Ca^{47} in the body was measured with whole-body counts at Brookhaven.

This study provided information that was used to formulate a computer model of calcium biokinetics in the body. This study was funded by the U.S. Atomic Energy Commission.

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BNL-43. The Study of Menstruation and Resulting Iron Deficiency Using Whole-Body Counting

IN 1963, SCIENTISTS at the Medical Research Center of Brookhaven National Laboratory studied iron absorption among nine women with various menstrual histories, including six parous (borne children) women with histories of heavy menses and related hypochromic anemia (abnormally low hemoglobin content in red cells), and one nulliparous (not borne a child) unmarried woman with normal menses and a normal blood count. A post-menopausal patient with marked iron-deficiency due to phlebotomy (bloodletting) treatment for polycythemia vera (a malignant excess of red blood cells), but no blood loss during the study period, served as a comparison subject.

One to 10 microcuries of iron-59 (Fe^{59}) in 250 micrograms of carrier (stable) iron were administered orally to each subject following an overnight fast. Serial body counts were obtained over the subsequent 4 to 10 hours to establish

each subject's Fe^{59} activity level. Each patient's hemoglobin, microhematocrit, red blood-cell count, and red cell indices were determined on the day of Fe^{59} administration, together with plasma iron and unsaturated iron-building capacities. Between days 10 and 30, several blood samples were obtained from each patient and measured for Fe^{59} level.

The results of this study showed that menstrual blood loss in women with excessive bleeding was 110 to 550 milliliters, whereas normal women lost only 33 to 59 milliliters of blood during menstruation. The heavily menstruating women were found to have much greater iron absorption compared to normal women. This research was supported by the U.S. Atomic Energy Commission.

References

Price, D.C., E.M. Forsyth, S.H. Cohn, and E.P. Cronkite. "The Study of Menstrual and Other Blood Loss, and Consequent Iron Deficiency, by Fe^{59} Whole-Body Counting." *The Canadian Medical Association Journal.* Vol. 90, Jan. 11, 1964, pp. 51–54. ❑

BNL-44. Characterizing Gamma Globulin Levels in Multiple Sclerosis with Iodine-131

IN 1964, researchers from the Medical Department of Brookhaven National Laboratory in cooperation with scientists from medical departments at Bowman Gray School of Medicine of Wake Forest University, North Carolina; the University of California, Los Angeles; and the Jewish Chronic Diseases Hospital, New York conducted a study involving 21 patients with established cases of multiple sclerosis. The objective of this study was to determine the level of gamma globulin in the blood and cerebrospinal (brain and spinal cord) fluid and the exchange rate between the two. Male and female hospitalized patients between 29 and 66 years of age, who had been symptomatic from 5 to 25 years, were studied.

Gamma globulin obtained from normal donor serum was labeled with iodine-131 (I^{131}), using an established technique. Between 0.5 and 2.0 milligrams of I^{131}-labeled gamma globulin with 15 to 150 microcuries of I^{131} were administered intrathecally (through the covering of the spinal cord into the space between it and the spinal cord) to all the patients.

After the required samples of cerebrospinal fluid and blood were obtained, at least two of the same patients and four other multiple sclerosis patients received by intravenous injection between 1.2 and 2.4 milligrams of I^{131}-labeled gamma globulin with a radioactivity of between 29.1 to 152 microcuries. Blood samples were obtained. The amount of I^{131} activity was determined in the serum, in urine, and by whole-body techniques. Cerebrospinal fluid samples were obtained by spinal taps. The procedure was repeated with selected subjects, using 29 to 152 microcuries of gamma globulin labeled with I^{131} injected intravenously.

This study showed that gamma globulin transferred about 12 times faster from the cerebrospinal fluid to the plasma than the reverse path. This research was supported in part by the National Multiple Sclerosis Society and the U.S. Atomic Energy Commission.

References

Lippincott, S.W., S. Korman, L.C. Lax, and C. Corcoran. "Transfer Rates of Gamma Globulin Between Cerebrospinal Fluid and Blood Plasma (Results Obtained on a Series of Multiple Sclerosis Patients)." *Journal of Nuclear Medicine.* Vol. 6, 1966, pp. 632–644. ❑

BNL-45. Study of the Metabolism of Scandium Using Scandium-46 as Tracer

IN 1964, researchers at the Veterans Administration Hospital, Hines, Illinois, and Brookhaven National Laboratory conducted a collaborative study of the metabolism, tissue distribution, and biological turnover of radioactive scandium using scandium-46 (Sc^{46}) as a tracer. Study subjects were six male and six female patients, ranging in age from 52 to 77 years, with various chronic diseases, including cancer.

Fifty microcuries of several Sc^{46}-labeled compounds were administered intravenously. Blood samples were drawn 1, 4, 8, 24, 48, and 72 hours after administration of the tracer. Urine and stool samples were collected throughout the study. Scandium retention in the body was measured by whole-body counting of selected subjects over a period of 1 to 7 months. Tissue

samples were obtained at autopsy from three subjects who died as a consequence of their disease during the study, and levels of Sc^{46} were measured.

This experiment showed that scandium uptake was greatest in the spleen and that the biological retention half-time was about 1,400 days. This research was supported by the U.S. Atomic Energy Commission.

References

Rosoff, B., and H. Spencer. "Metabolism of Scandium-46 in Man." *International Journal of Applied Radiation and Isotopes.* Vol. 16, 1965, pp. 479–485. ❑

BNL-46. Use of Whole-Body Counting to Evaluate the Metabolism of Proteins Labeled with Iodine-131

IN APPROXIMATELY 1964, researchers from the Medical Research Center of Brookhaven National Laboratory, in collaboration with medical personnel from the Jewish Chronic Disease Hospital, New York and the Bowman Gray School of Medicine at Wake Forest University, North Carolina conducted an extensive study on serum proteins in neoplastic (abnormal cell growth, such as a tumor) diseases.

Two proteins, gamma globulin and albumin, both labeled with iodine-131 (I^{131}), were administered to normal subjects and patients with various diseases (including multiple myeloma, breast cancer, and lymphoma) to measure the degradation rate of these proteins in the serum. Iodine-131–labeled gamma globulin and albumin containing 17 to 60 microcuries of I^{131} were administered by injection. Serum and urine samples were measured for radioactivity and total-body counting techniques were conducted to measure retention and clearance times. Over 70 subjects were employed in this study and monitoring continued for as long as 60 days.

In addition to establishing the turnover rate of proteins in certain diseases, this experiment demonstrated that whole-body counting was preferred over serum/urine sampling for accuracy and simplicity. This research was supported by the U.S. Atomic Energy Commission.

References

Cohen, S.H., S.W. Lippincott, and S. Korman. "Protein Metabolism in Neoplastic Diseases Using the Whole-Body Counting Technique." In *Clinical Uses of Whole-Body Counting: Proceedings of a Panel, International Atomic Energy Agency.* Vienna, Austria, June 28–July 2, 1965, pp. 212–231. ❑

BNL-47. Study of Skeletal Discrimination Between Calcium and Strontium Using Calcium-47 and Strontium-85

A STUDY WAS CONDUCTED at Brookhaven National Laboratory during 1964 to 1965 on the uptake and metabolism of calcium and strontium in bone. Calcium and strontium are chemically similar, and the purpose of this study was to determine whether the skeleton discriminates between uptake of strontium and calcium during normal bone formation. Seven healthy male subjects ranging in age from 53 to 80 years were selected for this study and placed on a regulated diet in the metabolic ward of the hospital.

Plasma calcium levels were evaluated and found to be within normal range before the subjects were injected intravenously with 20 microcuries of calcium-47 (Ca^{47}) and 15 microcuries of strontium-85 (Sr^{85}) as chlorides. Concentrations of Ca^{47} and Sr^{85} were measured in 24-hour urine and fecal specimens daily for 10 days. Plasma concentrations of Ca^{47} and Sr^{85} were also measured periodically for 10 days. The whole-body retention of Ca^{47} and Sr^{85} was determined by direct *in vivo* counting in the Brookhaven whole-body counter for 30 days post-injection.

This study showed that strontium predicted calcium uptake, retention, and excretion, but that calcium was slightly preferred to strontium by the skeleton as a mineral constituent. This research was supported by the U.S. Atomic Energy Commission.

References

Cohn, S.H., S.R. Bozzo, J.E. Jesseph, C. Constantinides, E.A. Gusmano, and J.S. Robertson. "Strontium and Calcium Skeletal Discrimination Determined by Compartmental Analysis."

Journal of Applied Physiology. Vol. 21, 1966, pp. 67–72. ❑

BNL-48. Evaluation of Thyroid Function and Anatomy Using Technetium-99m Pertechnetate and Iodine-131

BETWEEN 1964 AND 1966, a study was conducted at Brookhaven National Laboratory to evaluate thyroidal uptake of technetium-99m pertechnetate ($Tc^{99m}O_4$) relative to health status of the subject, and to compare this imaging procedure with other thyroid function tests. A total of 208 studies were conducted using 193 patients hospitalized for evaluation of suspected thyroid disease or for other non-thyroid–related reasons.

Between 2.0 and 2.6 millicuries of $Tc^{99m}O_4$ were administered intravenously to the subjects, and its distribution was monitored in the 143 non-thyroid–suppressed subjects, using a sodium iodide (NaI) crystal detector over the neck area. A phantom containing 3 percent of the activity administered to the subjects was used as the standard. Many patients also underwent a protein-bound iodine test before or after the $Tc^{99m}O_4$ study; the test used an unreported amount of iodine-131 (I^{131}) given orally, followed by thyroid counting for I^{131} for 24 hours. Blood samples obtained from 47 patients after the $Tc^{99m}O_4$ scanning procedure were analyzed to determine the Tc^{99m} activity per liter of plasma. Thyroid size, the ratios of $Tc^{99m}O_4$ in the thyroid to that in the plasma, and thyroid technetium space were calculated.

Technetium-99m pertechnetate imaging was found to have some advantages over the I^{131} test in the diagnosis and monitoring of thyroid disease, and was recommended for physiological and anatomical studies of the thyroid. This study was supported by the U.S. Atomic Energy Commission.

References

Atkins, H.L., and P. Richards. "Assessment of Thyroid Function and Anatomy with Technetium-99m as Pertechnetate." *Journal of Nuclear Medicine.* Vol. 9, No. 1, January 1968, pp. 7–15. ❑

BNL-49. Metabolic Study of Technetium-99m-DTPA as an Improved Brain and Kidney Scanning Agent

IN THE LATE 1960s, researchers at the Medical Research Center of Brookhaven National Laboratory studied the metabolism of diethylenetriaminepentaacetic acid labeled with technetium-99m (Tc^{99m}-DTPA) as a basis for its use as an improved brain and kidney scanning agent. Hospitalized patients participated in the study.

Five hundred microcuries of Tc^{99m}-DTPA were administered intravenously to each of 12 subjects believed to be free of kidney disease. Retention of activity was evaluated in a whole-body counter. Blood and 24-hour urine samples were measured to determine the Tc^{99m}-DTPA excreted by the body. Two patients received injections of 3 microcuries of Tc^{99m}-DTPA and were whole-body counted several times over a 24-hour period. Three patients were injected with 12 millicuries of Tc^{99m}-DTPA and underwent several profile scans during the following two hours. A single patient received 13 millicuries and was whole-body scanned after 1 hour. One patient was injected with 14 millicuries and underwent seven serial kidney scans during the following 2 hours. It is unclear whether the latter 7 patients were a subset of the first 12, or if the original subject pool was actually 19.

The results indicted that Tc^{99m}-DTPA is distributed uniformly throughout the extracellular space without concentration in any organ and is rapidly cleared from the body.

The study further showed that Tc^{99m}-DTPA is effective as a brain and kidney imaging agent and also has use as an imaging agent in vascular studies. This study was funded by the U.S. Atomic Energy Commission.

References

Hauser, W., H.L. Atkins, K.G. Nelson, and P. Richards. "Technetium-99m DTPA: A New Radiopharmaceutical for Brain and Kidney Scanning." *Radiology.* Vol. 94, No. 3, March 1970, pp. 679–684. ❑

BNL-50. Study of Tryptophan Metabolism in Humans with Various Types of Anemia Using Carbon-14

IN THE LATE 1960s, Brookhaven National Laboratory researchers studied tryptophan metabolism in humans with various types of anemia using tryptophan labeled with carbon-14 (C^{14}) as a tracer. The purpose of this study was to identify abnormalities in tryptophan metabolism in advanced anemia. Seven hospitalized patients, ranging in age from 12 to 67 years, with red cell anemias were selected as study subjects.

Tryptophan (approximately 12 to 31 milligrams) with approximately 100 microcuries of C^{14} was administered orally to each patient with a loading dose (2 grams) of unlabeled tryptophan. Exhaled carbon dioxide was collected from each subject for 27 hours to be analyzed for $C^{14}O_2$. Urine was also collected and analyzed for C^{14} levels.

Study results indicated abnormal enzyme activities. Some enzymes involved in tryptophan metabolism are associated with some types of anemias. The study was supported by the U.S. Atomic Energy Commission.

References

Hankes, L., R. Brown, L. Schiffer, and M. Schmaeler. "Tryptophan Metabolism in Humans with Various Types of Anemias." *Blood: The Journal of Hematology.* Vol. 32, No. 4, October 1968, pp. 649–661. ❑

BNL-51. Studies on the Effects of a High-Calcium Diet on Osteoporosis, Using Calcium-47

IN 1967, SCIENTISTS at the Medical Research Center of Brookhaven National Laboratory conducted a study of the role of dietary calcium in osteoporosis in humans. Seven patients, including two females and five males ranging in age from 58 to 89 years, participated in the study. All exhibited slight to severe symptoms of osteoporosis. Five of the seven were non-ambulatory as a result of the disease.

Subjects were fed a diet high in calcium and phosphorus for approximately 20 days. During the latter 10 days, calcium-47 (Ca^{47}) tracer studies were conducted. Each patient received 25 microcuries of Ca^{47} as calcium chloride by intravenous injection. Blood samples were drawn at 1 and 6 hours and daily thereafter for 10 days postinjection. Complete 24-hour collection of urine and feces and whole-body counting was continued for 10 days to measure retention of Ca^{47} by the body. Patients then received a calcium supplement for an additional 20 days. During the latter 10 days of this period, the tracer study was repeated.

This study showed that a diet high in calcium had a small, positive impact on osteoporosis. This work was funded by the U.S. Atomic Energy Commission.

References

Cohn, S.H., C.S. Dombrowski, W. Hausner, and H.L. Atkins. "High Calcium Diet and the Parameters of Calcium Metabolism in Osteoporosis." *The American Journal of Clinical Nutrition.* Vol. 21, No. 11, 1968, pp. 1,246–1,253. ❑

BNL-52. Studies on the Conversion of Pyruvate and Lactate to Glucose Using Carbon-14

A COLLABORATIVE STUDY was conducted in 1968 by researchers at Brookhaven National Laboratory and Case Western Reserve University, Cleveland, Ohio, on the conversion of lactate and pyruvate to glucose. Three normal subjects—two males and one female between 22 and 42 years of age—were studied at the Clinical Research Center, University Hospital, Cleveland.

After fasting overnight, the subjects were injected with 50 microcuries of sodium L-lactate-3 labeled with carbon-14 (C^{14}). The remaining six subjects, all females between the ages of 17 and 64, were studied at the Medical Research Center, Brookhaven National Laboratory. Three of these subjects were administered 50 microcuries of C^{14}-labeled DL-lactate-2; the others received 50 microcuries of C^{14}-labeled pyruvate-2. A blood sample was obtained from each subject 1 hour after injection and the glucose isolated and measured for radioactivity.

The results of this study suggested that metabolism of lactate in humans followed the observed path for animals. The study was funded by the National Institutes of Health and the U.S. Atomic Energy Commission.

References

Hostetler, K.Y., H.R. Williams, W.W. Shreeve, and B.R. Landau. "Conversion of Specifically Carbon-14–Labeled Lactate and Pyruvate to Glucose in Man." *The Journal of Biological Chemistry.* Vol. 244, No. 8, April 1969, pp. 2,075–2,077.

Memorandum. W.W. Shreeve and A.R. Hennes to the BNL Committee for the Use of Isotopes in Humans. March 25, 1957. Brookhaven National Laboratory Project H-48, Brookhaven National Laboratory. Clinical Research Center, Bldg. 490, Human Medical Research Protocols. ❑

BNL-53. Study of Glucose Metabolism in Patients with Gout Using Carbon-14–Labeled Glucose

IN 1968, RESEARCH findings were published describing the metabolic pathway of sugar (glucose) in patients with elevated levels of uric acid (hyperuricemia) and gout. This study was conducted at the Intermediary Metabolism Research Unit, University of Natal, Durban, South Africa. A researcher from Brookhaven National Laboratory also collaborated on the study. A group of 10 male patients, ages 39 to 51 years, with elevated blood uric acid levels was studied. Eight of these 10 had experienced previous attacks of gout. Ten males subjects, ages 37 to 47 years, with normal uric acid levels were included as controls. Five of the 10 hyperuricemic patients had histories of abnormal glucose tolerance, as did 3 of the control group. All subjects in the study were Indian.

All subjects fasted for approximately 10 hours before testing and were given an oral glucose load to which had been added glucose labeled with carbon-14 (C^{14}). The test was repeated 2 days later, using glucose-6–C^{14}. Approximately 25 microcuries of C^{14} were used in each test, except for two cases where individuals received 50 microcuries of each labeled compound. Respired carbon dioxide was collected from subjects 60 and 120 minutes after administrations of the radioactive material for $C^{14}O_2$ analysis. Blood samples were drawn at the same time. Radioactivity levels were measured in the samples.

The study showed that glucose was metabolized in essentially the same way by both groups. This work was supported in part by the South African Energy Board, the South Africa Council for Science and Industrial Research, the Rockefeller Foundation, and the U.S. Atomic Energy Commission.

References

Kallie, R.N., W.W. Shreeve, S.M. Joubert, and M.C. Path. "Studies in Primary Hyperuricemia III. The Conversion of C^{14} to Breath $C^{14}O_2$ From Glucose-1-C^{14} and Glucose-6-C^{14} in Hyperuricemia and Gout." *South African Medical Journal.* May 1, 1968. pp. 473–476. ❑

BNL-54. Experimental Lymph Node Imaging with Technetium-99m Sulfur Colloid

IN 1968 TO 1970, scientists at the Medical Research Center of Brookhaven National Laboratory conducted experiments to determine the suitability of technetium-99m (Tc^{99m})–sulfur colloid for imaging lymph nodes. Subjects for this study included an unstated number of cancer patients with various malignancies. The lymph node studies were not considered an essential aspect of patient management.

A gelatin-stabilized preparation of Tc^{99m}-sulfur colloid was prepared. After testing the preparation in laboratory animals, the Tc^{99m}-sulfur colloid was administered in amounts of 240 to 1,800 microcuries by subcutaneous injection to the feet of the cancer patients. In addition, a female patient with metastatic breast cancer was administered 2,200 microcuries of Tc^{99m}-sulfur colloid subcutaneously in the left side of her abdomen. The uptake and retention of the injected material in nearby lymph nodes was measured by rectilinear scanning and a scintigraph camera.

The results of this study showed that the best time to scan was 2.5 to 3 hours after injection. The investigators concluded that this technique had application for diagnostic imaging of Hodgkin's disease (a malignancy of the lymphatic system). These studies were supported by the U.S. Atomic Energy Commission.

References

Atkins, H., W. Hauser, and P. Richards. "Visualization of Mediastinal Lymph Nodes after Intraperitoneal Administration of Tc^{99m}-Sulfur Colloid."

Nuclear Medicine. Vol. 9, No. 3, October 1970, pp. 275–278.

Hauser, W., H.L. Atkins, and P. Richards. "Lymph Node Scanning with Tc^{99m}-Sulfur Colloid." *Radiology.* Vol. 92, No. 6, May 1969, pp. 1,369–1,371. ❑

BNL-55. The Comparison of Two Forms of Tryptophan in Patients with Scleroderma, Using Carbon-14 as a Tracer

FROM 1968 TO 1971, researchers from Brookhaven National Laboratory conducted a study to compare the metabolic patterns of two forms of tryptophan (the D- and L-isomers) in patients with scleroderma (chronic hardening and shrinking of connective tissue in any organ of the body, including the skin) using tryptophan compounds labeled with carbon-14 (C^{14}) as a tracer. The purpose of this study was to evaluate abnormal tryptophan metabolism in scleroderma patients. The study subjects were five females with scleroderma, ranging in age from 40 to 60 years.

Each subject was given orally between 17 and 113 milligrams of one or more forms of C^{14} -labeled tryptophan, having between 10 and 114 microcuries C^{14}, together with 2 grams of unlabeled L-tryptophan. Fifteen-minute samples of expired $C^{14}O_2$ were collected for a 4-hour period after the administration and at 2-hour intervals thereafter, and were analyzed for C^{14} activity. Four consecutive 24-hour urine collections were also analyzed.

The study showed that scleroderma patients have an altered metabolic step in the tryptophan metabolic pathway. This study was supported in part by the American Cancer Society, the National Cancer Institute, and the U.S. Atomic Energy Commission.

References

Hankes, L., R. Brown, J. Lekelm, M. Schmaeler, and J. Jesseph. "Metabolism of C^{14}-Labeled Enantiomers of Tryptophan, Kynurenine, and Hydroxynurenine in Humans with Scleroderma." *The Journal of Investigative Dermatology.* Vol. 58, No. 2, 1972, pp. 85–95. ❑

BNL-56. Metabolic Studies on Normal and Acromegalic Subjects Using Carbon-14–Labeled Pyruvate

IN 1969, RESEARCHERS from Brookhaven National Laboratory and the Department of Endocrinology and Metabolism at Karolinska Hospital, Stockholm, Sweden, collaborated on a study of human metabolism of pyruvate. A total of 32 studies were performed on 6 acromegalic patients and 17 non-acromegalic subjects. (Acromegaly is an endocrine disorder also called pituitary gigantism that is characterized by abnormal growth and swelling of the face, hands, and feet.)

Four of the non-acromegalic (normal) subjects were given human growth hormone prior to the study. All subjects were administered 20 microcuries of carbon-14–labeled pyruvate (2-C^{14}-sodium-pyruvate) by intravenous injection. This was followed by injection of 100 microcuries of tritium (H^3)-labeled water in normal saline. Patients remained at bed rest for 2 hours. Breath samples were collected at 15, 30, 60, and 120 minutes after injection and analyzed for C^{14}-labeled carbon dioxide. One hour after injection, a blood sample was drawn and analyzed for labeled and unlabeled glucose, free fatty acids, and H^3-labeled water.

These studies showed that acromegalics with a diabetic tendency exhibited a lowered glucose tolerance and impaired pyruvate oxidation. This study was supported by the U.S. Public Health Service and the U.S. Atomic Energy Commission.

References

Shreeve, W.W., E. Cerasi, and R. Luft. "Metabolism of [2-C^{14}]-Pyruvate in Normal, Acromegalic, and HGH-Treated Human Subjects." *Acta Endocrinologica.* Vol. 65, 1970, pp. 155–169. ❑

BNL-57. Measurement of Whole-Body Potassium Using Potassium-42 as Tracer and a Cesium-137 Gamma Source

IN 1969 AND 1970, scientists in the Medical Department of Brookhaven National Laboratory, examined the total-body distribution of potassium using potassium-42 (K^{42}) as a tracer and a whole-body counter. Objectives included *in vivo*

calibration of the counter and determination of the normal range of potassium values as a function of age, gender, body weight, and other parameters. Participating in the study as subjects were 425 normal volunteers, including obese children.

Some subjects were administered K^{42}; others were exposed to a broad beam cesium-137 (Cs^{137}) source. Total body counts were taken at 0.5, 3, 6, 24, and 30 hours after intravenous injection of 0.3 microcurie of K^{42}. Subjects also were counted over a broad beam Cs^{137} source to determine the absorption correction factor for potassium-40 (K^{40}) in the body. As part of a study on the measurement of lean body mass, the grossly obese children and the children of normal body weight were orally administered 0.1 microcurie of K^{42} and were then counted in the whole-body counter to compare measurement results. The levels of potassium in the study population were measured and expressed as a function of age and gender.

The study showed that the calibration factor was about ±3 percent for the study group, which varied in body weight from 26.8 to 145.5 kilograms. This work was supported by the U.S. Atomic Energy Commission.

References

Cohn, S.H., and C.S. Dombrowski. "Absolute Measurement of Whole-Body Potassium by Gamma Ray Spectrometry." *Journal of Nuclear Medicine.* Vol. 11, No. 6, June 1970, pp. 239–246. ❑

BNL-58. Studies on the Kinetics of Halothane Using Bromine-82

IN THE EARLY 1970s, researchers at the Medical Department of Brookhaven National Laboratory; the Department of Anesthesiology of Columbia University, New York; and the University of Liverpool, England, conducted collaborative studies on the uptake, distribution, and excretion of halothane, an inhalation anesthetic, that had been labeled with radioactive bromine-82 (Br^{82}).

Four volunteer subjects inhaled 2.5 microcuries of Br^{82}-labeled halothane in a single breath. Activity in the body was measured by whole-body counting at 1-minute intervals. Subjects also received an oral administration of 2.5 microcuries of Br^{82}-labeled ammonium bromide to determine, by comparison, whether Br^{82} dissociated from the halothane after administration.

The study showed that concentrations of halothane were initially high in upper parts of the body and low in lower parts of the body. Diffusion equilibrium throughout the body was reached in about 24 minutes. This work was supported by the U.S. Atomic Energy Commission.

References

Mark, L.C., I.C. Geddes, J.R. Scherrer, C.S. Dombrowski, and S.H. Cohn. "Pharmacokinetics of Halothane in Man: A Novel Approach." *International Journal of Applied Radiation and Isotopes.* Vol. 22, 1971, pp. 171–175. ❑

BNL-59. Comparison of Technetium-99m and Iodine-123 for Thyroid Imaging

IN THE EARLY 1970s, researchers in the Medical and Chemistry Departments of Brookhaven National Laboratory, evaluated technetium-99m (Tc^{99m}) and iodine-123 (I^{123}) to determine their relative effectiveness as thyroid imaging agents. One hundred patients were included in the study. Of these, 5 were hypothyroid (having abnormally low thyroid activity), 77 were euthyroid (having normal thyroid activity), 15 were hyperthyroid (having abnormally high thyroid activity), 2 had chronic thyroiditis, and 1 had subacute thyroiditis.

Each subject first received between 2.5 and 3.0 millicuries of Tc^{99m} pertechnetate ($Tc^{99m}O_4$) intravenously and was examined by a gamma camera scanning instrument 30 minutes later. Iodine-123 (100 to 350 microcuries) as sodium iodide was then administered orally to most subjects; some received 60 to 75 microcuries of I^{123}. Uptake measurements and scintiphoto-graphic images were obtained 18 hours later. Two patients participated in repeat studies.

Overall, I^{123} was found to be superior to Tc^{99m} as a thyroid imaging agent. This was attributed to the greater concentration of I^{123} in the thyroid, although some unexplained discrepancies between Tc^{99m} and I^{123} images were found. This research was funded by the U.S. Atomic Energy Commission.

References

Atkins, H.L., J.F. Klopper, R.M. Lambrecht, and A.P. Wolf. "A Comparison of Technetium-99m and Iodine-123 for Thyroid Imaging." *The American Journal of Roentgenology, Radium Therapy and Nuclear Medicine.* Vol. 117, No. 1, January 1973, pp. 195–201. ❑

BNL-60. Studies on Calcium Metabolism and Chronic Renal Failure Using Calcium-47

IN A COLLABORATIVE STUDY conducted in the early 1970s, researchers at the Medical Research Center of Brookhaven National Laboratory, the Nassau County Medical Center, and the Health Sciences Center, State University of New York at Stony Brook, investigated calcium metabolism in humans with chronic renal (kidney) failure using calcium-47 (Ca^{47}) as a tracer. Study subjects were two groups of patients with chronic renal failure who had undergone treatment for kidney disease prior to the study. The first group consisted of four males and two females between 46 and 63 years of age with slight-to-mild kidney failure. The second group consisted of seven subjects—five females and two males between the ages of 17 and 53 years—with severe kidney failure.

All subjects ingested a constant diet with fixed calcium and phosphorus levels for 7 days before and 10 days after administration of the Ca^{47} tracer. Experimental subjects received 20 microcuries of Ca^{47} intravenously. The level of Ca^{47} was measured in the blood 1 and 6 hours after injection and daily thereafter for the next 9 days. Stool and urine samples were collected over a 24-hour period and monitored for radioactivity. The concentration of Ca^{47} remaining in the body was measured with the Brookhaven whole-body counter.

This experiment showed that calcium metabolism in the group with mild kidney failure did not differ significantly from the normal population. Those with severe kidney failure exhibited a number of significant changes in the metabolism of calcium and phosphorus. This research was funded in part by the U.S. Atomic Energy Commission.

References

Letteri, J. M., K.J. Ellis, D.P. Orofino, S. Ruggieri, S.N. Asad, and S.H. Cohn. "Altered Calcium Metabolism in Chronic Renal Failure." *Kidney International.* Vol. 6, 1974, pp. 45–54. ❑

BNL-61. Studies of Glucose Tolerance in Obese Humans Using Glucose Labeled with Carbon-14 and Tritium

IN APPROXIMATELY **1970,** researchers at Brookhaven National Laboratory used glucose (simple sugar) labeled with carbon-14 (C^{14}) and tritium (H^3) to study the human response to cortisone glucose tolerance testing. Ten female subjects of normal weight between 17 and 35 years of age, and 19 obese females between 17 and 52 years of age, were included in the study. All nonobese subjects were in the hospital for at least 48 hours prior to metabolic studies and on diets of 1,600 to 2,000 calories, with 200 to 250 grams of carbohydrates per day. Obese subjects received 1,800 to 2,000 calories daily, with 200 to 300 grams of carbohydrates.

All subjects received an oral dose of glucose in an amount proportional to body-surface area. The glucose contained 40 to 50 microcuries of glucose-1-C^{14} and 250 to 500 microcuries of glucose-1-H^3. Blood samples were drawn at 30-minute intervals and analyzed for tritiated glucose and tritiated water. Breath was monitored almost continuously for $C^{14}O_2$. Body water space was also determined using tritiated water (250 to 500 microcuries of H^3OH) administered intravenously to the fasting subjects. Blood samples were drawn at 1 and 2 hours to measure H^3 activity. All subjects also received a conventional, unlabeled intravenous cortisone glucose tolerance test.

This study indicated metabolic differences between obese and nonobese subjects. This research was supported by the U.S. Atomic Energy Commission.

References

Shreeve, W.W., A.J. Tashjian, N. Oji, R.H. Slavinski, and M. Hoshi. "Formation of $C^{14}O_2$ and H^3OH from Glucose-1-C^{14}, -1-H^3 During Oral Cortisone Glucose Tolerance Tests in Obese

Patients." *Metabolism.* Vol. 20, No. 3, March 1971, pp. 280–292. ❑

BNL-62. Measurement of Total-Body Calcium, Sodium, Chlorine, Nitrogen, and Phosphorus by Neutron Activation Analysis

IN 1970 AND 1971, researchers at the Medical Research Center of Brookhaven National Laboratory examined the feasibility of using neutron activation analysis to measure levels of total-body calcium, sodium, chlorine, phosphorus, and nitrogen in humans. A total of 17 patients ranging in age from 15 to 70 years participated as subjects. This group consisted of four females with metastatic breast cancer, four females and two males with osteoporosis, two females with chronic kidney failure, and one male with Cushing's disease.

The subjects were exposed to a uniform neutron depth flux from 14-MeV (million electron volt) neutrons. Two 15-minute counts were then taken, using a whole-body counter.

The results indicated that the amounts of calcium, sodium, chlorine, nitrogen, and phosphorus in the subjects' bodies could be determined using neutron activation. The average radiation dose to patients using this technique was estimated to be 0.637 rem. The researchers concluded that the technique held promise for use in medical research and diagnosis. This work was supported by the U.S. Atomic Energy Commission.

References

Cohn, S.H., C.S. Dombrowski, and P.G. Fairchild. "*In Vivo* Neutron Activation Analysis of Calcium in Man." *International Journal of Applied Radiation and Isotopes.* Vol. 21, 1970, pp. 127–137.

Cohn, S.H., and C.S. Dombrowski. "Measurement of Total-Body Calcium, Sodium, Chlorine, Nitrogen, and Phosphorus in Man by *In Vivo* Neutron Activation Analysis." *Journal of Nuclear Medicine.* Vol. 12, No. 7, July 1971, pp. 499–505. ❑

BNL-63. Effectiveness of Technetium-99m-DTPA in Measuring Glomerular Filtration Rate

IN 1970 AND 1971, researchers at Brookhaven National Laboratory compared the effectiveness of technetium-99m-diethylenetriamine-pentaacetic acid (Tc^{99m}-DTPA) with that of sodium iothalamate labeled with iodine-125 (I^{125}), for measuring glomerular filtration rates in evaluation of kidney disease. Technetium-99m and I^{125} were used as tracers in this study. The subjects were 11 patients under investigation for hypertension (high blood pressure) who had normal or slightly diminished kidney function, as determined by other methods.

Each subject received a single intravenous injection of approximately 3 millicuries of Tc^{99m}-DTPA and 50 microcuries of I^{125}-sodium iothalamate. Urine samples and nine blood samples were obtained from each patient at regular intervals during the 24 hours after the administration. Measures of plasma concentration and urinary excretion of Tc^{99m}-DTPA were obtained from each subject, using a known standard of Tc^{99m}-DTPA for comparison.

The results indicated that Tc^{99m}-DTPA, rapidly prepared by a kit method, was an effective agent for measuring glomerular filtration rates in suspected kidney disease. This research was supported by the U.S. Atomic Energy Commission.

References

Klopper, J.F., W. Hauser, H.L. Atkins, W.C. Eckelman, and P. Richards. "Evaluation of Tc^{99m}-DTPA for the Measurement of Glomerular Filtration Rate." *Journal of Nuclear Medicine.* Vol. 13, No. 1, January 1972, pp. 107–110. ❑

BNL-64. Total-Body Neutron Activation Analysis

BETWEEN 1970 AND 1972, scientists at the Medical Research Center of Brookhaven National Laboratory, developed a method for analyzing total-body content of the elements calcium, sodium, chlorine, aluminum, and potassium. This method involved exposing a subject to a broad-beam neutron source and counting certain neutron-activation products in the human, using a whole-body counter. The neutrons were generated by an external plutonium-238, beryllium

oxide ($Pu^{238}O_2$-Be) neutron source as fourteen 50-curie sources arranged in a planar array. The levels of nitrogen-13, calcium-49, sodium-24, chlorine-38, and aluminum-28 produced in the body by neutron activation were determined from the resulting gamma-ray spectrum.

One male subject was irradiated for 5 minutes, then counted 3 minutes after exposure. The same patient was later exposed to a source of 14-MeV (million-electron-volt) neutrons (from an accelerator) and counted 6 minutes after exposure for comparison of activation product spectra. The radiation absorbed dose to the subject was estimated to be 277 millirems for each exposure.

The results of the study indicated that the plutonium/beryllium array produced a neutron source that was more uniform than the 14-MeV neutron source for total-body neutron activation analysis and body composition studies. This research was supported by the U.S. Atomic Energy Commission.

References

Cohn, S.H., K.K. Shulka, C.S. Dombrowski, and R.G. Fairchild. "Design and Calibration of a 'Broad-Beam' $Pu^{238}O_2$-Be Neutron Source for Total-Body Neutron Activation Analysis." *Journal of Nuclear Medicine.* Vol. 13, No. 7, July 1972, pp. 487–492. ❑

BNL-65. Study of the Effects of a High-Sucrose Dietary Intake Using Carbon-14

IN 1973, researchers at Brookhaven National Laboratory studied the acute and chronic effects of a high-sucrose (table sugar) diet intake on plasma triglyceride (a form of fatty acid) levels in comparison to those produced by a high-starch diet. Twenty females and three males between the ages of 16 and 47 years were included in the study. All but two females and one male were grossly overweight.

Subjects were hospitalized and given a diet consisting of 2,200 to 3,000 calories per day, of which 50 percent were from carbohydrate, 15 percent from protein, and 35 percent from fat. After overnight fasting, subjects received an oral dosage of sucrose labeled with 40 microcuries of carbon-14 (C^{14}). Blood was sampled frequently during the first 3 hours for measurement of C^{14}-labeled glucose and at 0, 1, 3, 6, and 12 hours for C^{14}-labeled triglycerides in the plasma. Breath was collected during the first 3 hours after ingestion and measured for C^{14}-labeled carbon dioxide. Other diets were also studied.

Among other findings, this experiment showed that triglycerides peaked very rapidly (3 to 6 hours) after ingestion of sugar. This research was funded by the U.S. Atomic Energy Commission.

References

Wu, C.H., M. Hoshi, and W.W. Shreeve. "Human Plasma Triglyceride Labeling after High-Sucrose Feeding. I. Incorporation of Sucrose-U-C^{14}." *Metabolism.* Vol. 23, No. 12, December 1974, pp. 1,125–1,139. ❑

BNL-66. Studies of the Uptake of Metabolites of Tryptophan Using Carbon-14

IN THE MID 1970s, researchers at Brookhaven National Laboratory studied the uptake of metabolites of tryptophan using carbon-14 (C^{14}) as a tracer. This was done to determine if reliable metabolism studies could be conducted using tryptophan and several of the isomers labeled with C^{14}, and if tryptophan metabolites are bound to proteins in blood. Study subjects were volunteers and included five white female scleroderma patients 40 to 60 years in age.

Tryptophan, or D- or L-kynurenine, or D- or 1-3-hydroxykynurenine was administered to each subject in amounts ranging from 10 to 50 microcuries of C^{14}, depending on the compound. Ten milliliters of blood were drawn from each subject after administration of tryptophan and analyzed for C^{14} content.

The study provided new information on metabolites and showed that the amino acids were bound to proteins in circulating blood. This study was supported in part by the U.S. Department of Health, Education, and Welfare and the U.S. Energy Research and Development Administration.

References

Hankes, L., and M. Schmaeler. "The Uptake of C^{14}-Labeled Hydroxanthranilic Acid and Enantiomers of Tryptophan, Kynurenine, and Hydroxykynurenine in Human Blood." In *Proceedings of*

the Society for Experimental Biology and Medicine. Vol. 149, 1975, pp. 1,063–1,068. ❑

BNL-67. Comparison of Tryptophan Metabolism Using Carbon-14–Labeled Tryptophan

IN 1975 AND 1976, Brookhaven National Laboratory researchers collaborated with the South African Atomic Energy Board, Pretoria, South Africa, to evaluate tryptophan metabolism in South African gold miners and compare it with that of previously studied American female scleroderma patients. Six white male patients at a South African hospital volunteered for the study. These subjects were between 40 and 60 years of age and suffering from silicosis-induced scleroderma.

A 2-gram loading dose of unlabeled tryptophan was administered to each subject. Five days later, 9 to 31 milligrams of carbon-14 (C^{14})–labeled tryptophan kynurenine-keto, or hydroxy-l-kynurenine-keto labeled with 21 to 26 microcuries of C^{14} was orally administered to each subject 1 hour after breakfast. Urine was collected for consecutive 24-hour periods after administration and analyzed for C^{14} activity.

This study confirmed the earlier finding that some scleroderma patients have an altered step in the tryptophan metabolic pathway. The relationship between silicosis of the lung and later development of scleroderma was unexplained by the study. The study was supported by the South African Council for Scientific and Industrial Research, the National Institutes of Health, and the U.S. Energy Research and Development Administration.

References

Hankes, L., E. DeBruin, C. Jansen, L. Vorster, and M. Schmaeler. "Metabolism of C^{14}-Labeled L-tryptophan, L-kynurenine, and Hydroxy-L-Kynurenine in Miners with Scleroderma." *SA Medical Journal.* Vol. 51, March 19, 1977, pp. 383–390. ❑

BNL-68. Changes in Body Composition with Age Determined by Total-Body Neutron Activation Analysis

IN 1975 AND 1976, several related studies were conducted at Brookhaven National Laboratory involving use of total-body neutron activation analysis to determine body levels of calcium, phosphorus, and potassium. The populations studied included 40 white women, 39 white men, 28 black women, and 21 black men. Each of the subjects received a 5-minute total-body exposure to a planar array of 14 neutron radiation sources. The source of external neutrons was 14 capsules each containing 50 curies plutonium-238 mixed with beryllium. The neutron flux activated stable elements in the irradiated subject, and the subsequent gamma emissions from the body were then counted in the Brookhaven whole-body counter.

In the first study, the age-related changes in body chemical composition were measured in a normal black population ranging in age from 30 to 80 years. The levels of total-body calcium, phosphorus, sodium, and chlorine were measured by gamma counting for neutron-induced calcium-49, aluminum-28, sodium-24, and chlorine-38. These data were compared to values observed on a normal white population in a previous study. This study showed that black men and women had significantly higher total-body calcium, phosphorus, sodium, chlorine, and potassium than that of a white population with the same ages and sex. However, the rates of mineral loss with aging were similar.

Two additional studies reported changes in body chemical composition with age in adult males and females and the effect of aging on bone mass mineral loss in adult women. These studies showed that women lose calcium at 0.37 percent per year before the age of 50 and 1.1 percent per year afterwards, and that men lose calcium at 0.7 percent per year. The rates of total-body phosphorus and potassium loss are directly related to that of calcium. These studies were supported by the U.S. Energy Research and Development Administration.

References

Cohn, S.H., C. Abesamis, I. Zanzi, J.F. Aloia, S. Yasumura, and K.J. Ellis. "Body-Elemental Composition: Comparison Between Black and White

Adults." *American Journal of Physiology.* Vol. 232, No. 4, pp. E419–E422.

Cohn, S.H., A. Vaswani, I. Zanzi, and K.J. Ellis. "Effect of Aging on Bone Mass in Adult Women." *American Journal of Physiology.* Vol. 230, No. 1, January 1976, pp. 143–148.

Cohn, S.H., A. Vaswani, I. Zanzi, J.F. Aloia, M.S. Roginsky, and K.J. Ellis. "Changes in Body Chemical Composition with Age Measured by Total-Body Neutron Activation." *Metabolism.* Vol. 25, No. 1, Jan. 1976, pp. 85–96. ❑

BNL-69. Study of Krypton-79 Biokinetics

In 1976, investigators of the Applied Science and Medical Departments, Brookhaven National Laboratory, studied the total-body retention and clearance of krypton gas using the isotope krypton-79 (Kr^{79}). Krypton is a noble gas produced during uranium fission in nuclear power plants (mainly Kr^{85}), and little information was available at that time on the metabolism of krypton in man. The purpose of this study, therefore, was to determine the uptake of krypton by the body and its short-and longer-term biological retention after inhalation using Kr^{79}.

Twelve male and four female adult volunteer subjects with no known respiratory disorders participated in this study. The subjects ranged in age from 30 to 61 years, and in weight from 124 to 234 pounds. These broad ranges were chosen to determine differences in retention according to age, respiratory volume, and percent body fat. Each of the subjects inhaled 130 to 1,250 microcuries of Kr^{79} gas mixed with normal breathing air during exposures of about 10 minutes, and were then counted in the Brookhaven whole-body counter to determine body retention of Kr^{79} over time.

This study showed that krypton deposited in different body compartments (lungs, muscles, and fatty tissues), each clearing at different rates, with retention half-times ranging from a few seconds to almost 10 hours. Krypton was retained longest in fatty tissues. Longer retention times correlated well with increasing amount of body fat, which acted as a repository in the body for krypton. This research was supported by the U.S. Energy Research and Development Administration.

References

Ellis, K.J., S.H. Cohn, H. Susskind, and H.L. Atkins. "Kinetics of Inhaled Krypton in Man." *Health Physics*, Vol. 33, 1977, pp. 515–522. ❑

BNL-70. Study of Xenon-127 Retention

In 1976, investigators of the Applied Science and Medical Departments, Brookhaven National Laboratory, studied the total-body retention and clearance of xenon gas using the isotope xenon-127 (Xe^{127}). Xenon was used in nuclear medicine clinics in routine studies of lung ventilation and perfusion as an aid to diagnosis of pulmonary disease. The purpose of this study was to determine the uptake of xenon by the body and its short-and longer-term biological retention after inhalation, and how these values are influenced by amount of body fat.

Seven male and five female volunteer subjects with no known pulmonary disease participated in this study. The subjects ranged in age from 29 to 61 years, and in weight from 110 to 306 pounds to determine differences in man according to age, respiratory volume, and percentage body fat. Each of the subjects inhaled up to 100 microcuries of Xe^{127} gas mixed with normal breathing air during exposure periods of 10 to 30 minutes, and were then counted in the Brookhaven whole-body counter to determine body retention of Xe^{127} over time. The subjects then repeated the study at different concentrations of Xe^{127} in breathing air.

This study showed that xenon totally cleared from the body three days after inhalation and that longer retention times correlated well with increasing amounts of body fat, which acted as a repository in the body for xenon gas. The results of this study were used to estimate radiation doses to nuclear medicine patients undergoing diagnostic examinations. This research was supported by the U.S. Energy Research and Development Administration.

References

Susskind, H., H.L. Atkins, S.H. Cohn, K.J. Ellis, and P. Richards. "Whole-Body Retention of Radioxenon." *Journal of Nuclear Medicine*, Vol. 18, 1977, pp. 462–471. ❑

Hanford Sites

HS-1. Ingestion of Iodine-131 in Milk by Hanford Employees

In 1963, milk from dairy cows fed iodine-131 (I^{131}) was consumed by eight General Electric/Hanford workers either as a single dose or as several daily doses. During the study, the amount of iodine in the cows' diet was increased from 5 milligrams per day to 2 grams per day. The resulting uptake by the human thyroid was determined in Hanford's whole-body counter facility. Participants were Hanford scientists who had volunteered to drink the milk and be counted over a period of approximately 1 month. This work was supported by the U.S. Atomic Energy Commission. (Previously described in #41 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

References

Watson, E.C., I.C. Nelson, D.H. Wood, R.O. McClellan, and L.K. Bustad. "Effect of Varying Stable Iodine in Diets of Cows Fed I^{131} on Uptake of I^{131} in Man Drinking the Milk—An Abstract." In *Biology of Radioiodine: Proceedings of the Hanford Symposium on the Biology of Radioiodine, Richland, Washington, July 17–19, 1964.* Oxford: Pergamon Press, 1964, p. 339.

Handwritten Monthly Report. J.K. Soldat to R.F. Foster. July 1963. Pasco, WA: Washington State University Tri-Cities Campus, PNL, DOE Richland Public Reading Room, I^{131}, Open Shelving, PNL-936 9-DEL. ❑

HS-2. Intentional Release of Iodine-131 at Hanford in 1963

In July 1963, the Hanford Laboratory conducted a study that involved the release of 120 microcuries of iodine-131 (I^{131}) into the environment. These releases were designed to characterize the dispersion of radiation. The purpose of the experiment was to enable scientists to determine the fraction inhaled by men, the amount taken up by the thyroid, and the retention half-time of radioiodine in human thyroid.

Two volunteer subjects (Hanford employees), were stationed in the expected path of the radiation cloud. These subjects intentionally inhaled I^{131} from the release and were subsequently measured for thyroidal uptake of I^{131}. These experiments were performed under contract with the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995, and since revised)

References

Gamertsfelder, C.C. "Plans and Hazard Analysis for the First Hanford I^{131} Field Release Test." Richland, WA: Hanford Atomic Products Operation, Physics and Instruments Laboratory, HW-78312, July 19, 1963. Pasco, WA: Washington State University Tri-Cities Campus, PNL, DOE Richland Public Reading Room, I^{131}, Open Shelving.

Handwritten Monthly Report. J.K. Soldat to R.F. Foster. July 1963. Pasco, WA: Washington State University Tri-Cities Campus, PNL, DOE Richland Public Reading Room, I^{131}, Open Shelving, PNL-9369-DEL.

Monthly Report. Senior Engineer to R.F. Foster. August 23, 1963. Pasco, WA: Washington State University Tri-Cities Campus, PNL, DOE Richland Public Reading Room, I^{131}, Open Shelving, PNL-9370. ❑

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HS-3. Absorption of Tritium Oxide Through the Skin

In 1951, scientists in the Biology Section, Radiological Sciences Department, General Electric Hanford Company examined the percutaneous (through the skin) absorption of tritium (H^3) oxide-labeled water vapor in animals and humans. A total of 14 subjects participated in the study.

Twelve subjects were exposed over about 10 square centimeters on the forearm, and two were exposed on the abdomen. One of the arm-exposed subjects also received atmospheric whole-body exposure while breathing H^3-labeled air through a respirator. Urine samples were collected from all 14 subjects over a 48-hour period.

The study results indicated that absorption of H^3 through the skin and lungs from an H^3-contaminated atmosphere contributed similarly to the total-body burden as exposure by H^3-water vapor. As a result of this finding, the researchers

recommended a 50 percent reduction in the permissible maximum level for atmospheric tritium oxide. This study was funded by the U.S. Atomic Energy Commission. (This experiment was referenced in the Markey report.)

References

DeLong, C.W., R.C. Thompson, and H.A. Kornberg. "Percutaneous Absorption of Tritium Oxide." *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine.* Vol. 71, No. 6, June 1954, pp. 1,038–1,045. ❑

HS-4. Calibration Studies Using Zinc-65

IN 1959, researchers at the General Electric Hanford Company, Atomic Products Operation conducted studies on the retention and distribution of zinc-65 (Zn^{65}) in the human body to establish calibration values for bioassay and *in vivo* counting.

In September 1959, one subject (a Hanford worker) was orally administered an unstated amount of Zn^{65} and the amount remaining in the body was measured by whole-body counting. The uptake of ingested Zn^{65} was found to be 35 percent or about twice the amount expected from results of animal studies. Over time, different values for different individuals suggested that different distribution patterns should be considered.

In March 1960, a study involving one subject showed that Zn^{65} deposited initially in the liver and later in the head and legs. The General Electric Hanford Company was operated at Richland, Washington, for the U.S. Atomic Energy Commission.

References

Bioassay Laboratory Monthly Report, September–1959. Richland, WA: General Electric Hanford Atomic Products Operation. October 1, 1959.

Radiation Protection Operation Report for the Month of March, 1960. Richland, WA: General Electric Hanford Atomic Products Operation. April 11, 1960. ❑

HS-5. Study of Metabolism of Strontium Using Strontium-85 as a Tracer

A STUDY WAS CONDUCTED in 1963 by scientists of the General Electric Hanford Laboratories to (1) determine whether ingested strontium is excreted in human body hair in measurable amounts, (2) determine whether analysis of hair samples was an accurate indicator of strontium uptake in man, and (3) investigate the biological retention of ingested strontium in man.

Two Hanford scientists voluntarily ingested a solution containing a few microcuries of strontium-85 (Sr^{85}). The exact amounts administered are not known. Hair clippings and facial shavings were then obtained from the subjects and analyzed for Sr^{85} content.

The results of this study showed that Sr^{85} could not be measured in small samples of body hair. This study was discontinued and the results were never published. The Hanford Laboratories were operated by the General Electric Hanford Company for the U.S. Atomic Energy Commission.

References

Letter. T. Beasley to D.R. Fisher. May 29, 1995.

Letter. B.I. Griffin to D.R. Fisher. May 2, 1995.

Memorandum. D.R. Fisher to file. April 27, 1995. ❑

HS-6. Whole-Body Counting Studies of the Measurement of Phosphorus-32

DURING 1963 TO 1964, a researcher at the General Electric Hanford Company developed techniques for the whole-body measurement of phosphorus-32 (P^{32}). The purpose of this study was to develop a more sensitive method for measuring the level of beta-emitting radioisotopes in the body.

Three patients at the University of Oregon Medical school who had received P^{32} therapy for blood diseases participated as subjects. Two other volunteer subjects at the Seattle Swedish Hospital were administered P^{32} by injection for calibration study purposes only. Each of the subjects was counted for P^{32} in the Hanford whole-body counter.

These studies provided P^{32} calibrations for measurement equipment that later was used in studies of P^{32} in people who consumed fish from the Columbia River. This work was supported by the U.S. Atomic Energy Commission.

References

Palmer, H.E. "Determination of P^{32} *In Vivo*." *Health Physics*. Vol. 12, 1966, pp. 605–608. ❑

HS-7. Distribution and Excretion of Technetium-95 and Technetium-96 in Humans

IN APPROXIMATELY 1965, scientists at the Battelle Memorial Institute's Pacific Northwest Laboratory collected data to establish exposure limits for personnel engaged in the handling of technetium isotopes and for workers in areas where inadvertent exposure might occur.

Eight normal volunteers, between the ages of 23 and 40 years, received 20 microcuries of technetium-95 (Tc^{95}) and 60 microcuries of Tc^{96} as pertechnetate. Administrations were by intravenous injection to four subjects, and orally to the other four. Samples of blood, urine, sweat, tears, and intestinal mucosae (biopsies of stomach, duodenal, and rectal mucosae were obtained from three individuals) were collected for the first week; total urine and feces were collected for an additional 8 to 10 days.

The study results indicated that there was no detectable difference between the intravenous and oral administrations in relation to the rate and route of excretion, and the amount excreted. Technetium was found to concentrate primarily in the stomach and gastrointestinal tract, with little or no concentration in the liver or kidney. Blood and urine analyses together were found to provide the best method for assessing external depositions of technetium as pertechnetate following accidental exposure.

The researchers concluded that the recommendations of the International Commission on Radiological Protection on the maximum permissible body burdens and air and water concentrations of technetium as pertechnetate, needed to be reevaluated. This study was funded by the U.S. Atomic Energy Commission. (This experiment was referenced in the Markey report.)

References

Beasley, T.M., H.E. Palmer, and W.B. Nelp. "Distribution and Excretion of Technetium in Humans." *Health Physics*. Vol. 12, 1966, pp. 1,425–1,435. ❑

HS-8. Study of Promethium Metabolism and the Effects of DTPA on Promethium Metabolism

IN 1967, SCIENTISTS at Battelle Memorial Institute's Pacific Northwest Laboratory and the Hanford Environmental Health Foundation, conducted a collaborative study on the effects of DTPA (diethylenetriaminepentaacetic acid, a chelating agent) on the retention of promethium-143 (Pm^{143}). The purpose of the study was to develop an excretion model for diagnosis of promethium exposure, to form a basis for radiation exposure, and to determine the radiation dose from accidental exposures.

A total of 14 volunteers participated in the study. Six received approximately 0.1 microcurie of Pm^{143} intravenously; two received 10 microcuries of Pm^{143} orally; the final six received 0.1 microcurie of Pm^{143} intravenously, followed at various intervals by intravenous administration of 1 gram DTPA to study its effectiveness in combining with promethium to enhance its rate of excretion. Whole-body counts and excreta measurements were conducted for up to 1 year following these administrations.

Results indicated that DTPA is effective in significantly reducing the body content of promethium when administered within about 1 hour following its entry into the bloodstream. This study was funded by the U.S. Atomic Energy Commission. (This experiment was referenced in the Markey report.)

References

Palmer. H.E., I.C. Nelson, and G.H. Crook. "The Uptake, Distribution, and Excretion of Promethium in Humans and the Effect of DTPA on those Parameters." *Health Physics*. Vol. 18, 1970, pp. 53–61. ❑

HS-9. Whole-Body Counting Studies Using Iron-59

IN THE LATE 1960s, researchers in the Department of Medicine, University of Washington, Seattle and Battelle Memorial Institute's Pacific Northwest Laboratory conducted studies to demonstrate the utility of the whole-body counter for measuring iron-59 (Fe^{59}) in humans and to establish the quantitative validity of measuring Fe^{59} absorption and loss by this technique.

Several healthy subjects were orally administered 1 microcurie of Fe^{59}. Whole-body counts were obtained immediately after the administration and at 3 to 7 hours thereafter. Subjects then received 1 microcurie of Fe^{59} by direct intravenous injection. Whole-body counts were repeated and compared for consistency. Negligible differences were found between the measurements of interests obtained following oral administration and those obtained following intravenous injection.

Another study was conducted to assess the differences in counting efficiency for Fe^{59} circulating in the blood, and the Fe^{59} localized in the red bone marrow. The researchers were supported by the U.S. Public Health Service and the U.S. Atomic Energy Commission.

References

Palmer, H.E., J.D. Cook, K.G. Pailthorp, and C.A. Finch. "A Whole-Body Counter for Precision *In Vivo* Measurement of Radio-Iron." *Physics in Medicine and Biology.* Vol. 15, No. 3, 1970, pp. 457–465.

Palmer, H.E., J.D. Cook, K.G. Pailthorp, and C.A. Finch. *The Precision In Vivo Measurement of Radioiron by Whole-Body Counting.* Seattle, WA: University of Washington, Department of Medicine. ❑

HS-10. Alternative Method for Measuring Iron Uptake Using Iron-59

A STUDY WAS CONDUCTED in 1969 at the Department of Medicine, University of Washington, Seattle in collaboration with Battelle Memorial Institute's Pacific Northwest Laboratory on three normal subjects between the ages of 25 and 40 years.

One microcurie of iron-59 (Fe^{59}) as ferrous sulphate in water was administered orally to each of the subjects. Whole-body counts were obtained immediately following the oral ingestion, and again 3 and 7 hours later. The latter count was immediately followed by an injection of Fe^{59} in the form of sodium citrate bound with fresh plasma. The experiment was conducted to evaluate a new (about 1970) technique for whole-body counting, namely the use of longitudinal scan geometry. This technique was tested using different biological distributions of Fe^{59} in the body, including point sources, moving sources, and metabolical sources.

The study demonstrated that the longitudinal scan geometry was suitable for measuring radioactivity in humans. The research was supported by grants from the U.S. Public Health Service and the U.S. Atomic Energy Commission.

References

Cook, J.D., H.E. Palmer, K.G. Pailthorp, and C.A. Finch. "The Measuring of Iron Absorption by Whole-Body Counting." *Physics in Medicine and Biology.* Vol. 15, No. 3, 1970, pp. 467–473.

Letter. C.A. Finch to S. Marks. July 17, 1984. Pacific Northwest Laboratory General Human Subjects, Box Alan Rither, PNL-9055-DEL. ❑

Idaho Sites

IS-1. Administration of Radioactive Material to Volunteers to Test or Calibrate Analytical Equipment

FROM 1965 TO 1972, as many as 18 employees at the U.S. Atomic Energy Commission's Health Services Laboratory at the National Reactor Testing Station in Idaho voluntarily swallowed radioactive material or inhaled radioactive noble gases, prior to being placed in whole-body counters. The following radionuclides were used in the experiments: argon-41, potassium-42, manganese-54, cobalt-60, zinc-65, krypton-85m, zirconium-95/niobium-95, ruthenium-106, silver-110m, iodine-131, cesium-132, xenon-133, cesium-137, and cerium-144.

In most of the ingestion cases, the radioactive material was encapsulated in plastic so that no

radioactive material was absorbed into body tissues. These measurements were performed to develop and evaluate new whole-body counting equipment and to calibrate that equipment. The whole-body counting equipment was used to measure the amount of radioactivity inside the body of occupational radiation workers exposed to radioactive material. Policies for conducting these experiments limited radiation doses to volunteers to levels below the occupational radiation-protection guidelines in effect at the time. (This experiment was referenced in the Markey report and included in *The DOE Roadmap* of February 1995.)

References

Anderson, J.I., and D.G. Olson. "A Rotational Technique for Assessing Quantity and Distribution of Body Radioactivity." *Health Physics.* Vol. 13, 1967, p. 719.

Anderson, J.I., and D.G. Olson. "Computerized Helical Scanning to Determine the Location of Specific Nuclides in the Human Body." *Health Physics.* Vol. 23, 1972, p. 325.

Howard, L.E., J.H. Spikard, and M. Wilhelmsen. "A Human Radioactivity Counter and Medical Van." *Health Physics.* Vol. 21, 1971, p. 417.

Olson, D.G. "A Direct Calibration Using Gamma Spectrometry for Measuring Radioactivity in Humans." *Health Physics.* Vol. 14, 1968, p. 438.

Sill, C.W. *Some Guidelines for Studies Involving Internal Administration of Radioactive Materials to Human Volunteers.* Idaho Falls, ID: Idaho Operations Office, U.S. Atomic Energy Commission, IDO-12058, October 1966. ❑

IS-2. Controlled Environmental Radioiodine Tests (CERT)

U.S. ATOMIC ENERGY COMMISSION scientists and other professionals at the National Reactor Testing Station in Idaho conducted the Controlled Environmental Radioiodine Tests (CERT) to study the transport of radioiodine through the air-vegetation-cow-milk-human food chain from 1963 through 1968. Five of the 24 CERT tests involved exposure of volunteers to iodine-131 (I^{131}) to study the transport of radioiodine to and through the human body.

In the first test, CERT No. 1, seven individuals consumed milk from a cow that had grazed in a pasture where the radioiodine was deposited, and their uptake of radioiodine was determined by thyroid gland monitoring. The average thyroid dose was 0.39 rad; the maximum thyroid dose was 0.63 rad.

In CERT Nos. 2, 7, and 10, three individuals, seven individuals, and one individual, respectively, were reportedly exposed during radioiodine releases over the pasture to determine their intake of I^{131} by inhalation.

The number of individuals involved in a similar inhalation experiment during CERT No. 11 was not listed in published reports; however, whole-body counting logs indicate that 10 individuals were apparently involved.

Thyroid doses from inhalation during CERT No. 2 were no greater than 0.015 rad, and the reported thyroid activity observed during CERT No. 7 was about the same as that in CERT No. 2. Thyroid doses to volunteers were not reported for CERT Nos. 10 and 11. The volunteers were employees of the U.S. Atomic Energy Commission. (This experiment was referenced in the Markey report and included in *The DOE Roadmap* of February 1995.)

References

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Hawley, Jr., C.A., Editor. *Controlled Environmental Radioiodine Tests at the National Reactor Testing Station 1965 Progress Report.* Idaho Falls, ID: Idaho Operations Office, U.S. Atomic Energy Commission, IDO-12047, February 1966. ❑

Lawrence Berkeley Laboratory

LBL-1. Treatment of Leukemia with Phosphorus-32

BETWEEN 1936 AND 1947, patients with various types of leukemia were treated with phosphorus-32 (P^{32}) with and without supplemental x-ray treatments. Approximately 129 patients with chronic myelogenous leukemia and 100 patients with chronic lymphatic leukemia were treated at the Radiation Laboratory and the Donner Laboratory of the University of California in Berkeley and San Francisco. Previously it had been demonstrated that radiophosphorus concentrated in the bone marrow and soft tissue of leukemic mice. Therefore, it was expected that P^{32} would provide a highly localized radiation source for human leukemic patients.

Patients were administered 1 to 2 microcuries of P^{32} per week for 4 to 8 weeks, although higher doses were also included. Approximately half of the patients studied had previously received x-ray treatment.

It was found that P^{32} treatment increased the quality of life for chronic myelogenous leukemic patients, but did not prolong the duration of life. In the case of chronic lymphatic leukemia patients, the quality of life was improved and the duration was prolonged. Based on these findings, an unspecified number of chronic lymphatic patients were treated with P^{32} through 1960. This research was partly supported by grants from the International Cancer Research Foundation. (Included in *The DOE Roadmap* of February 1995)

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Lawrence, J.H., B.V.A. Low-Beer, and J.W.J. Carpender. "Chronic Lymphatic Leukemia." *Journal of the American Medical Association.* Vol. 140, 1949, pp. 585–588. ❑

LBL-2. Metabolic Studies of Bone Tumors Using Strontium-89

AN EXPERIMENT WAS conducted in 1942 at the Radiation Laboratory of the University of California, Berkeley on the uptake of radiostrontium by bone tumors. Strontium-89 (Sr^{89}) was administered to six subjects prior to biopsy or amputation. Tissue samples were collected and analyzed to determine the Sr^{89} uptake.

The subjects consisted of five males and one female, ranging in age from 9 to 54 years. Five of the subjects received intravenous injection solutions which ranged from 326 to 1,462 microcuries. The sixth subject was given 1,183 microcuries of Sr^{89} orally.

This experiment showed that Sr^{89} had therapeutic value in treating certain types of bone cancers. Some of these cancer patients also received therapeutic amounts of Sr^{89} (a few millicuries), but details are not available. This research was supported by the Rockefeller Foundation and the Columbia Fund for Medical Physics. (Included in *The DOE Roadmap* of February 1995)

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Treadwell, A. de G., B.V.A. Low-Beer, H L. Friedell, and J.H. Lawrence. "Metabolic Studies on Neoplasm of Bone with the Aid of Radioactive Strontium." *American Journal of the Medical Sciences.* Vol. 204, 1942, pp. 521–523. ❑

LBL-3. Inhalation Studies Using Carbon-11

FROM 1944 TO 1945, the Aero Medical Laboratory, University of California, Berkeley and the Department of Physiology, Columbia University conducted a collaborative study using carbon-11 (C^{11}). The radioactive carbon was used as a tracer to determine whether carbon monoxide (CO) oxidizes to carbon dioxide (CO_2) in the human body.

The subjects consisted of four men, including three of the researchers conducting the experiment. The four men inhaled a relatively large amount of CO labeled with C^{11}, after which they breathed oxygen. During this time, their expired CO_2 was collected and measured for C^{11}, the presence of which would prove that the human body could convert CO to CO_2. Geiger counters

were placed over various parts of the body (thigh, chest, spleen, and liver) to measure the uptake and elimination of CO_2. The CO oxidized to CO_2 amounted to less than 0.1 percent of the CO lost from the blood. This work was supported by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

References

Lawrence, J.H. *Positron Emitting Isotopes: Investigative and Diagnostic Studies.* Berkeley, CA: Lawrence Berkeley Laboratory, John Hundale Lawrence Files, pp. 247–262. Accession 434-92-0066, File Code 19-14-6, Carton 15, Folder "Positron Emitting Isotopes."

Tobias C.A., J.H. Lawrence, F.J.W. Roughton, W.S. Root, and M.I. Gregersen. "The Elimination of Carbon Monoxide from the Human Body with Reference to the Possible Conversion of CO to CO_2." *American Journal of Physiology.* Vol. 145, No. 2, December 1945, pp. 253–263. ❑

LBL-4. Inhalation of Zirconium-89 on Smoke Particles

INHALATION STUDIES were conducted at Lawrence Berkeley Laboratory in approximately 1945 using an active smoke containing zirconium-89 (Zr^{89}). One member of the research team was the only subject. The purpose of this experiment was to determine the degree of retention by the lungs of very finely divided active smoke suspended in air. The results showed that almost 100 percent of the inhaled activity (about 0.5 microcurie of Zr^{89}) was retained within the lungs and upper respiratory tract. This work was supported by the U.S. Atomic Energy Commission. (Previously described in #30 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

References

Scott, K.G., D. Axelrod, J. Crowley, and J.G. Hamilton. "Deposition and Fate of Plutonium, Uranium and Their Fission Products Inhaled as Aerosols by Rats and Man." *Archives of Pathology.* Vol. 48, No. 1, July–December 1949, pp. 31–54. ❑

LBL-5. Radioactive Phosphorus as a Possible Diagnostic Procedure for Breast Tumors

IN 1946, the University of California Hospital, San Francisco, employed phosphorus-32 (P^{32}) in tracer studies to develop a new diagnostic procedure for distinguishing between malignant and benign breast tumors. Twenty-five female patients with breast tumors were included in the study. All patients had been scheduled for surgery.

Each patient was intravenously administered 300 to 500 microcuries of P^{32} as sodium phosphate 24 or 48 hours prior to surgery. Surface measurements were made over the tumor and over a control area on the opposite normal breast, 2, 4, 6, and 20 hours after the injection of P^{32}. An increase in counts was found over the surface of malignant tumors, whereas counts were not elevated over benign tumors. The malignancy of the tumor was determined after surgical removal.

Results indicated that P^{32} might be used as a diagnostic procedure for breast cancer, except for very slow-growing or deep-seated cancers. (Included in *The DOE Roadmap* of February 1995)

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Low-Beer, B.V.A., H.G. Bell, H.J. McCorkle, R.S. Stone, H.L. Steinbach, and W.B. Hill. "Measurement of Radioactive Phosphorus in Breast Tumors in Situ: A Possible Diagnostic Procedure." *Radiology.* Vol. 47, pp. 429–496. ❑

LBL-6. Comparison of the Uptake of Zirconium-95 in Tumor and Normal Tissue

IN 1946, at the University of California, San Francisco and the Crocker Radiation Laboratory, University of California, Berkeley research was carried out to study the uptake and deposition of zirconium. The subject, a 55-year-old female patient with a reticulo endothelial tumor that had arisen in the spleen and then metastasized to the liver and left leg, was given a test dose of zirconium-95 (Zr^{95}).

The subject was administered 1.76 millicuries of Zr^{95} in saline by intravenous injection 24 hours prior to a scheduled midthigh amputation of the

left leg. Samples of the tumor, as well as normal tissue, were later obtained from the limb for Zr^{95} assay.

The tumor was found to have greater uptake of Zr^{95} than the normal tissues of the body. External counting 2 hours after the Zr^{95} injection showed that the liver contained about 90 percent of the total measurable deposition and the tumor had about 10 percent of the total deposition. This study was supported by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

References

Low-Beer, B.V.A., K.G. Scott, J.G. Hamilton, and R.S. Stone. "Comparative Deposition of Zr^{95} in a Reticulo Endothelial Tumor to Normal Tissues in a Human Patient." Berkeley, CA: University of California Radiation Laboratory, UCRL-68. ❑

LBL-7. Autoradiographic Studies of the Distribution of Radiolabeled Lewisite and Mustard Gas on Skin

THIS EXPERIMENT was conducted in 1947 at the Crocker Radiation Laboratory, University of California, Berkeley and the University of California Medical School in San Francisco. The experiment sought to determine the distribution of mustard and lewisite in skin and eye tissues. These two chemical-warfare gases were labeled with radioactive sulfur (S^{35}) and radioactive arsenic (As^{74}). Small areas of the skin of four normal subjects were exposed to the two labeled gases.

Two experiments were performed with mustard gas labeled with S^{35}. The first involved a 10-minute exposure to 475 micrograms of labeled chemical; the second, a 15-minute exposure to 475 micrograms. In both cases, the exposed area was 0.43 square centimeter and biopsy specimens of these areas were taken 24 hours after exposure.

Two experiments were also performed on lewisite labeled with 10 micrograms of As^{74}; the first involved a 10-minute exposure to 475 micrograms of lewisite; the second, a 15-minute exposure to 475 micrograms. The new technique of autoradiography was used to determine the skin layer at which the fixation took place on the biopsied human skin samples. Lewisite was found to fix primarily in the epidermis, and mustard gas fixed in both the epidermis and dermis. (Included in *The DOE Roadmap* of February 1995)

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Axelrod, D.J., and J.G. Hamilton. "Radio-Autograph Studies of the Distribution of Lewisite and Mustard Gas in Skin and Eye Tissues." *American Journal of Pathology*. Vol. 23, 1947, pp. 389–411. ❑

LBL-8. Injection of Americium-241

ON JUNE 10, 1947, at the University of California, San Francisco a 16-year-old Chinese male patient at the Chinese Hospital in San Francisco, identified as Cal-A, with osteogenic sarcoma of the left femur and general metastases, received an intramuscular injection of americium-241 (Am^{241}). The estimated activity administered was about 0.2 microcurie. The same day, two rats were given intramuscular injections of 1 milliliter of solution made from the same specifications as the Cal-A injection.

Readings of the subject's urine and feces were collected through at least June 24, 1947. On June 12, 1947, the subject's leg was amputated at the left midthigh. Samples of the amputation tissue were dissected the next day. The samples were measured for isotope uptake, as the tumor was expected to have higher uptake than normal body tissues. Studies were made of the tumor; the bone tissue in which the tumor was found; the surrounding tissues, both bone and connective; and the muscles. Measurements from the amputated tissues were compared with the rat data; the patient was discharged on July 27, 1947.

Rat data showed considerable uptake by the liver; human data appeared to show 13 to 20 percent uptake by the bone. The patient died of preexisting ailments on June 15, 1948.

The experiment appears to have been done as a comparison to previous human studies involving plutonium, as data sheets for Cal-A show standards for measurements set against Cal-1 (a human injected with plutonium-238). (Included in *The DOE Roadmap* of February 1995)

References

Lawrence Berkeley Laboratory, Joseph G. Hamilton Records, Archives and Records Office, Folder Am H (95H). ❑

LBL-9. Uptake of Iodine-131 in Thyroids of Psychiatric Patients

FROM JULY 1949 TO APRIL 1950 a cooperative research project was conducted by the Departments of Psychiatry, Radiology, and Medicine at the University of California Medical School and the Langley Porter Clinic in San Francisco. The objective of this project was to determine whether thyroid function was normal or abnormal in persons with mental illness. Sixty-five subjects were selected from the regular in-patient group at the Langley Porter Clinic.

Among the subjects were patients with schizophrenia, manic-depression, mixed psychoneurosis, and anorexia nervosa. A control group was selected of volunteers from the clinic's, clerical, and medical staff.

Subjects were injected with 150 microcuries of iodine-131 (I^{131}); subsequently, the concentration of I^{131} in the thyroid was then measured six times over a 72-hour period. The test and control groups underwent medical and psychiatric evaluations, including serum-bound iodine, basal metabolism, plasma cholesterol, and electroencephalogram.

No abnormal thyroid function was found in the group with mental illness and no significant differences were detected between the patients and the controls in this study. This study was partly funded by the U.S. Atomic Energy Commission. (Previously described in #2 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

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Stone, R.S. *Biological Effects of Radiations from External and Internal Sources, Progress Report July 1, 1949 to April 15, 1950.* San Francisco: University of California Radiation Laboratory, April 1950. U.S. Department of Energy Archives, Record Group 326, U.S. Atomic Energy Commission, Box 3358, Folder 22. ❑

LBL-10. Sodium-24 Uptake Studies on Patients with Rheumatoid Arthritis

DURING THE MID-1940s through the early 1950s, Lawrence Berkeley Laboratory conducted studies on the uptake of sodium-24 (Na^{24}) to evaluate vascular abnormalities in persons with rheumatoid arthritis.

Sodium-24 was administered by intravenous injection, usually in 50-microcurie amounts. Systemic transport of Na^{24} was followed, using two gamma counters: one in the subject's hand, the other placed under a knee.

The results showed an impeded blood flow in diseased areas of the body. Uptake of Na^{24} in the knee joint was also studied after three patients drank a solution of sodium chloride labeled with Na^{24} in water. (Included in *The DOE Roadmap* of February 1995)

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Tobias, C. *Sodium Uptake Studies.* Berkeley, CA: Lawrence Berkeley Laboratory, Cornelius A. Tobias Papers, Accession 434-89-100, File Code 10-08-063, Carton 25/38, Folder "Sodium Uptake Studies." ❑

LBL-11. Blood Volume Studies with Iron-59, Phosphorus-32, and Chromium-51 Involving Inmates at San Quentin Prison

FROM 1949 TO THE LATE 1950s, the University of California conducted studies involving radioactive isotopes using inmates at San Quentin Prison as volunteer subjects. Studies included the following: (a) 1949 to 1951: studies on red blood-cell production—Blood was drawn from participants, labeled with iron-59 (Fe^{59}), and reinjected into the respective subjects. Four samples were drawn at specific intervals over the next 2 hours. The procedure was repeated for 4 successive days, during which Fe^{59}-labeled red blood cells were counted. (b) 1950: studies on blood volume—At least 13 participants had blood drawn, labeled with phosphorus-32 (P^{32}), and reinjected. Blood volume in the subjects

was subsequently measured. (c) late 1950s: Studies on red cell volume—Chromium-51 (Cr^{51}) was used as a label to measure red blood-cell volume in 201 healthy participants. (Included in *The DOE Roadmap* of February 1995)

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Letter. J.H. Lawrence to J.H. Corley. August 17, 1949. Lawrence Berkeley Laboratory, Administrative Files of Administrative Assistants to the Directors of the Biology and Medicine Division and Donner Laboratory, Accession 434-90-0209, File Code 16-5-22, Carton 2, Folder "Historical Donner Laboratory." ❑

LBL-12. Blood and Tissue Studies with Iron-59

THIS RESEARCH was conducted at the Donner Laboratory, University of California, Berkeley in the early 1950s. The purpose of this study was to investigate the rates and pathways of iron transport in the human body, including the differences in iron turnover rates between normal individuals and patients with anemia. The subjects consisted of 22 individuals with anemia and other diseases and 16 normal individuals.

Between 5 and 30 microcuries of radioactive iron-59 (Fe^{59}) globulin were injected intravenously to label the circulating plasma iron globulin. External radiation measurements were made on the liver, spleen, and bone marrow using a gamma-fluorescence detector. In addition, plasma and whole-blood samples were analyzed for Fe^{59} content.

The results showed that iron turnover rates varied, the exact rate depending on the disease state of the patient. This research was partly funded by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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Huff, R.L., C.A. Tobias, and J.H. Lawrence. "A Test for Red Cell Production." *Acta Haematologica.* Vol. 7, No. 3, March 1952, pp. 129–143. ❑

LBL-13.

(Duplicate of LBL-10 in *The DOE Roadmap*)

LBL-14. Studies on the Rate of Uptake of Iodine-131 in the Thyroid

IN THE EARLY 1950s, studies were conducted at the University of California, San Francisco on various aspects of thyroid function in patients with normal and abnormal thyroid glands. The 427 study participants included patients with normal and abnormal thyroids as well as goiters or uncertain thyroid functions.

After the subjects drank a solution containing approximately 100 microcuries of iodine-131 (I^{131}), an external gamma counter was placed over the thyroid to measure the uptake of radioiodine. A good correlation was found between high rates of uptake and hyperthyroidism, and between lower rates and absence of hyperthyroidism.

Further research was also conducted to study aspects of the physiology of the thyroid and other endocrine glands. Studies were conducted on obese patients, and on adult and child hyperthyroid patients requiring thyroid stimulating hormone. This research was funded by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

References

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Thyroid." *Radiology.* Vol. 57, No.1, July 1951, pp. 37–47.

Annual Report of Cancer Activities of the Radiological Laboratory. San Francisco: University of California School of Medicine, 1953, pp. 1–9. Special Collections, The Library, University of California, San Francisco. ❑

LBL-15. Measures of Body Fat and Related Factors in Normal Adults Using Potassium-40, Cesium-137, and Tritium

DURING 1950 TO 1960, the Donner Laboratory at the University of California, Berkeley, in collaboration with the California State Department of Public Health and the Bureau of Public Health Nutrition, conducted a series of experiments using natural potassium-40 (K^{40}) and cesium-137 (Cs^{137}) to measure body composition. The experiments were designed to accurately determine the human body's total water content, body fat, protein content, and bone mineral content. In all, 2,301 healthy volunteers were used for these experiments.

The laboratory analyses included measurements of total-body water after an oral tracer dose of tritium, analysis of specific gravity by the helium dilution technique, and whole-body counting of K^{40}. This study was partly supported by a grant from the National Institutes of Health. (Included in *The DOE Roadmap* of February 1995)

References

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LBL-16. Study of Ascitic Fluid Using Tritium-Labeled Water and Phosphorus-32

DURING 1951 AND 1952, the University of California Donner Laboratory and the Highland Alameda County Hospital, Oakland conducted experiments to determine the total amount of ascitic fluids in humans. Tritium (H^3) was used to trace the flow of water into, and out from, the peritoneal cavity.

Six patients with ascites (a condition characterized by fluid buildup in the peritoneal cavity) were injected with 2 microcuries of tritium-labeled water, either intravenously or intraperitoneally. Over the following 7 to 24 hours, samples of blood and ascitic fluid were taken. Blood samples were labeled with phosphorus-32 (P^{32}) and 1 milliliter of the labeled blood was injected into the peritoneal cavity.

This study showed that the water content of ascitic fluid entered and left the peritoneal cavity at a very rapid rate. It also showed that the peritoneal surfaces of both normal and diseased subjects reabsorbed large volumes of fluid. This work was supported by the Life Insurance Medical Research Fund and the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

References

Prentice, T.C., W. Siri, and E.E. Jones. "Quantitative Studies of Ascitic Fluid Circulation with Tritium-Labeled Water." *American Journal of Medicine.* Vol. 13, No. 6, December 1952, pp. 668–673. ❑

LBL-17. A Physiological Study in the Peruvian Andes Using Iron-59

THE DONNER LABORATORY of Medical Physics, University of California, Berkeley used iron-59 (Fe^{59}) in high-altitude studies similar to the previously conducted studies using tritium (H^3). The purpose of these experiments was to investigate the physiology of reduced barometric pressure, particularly as seen in high-altitude flights, and the physiology and treatment of various hematopoietic (blood-forming) disorders, especially polycythemia rubra vera, leukemia, and aplastic anemia.

In these studies, reported in 1952, healthy subjects (medical students from the University of San Marcos, Lima, Peru) and native Peruvians in the Andes mountains were studied. Four Andean natives suffering from pulmonary silicosis (as well as high-altitude polycythemia rubra vera) were also studied.

A few micrograms of Fe^{59} were incubated for 20 minutes with 10 to 20 milliliters of the subject's plasma and then injected into the subjects. After injection, Fe^{59} analysis was made on plasma samples taken at hourly intervals for 4 to 5

hours. Acclimatization to high altitude was found to be related to changes in blood volume, plasma volume, and red blood-cell mass. Postexposure plasma-iron turnover rates and red cell renewal rates increased to roughly twice their normal values in less than 12 hours at high altitude. This study was supported by the U.S. Navy, the U.S. Air Force, and the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

References

Lawrence, J.H., R.L. Huff, W. Siri, L.R. Wasserman, and T.G. Hennessy. "A Physiological Study in the Peruvian Andes." *Acta Medica Scandinavica.* Vol. 142, No. 2, 1952, pp.117–133. ❑

LBL-18. Studies on the Metabolism of Glycine Labeled with Carbon-14

DURING THE EARLY 1950s, researchers at the University of California Donner Laboratory conducted studies on human carbon metabolism using carbon-14 (C^{14}). Twelve patients participated in two studies that examined the distribution, retention, and excretion of C^{14}.

In one study, four patients, ranging in age from 29 to 52 years, were intravenously administered 100 microcuries of C^{14}-labeled glycine (an essential nutrient and a dietary supplement). Activity as $C^{14}O_2$ was measured in their exhaled breath and in tissue samples subsequently collected at autopsy. Five additional patients received similar injections and C^{14} activity was measured in their urine samples.

In a second study, which examined the retention of C^{14} in hemoglobin precursors, three patients were administered 100 microcuries of C^{14}-labeled glycine and activity was measured in hippuric acid isolated from their urine samples.

The results of these studies showed that exhalation of $C^{14}O_2$ was the primary route of C^{14} excretion, with a small percentage being excreted through urine. The studies also showed a small concentration in tissue and a biological retention half-time for C^{14} of 50 days. Finally, the studies showed that retention in the blood was due to absorption by newly formed cells, not long-lived existing cells. This work was supported by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995, and since revised)

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Berlin, N.I., C. Hewitt, and C. Lotz. "Hippuric Acid Synthesis in Man After the Administration of [α-^{14}C] Glycine." *The Biochemical Journal.* Vol. 58, 1954, pp. 498–503. ❑

LBL-19. Astatine-211 and the Thyroid

THE OBJECTIVE of this experiment was to test the uptake of astatine-211 (At^{211}) and to evaluate its potential benefits in the treatment of thyroid diseases. Eight subjects were injected with 50 microcuries of the 7-hour half-life alpha emitter At^{211}. These experiments were conducted at the University of California Hospital during early 1954. (Previously described in #37 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

References

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LBL-20. Body Water at Sea Level and at High Altitudes by Tritium Analysis

IN 1954, SCIENTISTS from the Donner Laboratory, University of California, Berkeley, and the Instituto de Biologia Andina, Lima, Peru, used tritium (H^3) to determine changes in weight and total-body water for subjects living in Lima at high altitudes and at sea level. Two groups of subjects were studied. The first group consisted of 15 young male medical students; the second group consisted of 13 normal male Peruvian Indian mine workers.

The tritium was administered both orally and intravenously. The mean values of body water for the two groups was normal for their age range and occupations. This research was supported by the U.S. Public Health Service, the U.S. Atomic Energy Commission, and the U.S. Air Force. (Included in *The DOE Roadmap* of February 1995)

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LBL-21. High-Energy-Beam Irradiation of Breast Cancer Patients

DURING THE 1950s AND EARLY 1960s, researchers at Donner Laboratory and Lawrence Radiation Laboratory, University of California conducted studies on therapeutic heavy particle beam irradiation. The purpose of these studies was to evaluate the results of pituitary irradiation in the treatment of a variety of hormone-dependent diseases.

An early study involved 26 breast cancer patients ranging in age from 27 to 70 years who received between 14,000 and 30,000 rads of 340-MeV (million electron-volt) radiation to the pituitary gland over periods of 9 to 63 days. Beginning in 1954, 159 breast cancer patients received therapy involving 900-MeV alpha particles produced by an accelerator. All patients were either in a terminal state or a state of rapid disease advancement despite all routinely available treatment. Radiation doses to the pituitary ranged from 14,000 to 17,000 rads delivered over 11 days. During the course of treatment, patients also underwent various diagnostic tests involving the use of internally administered iodine-131, carbon-14, and calcium-47. The results of these studies showed limited supression of tumor growth.

Beginning around 1956, 79 diabetes patients received heavy particle therapy in an attempt to slow degeneration of the retina. Doses ranged from 8,000 to 12,000 rads delivered over 11 days. The results of the study showed that diabetics with advanced complications did not benefit much from this therapy. Also beginning around 1956, 21 patients received therapy for acromegaly (a disease characterized by enlargement of the head, hands, feet, and thorax). Doses ranged from 3,000 to 7,200 rads delivered over 11 days. Follow-up studies showed beneficial changes in patients.

From 1957 to 1961, three female patients with Cushing's disease received therapy of 5,000 to 10,000 rads delivered over 11 days. All showed some benefit, from minor improvement to general remission. Three patients received up to 10,000 rads over 11 days to treat malignant exophthalmos. One patient showed beneficial results.

In 1958, one breast cancer patient was treated with direct tumor therapy (not pituitary irradiation) of 2,500 rads over 6 days and experienced temporary remission. These studies were supported by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995, and since revised)

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LBL-22. Iron-59 Metabolism in Patients with Cancer and Anemic Conditions

STUDIES WERE CONDUCTED in 1959 at the University of California Lawrence Radiation Laboratory on the metabolism of iron in humans using iron-59 (Fe^{59}) as a tracer. The aim of these studies was to determine the effects of age, gender, and health status on iron metabolism in humans. Approximately 80 cancer patients and subjects with various anemias, hemochromatosis (a disease characterized by an excessive absorption of iron), and iron deficiencies were used in these studies.

The rate of hemoglobin synthesis, mean red blood-cell life span, and mean time required for hemoglobin formation within the total red cell volume were measured. Gastrointestinal bleeding was correlated with iron and red cell movement in seven subjects. This work was supported by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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LBL-23. Radionuclide Studies to Determine Bone Marrow Distribution in Humans

IN THE EARLY 1960s, at the Donner Laboratory and the Lawrence Radiation Laboratory, University of California, Berkeley, iron-52 (Fe^{52}), iron-59 (Fe^{59}) and technetium-99m (Tc^{99m})–sulfur colloid were administered to study marrow distribution. The marrow, liver, and spleen were then imaged, using conventional scanners or scintillation cameras. Administered activities ranged from 3 to 100 microcuries. Samples of bone marrow, plasma, red cells, and liver were analyzed to determine tissue activity over time. Subjects included hospital patients and normal volunteers, including children. This work was supported in part by the U.S. Atomic Energy Commission and in part by a grant from the National Cancer Institute of the National Institutes of Health. (Included in *The DOE Roadmap* of February 1995)

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Van Dyke D.C., H.O. Anger, and Y. Yano. "Progress in Determining Bone Marrow Distribution *In Vivo*." *Progress in Atomic Medicine.* Vol. 2, 1968, pp. 65–84. ❑

LBL-24. Iron Kinetics and Hemoglobin Synthesis in Human Subjects with Iron-59–Bound Plasma

THIS STUDY WAS conducted in approximately 1959 at the University of California, Berkeley in collaboration with the Veterans Administration in Boston. Its purpose was to develop a suitable mathematical model of hemoglobin synthesis, using sequential measurements of iron-59 present in human plasma, red cells, and peripheral blood. Data were obtained from 13 normal, healthy subjects (1 female and 12 male volunteers) between the ages of 24 and 72 years, and 6 male hospital patients with endogenous hemochromatosis.

Five to 20 milliliters of plasma labeled with 10 to 40 microcuries of iron-59 (Fe^{59}) were intravenously injected into the subjects. Plasma and erythrocyte radioactivity were measured with a scintillation counter. This study was supported by the U.S. Atomic Energy Commission with partial support by a grant from the U.S. Public Heath Service. (Included in *The DOE Roadmap* of February 1995)

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LBL-25. Intestinal Iron Absorption Studies Using Iron-52, Iron-55, and Iron-59

IN A STUDY CONDUCTED at the Donner Laboratory, University of California, Berkeley in 1966, radioactive isotopes of iron were used to measure the rate of iron absorption into the plasma and its distribution in the gastrointestinal tract.

Forty microcuries of iron-52 (Fe^{52}) were administered orally to six fasting normal subjects. Just prior to the oral dose, iron turnover studies were performed using 2 microcuries of transferrin-bound iron-59 (Fe^{59}) injected intravenously; the subjects were then whole-body counted. For the iron turnover studies, 20 to 30 microcuries of iron-55 (Fe^{55}) were injected into the same subjects. Photoscans of the abdomen using the Anger positron camera were taken throughout the study. The maximum rate of intestinal iron absorption was found to occur at the time when iron was in the upper gastrointestinal tract. This work was supported by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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LBL-26. Chromium-51 Metabolism Studies in Patients with Hemochromatosis

CHROMIUM-51 METABOLISM studies were conducted at Lawrence Berkeley Laboratory on healthy males and on patients with hemochromatosis (a disease characterized by an excessive absorption of iron).

Five normal male subjects were injected with 100 microcuries of chromium-51 (Cr^{51}) to study the retention of chromium. This study was conducted to show that hemochromatic diabetes was due to the exclusion of chromium from either the carrying agent or from the liver because of saturation by iron.

Eleven subjects were injected with Cr^{51}-chloride. Among the subjects were patients with varying degrees of hemochromatosis, including two hemochromatotic patients depleted of excess iron and two subjects with excess iron but no clinical disease. All of the subjects were followed by whole-body counting for up to 6 months.

The results showed that the exclusion of chromium occurs principally at binding sites in the liver. Two further studies were conducted on chromium metabolism using plasma analysis, Cr^{51} clearance rates, the whole-body scanner, and the whole-body counter. This work was supported by the U.S. Department of Energy. (Included in *The DOE Roadmap* of February 1995)

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LBL-27. Calcium-47 Retention Studies in Juvenile Diabetics

THIS RESEARCH was conducted at the Berkeley Donner Laboratory in the early 1970s. This study was undertaken to determine the rate of uptake and retention of calcium-47 (Ca^{47}) in juvenile diabetics. The subjects consisted of eight healthy individuals, of various ages and diets, and three juvenile diabetics (ages 23, 26, and 26).

One to 25 microcuries of Ca^{47} was intravenously administered and the retention of Ca^{47} in the whole body was determined by direct *in vivo* counting.

The whole-body retention of Ca^{47} did not significantly vary over the wide range of calcium and protein intakes and ages of healthy subjects. Diabetics excreted Ca^{47} at a higher rate.

This work showed a decreased rate of bone mineralization in diabetics. The research was supported by the U.S. Energy Research and

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LBL-28. Whole-Body Counting Studies on the Retention of Copper-67 and Phosphorus-32 and Chromium-51

IN THE MID- TO LATE 1970s, the University of California Lawrence Berkeley Laboratory conducted studies on the retention of radionuclides in humans. The subjects were healthy individuals and patients with a variety of diseases.

Four subjects were injected with 100 microcuries of copper-67 (Cu^{67}) to determine copper uptake, retention, and excretion rates. Of the four subjects, three were healthy, and one had a copper storage disease. The results showed that there is no abnormality of total-body turnover of copper when iron stores are normal. Results also showed that for the subject with the copper storage disease, the excretion of copper was slower than for normal subjects by a factor of two.

Six subjects with diseases related to bone marrow production were injected with 1 to 5 millicuries of phosphorus-32 (P^{32}) to determine excretion rates. This was one of the first published studies on human whole-body phosphorus turnover.

Five subjects received injections of 100 microcuries of chromium-51 (Cr^{51}). The whole-body retention and excretion rates of Cu^{67}, P^{32}, and Cr^{51} were reported. This work was supported by the U.S. Department of Energy. (Included in *The DOE Roadmap* of February 1995 and since revised.)

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LBL-29. Metabolism of Carbon-14–Labeled Methionine in Schizophrenics

THIS RESEARCH was conducted in the 1980s at the Lawrence Berkeley Laboratory. Researchers suspected that a defect in the methyl-carbon metabolic pathway was a causative factor in schizophrenia. Methionine labeled with carbon-11 (C^{11}) or carbon-14 (C^{14}) was administered to both schizophrenics and healthy subjects to test this hypothesis. The oxidation of methionine was studied in seven unmedicated schizophrenics, and the effect of high and low methionine in the diet was studied in control subjects. This research was supported by the National Institute of Mental Health, the Donner Laboratory, and the U.S. Department of Energy. (Included in the DOE Roadmap of February 1995)

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LBL-30. Experimental Therapy of Multiple Myeloma with Phosphorus-32, Strontium-89, and Yttrium-90

FROM 1939 TO 1949, twenty-one male and female patients, ranging in age from 29 to 66 years, at the Donner Laboratory, University of California Radiation Laboratory, Berkeley received experimental radioisotope treatments for multiple myeloma.

Nine patients received phosphorus-32 (P^{32}) and strontium-89 (Sr^{89}); 11 received P^{32} alone; and 1 received colloidal yttrium-90. Levels of the administered activity differed for each patient. Subjects received 1 to 21 oral or intravenous administrations of activity, with total activity ranging from 0.3 to 103 millicuries.

The results of the treatment with P^{32} or Sr^{89} were no better than results obtained from treatment with x-rays or stilbamidine. The Donner Laboratory was supported by the U.S. Atomic Energy Commission.

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LBL-31. Experimental Therapy of Polycythemia Vera Using Phosphorus-32 and X-Rays

BETWEEN 1939 AND 1969, researchers at the Donner Laboratory, University of California Radiation Laboratory, Berkeley treated 181 polycythemia vera patients using intravenously administered phosphorus-32 (P^{32}) phosphate, or P^{32} plus x-rays. Doses usually totaled between 15 and 45 millicuries of P^{32} per patient. X-ray absorbed doses varied greatly between patients.

Excellent results were achieved in many cases, and the life expectancy was extended to nearly normal using this treatment. However, some of the polycythemia vera patients later developed splenic metaplasia and acute leukemia.

Follow-up studies were conducted in the late 1960s to evaluate the overall effectiveness of the therapy and to determine whether there was a relationship between therapy for polycythemia vera and the later incidence of leukemia. These studies indicated that the development of splenic myeloid metaplasia and acute leukemia are part of the evolutionary history of polycythemia vera, and that the incidence of acute leukemia in patients treated with P^{32} may be a result of prolonged survival rather than a direct effect of radiation dose. The Donner Laboratory was supported by the U.S. Atomic Energy Commission.

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Wasserman, L.R., J.H. Lawrence, N.I. Berlin, R.L. Dobson, and S. Estern. "The Bone Marrow Picture in Polycythemia Vera Before and After Treatment with Radioactive Phosphorus." *Acta Medica Scandinavica*. Vol. 143, No. 6, 1952, pp. 443–449. ❑

LBL-32. Studies of Iodine-131 Uptake in Hypothyroid Children

DURING THE EARLY 1940s, researchers at the University of California Medical School, San Francisco conducted tracer studies, using iodine-131 (I^{131}) as sodium iodide as tracer, to measure the metabolism of iodine in normal and hypothyroid children.

Ten hypothyroid children and young adults ranging in age from less than 1 year to 19 years served as subjects. The amounts of I^{131} administered were about 25 to 50 millicuries, or what the researchers thought to be less than one-fiftieth the amount of radioiodine necessary to produce biologic changes. Uptake was measured with a Geiger counter. Six subjects were administered additional radioiodine a few months later. The results were compared with the radioiodine uptake of three normal children in a separate study.

This study showed that the thyroids of children with hypothyroidism and without goiters concentrated only small amounts of iodine compared to the thyroids of normal children or adults. This

work was supported by grants from the Christine Breon Fund for Medical Research and the American Cyanamid Corporation. The principal investigator continued these studies and was supported by the Manhattan Engineer District (MED) during World War II. The University of California Medical School, San Francisco received funding from the MED through a contractual arrangement, and intermittently shared facilities and personnel with the MED-funded predecessors to LBL.

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LBL-33. Studies on Patients Treated with Total-Body X-Ray Irradiation

FROM 1942 TO 1946, researchers at the University of California, San Francisco conducted studies on the blood of patients at the University Hospital who had received therapeutic total-body irradiation (and directed tumor irradiation, in some cases). Patients were selected for radiation therapy by hospital staff physicians and radiation treatments were administered as part of the normal course of therapy for these patients. Only the ancillary blood studies were sponsored by the Manhattan Project.

Sixteen male and 13 female patients ranging in age from 20 to 75 years with metastatic carcinoma, lymphoma, or arthritis were studied. Patients received a series of daily fractional exposures of 5 to 50 roentgens, measured at the skin-surface entry point, with totals ranging from 100 to 300 roentgens. Patient blood samples were studied individually for up to 3 years after treatment. The purpose of this study was to determine whether the analysis of blood changes could be used to indicate occupational radiation exposures in workers on the Manhattan Project.

The studies of blood samples obtained at intervals from the treated patients showed an immediate decrease in the number of white blood cells that are formed in lymphoid tissue, followed by recovery to normal levels during the post-treatment period. Monocytes (very large white blood cells) increased in number during treatment, but returned to normal levels after treatment was completed. Significant deviations in total white blood-cell count were observed during both early and late post-treatment periods. The red blood-cell count and the concentration of hemoglobin decreased during treatment, but recovered during the early post-treatment period. A temporary anemia condition was observed in many patients during the late post-treatment period. These studies were supported by the Health Division of the Metallurgical Laboratory (a Manhattan Project site located in Chicago).

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LBL-34. Studies Using Radioactive Isotopes of Nitrogen, Argon, Krypton, and Xenon

BETWEEN 1943 AND 1949, the Divisions of Medical Physics and Medicine, and the Radiation Laboratory, University of California, Berkeley conducted studies on the exchange of isotopes of nitrogen, argon, krypton, and xenon gases between the body and the surrounding air. The isotopes used for this research included nitrogen-13, argon-41, krypton-79, krypton-81, krypton-85, xenon-127, xenon-133, and xenon-141. Fifteen subjects ranging in age from 17 to 26 years participated.

Subjects inhaled one of these radioactive gases for 30 to 120 minutes to receive an administered activity of about 0.4 millicurie of each isotope. The subjects were then either placed in a high-altitude chamber to simulate decompression or flown in airplanes to specific altitudes. The hands, legs, and knees of the subjects were placed into specially constructed Geiger counters to measure uptake and elimination rates of the gas isotopes. Counting of the isotopes continued for 1 hour after actual or simulated flight. Many of the subjects exercised at various "altitudes" in order to bring on "the bends," or the formation of nitrogen bubbles in the blood and tissues characterized by pain in the joints and abdomen. The subjects classified the degree of pain caused by the bends and this information was compared to the subjects' desaturation curves.

This study showed that diffusion plays very little role in the uptake of various gases by tissues, and that the rapidity of gas exchange is dependent on the ability of the blood to carry gas as well as the rate of perfusion of the tissues by blood. This work was supported by the Office of Scientific Research and Development and the Columbia Foundation. The Divisions of Medical Physics and Medicine, and the Radiation Laboratory at the University of California, Berkeley were supported by the U.S. Atomic Energy Commission.

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LBL-35. Blood Oxygen Studies in Polycythemia Vera Patients and Normal Subjects Using Colloids of Zirconium-95 and Yttrium-90

IN APPROXIMATELY 1944 to 1947, scientists at the Donner Laboratory, University of California Radiation Laboratory, Berkeley conducted studies on blood oxygen saturation to learn more about the disease polycythemia vera. These studies involved measurements on 74 subjects, 48 of whom were polycythemia vera patients. Among the remainder, 18 were normal, healthy subjects, 4 had hypochromic anemia, and 3 had erythrocytosis (overproduction of red blood cells) and chronic pulmonary or cardiac disease. Blood volumes were determined for some of these subjects using colloids of zirconium-95 (Zr^{95}) and yttrium (probably Y^{90}, although not stated), or by the use of radioactively labeled red blood cells. No further details were given with regard to specific procedures or amounts of radionuclides administered as part of these studies. All patients also received chest x-rays to exclude polycythemia patients with pulmonary disease.

These studies showed that arterial blood oxygen saturation in polycythemia vera was within normal limits in resting subjects. This research was supported by the International Cancer Research Foundation, the U.S. Public Health Service, and the Sara Welt Fund. The Donner Laboratory was supported by the U.S. Atomic Energy Commission.

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LBL-36. Experimental Breast Cancer Treatment Studies Using Phosphorus-32

BETWEEN 1945 AND 1954, researchers at the University of California Medical School, San Francisco treated 89 breast cancer patients with phosphorus-32 (P^{32}) in combination with surgery

and x-ray therapy. The treatment protocol included intravenous administration of 20 to 30 microcuries of P^{32} as sodium hypophosphate per kilogram of body weight, two or three times a week over 2 to 4 weeks. In addition, the treatment included local x-ray exposure up to 4,000 roentgens within 35 days. Total administered activity P^{32} ranged from 5.0 to 25.2 millicuries. In 1945 and 1946, eight additional breast cancer patients were treated. Treatments were suspended in 1947 because of concern regarding possible subsequent radiation-induced hematologic effects of internally deposited P^{32}. Treatments were resumed in 1951 after no evidence of adverse effect had been observed among the previously treated patients, and an additional 81 subjects were treated over the next 4 years.

Follow-up of the treated patients through 1954 showed that 5 of the 8 patients treated during 1945 and 1946 were still alive, as were 75 of the 85 treated in 1951 or later.

The researchers concluded that further investigations and an expanded clinical experience were needed before a definitive conclusion could be reached about the success of this experimental treatment method. The University of California Medical School, San Francisco, received funding from the U.S. Atomic Energy Commission (AEC) through a contractual arrangement, and intermittently shared facilities and personnel with the AEC-funded predecessors to Lawrence Berkeley Laboratory.

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LBL-37. Experimental Thyroid Cancer Treatment Using Iodine-131

BETWEEN 1945 AND 1954, researchers in the Department of Radiology, University of California Medical School, San Francisco evaluated the use of iodine-131 (I^{131}) in the treatment of thyroid cancer. The cases of 124 patients with confirmed primary thyroid cancer were studied.

Most patients had received 1 to 2 millicuries of I^{131} to test their thyroid function before surgery. Of these patients, 101 showed no detectable tumor or I^{131} uptake after surgery. Among these subjects, 14 received 25 to 50 millicuries of I^{131} on one or two occasions; were then given thyroid extract; and were later checked for recurrence or development of radiation-induced effects. The 23 patients with inoperable thyroid cancer received 100 millicuries of I^{131}. This was administered once monthly until there was no evidence of tumor tissue as indicated by the absence of I^{131} uptake, or until adverse effects of the treatment were observed.

The results showed that treatment of thyroid cancer with I^{131} often was not effective. Radiation-induced depression of all cell types in the circulating blood and bone marrow was evident to widely varying degrees, with the greatest effect being observed at the highest total I^{131} activity. However, the magnitude of the effect was not always correlated with the level of I^{131} activity. This research was funded by the U.S. Atomic Energy Commission.

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LBL-38. Metabolism and Effects of Iodine-131

A STUDY WAS CONDUCTED in 1947 and 1948 at the Radiation Laboratory, University of California, Berkeley to learn more about the effects of iodine-131 (I^{131}) and its metabolism in normal subjects and patients with thyroid disorders. The objective of this study was to measure the uptake of I^{131} in the thyroid and the rate of its excretion in urine in order to determine the metabolism of iodine and its concentration in other sites in the body. Subjects included a few healthy physicians from the University of California Hospital, a series of patients with thyroid nodules but otherwise-normal thyroid function, and a group of subjects with confirmed thyroid cancer.

The normal subjects and patients with nodules received an oral dosage of 0.25 millicurie of I^{131}. Subjects treated for hyperthyroidism received 0.25 to 4.0 millicuries or up to 12 millicuries over an extended period of time. Subjects with thyroid cancer received 2 millicuries at two different times, and one patient received 59 millicuries. Measurements were made at various times to measure I^{131} activity in the subjects' thyroids and urine.

Normal thyroids were found to retain between 5 and 35 percent of the ingested I^{131}. This study also showed that the uptake of iodine in the thyroid was related to the degree of thyroid function. No adverse clinical effects of radioiodine were observed in most patients, including the patient receiving the greatest amount of I^{131}. This work was supported by the U.S. Atomic Energy Commission.

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LBL-39. Studies Using Phosphorus-32 and Other Radioisotopes

FROM 1948 TO 1949, at the Laguna Honda Home in San Francisco (a hospital for destitute patients), researchers from the Laboratory of Experimental Oncology, University of California, conducted a variety of studies using phosphorus-32 (P^{32}) and other radioisotopes. Sixty-one patients participated as subjects.

Three patients underwent experimental therapy using various radioactive compounds. In the Laboratory's Isotope Unit, 43 patients participated in uptake, excretion, and tissue assay studies involving P^{32}. Seven patients participated in iodine-131 uptake studies. Uptake, excretion, and tissue assay studies were conducted on five patients using zirconium-95 and niobium-95, two patients using copper-64, and one patient using gallium-72. The research fellows working in the Isotope Unit were funded by the National Cancer Institute and the U.S. Atomic Energy Commission.

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LBL-40. Studies of Electric Potentials in the Stomach Using Sodium-24

FROM 1948 TO 1949, researchers at the University of California Medical School, San Francisco investigated the electric potentials across cells in the lining of the stomach in order to better understand their relationship with physiologic processes in the stomach. Two patients of the Laboratory of Experimental Oncology at the Laguna Honda Home participated as subjects. Both received open surgical incisions in the stomach wall through which samples of stomach juices and electric measurements were obtained.

An unspecified amount of sodium-24 (Na^{24}) was administered by intravenous injection to each patient to determine the time between injection and the appearance of the Na^{24} in the stomach. This interval was found to be less than 3 min-

utes. Attempts to correlate sodium and hydrogen ions were unsuccessful.

The studies were not completed. This work was funded by the National Cancer Institute through the University of California School of Medicine. The University of California Medical School, San Francisco, received funding from the U.S. Atomic Energy Commission (AEC) through a contractual arrangement, and intermittently shared facilities and personnel with the AEC-funded predecessors to Lawrence Berkeley Laboratory.

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LBL-41. Studies of Methionine Metabolism Using Sulfur-35 as Tracer

IN 1948 AND 1949, researchers at the University of California Medical School, San Francisco; the Division of Biochemistry, University of California, Berkeley; the Metabolic Research Unit and the Department of Medicine, U.S. Naval Hospital, Oakland; and the Department of Chemistry, Mills College conducted collaborative studies on methionine metabolism using sulfur-35 (S^{35}) as a tracer of the metabolic processes involved. The purpose of these studies was to determine whether methionine was metabolized differently in patients with chronic liver disease, idiopathic hypoproteinemia (an abnormal decrease in the amount of protein in the blood), or Cushing's syndrome.

Amounts of S^{35}-labeled DL-methionine ranging from 25 to 100 microcuries were administered by intravenous injection to three normal males, ages 19, 20, and 26 years; and to five patients with chronic illnesses, four males aged 22 to 43 years and one 39-year-old female. All subjects fasted before and after the injection. Blood, urine, and fecal samples were collected and analyzed for S^{35} to determine the turnover rate of methionine into plasma protein and the rate of excretion.

This study showed that the three patients with chronic liver damage had a lower rate of incorporation of the S^{35}-labeled methionine. The patient with Cushing's syndrome showed a pattern of metabolism similar to that of the control subjects, and the patient with idiopathic hypoproteinemia had an excessive rate of protein plasma turnover. This work was supported by the U.S. Navy and the Office of Naval Research, the latter under a contract with the University of California. The University of California Medical School, San Francisco, received funding from the U.S. Atomic Energy Commission (AEC) through a contractual arrangement, and intermittently shared facilities and personnel with the AEC-funded predecessors to Lawrence Berkeley Laboratory.

References

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Kinsell, L.W., S. Margen, H. Tarver, J. McB. Frantz, E.K. Flanagan, M.E. Hutchin, G.D. Michaels, and D.P. McCallie. "Studies in Methionine Metabolism. III. The Fate of Intravenously Administered S^{35}-Labeled Methionine in Normal Adult Males, in Patients with Chronic Hepatic Disease, 'Idiopathic' Hypoproteinemia and Cushing's Syndrome." *Journal of Clinical Investigation*. Vol. 29, 1950, pp. 238–250. ❑

LBL-42. X-Ray Irradiation of the Normal Pituitary Gland During Conventional Cancer Therapy

BETWEEN 1948 AND 1949, at the Laguna Honda Home (a hospital for destitute patients) in San Francisco, the Laboratory of Experimental Oncology, University of California, conducted a study on the effects of adjuvant x-ray irradiation of the normal pituitary gland, during treatment of cancers in other tissues (e.g., skin melanoma, breast, and prostate).

The study was designed to deliver 8,000 to 10,000 rads to the subject's pituitary gland in hopes that the reduced secretion of pituitary hormones would benefit the cancer treatment. At least one patient, a 60-year-old female with breast cancer and metastases of the skin, was

treated by irradiation of her pituitary gland. Clinical laboratory indicators were evaluated to determine whether hypophysectomy by irradiation would be more effective than surgical removal of the pituitary gland.

Follow-up results of this study were apparently not reported. The Laboratory of Experimental Oncology at Laguna Honda Home was funded by the National Cancer Institute. The study was performed with support of a U.S. Atomic Energy Commission research fellow.

References

Laboratory of Experimental Oncology Annual Report 1948–1949. San Francisco: University of California at San Francisco, 1949, pp. 16–17 Special Collections Library, San Francisco Record Series: School of Medicine, Committee Reports 1917–1957, Carton 1, Folder "School of Medicine Research Committee 3." ❑

LBL-43. Experimental X-Ray Irradiation of the Pituitary in Patients with Melanoma or Hormonally Influenced Tumors

IN 1949 OR 1950, at the Laguna Honda Home in San Francisco (a hospital for destitute patients), researchers from the Laboratory of Experimental Oncology, University of California, San Francisco collaborated in a study of pituitary irradiation and its effect on advanced melanoma and breast cancer. The purpose of this experimental therapy was to induce hypophysectomy (removal or destruction of the pituitary) with radiation. It was hoped that this technique would interrupt the influence of pituitary hormones, which were believed to stimulate tumor growth.

Three female patients, two with advanced carcinoma of the breast and one with disseminated melanoma, received between 8,500 and 10,000 rads of x-ray radiation to their pituitary glands. However, no visible changes in the pituitary or in the clinical parameters under the control of pituitary hormones were apparent during initial observation.

Preliminary conclusions were that the pituitary is extremely resistant to x-rays. The project was sponsored by the Cancer Research Institute, School of Medicine, University of California, San Francisco, and partially funded by grants from the National Cancer Institute. It was also supported by the U.S. Atomic Energy Commission.

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Application for Cancer Funds SF-1-50. Renewal (for 4th fiscal year) Report, Laboratory of Experimental Oncology, Laguna Honda Home, San Francisco, California, March 6, 1950, File Code 19-14-5, Carton 1/3, Folder "Applications for Cancer Funds." ❑

LBL-44. Blood Volume Studies Using Radioactive Phosphorus-32 as Tracer

FROM 1949 TO 1950, researchers at the Donner Laboratory, University of California Radiation Laboratory, Berkeley and at the Highland Alameda County Hospital, Oakland conducted studies on blood volume and the oxygen carrying capacity of the blood, using phosphorus-32 (P^{32}). The labeling technique consisted of incubating 5 milliliters of the patient's blood with 500 microcuries of P^{32} (as sodium or orthophosphate in saline) for 2 hours. After additional processing and washing, the blood cells were injected into the same patient.

The purpose of one study was to determine the relation between the hematocrit (the percentage of the blood volume occupied by cells) and the total red cell volume, and to investigate the pathologic physiology of the blood volume in leukemia. Blood volumes were determined with P^{32}-labeled red blood cells in 24 cases of chronic lymphatic leukemia and 17 cases of chronic myelogenous leukemia, using hospital patients as subjects. Results showed that the variation of total red cell volume for a given hematocrit is so large that it is of negligible value for the prediction of the total red cell volume in either normal subjects or patients with chronic leukemia. Determination of the blood volume is of considerable value in the treatment of chronic leukemia patients.

The purpose of the second study was to determine normal blood volume and plasma volume in healthy adult women, using the same technique of labeling blood cells with P^{32}. The 16 healthy volunteers ranged in age from 22 to 48 years. Results of these studies showed that blood volumes in the males did not differ from

those in a similar normal male population, despite differences in percentages of body fat.

A third study was conducted to determine blood loss and red cell turnover rates (in terms of cubic centimeters per kilogram of body weight) during thoracic surgery. Twenty-seven patients ranging in age from 21 to 57 years participated as subjects. The patients' surgeries were conducted in association with tuberculosis therapy. This study provided data on blood loss for various thoracic surgical procedures and demonstrated the feasibility of using this technique to make accurate blood volume determinations. It is of considerable clinical value to know the blood volume in thoracic surgical patients.

A study involving 12 prisoners who were evaluated for total red blood-cell volume and plasma volume was mentioned; however, details were not provided in the supporting documents. These studies were supported in part by the U.S. Public Health Service and the U.S. Atomic Energy Commission.

References

Berlin, N.I., J.H. Lawrence, and J. Gartland. "The Blood Volume in Chronic Leukemia as Determined by P^{32}-Labeled Red Blood Cells." *Journal of Laboratory and Clinical Medicine*. Vol. 36, 1950, pp. 435–439.

Berlin, N.I., G.M. Hyde, R.J. Parson, J.H. Lawrence, and S. Port. "Blood Volume of the Normal Female as Determined with P^{32}-Labeled Red Blood Cells." In *Proceedings of the Society of Experimental Biology and Medicine*. Vol. 76, 1951, pp. 831–832.

Berlin, N.I., D.F. Rowles, G.M. Hyde, R.J. Parsons, P.C. Samson, and S. Port. "The Blood Volume and Blood Turnover in Thoracic Surgery as Determined by P^{32}-Labeled Red Blood Cells." *Surgery, Gynecology, and Obstetrics*. Vol. 92, 1951, pp. 712–716. ❑

LBL-45. Studies on the Distribution of Gases, Water, and Electrolytes in the Human Body Using Carbon-11, Sodium-24, and Iodine-131

DURING THE LATE 1940s AND EARLY 1950s, studies on carbon monoxide metabolism and the *in vivo* analysis of human body composition were conducted by researchers at the Donner Laboratory, University of California Radiation Laboratory, Berkeley. Tracer doses were administered during studies to both normal subjects and subjects with various diseases.

One specific objective of the studies was to identify the function of the liver in carbon monoxide metabolism. Carbon monoxide labeled with carbon-11 (C^{11}) was employed for this purpose. These studies measured the rate of equilibration of (stable) heavy water (deuterium oxide [D_2O]) and sodium-24 (Na^{24}) in normal subjects following the injection of a saline solution labeled with Na^{24}. Samples of plasma, drawn at intervals following the injection, were used to measure total-body water and sodium content.

Some of these studies involved measuring the total sodium space and total-body sodium in older subjects, particularly patients with cardiac edema and other health problems, for comparison to normal subjects. The subjects—cardiac patients and normal volunteers (including 10 young normal adults, 13 older adults, 11 elderly adults with cardiovascular disease, and 20 elderly adults with congestive failure and edema)—were administered 100 microcuries of Na^{24} in isotonic sodium chloride. Blood samples were later drawn and counted for Na^{24}.

Differences were found in total sodium space between young and old normal adults. These differences corresponded to an increase in age, and a marked increase in cardiac edema. Additional studies were made of Na^{24} clearance from a limb as measured by *in vivo* counting in normal subjects and cardiac patients. Iodine-131 was also used for some of these studies to determine whether impaired circulation and altered fluid spaces had any effect on the Na^{24} distribution curve. This research was supported in part by a grant from the Office of Naval Research and by the U.S. Atomic Energy Commission.

References

Warner, G.F., E.L. Dobson, C.E. Rodgers, M.E. Johnston, and N. Pace. "The Measurement of Total Sodium Space and Total-Body Sodium in Normal Individuals and in Patients with Cardiac Edema." *Circulation*. Vol. 5, 1952, pp. 915–919.

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Correspondence. University of California to Office of Naval Research, May–December 1949. University of California, University Archives, Office of the President, Correspondence and Papers, CU-5, Carton 760, Folder 748-L. ❑

LBL-46. Total-Body Water Studies Using Tritium as a Tracer

DURING THE EARLY 1950s, researchers at the Donner Laboratory, University of California Radiation Laboratory, Berkeley conducted studies on total-body water measurements using tritium (H^3) as a tracer. Thirty-seven patients at the Highland Alameda County Hospital, ranging in age from 30 to 80 years, and 20 normal male volunteers, ranging in age from 20 to 56 years, from San Quentin Prison participated as subjects.

Subjects were intravenously administered 2 millicuries of water labeled with H^3. Blood samples were drawn at intervals of 2, 4, and 6 hours and the H^3 activity in the plasma was measured.

This study showed that total-body water varies greatly from individual to individual, reflecting the variation in body fat. In pathologic states, where lean body mass cannot be assumed to remain constant in composition, body water determinations are of limited value without a method for measuring body fat. This work was supported by the U.S. Atomic Energy Commission.

References

Prentice, T.C., W. Siri, N.I. Berlin, G.M. Hyde, R.J. Parsons, E.E. Joiner, and J.H. Lawrence. "Studies of Total-Body Water with Tritium." *Journal of Clinical Investigation.* Vol. 31, 1952, pp. 412–418. ❑

LBL-47. Liver Blood Flow Studies Using Phosphorus-32 as a Tracer

DURING THE EARLY 1950s, scientists at the Donner Laboratory, University of California Radiation Laboratory, Berkeley studied the blood flow through the liver by measuring the removal rate of colloidal particulate matter from the blood stream. In this study, the particulate matter was colloidal chromic phosphate labeled with phosphorus-32 (P^{32}).

Subjects for this study were 29 healthy fasting men between the ages of 20 and 26. Each received an intravenous injection of colloidal chromic phosphate containing 2 to 4 microcuries of P^{32}. Subsequently, blood samples were drawn at frequent intervals and measured for blood volume and specific activity.

The study found the average particulate disappearance rate corresponded to a liver blood flow of 1.5 to 1.8 liters per minute. This experiment was supported by the Office of Naval Research and the U.S. Atomic Energy Commission.

References

Dobson, E., G. Warner, C. Finney, and M. Johnston. "The Measurement of Liver Circulation by Means of the Colloid Disappearance Rate." *Circulation.* Vol. 7, May 1953, pp. 690–695. ❑

LBL-48. Blood Volume Studies in Cirrhosis Using Phosphorus-32–Labeled Red Blood Cells

DURING THE EARLY 1950s, researchers at the Donner Laboratory, University of California Radiation Laboratory, Berkeley and at the Highland Alameda County Hospital, Oakland conducted studies on blood volume in cirrhosis patients using phosphorus-32 (P^{32}).

Twenty-eight patients with portal cirrhosis of the liver participated as subjects. Blood volume in each subject was measured using an established technique that included labeling 5 milliliters of blood drawn from the patient with 500 microcuries of P^{32}, and reinjecting 1 milliliter.

The results of these studies showed that cirrhosis patients may exhibit various levels of total blood volume, red cell volume, or plasma volume. The study also showed that neither red cell volume nor plasma volume can be predicted from total cell volume in a blood sample. This work was supported in part by the U.S. Atomic Energy Commission.

References

Berlin, N.I., J.H. Lawrence, and J. Gartland. "The Blood Volume in Chronic Leucemia as Determined by P^{32}-Labeled Red Blood Cells." *Journal of Laboratory and Clinical Medicine.* Vol. 36, 1950, pp. 435–439.

Hyde, G.M., N. Berlin, R.J. Parsons, J.H. Lawrence, and S. Port. "The Blood Volume in Portal Cirrhosis as Determined by P^{32}-Labeled Red Blood Cells." *Journal of Laboratory and Clinical Medicine*. Vol. 39, 1952, pp. 347–358. ❑

LBL-49. Studies of the Metabolism of Tritium-Labeled Cholesterol

DURING THE EARLY 1950s, researchers at the Donner Laboratory, University of California Radiation Laboratory, Berkeley conducted cholesterol metabolism studies using tritium (H^3) as a tracer. The purpose of these studies was to investigate the relationship between dietary fat (lipids) and the development of atherosclerosis (hardening of the arteries) by tracing the absorption and turnover of ingested cholesterol in various compartments of the blood.

Four patients ranging in age from 42 to 69 years, all of whom had some degree of atherosclerosis, participated as subjects. Three were orally administered H^3-cholesterol dissolved in warm vegetable oil emulsified into whole milk. The fourth patient received the H^3-cholesterol in crystalline form dispersed in milk. The specific activity of the ingested H^3 varied from 0.48 to 1.07 millicuries per gram of cholesterol (depending on the preparation used). Blood and tissue cholesterol samples were assayed to determine the rate and magnitude of the appearance of ingested cholesterol in the various blood compartments.

The studies showed that cholesterol absorption in man is slow and inefficient. The Donner Laboratory was supported by the U.S. Atomic Energy Commission.

References

Biggs, M.W., D. Kritchevsky, D. Colman, J.W. Gofman, H.B. Jones, F.T. Lindgren, G. Hyde, and T.P. Lyon. "Observations on the Fate of Ingested Cholesterol in Man." *Circulation*. Vol. 6, September 1952, pp. 359–366. ❑

LBL-50. Study of Sodium-24 Metabolism in Normal Individuals and Patients with Ascites

DURING THE EARLY 1950s, the Departments of Physiology and Medicine, University of California Medical School, San Francisco; the University of California Medical Service of the San Francisco Hospital; the San Francisco Department of Public Health; and the Donner Laboratory, University of California Radiation Laboratory, Berkeley conducted collaborative studies of sodium metabolism in humans using sodium-24 (Na^{24}). The purpose of the studies was to determine the "sodium space" and body sodium content, exchangeable with Na^{24}, in normal adult subjects with no history of electrolyte or fluid imbalance, and in patients with ascites (fluid accumulation in the abdominal cavity) due to liver damage associated with advanced chronic hepatitis.

Study subjects included 15 normal (13 male and 2 female) hospital convalescents ranging in age from 42 to 85 years and with no history of electrolyte or fluid imbalance who served as study controls; and 20 cirrhotic patients, 15 males and 5 females, ranging in age from 38 to 69 years with ascites. Each subject received an injection of approximately 100 microcuries of Na^{24}. Blood samples were drawn 12, 24, and 40 hours after the injection and analyzed.

The studies showed sodium space and body sodium content of the patients with ascites were markedly higher than those of normal subjects and that the increase was roughly proportional to the degree of ascites clinically observed in the patient. This work was supported by the Office of Naval Research and the U.S. Atomic Energy Commission.

References

Warner, G., N. Sweet, and E. Dobson. "'Sodium space' and body sodium content, exchangeable with sodium-24, in normal individuals and patients with ascites." *Circulation Research*. Vol. 1, 1953, pp. 486–490. ❑

LBL-51. Measurement of Total "Sodium Space" and Total-Body Sodium Using Sodium-24 as a Tracer

DURING THE EARLY 1950s, researchers at the Donner Laboratory, University of California Radiation Laboratory, Berkeley; the Department of Physiology, University of California, Berkeley; and the University of California Medical Service Hospital, San Francisco conducted a study to measure the total "sodium space" and total-body

sodium contents using sodium-24 (Na^{24}) as a tracer.

Four groups of adult male subjects participated, including 10 normal subjects, ages 21 to 29; 13 normal subjects, ages 42 to 83; 10 subjects ages, 40 to 75 with cardiovascular disease; and 14 subjects ages, 40 to 72 with cardiovascular disease, congestive heart failure, and edema. Each subject was intravenously administered approximately 100 microcuries of Na^{24}. Activity was measured in a single blood sample drawn 24 hours after administration.

The results of the study showed an increase in sodium content consistent with age. In subjects with congestive heart failure and edema, there was a marked increase in total sodium space and total-body sodium. This work was supported by the Office of Naval Research and the U.S. Atomic Energy Commission.

References

Warner, G.F., E.L. Dobson, C.E. Rodgers, M.E. Johnston, and N. Pace. "The Measurement of Total 'Sodium Space' and Total-Body Sodium in Normal Individuals and in Patients with Cardiac Edema." *Circulation.* Vol. 5, June 1952, pp. 915–919. ❑

LBL-52. Study of the Effects of Injection Volume on Intramuscular Sodium Clearance Rates Using Sodium-24

DURING THE EARLY 1950s, researchers from the Donner Laboratory, University of California Radiation Laboratory, Berkeley and the Department of Physiology, University of California, Berkeley conducted studies to measure the effect of injection volume on the intramuscular clearance rate of sodium using sodium-24 (Na^{24}). The purpose of this study was to develop a practical method for measuring regional blood flow.

Six normal males between the ages of 20 and 30 years each received intramuscular injections of 5 microcuries of Na^{24} as isotonic sodium chloride into the calf muscles of both legs. The volume of the injection into one leg was 1.0 milliliter, while the volume of the injection into the other leg varied from 0.005 to 1.0 milliliters. Immediately after injection, external counters measured the activity remaining at the injection sites. These studies showed that the rate of clearance increased as the volume of the injection decreased. This work was supported by the Office of Naval Research and the U.S. Atomic Energy Commission.

References

Warner, G.F., E.L. Dobson, N. Pace, M.E. Johnston, and C.R. Finney. "Studies of Human Peripheral Blood Flow: The Effect of Injection Volume on the Intramuscular Radiosodium Clearance Rate." *Circulation.* Vol. 8, November 1953, pp. 732–734. ❑

LBL-53. Experimental Treatment of Bladder Tumors Using Cobalt-60 Beads

DURING THE EARLY 1950s, physicians in the Departments of Surgery, Urology, and Radiology, at the University of California Medical School, San Francisco treated 35 bladder cancer patients with radiocobalt beads.

Cobalt-60 (Co^{60}) beads, ranging in total administered activity from 20 to 90 millicuries per patient, were inserted into the bladder cavity. The beads delivered estimated doses of 5,000 to 6,000 rads to bladder wall tissue over a 7- to 10-day period. Some of the patients also received approximately 3,500 rads of x-ray radiation over a 35- to 40-day period.

The results of the study showed that non-infiltrating lesions could be treated successfully, but infiltrating lesions were only temporarily arrested. The University of California Medical School, San Francisco received funding from the U.S. Atomic Energy Commission (AEC) through a contractual arrangement, and intermittently shared facilities and personnel with the AEC-funded predecessors to Lawrence Berkeley Laboratory.

References

Hinman, F. Jr., J.W. Schulte, and B.V.A. Low-Beer. "Further Experience with Intracavitary Radiocobalt for Bladder Tumors." *The Journal of Urology.* Vol. 73, No. 2, February 1955, pp. 285–291.

Schulte, J.W., F. Hinman Jr., and B.V.A. Low-Beer. "Radiocobalt in the Treatment of Bladder

Tumors." *The Journal of Urology*. Vol. 67, No. 6, June 1952, pp. 916–924. ❑

LBL-54. Red Blood-Cell Studies in Leukemia Patients Using Carbon-14–Labeled Glycine

DURING THE EARLY 1950s, researchers at the Donner Laboratory, University of California Radiation Laboratory, Berkeley conducted studies of the life span of red blood cells in chronic leukemia using carbon-14 (C^{14})–labeled glycine.

Eight chronic leukemia patients, ranging in age from 24 to 68 years, participated as subjects. Each was intravenously administered approximately 100 microcuries of C^{14}. A blood sample was drawn and measured for activity.

These studies showed that non-hemorrhage-induced anemia in leukemia is the result of a shortened life span of the red blood cells. This work was supported by the U.S. Atomic Energy Commission.

References

Berlin, N.I., J.H. Lawrence, and H.C. Lee. "The Pathogenesis of the Anemia of Chronic Leukemia: Measurement of the Life Span of Red Blood Cells Glycine-2-C^{14}." *Journal of Laboratory and Clinical Medicine*. Vol. 44, December 1954, pp. 860–874. ❑

LBL-55. Study of the Effect of Thyrotropic Hormone Using Iodine-131

DURING THE EARLY 1950s, researchers at the University of California Pediatric Clinic, San Francisco conducted a study on the effect of thyrotropic hormone in children as measured by an increase in iodine-131 (I^{131}) uptake. The purpose of the study was to differentiate primary from secondary hypothyroidism (abnormally low thyroid activity) in infancy and childhood.

Five euthyroid (with normal thyroid function) children, and six hypothyroid children, ranging in age from 1 to 15 years, participated as subjects. Each subject was administered 15 to 40 microcuries of I^{131} either orally or through a polyethylene stomach tube. Uptake was measured after 24 hours. Thyrotropic hormone therapy was then initiated and continued over a period of 48 hours, after which I^{131} uptake was again measure

This study showed an increase in I^{131} uptake in euthyroid children, little or no difference in hypothyroid children assumed to have primary end-organ deficiency, and an increase in uptake in hypothyroid children with collateral signs of pituitary insufficiency. The results suggested a method for differentiating primary from secondary hypothyroidism in childhood. This work was supported by the University of California, the Playtex Park Research Institute, and the U.S. Atomic Energy Commission.

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Pickering, D.E., and E.R. Miller. "Thyrotropic Hormone in Infants and Children." *American Medical Association Journal of Diseases in Children*. Vol. 85, No. 2, 1953, pp. 135–140. ❑

LBL-56. Blood Volume Studies in Cancer Using Phosphorus-32

DURING THE EARLY 1950s, researchers at the Donner Laboratory, University of California Radiation Laboratory, Berkeley and at the Highland Alameda County Hospital, Oakland conducted studies on blood volume in cancer patients using phosphorus-32 (P^{32}). The purpose of this study was to determine whether advanced stages of cancer were associated with anemia.

Sixty-six cancer patients, including both males and females ranging in age from 24 to 86 years, participated as subjects. Blood volume in each subject was measured using a technique involving the labeling of 5 milliliters of blood drawn from the patient with 500 microcuries of P^{32}, and reinjecting 1 milliliter of labeled blood into the patient.

These studies indicated that 32 percent of the patients were anemic, possibly caused by a shortened red cell life span, as in leukemia. This study was supported by the U.S. Public Health Service. The Donner Laboratory was supported by the U.S. Atomic Energy Commission.

References

Berlin, N.I., G.M. Hyde, R.J. Parson, and J.H. Lawrence. "The Blood Volume in Cancer." *Cancer*. Vol. 8, No. 4, 1955, pp. 796–802. ❑

LBL-57. Blood Volume Studies in Pregnancy Using Phosphorus-32

DURING THE EARLY 1950s, researchers at the Donner Laboratory, University of California Radiation Laboratory, Berkeley and at the Highland Alameda County Hospital, Oakland investigated the anemia associated with pregnancy to better understand the relationship between anemia, blood volume, and total red cell volume. Blood volumes were determined using phosphorus-32 (P^{32})-labeled red blood cells in 181 women. These included 157 pregnant patients and 34 postpartum patients.

Blood volume in each subject was measured using a technique that included labeling 5 milliliters of blood drawn from the patient with 500 microcuries of P^{32}, and reinjecting 1 milliliter. Blood samples were obtained at various times after injection, before and after delivery.

The results of these studies showed a true anemia during the first and second trimesters of pregnancy, confirmed a progressive increase of plasma volume up to the 9th month of pregnancy, and showed a decrease in blood volume at delivery. This work was supported in part by the U.S. Atomic Energy Commission.

References

Berlin, N.I., C. Goetsch, G.M. Hyde, and R.J. Parsons. "The Blood Volume in Pregnancy as Determined with P^{32}–Labeled Red Blood Cells." *Surgery Gynecology and Obstetrics.* Vol. 94, 1952, pp. 173–176. ❑

LBL-58. Blood Volume Studies in Pre-Eclamptic Patients Using Phosphorus-32

DURING THE EARLY 1950s, researchers at the Donner Laboratory, University of California Radiation Laboratory, Berkeley and at the Highland Alameda County Hospital, Oakland conducted studies on blood volume in women with pre-eclampsia (hypertension due to pregnancy) using phosphorus-32 (P^{32}). Eight women in the last trimester of pregnancy and diagnosed with pre-eclampsia participated as subjects.

Blood volume in each subject was measured using a technique that included labeling 5 milliliters of blood that was drawn from the patient, with 500 microcuries of P^{32}, and reinjecting 1 milliliter.

These studies showed a reduction in total blood, red cell, and plasma volumes in participating patients. This work was supported in part by the U.S. Atomic Energy Commission.

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LBL-59. Lipid Metabolism Studies Using Tritium-Labeled Cholesterol

DURING THE EARLY 1950s, scientists at the Donner Laboratory, University of California Radiation Laboratory, Berkeley conducted studies on lipid metabolism using tritium (H^3) as a tracer. The purpose of these studies was to demonstrate a quantifiable metabolic defect in lipid metabolism.

The subjects of these studies were 10 hospital patients ranging in age from 34 to 52 years and included 2 with elevated cholesterol; 3 with clinical atherosclerosis; and 3 normal, healthy subjects. Each was administered 0.55 to 0.77 millicurie of cholesterol labeled with H^3 dissolved in warm vegetable oil, emulsified into whole milk, and mixed together with ice cream. Serum cholesterol measurements were made 1, 7, and 14 days after ingestion by analysis for H^3.

This study showed that patients with abnormal serum lipoprotein spectra carry a greater fraction of their newly absorbed cholesterol in the esterified form (an oxygen-linked form of cholesterol commonly found in the body) than do subjects with normal serum lipoprotein spectra. This research was supported by the U.S. Atomic Energy Commission.

References

Biggs, M.W., and D. Colman. "A Quantitative Metabolic Defect in Lipid Metabolism Associated

with Abnormal Serum Lipoproteins in Man." *Circulation.* Vol. 7, March 1953, pp. 393–402. ❑

LBL-60. Blood Volume Studies Using Dextran and Phosphorus-32–Labeled Red Blood Cells

DURING THE EARLY 1950s, researchers at the Donner Laboratory, University of California Radiation Laboratory, Berkeley and Highland Alameda County Hospital, Oakland conducted studies on blood volume following administration of dextran (a plasma substitute) using phosphorus-32 (P^{32})–labeled red blood cells.

The subject pool for this study consisted of 24 patients with chronic lymphocytic leukemia, 17 patients with chronic myelogenous leukemia, and 10 males with fractures (one of whom had liver cirrhosis). The latter 10 patients were administered dextran. Three patients who served as controls received only saline. Each subject (aside from the three controls) underwent two blood volume measurements using an established technique that included labeling 5 milliliters of blood drawn from the subject with 500 microcuries of P^{32} and reinjecting 1 milliliter.

The results of these studies showed an increase in blood volume among the 10 subjects administered dextran. The three control patients showed no significant change in blood volume. This work was supported by the U.S. Atomic Energy Commission.

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Meyer, L.M., N.I. Berlin, G.M. Hyde, R.J. Parson, and B. Whittington. "Changes in Blood Volume Following Administration of Dextran—Determined by P^{32}-Labeled Red Cells." *Surgery Gynecology and Obstetrics.* Vol. 94, 1952, pp. 712–714. ❑

LBL-61. Measurement of Blood Volume Using Chromium-51

DURING THE EARLY 1950s, researchers in the Department of Radiology, University of California Medical School, San Francisco with others in the Radioisotope Unit, Veterans Administration Hospital at Fort Miley, made measurements of blood volume using chromium-51 (Cr^{51}). The purpose of this study was to determine if the anemia observed in cancer patients is due to excessive red blood-cell destruction, or to increased plasma volume. One hundred seventy-five hospitalized patients with various types of cancer and 87 normal individuals participated as subjects.

A sample of blood was drawn from each subject, labeled with Cr^{51}, and reinjected intravenously. After 1 hour, another blood sample was drawn and activity was measured to determine blood volume, plasma volume, and red cell mass.

The studies showed that patients with nonmetastatic cancers exhibited lower-than-normal whole-blood volumes. Patients with all types of cancer, except colon cancer, had lower red cell masses and higher plasma volumes than normal. Patients with leukemia or cancer of the stomach, esophagus, or colon had higher than normal blood volumes. This work was supported by the U.S. Atomic Energy Commission.

References

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LBL-62. Body Composition Studies Using Tritium

IN THE EARLY 1950s AND 1960s, researchers at the Donner Laboratory, University of California Radiation Laboratory, Berkeley and the Division of Medical Physics, University of California, Berkeley conducted a series of studies on the fat, water, blood, and bone volumes in the human body. The procedure to determine a total water volume routinely made use of oral or injected tritium (H^3)-labeled water as a tracer.

The total-body water and body composition of 100 normal subjects, ages 20 to 80, was evaluated using tritium. The experiment was designed to determine the deviations in body composition in various body types, from lean to obese.

The results indicated not only wide variations in body compositions from lean to obese subjects,

but also wide variation in groups of subjects with similar densities or body water. This work was supported by the U.S. Atomic Energy Commission.

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LBL-63. Blood Studies in Congestive Heart Failure Using Phosphorus-32 and Sodium-24

IN 1950, researchers at the Donner Laboratory, University of California Radiation Laboratory, Berkeley conducted tracer studies using phosphorus-32 (P^{32}) and sodium-24 (Na^{24}) to determine total red cell volume, plasma volume, and sodium space in patients with congestive heart failure. This research was conducted to better understand the physiological processes involved.

Twenty-seven male and female patients at the Highland Alameda County Hospital, ranging in age from 34 to 84 years, were used as subjects. Blood, red cell, and plasma volumes were determined using established techniques. Five milliliters of blood samples from each subject were labeled with 500 microcuries of P^{32} and 1 milliliter of the labeled sample was reinjected into the subject. Exchangeable body sodium was determined by administering 100 microcuries of Na^{24} and then measuring the radioactivity in a plasma sample taken 18 hours after injection.

The study showed that 12 patients had normal blood, red cell, and plasma volumes. Fifteen patients had either an elevated blood volume, total red cell volume, or plasma volume. This work was supported by the U.S. Atomic Energy Commission.

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LBL-64. Experimental Cancer Therapy Using Gold-198, Yttrium-90, and Chromium-51

FROM 1950 TO 1955, cancer patients with ascites (cancer-caused fluid in the abdominal cavity) and pleural effusions (fluid in the chest cavity) were treated at the Donner Laboratory, University of California Radiation Laboratory, Berkeley and at the Alta Bates Hospital using gold-198 (Au^{198}) or yttrium-90 (Y^{90}).

Sixteen female patients ranging in age from 34 to 62 years were administered 23 to 120 millicuries of Au^{198} or Y^{90} by injection into the affected body cavity. Small samples of fluid were removed after 24 hours to assess the activity of the isotope remaining in the cavity. Two patients received injections in the chest and abdomen and one patient underwent three separate abdominal injections. Follow-up consisted of observation for the return of ascitic fluid. One patient was also administered 0.5 millicurie of chromium-51 (Cr^{51}). This material was deemed unsatisfactory, and the patient then was administered 61 millicuries of Y^{90}.

Of the 20 total treatments to the 16 patients, 11 were observed to render the patient free of ascites for a period of time. The Donner Laboratory was supported by the U.S. Atomic Energy Commission.

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LBL-65. Study of Local Blood Flow in Bone Marrow in Patients with Leukemia and Neoplastic Diseases Using Iodine-131

BETWEEN 1951 AND 1952, researchers at the Laboratory of Experimental Oncology, University of California, San Francisco; the National Cancer Institute; and the Division of Medicine and Cancer Research, University of California Medical School, San Francisco conducted studies on blood flow in human bone marrow using iodine-131 (I^{131}) as a tracer. The purpose of the studies was to determine the relative rates of clearance of I^{131} from the bone marrow, to ascertain the blood flow in human bone marrow, and to obtain information on the clearance rates from the gastrocnemius muscle.

A total of 44 patients, with various neoplastic diseases, lymphoblastomas, and leukemia participated as subjects. The subjects were 31 males ranging in age from 9 to 79 years, and 13 females between 5 and 63 years of age. Ten to 30 microcuries of I^{131} were injected into the marrow tissue of each patient. Most patients also received intramuscular injections of 10 to 30 microcuries of I^{131}. Activity was externally counted for 15 to 30 minutes following injection.

The results of these studies showed a selective increase in blood flow in the bone marrow in acute leukemia and in some cases of chronic lymphocytic leukemia and multiple myeloma. The studies also suggested that fundamental differences in the marrow vascular bed exist among the leukemic group of diseases. Use of I^{131} to evaluate blood flow in bone marrow was considered a research tool in studying cancer patients and applied over time, at least into the 1960s. The University of California Medical School, San Francisco received funding from the U.S. Atomic Energy Commission (AEC) through a contractual arrangement, and intermittently shared facilities and personnel with the AEC-funded predecessors to Lawrence Berkeley Laboratory.

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LBL-66. Localization of Deep-Seated Tumors Using Potassium-42

FROM 1954 THROUGH 1956, researchers at the University of California Medical School, San Francisco studied the effectiveness of potassium-42 (K^{42}) as an agent for localizing deep-seated tumors. The purpose of this study was to find better means of localizing deep tumors and to determine metabolic activity in tumor tissue.

Thirty-three patients were administered K^{42} to localize and identify deep-seated tumors by surface measurement methods. A scintillation counter with a collimator was used to localize tumors, which were presumed to have a high metabolism of potassium.

Available information indicates that the results of these studies were inconclusive. This work was supported by the U.S. Atomic Energy Commission.

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LBL-67. Measurement of Residual Fluid in the Fasting Stomach Using Zirconium-95/Niobium-95 as Tracer

DURING THE MID-1950s, researchers at the Department of Medicine and the Radioactivity Research Center, University of California Medical School, San Francisco measured the rate of

gastric fluid secretion and amounts of gastric fluid remaining in empty stomachs. These measurements were made using zirconium-95/niobium-95 (Zr^{95}/Nb^{95}) complex as a tracer. Thirty-six patients, none with clinical evidence of gastric retention, participated as subjects. Each was administered 0.5 microcurie of Zr^{95}/Nb^{95}, mixed with a quantity of water and a chelating agent (versene or EDTA). Within 1 minute, samples were drawn from the stomach and activity was measured to determine the amount of dilution.

The study showed that the gastric volume remaining after aspiration varied uniformly from 3 to 83 milliliters. Seventy-five percent of the participants had a residual volume of 20 milliliters or more. The University of California Medical School, San Francisco received funding from the U.S. Atomic Energy Commission (AEC) through a contractual arrangement, and intermittently shared facilities and personnel with the AEC-funded predecessors to Lawrence Berkeley Laboratory.

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LBL-68. Measurement of Sodium-24 Movement in Normal Subjects

DURING THE MID-1950s, researchers at the Donner Laboratory, University of California Radiation Laboratory, Berkeley conducted studies on the movement of sodium in the human body using sodium-24 (Na^{24}). The purpose of the studies was to correlate the early movement of sodium with age and gender to determine the relationship between blood circulation and aging.

Study subjects included 63 healthy male and 70 healthy female volunteers ranging in age from 22 to 90 years. Each subject was intravenously administered 30 to 50 microcuries Na^{24} as chloride ($Na^{24}Cl$). Movement of the radioisotope was measured for 35 to 120 minutes.

These studies showed that the sodium mixing rate slowed with increasing age, and that the mixing rate was generally higher among women than among men. This work was supported by the National Heart Institute, the National Institutes of Health, and the U.S. Atomic Energy Commission

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LBL-69. Aspirin Absorption Studies Using Carbon-14

DURING THE MID-1950s, researchers at the Donner Laboratory, University of California Radiation Laboratory, Berkeley conducted studies to determine and compare the absorption levels of two different aspirin products using an unstated amount of carbon-14 (C^{14}) as a tracer. Seven study subjects ingested aspirin that had been labeled with C^{14}. Measurement of exhaled C^{14} dioxide ($C^{14}O_2$) indicated the absorption rate of the aspirin.

The results of these studies indicated no difference in the absorption rate of the two products. The Donner Laboratory was supported by the U.S. Atomic Energy Commission.

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LBL-70. Studies on Protein-Bound Iodine-131 in Children

DURING THE MID-1950s, researchers at the Departments of Pediatrics and Radiology, University of California Medical School, San Francisco; the San Francisco Veterans Administration Hospital; and the San Francisco Children's Hospital conducted studies to measure protein-bound iodine in human plasma.

Fourteen children ranging in age from 4 to 14 years with poliomyelitis, but normal thyroid function, participated as subjects. Each received oral doses of 10 to 30 microcuries of iodine-131 (I^{131}) as a tracer. Blood samples were drawn at intervals and the plasma was treated with anionic resin. Samples were counted to determine the amount of plasma protein-bound iodine.

When compared with data from another study involving 27 euthyroid (normal thyroid) adults, this study showed that children appear to release protein-bound iodine earlier, and in greater amounts, than adults. The University of California Medical School, San Francisco, received funding from the U.S. Atomic Energy Commission (AEC) through a contractual arrangement, and intermittently shared facilities and personnel with the AEC-funded predecessors to Lawrence Berkeley Laboratory.

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LBL-71. Studies of Red Blood-Cell Production in Patients with Polycythemia Vera Using Iron-59 and Phosphorus-32

DURING THE 1950s AND EARLY 1960s, researchers at the Donner Laboratory, University of California Radiation Laboratory, Berkeley conducted studies on red blood-cell production using iron-59 (Fe^{59}). The purpose of these studies was to classify the patterns of red cell production in patients with polycythemia vera (a chronic disease characterized by an abnormal increase in red blood-cell production) to aid in diagnosis of the disease.

Sixty-four patients ranging in age from 6 to 78 years participated as subjects. For each subject, plasma was obtained from a blood sample and mixed with 10 to 40 microcuries of Fe^{59}. Five to 20 milliliters of this solution were then injected into the same donor. Blood samples were then drawn over the next 14 days and analyzed for plasma and red cell radioactivity. Surface measurements over the liver, spleen, and sacral bone marrow were also obtained to determine Fe^{59} activities in these organs. Plasma and red cell volumes were determined, independently, by conventional methods involving the administration of Fe^{59} and phosphorus-32 (P^{32}). Seven of the patients participated in repeat studies over a 12-year period. The clinical course and pathologic findings at postmortem examination (autopsy) on the patients were correlated with the previous study data.

The results of these studies provided data for classifying the diagnosis of polycythemia vera according to red cell activity and for determining appropriate therapy. This work was supported by the U.S. Atomic Energy Commission.

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LBL-72. Experimental Treatment of Cancer with Heavy Charged Particles

FROM THE MID-1950s THROUGH THE MID-1970s the Lawrence Berkeley Laboratory's 184-inch synchrocyclotron was used to create heavy particle beams for use in experimental treatment and clinical trials of cancer therapy. Early experiments included three cases of patient brain tumor irradiation in 1961 and 1962. Subsequent cases utilizing the Bragg peak of the 910-MeV (million electron volt) alpha-particle beam for treatment included at least six patients with brain tumors, three patients with pulmonary metastases, two patients with Parkinson's disease, and one case of acromegaly with large hypophyseal tumor. The maximum doses to the tumors in these cases ranged from 2,500 to 6,000 rads.

In the early 1970s, Donner Laboratory researchers began preparations for what would become the clinical trials of the program of cancer treatment with heavy charged particles. The tumors considered for treatment with heavy nitrogen

and heavy neon beams in this phase included craniopharyngioma, pinealoma, brain-stem tumor and glioblastoma multiforme, esophageal carcinoma, advanced carcinoma of the cervix, osteogenic sarcoma, Ewing's tumor, soft-tissue sarcomas and synoviomas (especially of childhood), chordomas and malignant tumors of the vertebral bodies, parotid and middle ear tumors, chest wall lesions, breast cancer, and carcinoma of the prostate. The total dose to the tumor site was between 5,000 and 7,000 rads.

Clinical trials in the mid-1970s were concerned with the establishment of a protocol and the study of technical matters such as dosimetry for the helium-ion beam and other heavy-ion therapies that were eventually used. The program at this point was supported by the U.S. Energy Research and Development Administration and by a grant from the National Cancer Institute.

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LBL-73. Studies of Human Growth and Development Involving the Use of Tritium, Sodium-24, and Iodine-131 as Tracers

FROM 1954 THROUGH THE EARLY 1970s, researchers at the Donner Laboratory, University of California Radiation Laboratory, Berkeley conducted studies of human growth and development in collaboration with several departments on the Berkeley campus, including the Institute of Human Development, the School of Optometry, the Department of Physiology-Anatomy, Medical Physics and Nutritional Sciences, and the Colwell Memorial Hospital. The researchers studied individuals who had been subjects in a series of earlier studies of the physical, physiological, and psychological aspects of childhood and adolescent growth that were initiated at Berkeley in the late 1920s and early 1930s.

The Donner Laboratory studies involved the 120 traceable participants among the Oakland Growth Study group, that in 1932 comprised about 200 male and females, who were members of the fifth grades at five schools in Oakland. This subgroup, all members in their thirties, participated in a comprehensive series of medical examinations that included about 100 different measures of physical status, body composition, urine and blood chemistries, renal and circulatory systems function, basal metabolism,

respiration, and sensory functions. Some of these tests involved the use of iodine-131 (I^{131}), tritium (H^3), and sodium-24 (Na^{24}) as tracers of the biological processes. The amounts of activity administered to each subject were not provided in the supporting documents. However, early test material mixtures contained about 0.17 millicurie of I^{131}, 2.0 millicuries of H^3, and 12.0 microcuries of Na^{24} together in 50 milliliters of water.

These studies yielded valuable information about changes in physiological measurements associated with growth, development, and the aging process. This work was funded by the U.S. Public Health Service. The Donner Laboratory was supported by the U.S. Atomic Energy Commission.

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LBL-74. Study of the Effects of Altitude on Red Cell Production and Volume Using Tritium, Phosphorus-32, and Iron-59

FROM SEPTEMBER 6 TO OCTOBER 10, 1957, researchers from Donner Laboratory, University of California Radiation Laboratory, Berkeley conducted blood studies in Bolivia using phosphorus-32 (P^{32}) and iron-59 (Fe^{59}). The purpose of the studies was to examine red cell production and volume at high altitudes. Four volunteer medical students and four Indian miners participated as subjects.

A series of tests were administered to the students in La Paz, Bolivia, and later repeated at a mountain laboratory at 17,000 feet of elevation. The same tests were administered to the miners, who had lived at an elevation of about 17,000 feet for about 4 years. Phosphorus-32 was administered in a blood volume test and Fe^{59} was administered in tests of plasma turnover, plasma volume, and red cell uptake. Tritium (H^3) was also administered in a total-body water test.

Preliminary study results showed that red cell volume has a slight tendency to increase at higher elevations, that plasma volumes remain the same, and that plasma turnover increases at higher altitudes. This work was supported by the U.S. Public Health Service and the U.S. Atomic Energy Commission, in cooperation with the University Mayor de San Andres, the High Altitude Cosmic Ray Laboratory, and the General and Labor Hospitals of La Paz, Bolivia.

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LBL-75. Estimates of Lean-Body Weight and Skeletal Size Using Tritium and X-Rays

DURING THE PERIOD from 1958 to 1959, scientists at the U.S. Naval Radiological Defense Laboratory, San Francisco and at the Donner Laboratory, University of California Radiation Laboratory, Berkeley collaborated in a study of lean-body weight and skeletal size in humans. The purpose of this study was to determine reference values for normal, healthy individuals. Thirty-one healthy Navy personnel served as subjects for a study of lean-body weight, total-body water, and skeletal size.

Total-body water was determined by the tritium space method using water labeled with an unreported amount of tritium (H^3) that was taken orally. Samples of urine were collected and analyzed for tritium activity. Using standard techniques, x-ray radiographs were taken of 22 of the same healthy subjects to determine the sizes of various skeletal structures, including the size of arm, leg, chest, and pelvis bones. The gonads received only negligible exposures, being outside the primary x-ray beam. The Donner Laboratory was supported by the U.S. Atomic Energy Commission.

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LBL-76. A Study of the Effectiveness of Silver-111 as a Tracer in Liver Functions Tests

IN APPROXIMATELY 1959, researchers from the San Francisco Veterans Administration Hospital and the University of California Medical School, San Francisco studied the human metabolism of radiosilver using silver-111 (Ag^{111}). The purpose of these studies was to determine if radioactive silver might be used as a tracer to measure liver function. The 24 study subjects included cirrhotic patients and patients with normal liver function. Ten to 30 microcuries of Ag^{111} were incubated with plasma obtained from each subject and were injected intravenously.

The results of the study showed that Ag^{111} was removed from the plasma principally by the liver, with the rate of removal being less in the cirrhotic subject than in the normals. Following maximal uptake, the clearance half-time of Ag^{111} in normal subjects was about 11 days, compared to 20 days in cirrhotic subjects. Seven of the patients involved in the study were considered terminally ill at the time of administration of the silver and subsequent autopsy specimens showed that the largest proportion of Ag^{111} in the body was deposited in the liver. One subject who had received radiosilver 8 days before death had 99.6 percent of the remaining radioactivity in the liver.

The study also showed that radiosilver was not a promising tracer for liver function assays (tests) due to the difficulty of its preparation and its long retention in the liver. The University of California Medical School, San Francisco received funding from the U.S. Atomic Energy Commission (AEC) through a contractual arrangement, and intermittently shared facilities and personnel with the AEC-funded predecessors to Lawrence Berkeley Laboratory.

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LBL-77. Iodine Uptake Studies in Thyroid Cancer Patients Using Iodine-131

DURING THE EARLY 1960s, researchers at the San Francisco and Berkeley campuses of the University of California conducted metabolic studies using iodine-131 (I^{131}) as tracers. Forty-three cancer patients at the Fort Miley Veterans Administration Hospital participated as subjects.

The studies showed that in some cancer patients, I^{131} remained in the bloodstream or concentrated in tumors and other tissues, rather than accumulate in the thyroid gland as expected. This phenomenon was described as "iodine trapping." This work was supported by the American Cancer Society and the University of California, San Francisco. The University of California Medical School, San Francisco, received funding from the U.S. Atomic Energy Commission (AEC) through a contractual arrangement, and intermittently shared facilities and personnel with the AEC-funded predecessors to Lawrence Berkeley Laboratory.

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LBL-78. Studies on Iron Loss Using Iron-59

DURING THE EARLY 1960s, researchers at the Donner Laboratory, University of California Radiation Laboratory, Berkeley conducted studies on daily total-body iron loss using iron-59 (Fe^{59}) as a tracer.

Twelve normal males ranging in age from 19 to 43 years participated as subjects. Two subjects received intravenous administration of 18 microcuries of Fe^{59} that had been incubated with plasma. Ten subjects received injections of 5 microcuries of Fe^{59} that had not been incubated with plasma. Activity was measured over the next 300 days by whole-body counting and by analysis of urine and stool samples.

These studies showed that the average daily iron loss rate was 0.03 percent, and that the whole-body counter was an accurate, simple means of measuring iron loss. This work was supported by the U.S. Atomic Energy Commission.

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LBL-79. Blood Volume Studies in Healthy Humans Using Chromium-51 as Tracer

DURING THE EARLY 1960s, scientists at the University of California Medical School, San Francisco conducted blood volume studies using chromium-51 (Cr^{51}) as tracer. The purpose of these studies was to collect data to develop standards for predicting normal values of red cell mass and plasma volumes, and to derive an equation that related blood volumes with height and weight. The subjects for this study were 17 healthy males, 101 healthy females, and 201 healthy male prison inmates.

Fifteen milliliters of each subject's blood were drawn and labeled with 50 to 200 microcuries of radioactive Cr^{51} as sodium chromate. Ten milliliters of the labeled blood were returned by intravenous administration to each subject. Blood samples were drawn within 35 minutes of administration for Cr^{51} analysis. Regression equations were derived, and from those equations, blood volume and red blood-cell volumes for males and females were estimated.

The results showed that females had a higher red cell volume and a lower plasma volume than males of comparable height and weight. The results also showed that age, physical habits, and muscularity had little influence on blood volume. This work was supported by the U.S. Public Health Service, American Heart Association, the Robert Harris Fund, and the James Edwards Memorial Fund. The University of California Medical School, San Francisco received funding from the U.S. Atomic Energy Commission (AEC) through a contractual arrangement, and intermittently shared facilities and personnel with the AEC-funded predecessors to Lawrence Berkeley Laboratory.

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LBL-80. Studies of Blood Flow to Bone Using Fluorine-18

DURING THE EARLY 1960s, researchers at the Donner Laboratory, University of California Radiation Laboratory, Berkeley conducted studies on blood flow to bone using fluorine-18 (F^{18}). The purpose of the studies was to correlate F^{18} distribution with skeletal growth rate and various disease states. One 19-year-old female with a leg fracture and four patients with Paget's bone disease participated as subjects.

Two hundred microcuries of F^{18} were administered intravenously to each subject, and the resulting activity in bone was assayed using a positron gamma camera.

The studies showed that distribution of F^{18} administered intravenously was uneven in normal skeletons, and was markedly altered in pathological conditions. Furthermore, F^{18} accumulated at fracture sites, tumor sites, and in the lesions of Paget's disease; a finding attributed to increased numbers of blood vessels (vascularity) in these areas. This work was supported in part by the U.S. Atomic Energy Commission.

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LBL-81. Blood Volume Studies Using Chromium-51 and Iodine-131 in Diagnosis of Aldosteronism

IN 1961, researchers at the University of California Department of Medicine; the Cardiovascular Research Institute; the Radioactivity Research Center; and the University of California Department of Statistics, San Francisco and Berkeley conducted blood volume studies to improve the diagnosis of hypertension and aldosteronism (a disorder caused by excessive secretion of the hormone aldosterone). An improved method for measuring total blood volume was tested on about 201 healthy male and 101 healthy female volunteers.

Samples of each subject's blood were labeled with 50 to 75 microcuries of Cr^{51} as sodium chromate, and reinjected. Samples of circulating blood were then counted for Cr^{51} activity. This method was applied as part of a study of hypertension and primary aldosteronism involving two hospital patients with aldosteronism and five patients with hypertension. Plasma volumes were also determined using iodine-131–labeled human serum albumin to allow calculation of true whole blood volume and body hematocrit (the percentage of the volume of a blood sample occupied by red cells).

The results showed that primary aldosteronism could be diagnosed by observing an increase in plasma volume with normal hematocrit. These studies were supported by the U.S. Public Health Service, the American Heart Association, and the Committee on Research of the University of California Medical School. The Radioactivity Research Center at the University of California Medical School, San Francisco was supported by the U.S. Atomic Energy Commission.

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LBL-82. Experimental Therapy for Leukemia Using Yttrium-90

IN JUNE OR JULY OF 1961, physicians at the Donner Laboratory, University of California Radiation Laboratory, Berkeley administered yttrium-90 (Y^{90}) to a 3-year-old child for treatment of acute leukemia. This resulted in an estimated 200 rads of internal radiation to the lymphatic tissue. The purpose of this effort was to treat acute leukemia with a form of Y^{90} that was thought to concentrate in lymphatic tissues.

The therapy resulted in a temporary remission with complete disappearance of all abnormal lymphocytes from the peripheral blood and bone marrow, and with little effect on the granulocytes or red cells. The Donner Laboratory was supported by the U.S. Atomic Energy Commission.

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LBL-83. Studies of Fatty Acid Metabolism Using Palmitic Acid Labeled with Carbon-14 as a Tracer

BETWEEN 1961 AND 1963, researchers at the University of California Medical School, San Francisco conducted metabolic studies using palmitic acid labeled with carbon-14 (C^{14}) as a tracer. The purpose of these studies was to examine the relationship between free fatty acids in the plasma and triglyceride fatty acids.

Two male subjects, ages 48 and 56 years, were intravenously injected with approximately 100 microcuries of palmitic acid labeled with C^{14} complexed to human serum albumin. Serial blood samples were drawn over the following 72 hours to measure C^{14} activity. This study showed that free fatty acids in the plasma are the major precursors of triglyceride fatty acids.

Palmitic acid labeled with C^{14} was used in two similar studies with different test subjects. Between January 1, 1962, and June 30, 1963, palmitic acid labeled with C^{14} was intravenously injected into young diabetic subjects hospitalized in the metabolism ward of Moffitt Hospital. In another study, a group of subjects over 40 years old received constant intravenous infusions of C^{14}-labeled palmitic acid during exercise.

This work was supported by the U.S. Public Health Service, the American Heart Association, and the Monterey and Napa Valley Heart Associations. The University of California Medical School, San Francisco received funding from the U.S. Atomic Energy Commission (AEC) through a contractual arrangement, and intermittently shared facilities and personnel with the AEC-funded predecessors to Lawrence Berkeley Laboratory.

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LBL-84. Bone Marrow Distribution of Iron Using Iron-59 and Iron-52 as Tracers

IN 1963, researchers at Donner Laboratory, University of California Radiation Laboratory, Berkeley conducted studies on bone marrow distribution using iron-59 (Fe^{59}) and iron-52 (Fe^{52}). The purpose of the studies was to evaluate methods for determining total marrow in the skeleton.

Three adult males—one normal control and two anemic patients—participated as subjects. Each received an intravenous injection of 40 microcuries of Fe^{59}. Distribution within the marrow was measured by whole-body scanning. One subject was administered an unstated amount of Fe^{52} to measure marrow distribution in selected areas of the body.

The results of these studies showed considerable peripheral extension of bone marrow after prolonged, massive stimulation. Increases in red cell production up to 13 times normal could be achieved without any great marrow extension. This work was supported in part by the U.S. Atomic Energy Commission.

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LBL-85. Physiological Studies on Mount Everest Climbers Using Iron-59 and Tritium

IN 1963, researchers at the Donner Laboratory, University of California Radiation Laboratory, Berkeley conducted high-altitude physiological studies using iron-59 (Fe^{59}) and tritium (H^3). Members of the 1963 American Mount Everest Expedition, including 17 healthy males ranging in age from 24 to 44 years, participated as subjects.

Plasma iron turnover rate, plasma volume, and red cell volume measurements were made by drawing a sample of blood, labeling it with Fe^{59}, and reinjecting it into the subject. Total body water was measured by orally administering tritium and analyzing the activity in subsequently collected urine samples. Studies were conducted both at the Donner Laboratory and in the field at various altitudes.

The studies showed increased plasma iron turnover rates and higher red cell volumes at high altitudes and a rapid decrease in red cell volume upon return to sea level. This work was supported by the U.S. Air Force Office of Scientific Research and the U.S. Atomic Energy Commission.

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LBL-86. Tumor Localization Studies Using Selenium-75, Mercury-197, Technetium-99m, and Strontium-85

IN THE MID-1960s, researchers at the Radioisotope Service; Veterans Administration Hospital; and the Radioactivity Research Center, University of California Medical School, San Francisco conducted brain scanning studies using selenium-75 (Se^{75}) in collaboration with the San Francisco Veterans Administration Hospital. The purpose of these studies was to determine whether radioactive selenium would improve diagnostic accuracy in scanning for brain and bone tumors. Fifty-two patients with intracranial disease and 25 patients with focal bone lesions participated as subjects.

Four microcuries of Se^{75} as sodium selenite per kilogram of body weight were administered intravenously to each subject, and scans were accomplished 1 to 6 days following injection. Preliminary brain scans were performed with either mercury-197 (Hg^{197}), 10 microcuries per kilo-

gram of body weight, or technetium-99m (Tc^{99m}), 100 microcuries per kilogram of body weight. Routine bone scans also were made after administration of 10 microcuries of strontium-85 (Sr^{85}).

The results of these studies showed that Se^{75} was superior to Sr^{85}, Tc^{99m}, or Hg^{197} in differentiating between brain tumors and vascular lesions, and superior also in differentiating bone tumors from non-neoplastic lesions. Because of its relatively long half-life (45 days), Se^{75} was recommended as a secondary scanning agent. The Radioactivity Research Center at the University of California Medical School, San Francisco was supported by the U.S. Atomic Energy Commission.

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LBL-87. Iron Kinetics Studies Using Iron-59

DURING THE LATE 1960s, researchers at the Donner Laboratory, University of California Radiation Laboratory, Berkeley conducted studies of erythropoiesis (red blood-cell formation and turnover) and developed new methods for investigating heme (the oxygen-carrying component of hemoglobin) synthesis and degradation in healthy and diseased subjects. The purpose of this work was to develop a simplified means of obtaining clinical information about heme synthesis, mean red-cell turnover time, and rates of iron storage exchange.

Two or more hospital patients, including a 9-year-old boy with cystic fibrosis and an enlarged spleen, participated as subjects. Each was intravenously administered plasma that had been labeled with 2 to 5 microcuries of iron-59 (Fe^{59}) as ferrous citrate. Plasma samples were obtained at 10,15, 20, 30, 45, 60, and 90 minutes following the injection to determine plasma iron-turnover rate. Whole-body scans were obtained the day after injection and again 2 weeks after injection. Plasma iron-turnover rate was determined by a blood sample at the time of the second scan. The Donner Laboratory was supported by the U.S. Atomic Energy Commission.

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LBL-88. Experimental Tumor Imaging Using Gallium-67

DURING THE LATE 1960s, researchers at the Donner Laboratory, University of California Radiation Laboratory, Berkeley in collaboration with the Oak Ridge Associated Universities, conducted studies on tumor imaging using gallium-67 (Ga^{67}). The purpose of these studies was to evaluate the effectiveness of Ga^{67} as a tumor-visualizing agent using the Anger whole-body camera, scintillation camera, and tomographic scanner. Eighteen patients, nine men and nine women with established diagnoses of malignant tumors, participated as subjects.

Approximately 4 millicuries of Ga^{67} citrate were administered to each subject by intravenous injection. In addition, one patient was administered an unspecified amount of technetium-99m for comparison of image quality using this radionuclide. Patient imaging took place over the next 6 days using cameras at various settings.

The results of these studies showed that Ga^{67} was useful in clinically evaluating the presence and distribution of malignant neoplastic tissue in humans. This work was supported by the U.S. Atomic Energy Commission.

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LBL-89. Study of Metabolic Abnormalities in Asparagine-Dependent Tumors Using Carbon-14

DURING THE LATE 1960s, researchers at the Donner Laboratory, University of California Radiation Laboratory, Berkeley used UL-L-asparagine (an amino acid) labeled with carbon-14 (C^{14}) to demonstrate and assess abnormalities in asparagine metabolism in L-asparagine–dependent tumors. The purpose of this study was to develop a method of assessing the effectiveness of treatment of this type of tumor.

Two female patients with advanced L-asparagine–dependent tumors, a nonwhite 19-year-old and a white 54-year-old, participated as subjects. They had malignant lymphatic tumors with primary bone involvement and multiple myeloma with widespread involvement of bone and organs, including the kidneys or stomach, respectively.

Each subject received 5 to 10 microcuries of C^{14}-UL-L-asparagine by intravenous injection, followed several weeks later by chemotherapy specific to their disease. Carbon-14 excretion, as measured by C^{14} activity in expired carbon dioxide ($C^{14}O_2$), was determined for each subject both before and after administration of the chemotherapy.

The percent of $C^{14}O_2$ excreted per minute was increased in both C^{14}-asparagine treated subjects after chemotherapy compared with the pre-chemotherapy values. The researchers concluded the $C^{14}O_2$ measurement method may be useful in assessing the effectiveness of treatment of this type of tumor and that it might form a basis for studying metabolic abnormalities associated with various neoplastic processes. This work was supported by the James Picker Foundation and the U.S. Atomic Energy Commission.

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LBL-90. Carbon-14 Bicarbonate Kinetics in Adult Males

AROUND 1969, researchers at the Donner Laboratory, University of California Radiation Laboratory, Berkeley conducted studies on normal bicarbonate-CO_2 excretion kinetics in resting and exercising humans.

In one study, 1.4 to 6.3 microcuries of sodium bicarbonate labeled with carbon-14 (C^{14}) as tracer were administered intravenously to 13 normal male subjects at rest, breathing normally into a breath-analysis apparatus. The $C^{14}O_2$ and total CO_2 excretion in the breath were monitored continuously in each subject for a minimum of 2 hours following injection.

In a related study, five of the same subjects were studied at rest and during physical exertion on an exercise bicycle. Before the administration of the C^{14}-bicarbonate, bicycle exercising was continued for a sufficient time to ensure that oxygen consumption and CO_2 production had reached a steady state. Two microcuries of C^{14}-labeled sodium bicarbonate were then injected intravenously; and the subject's $C^{14}O_2$ excretion was studied while the subject continued a constant level of exercise over the ensuing 2-hour period.

These studies showed that exertion of a limited group of muscles resulted in a selective increase in blood flow to these muscles without alteration of the absolute blood flow rate to unexercised muscles. This work was supported by the U.S. Atomic Energy Commission.

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LBL-91. Study of Methionine Metabolism in Folic-Acid–Deficient and Vitamin B_{12}-Deficient Patients Using Carbon-14

IN 1969, RESEARCHERS at the Donner Laboratory, University of California Radiation Laboratory, Berkeley conducted studies on metabolic abnormalities associated with deficiencies of B_{12} and folic acid, using carbon-14 (C^{14}) as a tracer.

Four patients were intravenously administered 11 to 15 microcuries of L-histidine (an amino acid) labeled with C^{14}. They then ingested various amounts of L-methionine (also an amino acid) prior to another administration of the labeled L-histidine. Their breath was analyzed for the presence of carbon dioxide labeled with C^{14}.

The results of the studies failed to show any effect of ingestion of L-methionine on the production of carbon dioxide labeled with C^{14} resulting from the administered L-histidine. This, in turn, failed to confirm in humans the results of previous animal studies. This research was supported by the U.S. Atomic Energy Commission.

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LBL-92. Visual Perception Studies Using Neutron Beams

IN THE EARLY 1970s, researchers at the Donner Laboratory, University of California Radiation Laboratory, Berkeley and the University of Washington Department of Radiology, Seattle conducted studies on the effects of neutron beam exposure on vision. The purpose of these studies was to duplicate and determine the cause of brilliant flashes and streaks reported by astronauts during space flights. Berkeley scientists had observed this effect as early as 1952.

In a 1976 follow-up experiment, six subjects were exposed to neutrons produced by the University of Washington's cyclotron. Each subject received a total dose of approximately 200 millirads during a 100-second exposure. All reported seeing colorless "stars" and "streaks," with intensity proportional to the energy level of the exposure.

In another study at the University of California at Berkeley three scientists were exposed to high-energy neutron beams produced at the Bevatron accelerator. All reported a variety of visual sensations in response to different experimental protocols.

The results of these studies suggested that the visual phenomenon experienced by astronauts was caused by interaction between the retina and alpha particles produced by neutron radiation encountered during space flight. This research was supported by the National Aeronautics and Space Administration and the U.S. Atomic Energy Commission.

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LBL-93. Nutritional Studies Using Carbon-14 as Tracer

IN 1971, RESEARCHERS at the Donner Laboratory, University of California Radiation Labora-

tory, Berkeley collaborated in nutritional studies using carbon-14 (C^{14}) as a tracer for serum glycerides in lipoproteins. The purpose of the study was to assess serum glyceride turnover rate during a period of acute weight loss to improve the understanding of lipoprotein metabolism and its role in obesity in humans. Eight obese but otherwise healthy females participated as subjects.

As part of a controlled, 63-day weight loss program, each subject was intravenously administered approximately 10 microcuries of glycerol labeled with C^{14}. Blood samples were obtained at specific time intervals and analyzed for C^{14} activity to determine glyceride turnover rate.

This study showed that glyceride turnover rate was higher for obese women than for normal-weight women. There was no significant change in turnover rate during periods of significant weight loss. This research was supported in part by the U.S. Atomic Energy Commission.

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Lawrence Livermore National Laboratory

LLNL-1. *In Vivo* Calibration Studies Using Humans Administered Niobium-92m, Barium-133, Palladium-103, Chromium-51, and Strontium-85

THE PURPOSE OF these studies was to develop accurate calibration factors for *in vivo* counting equipment and to cross-calibrate the various U.S. and European counting centers. Volunteer subjects were administered radionuclides at Harwell Laboratory (United Kingdom) and were whole-body or chest counted at the Lawrence Livermore National Laboratory and at other Department of Energy contractor *in vivo* counting facilities in the United States. Two subjects were from Lawrence Livermore Laboratory and the remainder were from the United Kingdom.

This study was broad in scope and spanned several years. From 1972 to 1976, three males inhaled palladium-103 and chromium-51–labeled microspheres and were counted in 14 labs in Europe and the United States. From 1979 to 1985, 19 men and women inhaled niobium-92m (Nb^{92m})–labeled microspheres and were counted at several labs. During the 1986 to 1988 period, two males were injected with barium-133; one of the two was also injected with strontium-85. During the 1988 to 1990 period, eight males (including five who earlier had inhaled Nb^{92m}) were exposed to Nb^{92m} and counted.

This research was jointly sponsored by the Atomic Energy Research Establishment—Harwell, British Nuclear Fuels, the General Electricity Generating Board, the International Atomic Energy Agency, and the U.S. Department of Energy (and its predecessor agencies). (Previously described in #15 on the original list of 48 experiments released by DOE in June 1994; included in *The DOE Roadmap* of February 1995, and since revised).

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LLNL-2. Ozone Effects on Overall and Regional Lung Function Using Nitrogen-13 and Oxygen-15

IN THIS COLLABORATION between the University of Washington, Seattle and Lawrence Livermore National Laboratory, the impact of ozone on the human lungs was studied. The objective was to determine the functional changes that might result from low ozone levels in smog.

Four healthy, male subjects were exposed to 0.4 part per million by volume concentrations of nonradioactive ozone for a total of 2.5 hours. Periods of exercise and rest were alternated during the exposure. The subjects then inhaled small quantities of radioisotope-labeled gas mixtures for the purpose of measuring lung function. The mixtures were similar to air, with an oxygen-to-nitrogen ratio of roughly 1 to 4; however, in the first mixture, a small amount of the nitrogen was a radioactive tracer, nitrogen-13. The second mixture contained a few percent of radioactive oxygen-15–labeled carbon dioxide.

The results of this test suggested that ozone caused nonuniform mechanical alteration to the central and peripheral airways. The study was performed under a contract from the U.S. Department of Energy from 1977 to 1978 and in part by a grant from the National Heart, Lung, and Blood Institute. (Previously described in #16 on the original list of 48 experiments released by DOE in June 1994; included in *The DOE Roadmap* of February 1995, and since revised.)

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LLNL-3. Decompression Sickness Studies Using Nitrogen-13 and Argon-41

THE LAWRENCE LIVERMORE NATIONAL LABORATORY and the U.S. Navy conducted studies during the 1980s using the radionuclide tracers nitrogen-13 (N^{13}) and argon-41 (Ar^{41}) to acquire information on the uptake and clearance of nitrogen gas in man. This research was performed to better understand decompression sickness of deep-sea divers; such sickness is thought to result from excessive accumulation of nitrogen in divers' bodies.

In these studies, a total of 11 healthy subjects (Navy volunteers) breathed air containing N^{13}; 2 of the 11 also breathed air containing Ar^{41} tracers. Each subject was monitored using gamma detectors to determine the concentration and location of the radioactive tracers contained in the subject's body as a function of time after uptake. The amounts of N^{13} and Ar^{41} inhaled depended on the amounts breathed by the sub-

jects. This air contained a few millicuries of N^{13} and a few dozen microcuries of Ar^{41} per liter of breathing air. Absorbed doses to subjects were estimated to be about 0.3 to 0.5 rad to the lungs and trachea and 0.01 rad to the whole body.

This work was supported by the Naval Medical Research Institute and the U.S. Department of Energy. (Previously described in #14 on the original list of 48 experiments released by DOE in June 1994; included in *The DOE Roadmap* of February 1995, and since revised)

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Los Alamos National Laboratory

LANL-1. Tritium Studies at Los Alamos Scientific Laboratory

DURING THE EARLY 1950s, Los Alamos Scientific Laboratory conducted studies on the human uptake, distribution, and retention of tritium (H^3). Three volunteers, all researchers working on the studies, participated as subjects. In one experiment, a male subject immersed his arm up to the elbow in water containing 0.1 millicurie of tritium per milliliter. This study showed that the rate of absorption through the skin was too slow to pose a hazard. The whole body would have to be immersed for more than 1 hour before the U.S. Atomic Energy Commission-recommended exposure limit was reached.

In another study, all three subjects inhaled for 4 to 5 minutes oxygen that was saturated with tritium water vapor (HTO) which, when condensed, contained 1.16 millicuries of tritium per milliliter of water. Results showed that 98 to 99 percent of the tritium was retained in the body after inhalation.

In a third study, the three subjects drank water containing tritium. Water volumes ranged from 100 to 1,000 milliliters (.33 to 4 cups) and level of activity ranged from 1,640 to 2,920 microcuries.

These studies showed that water absorption from the gastrointestinal tract begins 2 to 9 minutes after ingestion, that absorption is a linear function of time, and that absorption is proportional to the amount ingested. All these studies were used to establish standards for occupational exposure to tritium. This work was supported by the U.S. Atomic Energy Commission. (These experiments were referenced in the Markey report and included in *The DOE Roadmap* of February 1995)

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Pinson, E.A. *Lung Absorption of HTO by Man Upon Inspiration of HTO Water Vapor.* Los Alamos, NM: Los Alamos Scientific Laboratory, LA-1465, June 1952.

Pinson, E.A. *The Body Absorption of Ingested Tritium Water and the Water Dilution Volume of Man.* Los Alamos, NM: Los Alamos Scientific Laboratory, LA-1464, June 1952. ❑

LANL-2. Metabolism of EDTA in Humans Using Carbon-14

IN 1953, Los Alamos Scientific Laboratory conducted studies on the human metabolism of the chelating agent ethylenediaminetetraacetic acid (EDTA) labeled with carbon-14 (C^{14}). The purpose was to gain information that would help establish optimum dosage schedules and identify any harmful effects.

Twelve young healthy men served as subjects in four groups of three. One group was administered an intravenous injection of 2.2 milligrams of C^{14}-labeled EDTA; the second received an intramuscular injection of 2.2 milligrams; the third received oral administration of 1.5 milligrams; and the fourth group had 2.0 milligrams applied directly to the skin.

The studies showed that EDTA passed through the body essentially unchanged and that it was

excreted primarily by the kidney within 1 hour of intravenous injection and 1.5 hours after intramuscular injection. EDTA is poorly absorbed in the gastrointestinal tract and practically not at all through the skin. This work was supported by the U.S. Atomic Energy Commission. (Previously described in #43 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

References

Foreman, H., and T.T. Trujillo. "The Metabolism of C^{14} Labeled Ethylenediaminetetraacetic Acid in Human Beings." *The Journal of Laboratory and Clinical Medicine*. Vol. 43, No. 4, pp. 566–571.

Biomedical Research Group of the Health Division Annual Report 1953. Los Alamos, NM: Los Alamos Scientific Laboratory, LA-1690, 1954, p. 17. ❑

LANL-3. Radiation Exposure of Aircrews in Mushroom Clouds

DURING THE 1955 TEAPOT and the 1956 REDWING nuclear test series, manned aircraft were used to map the amount and distribution of radiation within some of the resulting "mushroom" clouds. The objective was to obtain information needed to plan for the safe and effective use of military aircraft in cloud areas during combat operations.

Studies conducted in 1953 using animal subjects in drone aircraft had previously shown that it would be safe for manned aircraft to enter atomic clouds relatively soon after detonation. Penetrations of clouds from low-yield detonations were made during Operation TEAPOT in 1955. Penetrations of the larger clouds from high-yield detonations were made during Operation REDWING in 1956. Special radiation exposure limits, in excess of the usual 3.9 roentgens maximum permissible exposure limit, were established for some of these flight crews.

During Operation TEAPOT, four Air Force officers were permitted to receive up to 15 roentgens, and two received this amount. Exposures of up to 25 roentgens were permitted during Operation REDWING, but no one received this amount. The largest exposures were approximately 15 roentgens for three officers.

Pre- and post-mission urine tests and evaluation in whole-body counters showed no significant internal deposition of fission products or unfissioned plutonium. This work was supported by the U.S. Atomic Energy Commission. (This experiment was referenced in the Markey report and included in *The DOE Roadmap* of February 1995)

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Headquarters Field Command. "Early Cloud Penetrations." *Report of Operation REDWING Project 2.66a.* Armed Forces Special Weapons Center, WT-1320. Reynolds Electrical and Engineering Co., Inc., Coordination and Information Center, Las Vegas, NV, CIC Document 68117.

Headquarters Field Command. "Manned Penetration of Atomic Clouds." *Report of Operation TEAPOT Project 2.8a.* Armed Forces Special Weapons Center, WT-1156. Reynolds Electrical and Engineering Co., Inc., Coordination and Information Center, Las Vegas, NV, CIC Document 12800.

Headquarters Field Command. "The Radiation Hazards to Personnel Within an Atomic Cloud." *Report of Operation UPSHOT/KNOTHOLE Project 4.1.* Armed Forces Special Weapons Center, WT-743. Reynolds Electrical and Engineering Co., Inc., Coordination and Information Center, Las Vegas, NV, CIC Document 40992. ❑

LANL-4. Determination of the Survival Time of Red Blood Cells by Chromium-51 Labeling

A STUDY WAS CONDUCTED by Los Alamos Scientific Laboratory in 1957 to determine the survival times of circulating red blood cells in healthy and diseased subjects. Thirty-two subjects (7 healthy and 25 diseased) received intravenous injection of samples of their own red blood cells that had been previously removed and tagged with radioactive chromium-51.

After tagging, the red cells were injected back into the donor, and the person's uptake and radioactivity were assessed in the whole-body counter. Half-times for the survival of the chromium tag were determined. Large volumes of urine were also obtained from the subjects and counted to determine excretion rates. This research was supported by the U.S. Atomic Energy Commission. (Previously described in #26

on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

References

"Application of Low Level *In Vivo* Counting Techniques to Clinical Investigations." *Annual Report of the Health Division 1957.* Los Alamos, NM: Los Alamos Scientific Laboratory, LA-2216, pp. 62–63. ❑

LANL-5. Studies of the Metabolism and Excretion of Alkali Metal Radionuclides in Humans

SCIENTISTS AT THE Los Alamos Scientific Laboratory conducted a series of studies to determine the metabolism and excretion of alkali metals as part of a general research program on the retention, excretion, and absorption of radioactive materials in humans.

Sodium-22, potassium-42, and rubidium-86 were administered orally to 10 normal, healthy subjects and were measured at various times thereafter in the whole-body counter. The distribution and retention patterns for these materials were determined periodically for about 1 year. Radiocesium was also administered and measured. These experiments are described separately, under LANL-8. This research was supported by the U.S. Atomic Energy Commission. (Previously described in #25 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

References

Richmond, C.R. "Retention and Excretion of Radionuclides of the Alkali Metals by Five Mammalian Species." *Biological and Medical Research Group of the Health Division Semiannual Report July–December 1959.* Los Alamos, NM: Los Alamos Scientific Laboratory, LAMS-2445, 1960, pp. 71–79. ❑

LANL-6. Absorption and Retention of Orally Administered Iron-59 in Humans

THIS STUDY WAS conducted at Los Alamos Scientific Laboratory in 1959. The purpose was to determine the absorption and retention of orally administered iron in subjects. A second objective was to evaluate the whole-body counting technique and equipment as a tool for measuring iron in the human body.

Sixty-six subjects were part of this test, including one pregnant woman and four children. Also included in the study were hospital patients with anemia, leukemia, or polycythemia rubra vera. Each of the study participants ingested 0.5 to 0.7 microcurie of iron-59 as ferrous citrate in water. The oral dose was followed with an additional 100 to 200 milliliters of tap water to wash the radioactive iron into the stomach. Body counting and fecal bioassay were used to determine the relationship between ingested, retained, and excreted iron.

The study showed that there was an apparent lack of iron absorption with leukemia and infection. Also, the pregnant woman absorbed larger amounts of iron. This study was supported by the U.S. Atomic Energy Commission. (Previously described in #40 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

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Lushbaugh, C.C., and D.B. Hale. "Clinical Applications of Whole-Body Counting: A Clinical Comparison of the Absorbability of Ferrous versus Ferric Salts in Normal Human Subjects." *Biological and Medical Research Group of the Health Division Semiannual Report July–December 1959.* Los Alamos, NM: Los Alamos Scientific Laboratory, LAMS-2445, 1960, pp. 337–347.

Lushbaugh, C.C., and D.B. Hale. "Determination of Absorbability of Oral Radioiron in Health and Disease in Man by Whole-Body Scintillometry." In *Radioactivity in Man Symposium.* Chicago, 1962. pp. 417–429. ❑

LANL-7. Determining Thyroid Uptake and Retention of Iodine-131

IN 1959, Los Alamos Scientific Laboratory conducted studies on whole-body measurement techniques for determining thyroid uptake of iodine-131 (I^{131}).

Seventeen normal subjects or patients, both men and women, ranging in age from 10 to 57,

drank water solutions containing 1.5 to 3.0 microcuries of I^{131} as sodium iodide. Study results showed that the whole-body liquid scintillation measurement technique together with a 3x3-inch collimated sodium iodide thyroid probe, provided a simple, valid means of determining whole-body iodide retention, thyroid uptake, and thyroid function.

Additional studies were conducted to address how thyroid retention changed with disease, chemotherapy, and metabolic status. These studies involved some of the same patients, but also added others. Six children whose thyroid gland had been removed were added, as was one patient with an overactive thyroid and another with an underactive thyroid. A total of 63 patients were administered I^{131} either orally or intravenously.

These studies showed that retention rates in diseased patients varied widely from normal rates, and that retention of I^{131} was influenced by therapy. This work was supported by the U.S. Atomic Energy Commission. (Previously described in #45 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995 and since revised.)

References

Lushbaugh, C.C., and D.B. Hale. "Clinical Applications of Whole-Body Scintillometry. III. Whole-Body Retention of Iodine-131 as a Method of Studying Thyroid Function in Man." *Biological and Medical Research Group of the Health Division Semiannual Report July–December 1959.* Los Alamos, NM: Los Alamos Scientific Laboratory, LAMS-2445, 1960, pp. 361–373.

Lushbaugh, C.C., and P.S. New. "Clinical Applications of Whole-Body Scintillometry. II. A Comparison of Three Different Methods of Determining Retention and Thyroid Uptake of Orally Administered I^{131}." *Biological and Medical Research Group of the Health Division Semiannual Report July–December 1959.* Los Alamos, NM: Los Alamos Scientific Laboratory, LAMS-2445, 1960, pp. 348–360. ❑

LANL-8. Long-Term Retention of Cesium-134 and Cesium-137 in Humans

FROM APPROXIMATELY 1959 to 1961, a study was conducted at the Los Alamos Scientific Laboratory on the long-term retention of radioactive cesium in humans. Four healthy, adult males participated in this study.

Two of the subjects received oral doses of 1 and 1.4 microcuries of cesium-134 (Cs^{134})as cesium chloride. The subjects were followed by whole-body counting for 106 and 910 days, respectively, to determine the gastrointestinal tract uptake and whole-body. The other two subjects were administered about 1 microcurie of cesium-137 (Cs^{137}) and were followed by whole-body counting for about 500 days.

This study showed that the biological retention half-time of cesium in humans was about 137 days. This work was supported by the U.S. Atomic Energy Commission. (Previously described in #25 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

References

Richmond, C.R., J.E. Furchner, and W.H. Langham. "Long-Term Retention of Radiocesium by Man." *Biological and Medical Research Group of the Health Division Semiannual Report January–June 1961.* Los Alamos, NM: Los Alamos Scientific Laboratory, LAMS-2627, 1961, pp. 163–174. ❑

LANL-9. Study of the Retention and Excretion of Iodine-131

IN 1960, a study was performed at Los Alamos Scientific Laboratory to determine the retention and excretion of iodine-131 (I^{131}). Twenty-six normal subjects, including 17 women, 3 men, 3 girls, and 3 boys participated in the study. Each volunteer was given an oral dose of liquid containing 8 microcuries of I^{131} as sodium iodide, and then measured for whole-body and thyroid content of I^{131} within 1 hour. Additional measurements were made on the 1st, 2nd, 3rd, 4th, 7th, 10th, 14th, and 18th days following the ingestion.

This study showed that approximately 20 percent of the ingested I^{131} was taken up by the thy-

roid gland, and the remaining 80 percent was excreted in the urine by the kidneys. This research was supported by the U.S. Atomic Energy Commission. (Previously described in #19 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

References

Lushbaugh, C.C., D.B. Hale, and C.R. Richmond. "Clinical Applications of Whole-Body Scintillometry. IV. Turnover Rate of Protein-Bound Iodide." *Biological and Medical Research Group of the Health Division Semiannual Report January–June 1960.* Los Alamos, NM: Los Alamos Scientific Laboratory, LAMS-2455, 1960, pp. 364–371. ❑

LANL-10. Absorption and Uptake of Iodine-131 and Sodium-24 in Humans

IN 1960, an experiment was conducted at Los Alamos Scientific Laboratory to determine the feasibility of *in vivo* measurements to study the absorption of radionuclides through the skin.

Liquid solutions of 10 microcuries of sodium-24 (Na^{24}) or 51 microcuries of iodine-131 (I^{131}) were placed on the palms of two volunteer subjects employed at the Laboratory. After allowing absorption to occur, the palms were washed and the subjects were counted periodically in the Laboratory's whole-body counter to determine the fraction of either radionuclide absorbed through the skin.

In a second experiment, two volunteer subjects ingested 0.18 microcurie of Na^{24} or 0.14 microcurie of I^{131} to determine the gastrointestinal absorption and whole-body retention of these radionuclides. This research was supported by the U.S. Atomic Energy Commission. (Previously described in #27 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

References

Van Dilla, M.A., C.R. Richmond, and J.E. Furchner. "Cutaneous Absorption by Human Subjects, I. Studies with Sodium-24 and Iodine-131." *Biological and Medical Research Group of the Health Division Semiannual Report July–December 1960.* Los Alamos, NM: Los Alamos Scientific Laboratory, LAMS-2526, 1961, pp. 164–171. ❑

LANL-11. Retention of Iodine-131 in Subjects with Inflammatory Liver Disease

IN 1960, A STUDY was conducted at Los Alamos Scientific National Laboratory on the use of an iodine-131 (I^{131})–labeled blood dye in determining liver function.

Ten normal subjects and 18 persons suffering from inflammatory hepatic disease were injected intravenously with 10 microcuries of I^{131}-labeled dye (rose bengal). The time/activity curves for retention of I^{131} in the bloodstream were determined, using the Los Alamos arm counter.

The blood retention curve was found to be a better measurement of liver function than the clearance rate of labeled rose bengal dye measured in urine. This research was supported by the U.S. Atomic Energy Commission. (Previously described in #28 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

References

Lushbaugh, C.C., D.B. Hale, and R. McGill. "The Use of the Arm Counter to Determine the Degree of Hepatic Function." *Biological and Medical Research Group of the Health Division, Semiannual Report January–June 1960.* Los Alamos, NM: Los Alamos Scientific Laboratory, LAMS-2455, 1960, pp. 223–229. ❑

LANL-12. Gastrointestinal Passage of Radioactive Particles Containing Manganese-54 and Uranium-235

IN THE EARLY 1960s, Los Alamos Scientific Laboratory conducted studies on the passage of radioactive particles through the human gastrointestinal tract. These studies addressed the issue of reentry and destruction of nuclear-powered space vehicles in the earth's atmosphere and subsequent ingestion of the resulting airborne particles by humans.

Fifty-seven normal adults participated. Each subject swallowed a gelatin capsule containing three radioactive particles. One particle was ceramic, about 150 microns in diameter, and contained approximately 150 picocuries of manganese-54. The other two particles were uranium carbide, about 175 microns in diameter, and contained an unspecified amount of uranium-235 activity. The total calculated radiation dose delivered to the gastrointestinal tract in these studies was extremely low—well below the maximum permissible level for these materials. Several subjects repeated the ingestion at different times of day to estimate the time-of-day variations. One subject repeated the test 10 different times to estimate the variation within a single individual.

The studies showed that particle density did not influence passage rate and that there was no significant holdup of particles in the digestive system. Transit times corresponded to individual bowel movement characteristics. This work was supported by the U.S. Atomic Energy Commission. (This experiment was referenced in the Markey report and included in *The DOE Roadmap* of February 1995.)

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Some Biological Aspects of Radioactive Microspheres. Los Alamos, NM: Biological and Medical Research Group, Los Alamos Scientific Laboratory, LA-3365-MS, June 20, 1965. ❑

LANL-13. Metabolism of Zinc-65 in Human Leukemia

A STUDY WAS CONDUCTED at Los Alamos Scientific Laboratory in early 1961 on the metabolism of zinc-65 (Zn^{65}) in human cancer patients with chronic leukemia. This experiment involved a single subject. A 15-year-old female patient with chronic myelogenous leukemia was given an oral dose of 0.6 microcurie of zinc-65 (Zn^{65}) as zinc chloride 137 days prior to death. One hour after administration and on days 1, 2, 3, 20, and 137 the subject was studied for whole-body Zn^{65} in the Los Alamos human counter. In addition, tissue samples were removed at autopsy and sampled for Zn^{65}.

The findings of this study showed that Zn^{65} was retained less tenaciously by the leukemia patient than by previously studied normal subjects. (See LANL-15.) This work was supported by the U.S. Atomic Energy Commission. (Previously described in #32 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

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Furchner, J.E., and C.R. Richmond. "Effect of Dietary Zinc on the Absorption of Orally Administered Zn^{65}." *Health Physics.* Vol. 8, 1962, pp. 35–40.

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Richmond, C.R., C.C. Lushbaugh, M.W. Rowe, and M.A. Van Dilla. "Metabolism of Zinc-65 in a Terminal Leukemia Case." *Biological and Medical Research Group of the Health Division Semiannual Report January–June 1961.* Los Alamos, NM: Los Alamos Scientific Laboratory, LAMS-2627, 1960, pp. 263–269.

Richmond, C.R., J.E. Furchner, G.A. Trafton, and W.H. Langham. "Comparative Metabolism of Radionuclides in Mammals-I: Uptake and Retention of Orally Administered Zn^{65} by Four Mammalian Species." *Health Physics.* Vol. 8, 1962, pp. 481–489. ❑

LANL-14. Iodine-131 Used to Determine Thyroid Uptake Measurement Techniques

IN 1961, Los Alamos Scientific Laboratory conducted studies intended to improve the accuracy of whole-body counting techniques for determining thyroid uptakes. Previous experience had shown that body mass influenced overall absorption and affected the accuracy of thyroid uptake measurements.

An unspecified number of subjects received oral administration of 8 microcuries of iodine-131. A

"mock iodine" mixture of barium-133 and cesium-134 equal to 2.48 microcuries was also administered to establish a control standard.

The results of these studies were used to establish normal human absorption values for men, women, and children of various ages. (Previously described in #45 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

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Lushbaugh, C.C. "Progress in Refinement of the Whole-Body Counting Technique for Determining Thyroid Uptake." *Biological and Medical Research Group of the Health Division Semiannual Report January–June 1961.* Los Alamos, NM: Los Alamos Scientific Laboratory, LAMS-2627, 1961, pp. 291–297. ❑

LANL-15. Uptake and Retention of Zinc-65

DURING 1961 AND 1962, a study was conducted at Los Alamos Scientific Laboratory on the uptake and retention of radioactive materials by subjects. Three males and one female between the ages of 29 and 48 received a single oral dose of 0.6 to 1.0 microcurie of zinc chloride in water. The subjects were evaluated for whole-body distribution and retention of zinc-65 (Zn^{65}) with time. These measurements were made in the Los Alamos whole-body center. Urine and feces were also obtained and analyzed for Zn^{65}. Measurements continued 416 to 664 days after the administration of Zn^{65}. These data were used to determine the retention and excretion of Zn^{65} in men and women for comparison with other animal species. This study was supported by the U.S. Atomic Energy Commission. (Previously described in #32 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

References

Richmond, C.R., J.E. Furchner, G.A. Trafton, and W.H. Langham. "Comparative Metabolism of Radionuclides in Mammals: I. Uptake and Retention of Orally Administered Zn^{65} by Four Mammalian Species." *Health Physics.* Vol. 8, 1962, pp. 481–489. ❑

LANL-16. Iron-59 Absorption in Normal Human Subjects

FROM MID-1961 TO MID-1962, a study was conducted at the Los Alamos Scientific Laboratory on the absorption of iron by normal subjects. The objective of the study was to determine whether the ferrous or ferric form was more readily absorbed.

A group of volunteers composed of 20 normal men and 30 normal women was included in the study. The subjects were divided randomly into two subgroups. Each subject received 0.27 microcurie of iron orally. Some received the iron in the form of ferrous citrate labeled with iron-59 (Fe^{59}). The others received the iron in the form of ferric chloride labeled with Fe^{59}. A whole-body count was performed immediately after ingestion and again 7 days later. At the time of the second body count, blood samples were drawn and characterized.

No difference was found in human uptake between the ferrous and ferric forms of iron. This study was supported by the U.S. Atomic Energy Commission. (Previously described in #40 on the original list of 48 experiments released by DOE in June 1994)

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Lushbaugh, C.C., and D.B. Hale. "Clinical Applications of Whole-Body Scintillometry I. Retention of Orally Administered Iron." *Biological and Medical Research Group of the Health Division Semiannual Report July–December 1959.* Los Alamos, NM: Los Alamos Scientific Laboratory, LAMS-2445, 1960, pp. 337–347.

Lushbaugh, C.C., and D.B. Hale. "Determination of Absorbability of Oral Radioiron in Health and Disease in Man by Whole-Body Scintillometry." In *Radioactivity in Man Symposium.* Chicago, 1962, pp. 417–429. ❑

LANL-17. Cutaneous Absorption of Strontium-85

FROM 1961 TO 1962, Los Alamos Scientific Laboratory conducted studies on the absorption of strontium-85 (Sr^{85}) through human skin. Radioactive strontium chloride was applied in a gauze patch to the forearm of two subjects and held in place with adhesive tape. The amount of Sr^{85}

administered was about 70 microcuries. After 2 days, one subject had absorbed 0.2 percent and the other had absorbed 0.6 percent.

The study showed that absorption through the skin occurred, but at very low levels. This work was supported by the U.S. Atomic Energy Commission. (Previously described in #44 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

References

Van Dilla, M.A., C.R. Richmond, J.E. Furchner, and M.W. Rowe. "Cutaneous Absorption of Radionuclides by Human Subjects. II. Strontium-85." *Biological and Medical Research Group of the Health Division Annual Report July 1961–June 1962.* Los Alamos, NM: Los Alamos Scientific Laboratory, LAMS-2780, 1962, pp. 154–157. ❑

LANL-18. Retention of Strontium-85

FROM 1961 TO 1962, Los Alamos Scientific Laboratory conducted studies on the whole-body retention of strontium-85 (Sr^{85}) in humans. Three male laboratory employees ingested 1.07 microcuries of Sr^{85} in 100 milliliters of tap water.

The studies showed that Sr^{85}, with its 65-day half-life, is suitable for studying short-term retention of fallout but not appropriate for long-term retention studies. This work was supported by the U.S. Atomic Energy Commission. (Previously described in #44 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

References

Furchner, J.E., M.A. Van Dilla, M.W. Rowe, and C.R. Richmond. "Retention of Strontium-85 by Man." *Biological and Medical Research Group of the Health Division Annual Report July 1961–June 1962.* Los Alamos, NM: Los Alamos Scientific Laboratory, LAMS-2780, 1962, pp. 43–49. ❑

LANL-19. Studies on the Retention of Iodine-131 in Humans

FROM 1961 TO 1962, Los Alamos Scientific Laboratory conducted studies on the retention of radioiodinated para-toluidine polyvinylpyrrolidone, also known as PVP-I^{131}. The purpose of the study was to determine whether PVP-I^{131} could be used to detect the presence of vascular leaks into the gastrointestinal or renal excretory tracts.

Eight adults were injected intravenously with 0.7 microcurie of PVP-I^{131}. Four of the subjects had medical conditions that included known internal bleeding. The study showed that the bleeding subjects lost the iodine more rapidly than the nonbleeding subjects—in one case, almost twice as fast—indicating that PVP-I^{131} was an effective detector of internal bleeding.

In a related study, one of these subjects drank a water solution containing 0.06 microcurie of PVP-I^{131} to determine retention in the thyroid gland. The study showed little retention, indicating that PVP-I^{131} is not readily absorbed. This work was supported by the U.S. Atomic Energy Commission. (Previously described in #45 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

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Lushbaugh, C.C., and D.B. Hale. "Clinical Applications of Whole-Body Counting: Retention of Raovin Iodine-131 as a Measure of Serum or Blood Loss." *Biological and Medical Research Group of the Health Division Annual Report July 1961–June 1962.* Los Alamos, NM: Los Alamos Scientific Laboratory, LAMS-2780, 1962, pp. 188–193. ❑

LANL-20. Thyroid Function Studies Using Sodium Iodide-131

FROM 1961 TO 1962, Los Alamos Scientific Laboratory conducted studies on human thyroid function using iodine-131 (I^{131}) administered as sodium iodide. At least two adult females received 0.5 microcurie by oral administration. Tests were repeated several times in combination with various drugs and uptakes were measured and compared.

These studies showed which drug therapies were most effective in treating thyroid disorders. This work was supported by the U.S. Atomic Energy Commission. (Previously described in #45 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

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LANL-21.

(Essentially a duplicate of LANL-15 in *The DOE Roadmap*)

LANL-22. Cesium-132 Metabolism in Humans

FROM 1962 TO 1963, a study was conducted at Los Alamos Scientific Laboratory to determine the retention and excretion of cesium-132 (Cs^{132}) in humans. The subjects were three male and one female normal, young adults in good health. These subjects were injected intravenously with 0.65 microcurie of Cs^{132} as cesium chloride. Three of the subjects were counted approximately 30 times over a 45-day period. Whole-body retention of Cs^{132} was determined by measurements of the subjects in the Laboratory's whole-body counters. This research was supported by the U.S. Atomic Energy Commission. (Previously described in #25 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

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Richmond, C.R., J.E. London, and J.E. Furchner. "Retention of Intravenously Administered Cesium-132 by Man." *Biological and Medical Research Group of the Health Division Annual Report July 1962–June 1963.* Los Alamos, NM: Los Alamos Scientific Laboratory, LAMS-3034, 1963, pp. 21–33. ❑

LANL-23. Thyroid Studies Using Small Amounts of Iodine-125 and Iodine-131

IN APPROXIMATELY 1963, Los Alamos Scientific Laboratory conducted studies on thyroid metabolism, using very small amounts of iodine-125 (I^{125}) and iodine-131 (I^{131}). The purpose was to determine the retention of iodine in the thyroid as a function of time, with a particular interest in radioiodine metabolism in children. Nineteen normal male and female subjects ranging in age from 4 to 46 drank approximately 10 nanocuries each of I^{125} and I^{131} mixed together in water.

Subsequent measurements showed that there was little difference in radioiodine metabolism between children and adults. This work was supported by the U.S. Atomic Energy Commission. (Previously described in #45 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

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Van Dilla, M.A., and M.J. Fulwyler. "Thyroid Metabolism in Children and Adults Using Very Small (Nanocurie) Doses of Iodine-125 and Iodine-131." *Health Physics.* Vol. 9, 1963, pp. 1,325–1,331.

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LANL-24. Studies of the Metabolism of Antituberculous Drugs Using a Carbon-14 Tracer

IN 1959, Los Alamos Scientific Laboratory scientists collaborated with physicians at the Department of Public Health and Preventive Medicine, Cornell University, New York Hospital Medical Center on a series of studies on the effects of certain drugs on the metabolism of isoniazid, a drug for treatment of tuberculosis.

Of the seven study subjects, five (four males and one female, ages 25 to 80 years) were Navajo Indian patients in the U.S. Public Health Service Hospital at Fort Defiance, Arizona. Two of the males were nontubercular and had no prior history of isoniazid therapy. Two other sub-

jects (one white, age 52 years, and one Hispanic, age 36 years) were tuberculosis patients in the Los Alamos Medical Center.

Intramuscular injections of 186 to 327 microcuries carbon-14 (C^{14})–labeled isoniazid chloride, followed by at least 100 milligrams of unlabeled isoniazid were administered to each subject. Four subjects received one or two repeat injections of C^{14}-labeled isoniazid at intervals of up to 5 weeks in combination with streptomycin and oral para-aminosalicylic acid (PAS). Two of these subjects also received oral pyridoxine.

These studies showed that labeled isoniazid was rapidly excreted in the urine (up to 95 percent in the first 24 hours). The metabolic products of isoniazid were found to be acetylisoniazid and isonicotinic acid. Neither pyridoxine nor PAS had an appreciable effect on isoniazid plasma turnover time or on urinary excretion rate. This work was supported by the U.S. Atomic Energy Commission, and in part by grants from the Navajo Tribal Council, the American Thoracic Society, and the U.S. Public Health Service.

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LANL-25. Clinical Applications of Whole-Body Scintillometry for Determining Cobalt-60–Labeled Vitamin B_{12} Absorption and Retention

STUDIES WERE CONDUCTED in 1961 at the Los Alamos Scientific Laboratory to determine the absorption and retention of vitamin B_{12} labeled with cobalt-60 (Co^{60}) in humans. Because of observed problems in the collection and measurement of excreta, the purpose of these studies was to determine the metabolism and turnover rate of vitamin B_{12} using the whole-body counter.

The subjects in this study were three healthy people and one patient with severe degenerative disease of the posterio-lateral columns of the spinal cord. Each subject was given 0.5 microcurie of Co^{60}-vitamin B_{12} orally. One hour after ingestion, each subject was given 1,000 micrograms of unlabeled vitamin B_{12} intramuscularly as a flushing dose. Each subject was then counted daily in the whole-body counter (HUMCO I) for the first week after ingestion and at frequent intervals throughout the following month.

The results of this study showed that the malabsorption of Co^{60}-vitamin B_{12} was easily measured using whole-body counting techniques. This work was supported by the U.S. Atomic Energy Commission.

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Oak Ridge Sites

OR-1. Early Gallium-72 Studies in Nuclear Medicine

STARTING IN ABOUT 1950, the Oak Ridge Institute of Nuclear Studies (ORINS) conducted studies

on the potential therapeutic uses of gallium-72 (Ga^{72}) in human subjects. Previous animal experiments at ORINS indicated that Ga^{72} might be effective in the treatment of bone tumors. Therefore, patients with various kinds of malignant bone tumors were studied with Ga^{72}.

Two types of studies were conducted among male and female patients referred to ORINS in 1950 and 1951; most of these 54 patients had late-stage (terminal) disease that was not amenable to surgery or external irradiation therapy.

In one study, 50 to 100 millicuries of Ga^{72} were administered intravenously to 21 patients with some hope of therapeutic benefit. In the other study, lesser amounts (10 to 50 millicuries) of Ga^{72} were administered to 34 other, similar patients, to determine the metabolism and biodistribution patterns of intravenously administered Ga^{72} in man. Several adverse reactions, typical of radiation toxicity, were observed in patients receiving greater than 50 millicuries of Ga^{72}.

These studies indicated that Ga^{72} was not suitable for therapy of bone tumors. As a result, subsequent studies focused on other isotopes, such as Ga^{67} or Ga^{68}. This work was supported by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995, and since revised.)

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OR-2. Colloidal Gold-198 Studies at Oak Ridge

IN THE 1950s, colloidal gold-198 was studied at the Oak Ridge Institute of Nuclear Studies for potential diagnostic and therapeutic applications in nuclear medicine. Colloidal gold-198 (Au^{198}) was administered intravenously in a therapeutic trial to terminally ill cancer patients to determine its metabolism and biodistribution.

More than 44 male and female patients with different types of cancer, including 6 with liver cancer and 8 with leukemia, were included in this study between 1949 and 1953. Gold-198 was administered in various amounts over the course of the patient's disease in the hope of demonstrating a therapeutic effect. In addition, activities of 2.3 to 33.0 millicuries were administered just prior to death to enhance the isotope concentrations in tissues and to study the biodistribution at time of autopsy. Gold Au^{198} was also administered by intracavitary injection to treat patients with cancer-related accumulations of fluid in the chest or abdominal cavities. This treatment resulted in the relief of symptoms in some cases.

These studies were conducted after earlier animal studies indicated that this agent had potential therapeutic benefit for patients with certain malignant diseases. Data on the metabolism, distribution, and effects of radiation associated with colloidal Au^{198} were compiled during the course of these experimental treatments, and at autopsy, in some cases.

The results of these trials indicated that intracavitary injection of colloidal Au^{198} was effective in relieving some of the symptoms of cancer-related fluid accumulations, but that Au^{198} colloid showed little promise for therapeutic benefit in patients with liver tumors. These studies were supported by the U.S. Atomic Energy Commission. (Previously described in #12 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995, and since revised)

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OR-3. Use of Serum Albumin Labeled with Iodine-131

IN THE EARLY 1950s, the Oak Ridge Institute for Nuclear Studies conducted experiments on the transfer of labeled serum albumin between the peritoneal cavity (within the abdominal cavity) and the blood vessels.

Eleven women hospitalized for ascites (accumulation of fluid in the peritoneal cavity) were the subjects of this study; nine had abdominal carcinomatosis and two had cirrhosis of the liver. These patients were administered intraperitoneally or intravenously with human serum albumin labeled with 200 to 300 microcuries of iodine-131 (I^{131}). Samples of ascitic fluid and blood were analyzed for I^{131}-labeled human serum albumin content.

The results showed complete equilibrium of the injected tagged albumin between compartments, and that a similar mechanism was involved in the accumulation of ascitic fluid in the two diseases studied. This work was supported by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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OR-4. Iodine-131 in the Treatment of Malignant Melanoma

THERAPEUTIC TRIALS were conducted at the Oak Ridge Institute of Nuclear Studies in 1951 to investigate the use of iodine-131 (I^{131}) in the treatment of malignant melanoma. A secondary objective was to determine the distribution of I^{131} in patients with this type of tumor both in the presence and in the absence of functioning thyroid tissue.

Two subjects were studied. The first subject was a 37-year-old man in the terminal stages of metastatic malignant melanoma of the liver. He received 100 microcuries of I^{131} orally. Three days later, the subject was given 57.6 millicuries of I^{131} orally. Tissue samples were obtained during the autopsy, 6 days after ingestion of the I^{131}.

The second subject was a 43-year-old woman with malignant melanoma of the arms and legs. This patient received three oral doses of I^{131} (305 millicuries, 69.7 millicuries, and 69.7 millicuries). Tissues samples were obtained by biopsy after each dose. Iodine-131 failed to localize the tumor and was judged ineffective for therapy of melanoma by this method. This work was supported by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995, and since revised)

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OR-5. Use of Iodine-131 Following Surgical Removal of Thyroid Cancers

BETWEEN 1950 AND 1974, 117 patients admitted to the Oak Ridge Institute of Nuclear Studies, Oak Ridge Associated Universities, with cancer of the thyroid, received at least one dose of therapeutic administration of iodine-131 (I^{131}) as a followup to surgical removal of the tumors. The purpose of the I^{131} was to destroy any possible cancerous thyroid tissue that was not removed surgically.

The project was terminated in October 1974 and ORAU personnel began compiling data and evaluating the clinical course of the patients. Eighty-seven of these patients were still alive at that time. This work was supported by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995, and since revised)

References

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OR-6. Comparison of the Metabolism of Rubidium-86 and Potassium-42

IN 1953, four patients at Oak Ridge Institute for Nuclear Studies with leukemia and carcinoma, participated in tracer studies to determine whether rubidium-86 (Rb^{86}) could be used as an analog for potassium-42 (K^{42}) in studying biological systems. Simultaneous intravenous injections of K^{42} and Rb^{86} were administered to the study participants. Multiple samples of plasma, red cells, and urine were obtained and analyzed from each patient.

The researchers concluded that Rb^{86} was a satisfactory substitute for K^{42} in biological studies. This work was funded by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995, and since revised)

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OR-7. Metabolism Studies Using Calcium-47

IN 1959, the metabolism of calcium was studied at the Oak Ridge Institute of Nuclear Studies. Eleven patients with various diseases, including bone lesions and breast cancer, were given calcium-47 (Ca^{47}).

Two of the patients were administered 70 microcuries intravenously and two patients received oral dosages of 138 and 104 microcuries, respectively. One patient received both an intravenous and an oral dose. Analyses for Ca^{47} were then made on blood, urine, feces, and saliva. Whole-body retention of Ca^{47} was also determined. Comparisons were made between intravenous and oral routes of administration. This research was funded by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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OR-8. Total-Body Irradiation Therapy of Hematologic Disorders

BETWEEN 1956 TO 1973, the Oak Ridge Institute for Nuclear Studies, Oak Ridge Associated Universities Medical Division studied the efficacy of total-body irradiation (TBI) on the treatment of hematological disorders, particularly leukemia, polycythemia rubra vera, and lymphoma. The purposes were to develop improved methods for irradiation therapy, to develop improved methods for assessing and treating accidental gamma and neutron radiation, to compile and evaluate related data, and to identify new and more precise endpoints that define human radiation dose-response.

The 194 male and female patients, all diagnosed with hematologic malignancy, ranged in age from 12 to 86 years. They were exposed to totals of 50 to 300 roentgens per treatment series. However, in 1970, one patient was exposed to 500 roentgens in preparation for an attempted bone marrow graft. The external gamma radiation sources were either cobalt-60 (Co^{60}) or ce-

sium-137 (C^{137}) used in two types of facilities: a medium-exposure-rate total-body irradiator (METBI) providing an exposure rate of 1.5 roentgens per minute from C^{137} and sources, and a low-exposure-rate total-body irradiator (LETBI) providing an exposure rate of 1.5 roentgens per hour from Co^{60} sources.

There was a higher frequency of remissions after 150 roentgens compared to 250 roentgens. The results showed that TBI-treated patients survived about as long as, but not significantly longer than, patients treated by standard chemotherapy. The use of TBI in conjunction with splenectomy in the treatment of one patient with chronic granulocytic leukemia was studied, but the response to the combined therapy was similar to TBI alone. The program, which was discontinued in 1974, was funded by the U.S. Atomic Energy Commission. (TBI was referenced in the Markey report and included in *The DOE Roadmap* of February 1995, and since revised.)

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OR-9. Studies Using Cobalt-57–Labeled Vitamin B_{12}

THIS RESEARCH, conducted in the early 1960s, was a collaborative effort between the Oak Ridge Institute of Nuclear Studies; the Long Island Jewish Hospital, Jamaica, New York; South Nassau Communities Hospital, Oceanside, New York; and Brookhaven National Laboratory. The studies sought to determine why the serum and plasma levels of vitamin B_{12} were elevated in patients with chronic myelocytic leukemia.

In one study, three patients in remission were intravenously administered 0.13 microcurie of vitamin B_{12} labeled with Co^{57}. The procedure was repeated twice in the same patients, after administration of loading doses of vitamin B_{12}.

In another study, 10 patients with various degrees of chronic myelocytic leukemia and 5 healthy individuals each received 3 or more intravenous injections of Co^{57}-labeled B_{12}. This research was supported by a grant from the National Cancer Institute and by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995, and since revised)

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OR-10. Iodine-131–Labeled L-Thyroxine Turnover by Whole-Body Counting

DURING 1966 AND 1967, a study was conducted by the Oak Ridge Institute of Nuclear Studies, Oak Ridge Associated Universities to compare the turnover of L-thyroxine (thyroxine is an iodine-containing hormone that exists normally in the thyroid gland) in subjects with hyperthyroidism, hypothyroidism, and normal thyroid functions.

Twenty to 40 microcuries of iodine-131 (I^{131}) labeled L-thyroxine were administered by intravenous injection to each of 10 patients with abnormal L-thyroxine metabolism and to 5 normal, healthy subjects for comparison. Body counting was conducted twice on the first day after the I^{131}-labeled L-thyroxine was administered, and daily thereafter. Daily thyroid counts were made on the subjects by standard methods. In addition, blood samples were obtained from five patients to compare blood turnover rates to whole-body counts with those of the patients with thyroid disease.

This study showed that whole-body counting provided quantitative information on the turnover of L-thyroxine. This work was funded by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995, and since revised)

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OR-11. Experimental Tumor Scanning with Gallium-67

FROM 1969 THROUGH 1977, Oak Ridge Associated Universities conducted studies on the use of gallium-67 (Ga^{67}) as a tumor-scanning agent in humans. Participating were 357 male and female patients ranging in age from 6 to 83 years. All had known, viable bone or soft tissue tumors associated with a wide variety of cancers.

All patients received at least one intravenous injection of 70 microcuries of Ga^{67} per kilogram of body weight, up to a total amount of 6 millicuries. Thirty-four of these patients received more than one injection. Several received a series of injections to study the therapeutic effect and to look for recurrence of disease.

In a related study, four patients were administered Ga^{67} by injection into the lymphatic structure of the feet.

These studies showed that gallium did not collect equally in all types of tumors. Rather, it collected in tumors of specific cellular types. The lymphatic injections showed no advantage to this approach, even in identifying tumors along the lymphatic vessels. In May 1976, the U.S. Food and Drug Administration approved Ga^{67} citrate for general diagnostic use. This work was supported by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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OR-12. Therapeutic Allogenic Transplantation of Human Bone Marrow

FROM 1970 TO 1973, Oak Ridge Associated Universities conducted a study to evaluate the effectiveness of combining high-dose total-body irradiation (TBI) with antilymphocyte-globulin as an immunosuppressive regimen to induce tolerance to a foreign bone marrow graft in humans.

Three patients were involved initially. Each was exposed to 500 roentgens, which corresponded to an average total-body absorbed dose of approximately 370 rads. Subsequent bone marrow grafts were successful in two patients. Failure of the graft in the third patient was determined to have resulted from an insufficient radiation dose. Accordingly, researchers requested and received approval to increase the exposure level to deliver an absorbed dose of 800 rads at the rate of 40 roentgens per minute.

The original protocol limited patients to those with acute leukemia. Researchers also requested and received approval to extend the procedure to patients with aplastic anemia. A fourth patient, with acute leukemia, was treated in 1973. This patient was exposed to a 694 roentgens total-body irradiation (TBI), but developed a severe graft-versus-host reaction that prevented a successful marrow transplant.

The Oak Ridge Institute of Nuclear Studies conducted a related study beginning in 1971 that was designed to identify objective signs and distinguish early graft-versus-host reactions from drug reactions, infections, and other complications related to or incidental to the marrow transplant/TBI procedure. In this study, skin biopsies were obtained from four patients or volunteers, without further exposing them to radiation of any kind.

This work was supported by the U.S. Atomic Energy Commission. (TBI was referenced in the Markey report and included in *The DOE Roadmap* of February 1995.)

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OR-13. Scandium-Augmented Gallium-67 Localization in Tumors

FROM 1972 TO 1973, Oak Ridge Associated Universities conducted a study to determine whether intravenous administration of stable

scandium citrate along with radioactive gallium increased the relative concentration of the gallium in tumors.

The study protocol proposed administration of scandium in doses ranging from 0.005 to 1.0 milligram per kilogram of body weight, followed by 100 microcuries of gallium-67 to 21 patients with known malignancies. The first patient to be treated experienced an adverse reaction to the scandium citrate but made a satisfactory recovery. Testing was suspended pending further investigation. There is no indication of further study. This work was supported by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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OR-14. Clinical Testing of Strontium-85m as a Bone Scanning Agent

FROM 1972 TO 1975, Oak Ridge Associated Universities conducted a study of strontium-85m (Sr^{85m}) as a bone scanning agent. Patients with known malignant tumors or suspected metastatic disease of the bone were administered up to 30 microcuries of Sr^{85m} per kilogram of body weight (approximately 2 microcuries per patient) by intravenous infusion. Results of the Sr^{85m} scans were compared with subsequent scans using strontium-85, fluorine-18, or technetium-99m. Four patients were involved in the study. This work was supported by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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OR-15. Comparison of Indium-111 and Bismuth-206 with Gallium-67 as Tumor Scanning Agents

FROM 1972 TO 1978, Oak Ridge Associated Universities conducted a study to determine the relative merits of indium-111 (In^{111}) and bismuth-206 (Bi^{206}) when compared to gallium-67 (Ga^{67}) as tumor imaging agents. In actual application, the study was limited to evaluating In^{111} and Ga^{67}.

In 1973, six cancer patients received simultaneous injections of In^{111} (0.011 microcurie per kilogram of body weight) and Ga^{67} (0.045 microcurie per kilogram). Three additional patients were studied during 1974.

The study showed that Ga^{67} was a better tumor scanning agent than In^{111}. After July 1974, no patients were scanned with In^{111} at Oak Ridge. This work was supported by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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OR-16. Use of an External Gadolinium-153 Source for Timing the Cardiac Cycle

FROM 1972 TO 1975, Oak Ridge Associated Universities conducted a study to determine the effectiveness of gadolinium-153 (Gd^{153}) as a noninvasive technique for evaluating specific stages of the cardiac cycle, notably the left ventricular ejection time.

A fine beam of gamma radiation from a Gd^{153} source, which was placed on the subject's back, was directed through the heart to a detector on the subject's chest. At least six patients were subjected to a radiation exposure of approximately 0.2 roentgen over a 1-inch-diameter area on their backs. The passage of blood through the left ventricle was determined by measuring the blockage of gamma rays emitted by the Gd^{153}. This work was supported by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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OR-17. Dysprosium-157 as a Clinical Imaging Agent for Solid Tumors

FROM 1973 TO 1977, Oak Ridge Associated Universities conducted a study to determine whether dysprosium-157 (Dy^{157}) could be used effectively as a tumor localizing agent in humans. Both bone tumors and soft-tissue tumors were considered. Thirty-four patients with known cancer were included.

This study was discontinued in 1977 after the investigators found that Dy^{157} did not provide better images of solid tumors than the technetium-99m phosphate compounds did for bone scans, nor was it better than gallium-67 citrate for soft-tissue tumors. This work was supported by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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OR-18.

(Included in *The DOE Roadmap* and now part of OR-8)

OR-19. Clinical Testing of a Line-Scanning Proportional Counter Camera Using Injected Iodine-125 and Technetium-99m

DIAGNOSTIC DOSES OF IODINE-125 and technetium-99m were administered to selected patients referred to Oak Ridge Associated Universities from the Oak Ridge Methodist Hospital for thyroid evaluation. The quality of images obtained by the camera using the two radioisotopes was evaluated and compared. Although these subjects were evaluated for preexisting disease, certain aspects of this study were experimental, and the objective was development of instrumentation and techniques for evaluating human thyroids. An estimated 100 subjects were studied. This study was conducted between August 27, 1975, and September 29, 1977. (Previously described in #33 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

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OR-20. Uranium Injections Into Terminally Ill Cancer Patients

FROM 1953 TO 1957, Oak Ridge National Laboratory and Massachusetts General Hospital conducted a cooperative study on the distribution and excretion of uranium in humans using terminally ill brain cancer patients as subjects. Participants included male and female patients ranging in age from 26 to 63 years. All were near death (in a coma or semicoma) prior to injection and were receiving usual hospital care for comatose patients.

Subjects were intravenously administered uranium-233 or uranium-235 as either uranyl nitrate hexahydrate (nine patients) or uranium tetrachloride (two patients) in amounts ranging from 4 to 50 milligrams.

The subjects died from their brain cancer within several months of injection. Study results indicated that 99 percent of the injected uranium cleared the blood within 20 hours, either depositing in the skeleton and kidneys or exiting through urine. This work was supported by the U.S. Atomic Energy Commission. (This experiment was referenced in the Markey report and included in *The DOE Roadmap* of February 1995.)

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Struxness, E.G., A.J. Luessenhop, S.R. Bernard, and J.C. Gallimore. "The Distribution and Excretion of Hexavalent Uranium in Man." In *Proceedings of the International Conference on the Peaceful Uses of Atomic Energy*, pp. 186–196. New York: United Nations, 1956. ❑

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OR-21. Pathologic Changes in Normal Thyroid Tissue After Large Doses of Iodine-131

IN THE EARLY 1950s, physicians at the Oak Ridge Institute of Nuclear Studies studied the histopathology of normal thyroid tissue subjected to high-dose radiation from incorporated iodine-131 (I^{131}). Ten hospital patients were included in this study (four men and six women). All required the removal of their thyroids for treatment of thyroid cancer, except for one patient with advanced metastatic melanoma (a tumor of melanin-pigmented cells in skin and elsewhere) who had a poor prognosis and short life expectancy. The purpose of this study was to evaluate the effectiveness of I^{131} in destroying normal thyroid tissue, which was considered to be a relatively radioresistant tissue.

Three of the patients received large amounts of I^{131} (totaling between 81 and 298 microcuries, which were intended to destroy the thyroid by radiation alone. Six received smaller but varying amounts totaling between 28 and 75 microcuries followed by thyroidectoy (surgical removal of the thyroid gland) 2 and 13 days after administration. The one remaining subject received a diagnostic rather than destructive amount totaling

75.4 microcuries but did not undergo surgery until 42 days after the initial administration of I^{131}. Thyroid tissues were histologically studied to determine the pathological effects of radiation and degree of completeness as a function of the radiation absorbed dose.

For 9 of the 10 subjects, the administration of radioiodine constituted beneficial medical therapy. The study of the effects of I^{131} on the thyroid of the terminal melanoma patient was not related to therapy. This study provided new information on the response of thyroid tissue to relatively large dosages from I^{131}. Variations in response were observed among the patients treated, and response was not well correlated with radiation absorbed dose. Complete necrosis of normal thyroid tissue was not observed, even following administration of large amounts of I^{131}. This experiment was supported by the U.S. Atomic Energy Commission.

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OR-22. Intracavitary Injection of Phosphate-32 as Colloidal Chromic Phosphate

IN THE EARLY 1950s, researchers in the Medical Division of the Oak Ridge Institute of Nuclear Studies conducted a study examining the metabolism and distribution of chromic phosphate ($CrPO_4$) labeled with phosphorus-32 (P^{32}) after intracavitary administration. Four patients with pleural effusion (fluid accumulation in the lungs) and six with ascites (fluid accumulation in the abdominal cavity associated with cancer) were chosen as subjects.

Subjects received an intracavitary injection of between 2.2 and 19.5 millicuries of colloidal P^{32} chromic phosphate. Following the intraperitoneal administration, the levels of P^{32} activity in the blood, urine, and the pleural and peritoneal fluids were measured at various time intervals. Tissue distribution of P^{32}-chromic phosphate also was studied in tissues obtained at autopsy from three patients who died as a consequence of their disease during the period of observation. The researchers concluded that colloidal P^{32}-chromic phosphate had potential to be useful in intracavitary therapy. This research was funded by the U.S. Atomic Energy Commission.

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Root, S., M. Tyor, G. Andrews, and R. Kniseley. "Distribution of Colloidal Radioactive Chromic Phosphate After Intracavitary Administration." *Radiology.* Vol. 63, August 1954, pp. 251–259. ❑

OR-23. Experimental Treatment of Chronic Leukemia Using Colloidal Gold-198

IN THE EARLY 1950s, physicians in the Medical Division of the Oak Ridge Institute of Nuclear Studies used colloidal gold-198 (Au^{198}) in the treatment of chronic leukemia. Six patients with previously untreated chronic leukemia and two additional patients with late-stage treated leukemia, were included in the study and followed for 3 to 8 months.

All patients in this study received from 23.0 to 45.5 millicuries of Au^{198} by intravenous injection. Three patients with previously untreated disease also received a second administration 2.5 to 5 months after the initial injection. Levels of Au^{198} activity were measured in the plasma, urine, and the red and white blood cells of the patients.

External counting studies using collimated gamma detectors showed that Au^{198} concentrated in the liver and spleen. All the patients with untreated leukemia exhibited a reduction in the size of the liver and spleen; five of the six showed an improvement in red cell values. Little or no improvement was observed in two patients with late stage disease. This research was supported by the U.S. Atomic Energy Commission.

References

Andrews, G.A., and M.P. Tyor. "Early Results of the Treatment of Chronic Granulocytic Leukemia with Intravenous Colloidal Gold-195." *Journal of Laboratory and Clinical Research.* Vol. 42, No. 5, 1953, pp. 777–778. ❑

OR-24. Intracavitary Colloidal Gold-198 in the Treatment of Effusions Due to Malignant Neoplasms

BETWEEN 1950 AND 1952, researchers in the Medical Division of the Oak Ridge Institute of Nuclear Studies conducted a pioneering program in the intracavitary use of colloidal gold (Au^{198}) for treatment of effusions (fluid accumulations) caused by malignant tumors. This treatment was expected to be palliative (resulting in relief, not cure); however, its ultimate value was unknown. The treatment program also provided the opportunity to study the metabolism, distribution, and tissue effects of Au^{198} in humans.

Over the 2-year period, 39 patients with tumor-related accumulations of fluid in one or more body cavities received intracavitary Au^{198} treatment to eliminate or reduce the fluid accumulations. This was done as an alternative to the conventional regimen of drainage of the fluid followed by x-ray therapy. The patients included both men and women ranging in age from 18 to 76 years.

The amount of radioactivity given was patient-specific, with typically 75 and 150 millicuries of colloidal Au^{198} being injected directly into the abdominal and pleural cavities, respectively. Some patients required multiple treatments over several weeks. The largest amount of Au^{198} given in a single administration was 187 millicuries. The largest total amount administered to a single patient was 659 millicuries over a 10-month period. In anticipation of postmortem studies, small additional amounts of Au^{198} were given to patients whose death appeared imminent if the previously administered Au^{198} had largely decayed. Daily blood and urine samples were measured for radioactivity. Activity retained in the body was assessed by Geiger counters. Tissue samples were obtained during routine surgical procedures or at autopsy.

Patients typically experienced some gastrointestinal effects of varying severity beginning 12 to 24 hours after Au^{198} administration and lasting for 2 to 3 days. However, there were no serious or prolonged adverse reactions, even with the largest amounts of Au^{198}. Slight, transient bone marrow depression was observed in most patients. Twenty-three patients experienced some degree of relief from fluid accumulations; no effect was observed in 2; evaluation was not possible in 14 patients because of early death from the underlying tumor or because of combined therapy.

Tissue studies showed that Au^{198} tends to be absorbed at the cavity surfaces rather than entering the tumor tissue. There was little evidence of radiation-induced changes in the tumors. A small amount of Au^{198} was found to have migrated slowly into the lymphatic system, and measurable amounts were detectable in major organs. A small amount of Au^{198} was excreted in the urine. Evidence of benefit of Au^{198} treatment in these cases appeared to be confined to the control of fluid accumulation, but the frequency and severity of adverse effects were less than with conventional therapy. This research was supported by the U.S. Atomic Energy Commission.

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OR-25. Study of Strontium and Calcium Metabolism Using Strontium-85 and Calcium-45

BETWEEN 1955 AND 1957, researchers at the Oak Ridge Institute of Nuclear Studies conducted a series of experiments to learn more

about the comparative metabolisms of strontium and calcium. The purpose of this research was to better understand the competition between strontium and calcium and the various processes that determine their uptake, retention, and excretion. A further purpose was to study strontium metabolism after single and continuous intakes.

The study subjects were 13 chronically ill patients —6 men and 7 women—with leukemia or other widespread malignant diseases of various types. The patients ranged in age from 9 to 73 years. Seven patients were administered one oral or intravenous dosage of between 5 and 20 microcuries of strontium-85 (Sr^{85}) while consuming an exclusively nonmilk diet. Four of these seven later received an equal amount of Sr^{85} while consuming a normal milk intake. Two patients ingested 1 to 3 microcuries of Sr^{85} per meal for about 20 days. Four other subjects received 1 to 3 microcuries of Sr^{85} and 2 to 6 microcuries of calcium-45 (Ca^{45}) per meal for 5 to 20 days.

Urine and fecal samples were collected from each patient for Sr^{85} and Ca^{45} analysis. Blood samples were also obtained from some of the patients to determine levels of Sr^{85} in plasma over time. Tissue samples were obtained from some of the patients at autopsy.

This study showed that Sr^{85} concentrations measured early in the experiment in blood, kidneys, spleen, thyroid, bones, and bone marrow were all approximately the same. These concentrations were much higher, however, than those measured in other tissues. When measured later, the strontium concentrations were higher in bones and lower in blood and soft tissues than those absorbed earlier. Calcium was absorbed more readily, and excreted less readily, than strontium. This research was supported by the U.S. Atomic Energy Commission.

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OR-26. Gastrointestinal Tract Studies Using Lanthanum-140 and Iron-59

IN THE EARLY 1960s, researchers in the Medical Division of the Oak Ridge Institute of Nuclear Studies used lanthanum-140 (La^{140}) citrate in human studies. The purpose was to investigate the importance of individual variations that may result in radiation dose to the intestinal tract from internal emitters.

In the first study, the subjects were 54 patients having normal intestinal tracts who were administered 10 to 20 microcuries of La^{140} in the citrate form under a variety of meal scenarios (2 hours before breakfast, with the noon meal, etc.) The purpose was to verify the assumptions being used at that time to describe a standardized intestinal tract in man. The results of this study showed that radiation dose estimates for individuals could vary significantly from dose estimates derived from generalized models.

In the second study, La^{140} was used to verify the completeness of information from analysis of stool collections for gastrointestinal absorption tests and to calculate the loss of unabsorbed iron-59 (Fe^{59}) when fecal collections are incomplete. Twenty-one patients participated as subjects in this study, with one subject receiving two treatments. Subjects received 20 microcuries of La^{140} and 2 microcuries of Fe^{59} orally. Results of the study indicated that La^{140} could be used to determine incomplete collections of stool samples, but that it could not be used to calculate the loss of unabsorbed Fe^{59} because the rates of passage through the intestinal tract are different. This study was supported by the U.S. Atomic Energy Commission.

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OR-27. Total-Body Irradiation and Attempted Bone Marrow Transplants in Acute Leukemia

IN A STUDY REPORTED IN 1961, researchers in the Medical Division of the Oak Ridge Institute of Nuclear Studies investigated combined total-body irradiation and bone marrow transplants as a possible treatment of leukemia. The researchers recognized that hazards were associated with the treatment of patients who had a very poor prognosis, had already been treated by means of chemotherapy, and were in clinical and hematologic relapse.

Eleven subjects—nine males and two females—were included in the study. Seven of the 11 subjects were children with acute leukemia of the primitive cell type. Nine of the subjects received various doses of radiation from cobalt-60 (Co^{60}) ranging from 210 to 940 rads in single administrations. One of the subjects received a total of 1,000 rads in two fractions (380 and 620 rads) 5 months apart. Another subject received 940 rads over a 9-day period. Seven of the subjects received bone marrow transplants between 1 and 7 days after irradiation. While several short-term remissions resulted, all patients died within 1 year of treatment.

This study suggested that total-body irradiation alone could produce short-term remission in some cases of leukemia. Temporary remission in the case of bone marrow transplants, however, was not proof of survival of the transplanted cell. In acute leukemia, the leukemic cells appeared to be radiosensitive, and profound cell destruction occurred after a single large dose of radiation. This study was funded by the U.S. Atomic Energy Commission.

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OR-28. Use of Iodine-130 to Study Thyroid-Stimulating Hormone in Cancer Patients

DURING THE PERIOD from 1965 to 1966, researchers in the Medical Division of the Oak Ridge Institute of Nuclear Studies studied the suitability of iodine-130 (I^{130}) as a tool for investigating the effects of thyroid-stimulating hormone on thyroid cancer.

Forty tests were conducted on 18 subjects, including 5 with healthy thyroids and 13 with thyroid cancer. Subjects were administered 0.1 to 5.0 millicuries of I^{130} and were counted to determine thyroid uptake at 4, 24, 48, and 72 hours. Some were also administered thyroid-stimulating hormone by intramuscular injection before or after I^{130}. Some received thyroid blocking before or after the administration of the hormone plus I^{130} administration. The uptake of I^{130} in neck lesions associated with thyroid cancer was measured in four subjects after their thyroids had been surgically removed.

The investigators found that thyroid-stimulating hormone did not affect the uptake or distribution of I^{130}. This study was supported by the U.S. Atomic Energy Commission.

References

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OR-29. Study of Uranium Excretion in Urine After Exposure to Uranium Oxide Dusts

IN 1944 TO 1945, a test was conducted at the Y-12 Plant, Oak Ridge to determine the rate of uranium excretion by workers occupationally exposed to uranium oxide dusts. The purpose of this test was to obtain information needed to interpret urinalysis results for workers involved in chemical processing of natural uranium compounds at the Y-12 Plant.

After the average uranium concentrations in urine were determined for a group of 168 chemical production workers, both male and female, from routine occupational exposure to uranium dusts in their work place, a special study was conducted. Two male volunteer workers at the Y-12 plant were deliberately exposed to high concentrations of airborne uranium oxide dust near a dryer in the bulk treatment department. The operator attempted to make the air more dusty (about 28 milligrams natural uranium per

cubic meter air) than would otherwise be normal. The subjects inhaled the dusty air for 30 minutes. Twenty-four-hour urine samples were collected prior to the test exposure and for 3 days following to determine the rate of uranium excretion before and after exposure.

This experiment showed that inhaled uranium dust was rapidly excreted and that the maximum rates of excretion occurred within 12 hours of exposure. The Y-12 Plant was operated for the U.S. Atomic Energy Commission.

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OR-30. Study of the Effects of Beta Rays on Skin Using Phosphorus-32

IN 1945, RESEARCHERS at Oak Ridge National Laboratory conducted an experiment to determine the threshold dose of beta radiation and induced skin reactions. A total of 10 normal, healthy adult volunteers were exposed to between 140 and 1,180 rads of localized external beta radiation to the skin surface from a plastic disk containing phosphorus-32 applied to the skin of the forearm or inner thigh. After exposure, the subjects' skin was monitored at increasing time intervals for a period of up to 8 months.

The results indicated that the threshold dose of beta radiation required to cause mild tanning of the skin is about 200 rads, and for erythema (reddening) is about 813 rads. This research was supported by the U.S. Atomic Energy Commission. (This experiment was referenced in the Markey report.)

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OR-31. Thyroid Metabolism of Iodine-131 in Single Versus Continual Ingestions

IN THE EARLY 1960s, scientists at Oak Ridge National Laboratory examined the thyroid uptake and bodily excretion of iodine-131 (I^{131}) in single and daily administrations to test the theory that I^{131} is metabolized in the thyroid at the same rate as stable iodine.

Five male volunteers ingested resin-treated milk containing protein-bound I^{131}. In the first stage of the experiment, the five received either 0.15 or 1.84 nanocuries of I^{131} per day for 4 to 63 days. Thyroid activity in all five subjects was measured with a scintillation counter and urinary excretion was monitored for two of these five.

In a second study, two subjects received a single administration of 92 nanocuries of I^{131} and thyroid uptake and urinary excretion were monitored.

The study found that the predicted uptake of I^{131} for the single dosages was slightly higher than expected, and that the continued ingestion uptakes came close to matching the predictions. This study was funded by the U.S. Atomic Energy Commission. (This experiment was referenced in the Markey report.)

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OR-32. Study of Decontamination of Skin Contaminated with Silver-110m

IN 1963, a researcher at Oak Ridge National Laboratory conducted a study to determine the depth of chemical penetration into skin by a solution of silver-110m (Ag^{110m}) in nitric acid, and to

evaluate the effectiveness of skin decontamination procedures and materials.

One drop containing 0.2 millicurie of Ag^{110m} was self-administered by the researcher to the skin of each arm and spread over an area of approximately 0.5 square inch. The skin was blotted and anesthetized, after which a sample of skin tissue was obtained to determine by autoradiography the depth of penetration of the Ag^{110m}. The area of skin on the other arm was decontaminated several times with detergent and water, and a second biopsy was performed after decontamination to determine by autoradiography the depth of penetration and amount of Ag^{110m} remaining in the skin. Each of the contaminated areas of skin was counted using a radiation detector to measure the Ag^{110m} activity present after each procedure.

The study showed that detergent was not effective in removing Ag^{110m} from the contaminated skin; however, abrasive removal of skin did remove some of the residual activity. This experiment was supported by the U.S. Atomic Energy Commission.

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Correspondence. G.S. Hill. "Human Skin Decontamination Study." Oak Ridge National Laboratory July 25, 1963. Oak Ridge/Energy Systems/ORNL (X-10), Collection Personnel Radiation Records, 1943–present, Dosimetry Data Management. ❑

University of California, Los Angeles

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UCLA-1. Early Experimental Imaging of the Thyroid Gland Using Iodine-131

IN 1951, the University of California, Los Angeles conducted a series of tests on humans to study the uptake of radioiodine into the thyroid gland. Additional tests were made on patients at the Sawtelle Veteran's Hospital. The main purpose of this study was to test a new automatic scanner and recorder.

Initial scans were made using a collimated gamma scintillation counter. This equipment enabled a record to be obtained on which an image of the gland was visible and which the researchers concluded was better than a total activity count for clinical studies of thyroid disease.

The second set of scans was made on a frozen tissue preparation obtained from a terminal patient who had been given 3 millicuries of iodine-131, 14 hours before his death. The measured total activity of the thyroid gland at the time it was scanned was about 50 microcuries.

The results of these tests led to increased use of this equipment for clinical diagnostic scans in other patients with thyroid disorders. This work was supported by the U.S. Atomic Energy Commission.

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UCLA-2. Zinc Metabolism Studies Using Zinc-65

DURING THE LATE 1950s, researchers at the University of California, Los Angeles; Boston University School of Medicine; and the Massachusetts Memorial Hospitals conducted studies on the metabolism of zinc using zinc-65 (Zn^{65}).

Twenty-one patients with neoplastic disease and one patient with generalized arteriosclerosis participated as subjects. Each was intravenously administered Zn^{65} as zinc ammonium citrate. The amounts of activity administrated were not reported.

These studies showed that zinc appeared rapidly in white blood cells and persisted for several weeks. It appeared less rapidly in red cells, but persisted much longer. The injected zinc concentrated in the liver and other major organs and was excreted slowly in urine and feces. This study was supported by the U.S. Atomic Energy Commission.

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Human Subjects." *Transactions of the Association of American Physicians.* Vol. 71, May 1958, pp. 322–336. ❑

UCLA-3. A Study of Strontium-85 and Calcium-47 Metabolism in Patients with Osteoporosis, Paget's Disease, and Metastatic Bone Tumors

IN 1959, RESEARCHERS at the University of California Medical School, Los Angeles conducted a series of studies on strontium-85 (Sr^{85}) metabolism using hospital patients with osteoporosis, other skeletal disorders (such as Paget's disease), and various cancers to determine the uptake and retention of strontium in selected tissues.

The study population included nine hospital patients and six normal volunteers. Five to 15 microcuries of Sr^{85} as the chloride were administered intravenously to each subject. The rates of Sr^{85} accumulation were determined for selected parts of the body, using a shielded sodium iodide gamma scintillation counter. Strontium-85 injections were repeated in some of the patients. Excretion rates of Sr^{85} in urine and stool were determined in one patient. Some of the patients also received tracer amounts of human serum albumin labeled with iodine-131 (I^{131}) by intravenous injection to determine the uptake and retention of protein-bound I^{131} for comparison to Sr^{85}.

These studies indicated that Sr^{85} uptake was normal in "nonsenile" osteoporotic patients, but reduced in patients with "senile" osteoporosis, due presumably to reduced capillary blood flow.

These studies continued from 1959 to 1962 and included additional injections of Sr^{85} and calcium-47 in other hospital patients with multiple myeloma and other diseases to improve understanding of the metabolism of strontium and calcium in man. The effects on strontium metabolism and calcium balance of administered prednisone, testosterone propionate, and adrenocorticotropic hormone were also studied in one patient. This work was supported by the U.S. Atomic Energy Commission.

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UCLA-4. Studies of Liver Function and Blood Flow Using Rose Bengal Iodine-131 and Colloidal Gold-198 in Normal and Diseased Subjects

IN THE LATE 1950s AND EARLY 1960s, researchers at University of California Medical School, Los Angeles and at the Los Angeles County Harbor General Hospital conducted tracer studies using iodine-131 (I^{131})–labeled rose bengal (a sodium salt stain) and colloidal gold-198 (Au^{198}). The purpose of this study was to determine whether the I^{131}-labeled rose bengal hepatogram provided an improved method for diagnosing jaundice.

At least 120 patients with a variety of liver and hepatobiliary tract diseases, and 45 subjects with normal liver functions participated in the study. Blood clearance half-times for intrave-

nously injected rose bengal I^{131} and colloidal Au^{198} were studied to assess liver blood flow and cell function. This allowed researchers to correlate functional abnormalities of the liver with vascular defects. The colloidal radiogold test was found useful for diagnosis of severe jaundice, ascites(fluid accumulation in the abdominal cavity) of unknown origin, and acute gastrointestinal tract hemorrhage.

In 1959, blood clearance stress tests using I^{131}-labeled rose bengal were performed on 23 subjects with normal liver function and compared with tests on 39 nonjaundiced patients having probable liver disease, and on 25 other patients with confirmed liver disease. This study confirmed that this test was more sensitive than tests then in use. Tracer studies using I^{131}-labeled rose bengal and colloidal Au^{198} were continued in 1960 to assess liver blood flow and cellular function in patients with congestive heart failure. Clearance rates of I^{131} and Au^{198} were determined. At least 13 subjects participated in these studies, including patients with congestive heart failure, hepatitis, jaundice, cirrhosis, and 1 subject with a normal liver.

The investigators showed that reduced blood flow occurred in liver cirrhosis but not in jaundice. This work was supported by the U.S. Atomic Energy Commission.

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UCLA-5. Tracer Studies Using Iodine-125, Iodine-131, and Gold-198 to Evaluate Functions of the Reticuloendothelial System

STUDIES WERE CONDUCTED in 1960 at the University of California Medical School, Los Angeles to develop tracer methods for evaluating the phagocytic (engulfing foreign matter and breaking it down chemically) and digestive functions

of the reticuloendothelial system (a defensive mechanism against foreign materials) in man.

Experiments were conducted using iodine-131 (I^{131}) colloidal agents administered to 8 normal subjects and 13 patients with various renal disorders. The amounts of I^{131} tracer administered as iodinated albumin aggregates were not stated. Blood clearance half-times for I^{131} were determined. Colloidal gold-198 (Au^{198}) was also administered to patients to evaluate uptake in liver cells for comparison with the metabolism of I^{131}-labeled proteins.

A study in 1961 at the Laboratory of Nuclear Medicine and Radiation Biology, University of California, Los Angeles used heat-treated serum albumin labeled with I^{131} to determine blood flow and reticuloendothelial system functions. The number of subjects involved in this study was not stated. A further study in 1961 involved clinical trials with colloidal suspensions of I^{131}-labeled human serum albumin to estimate phagocytic and proteolytic digestive functions of the reticuloendothelial system. Fifteen healthy subjects and an unstated number of patients with diseases involving the organs of the reticuloendothelial system participated.

In 1964, patients with cirrhosis of the liver were injected with albumin microaggregates labeled with I^{125}. The purpose of this study was to determine the extraction efficiency of the liver. After injection, samples of blood were obtained from catheters in the hepatic vein and a peripheral vein. It was determined that the extraction efficiency of the liver in cirrhosis is dependent to a large extent on the degree of portal hypertension. These studies were funded by the U.S. Atomic Energy Commission.

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UCLA-6. Retention of Vitamin B_{12} Labeled with Cobalt-60

IN 1960, RESEARCHERS at the Laboratory of Nuclear Medicine and Radiation Biology at the University of California, Los Angeles conducted studies on the whole-body retention of vitamin B_{12} labeled with cobalt-60 (Co^{60}).

In the first study, four normal volunteer subjects received an oral administration of 0.02 microcurie of Co^{60}-labeled vitamin B_{12}. The subjects were then monitored in the whole-body counter over a period of 7 days. The purpose of the study was to determine the retention of vitamin B_{12} in the whole body, liver, and intestinal tract, and to demonstrate the whole-body counter's sensitivity for measuring small amounts of gamma radioactivity in humans. The measurements showed a retention of 50 to 81 percent of the administered activity at 7 days post-ingestion of vitamin B_{12}.

The results of this study were compared with results of the routine Schilling test performed on four other hospital patients with pernicious anemia. These patients were injected with 0.5 microcurie of Co^{60}, which was accompanied by an injection of a flushing dose of nonlabeled vitamin B_{12}.

The conclusion of the study was that similar diagnostic information could be obtained using this Co^{60}-B_{12} whole-body counting technique with 96 percent less Co^{60} than that used with the Schilling test. These studies were funded by the U.S. Atomic Energy Commission.

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UCLA-7. Retention of Iodine-131–Labeled Human Serum Albumin

IN THIS 1962 STUDY at the University of California, Los Angeles the body retention of human serum albumin labeled with iodine-131 (I^{131}) was determined by frequent measurements of hospital patients and normal volunteers in the UCLA total-body counter.

Twenty subjects received an intravenous administration of approximately 5 microcuries of I^{131}-labeled human serum albumin (HSA). This study included normal subjects in addition to patients with various disorders, including: duodenal ulcer, hepatitis, lymphosarcoma, ulcerative colitis, and regional enteritis. Potassium iodide was given prior to I^{131}-labeled HSA administration to minimize thyroid uptake of the radioiodine. The subjects with ulcerative colitis retained only 14 to 31 percent of the human serum albumin after 14 days, while all other subjects retained over 40 percent after 14 days. This study was funded by the U.S. Atomic Energy Commission.

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UCLA-8. Study of Calcium Metabolism Using Calcium-47 as a Tracer

BETWEEN 1962 AND 1964, staff of the University of California Medical School, Los Angeles conducted calcium metabolism studies using calcium-47 (Ca^{47}) to determine the gastrointestinal absorption of calcium by humans.

Calcium-47 was administered orally to 11 patients at the Veterans Administration Hospital in Los Angeles. The administered activity is not stated. Some of the patients suffered from cirrhosis of the liver, osteoporosis, or hyperparathyroidism. Four were on calcium balance, and three were normal, healthy subjects. The investigators assayed the Ca^{47} in stool, urine, and blood and conducted total-body counts.

This study showed that calcium absorption rates in normal and osteoporotic subjects were highly variable and overlapped between groups. This study was funded by the U.S. Atomic Energy Commission.

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UCLA-9. Study of Lung Imaging Techniques Using Albumin Labeled with Iodine-131 and Iodine-125

BETWEEN 1963 AND 1965, the University of California Medical School, Los Angeles conducted

studies to develop new methods for imaging the lungs.

In these studies, albumin (a simple protein found in the body), labeled with 100 to 200 microcuries of iodine-131 (I^{131}) or iodine-125 (I^{125}), was administered by intravenous injection. The subjects' lungs were then scanned to produce an image to determine where the albumin deposited. Areas of impaired lung function were indicated by low uptake of I^{131} or I^{125}-albumin. Using this technique, lung tumors and other abnormalities were detectable before they were apparent on traditional x-rays.

These methods were tested on patients with a variety of lung disorders, including pneumonia, tuberculosis, and lung cancer. Subjects with normal lung function were also used for comparison. Approximately 100 subjects were used in these studies. This research was supported by the U.S. Atomic Energy Commission.

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UCLA-10. Strontium-85 Retention in Humans

A STUDY WAS CONDUCTED in 1964 at the University of California, Los Angeles on the skeletal retention of strontium-85 (Sr^{85}) in subjects after intravenous injection. The purpose of this study was to develop a correlation between body depositions of strontium and the amount excreted in urine at various times after injection. It was hoped that this information could be used to estimate the amounts of strontium-90 (Sr^{90}) fallout in people exposed to radioactive fallout from atmospheric weapons testing.

Twenty-three subjects, both men and women, were selected to participate in this study. The subjects ranged in age from 11 to 76 years and included 10 patients with osteoporosis, 4 cancer patients, 6 patients with other illnesses, and 3 normal healthy subjects. These subjects were each injected with 5 to 10 microcuries of Sr^{85} chloride.

The amount of Sr^{85} retained in the subjects' bodies was measured in the University's total-body counter at frequent intervals for up to several months post-injection. Radiation measurements were also selectively made over the knee and tibia midshaft (shin) areas of nine subjects to estimate the fraction of the total-body deposition in skeletal tissue. Complete collections of all urine and feces were obtained from 11 patients on metabolic balance regimens to determine calcium/strontium ratios.

The study showed that strontium intake and body deposition could be evaluated by urinalysis measurements. Funding for the study was provided by the National Institutes of Health and the U.S. Atomic Energy Commission.

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UCLA-11. Lung Scanning of Inhaled Radiopharmaceuticals Using Iodine-131 and Technetium-99m

DURING THE PERIOD 1964 TO 1968, the Laboratory of Nuclear Medicine and Radiobiology at the University of California, Los Angeles conducted studies on the use of radiolabeled compounds for the diagnosis of various pulmonary diseases in man. While most of these studies were in-

tended for the diagnosis of conditions in patients with disease, some of the studies were conducted using normal, healthy volunteer subjects.

Aerosols of albumin aggregate labeled with iodine-131 (I^{131}) and administered by inhalation were used to diagnose bronchial obstructions in patients with lung cancers and in normal volunteer subjects. The lungs of each subject were imaged using a gamma camera after administration of the aerosol. The number of subjects and the amounts of activity administered were not stated. The diffusion of gases across alveolar (air cells in the lungs) membranes was studied in an unstated number of normal, healthy subjects using ethylenediaminetetraacetic acid labeled with technetium-99m (Tc^{99m}-EDTA) administered by inhalation. The distribution of the Tc^{99m}-EDTA in the lungs was then determined by gamma camera imaging. The amount of Tc^{99m}-EDTA administered to each subject was not stated. These studies were funded by the U.S. Atomic Energy Commission.

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UCLA-12. Measurement of Loss of Iodine-131–Labeled Human-Serum Albumin in Children

IN 1967, nine healthy children aged 6 months to 12 years, and seven ill children aged 18 months to 14 years, participated in a study at the University of California, Los Angeles to determine the rate of loss of iodine-131 (I^{131})–labeled human serum albumin by using total-body counting. The study was designed to compare the retention between healthy and ill children and between children and adults.

After their thyroid uptake was blocked with Lugol's solution, the children were intravenously injected with 0.05 to 0.10 microcurie of I^{131}-albumin, estimated to impart an absorbed dose of about 10 millirads. Whole-body retention was studied for 3 weeks following injection.

This study showed that I^{131} was retained in healthy children with half-times ranging from 2 to 13 days, a period shorter than the 13- to 18-day adult retention period. The study was funded by the U.S. Atomic Energy Commission.

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UCLA-13. Copper-67 Absorption in Patients with Disorders of Iron Metabolism

IN APPROXIMATELY 1968, a preliminary study of copper absorption was conducted at the University of California, Los Angeles. Copper-67 (Cu^{67}) was used to measure total-body absorption and retention of elemental copper in seven patients with disorders of iron metabolism, and in two normal volunteers.

Subjects were orally administered an unstated amount of Cu^{67} with a small amount of stable copper. The absorption and retention were measured in the Total-Body Counter Facility over a period of 15 days. Due to the variability between patients of day-to-day measurements, the experiment produced only rough estimates of copper absorption and retention. This study was funded by the U.S. Atomic Energy Commission.

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UCLA-14. Total-Body Counting of Iodine-131–Labeled Gamma Globulins

AROUND 1968, researchers at the University of California, Los Angeles conducted a study of metabolic kinetics of gamma globulins. Gamma globulins labeled with an unstated amount of iodine-131 (I^{131}) or iodine-125 (I^{125}) were administered intravenously to 11 hospital patients. The rates of loss of these substances from the blood and from the body were measured over a period of 3 to 4 weeks.

This study showed that the blood concentrations of the g-type gamma globulin labeled with I^{131} cleared with a half-time of 10 to 32 days. The time range for complete clearance of I^{131} from the body was 9 to 60 days. In patients who also received the m-type gamma globulin, the rate of metabolism was faster, showing a clearance half-time of 1.3 to 20 days. This work was funded by the U.S. Atomic Energy Commission.

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UCLA-15. Study of Manganese-54 and Copper-67 Absorption and Retention

IN A 1969 STUDY conducted at the University of California, Los Angeles, 14 subjects were administered isotopes of manganese and copper to determine the absorption and retention rates of these elements. The subjects were seven patients with hemochromatosis (excessive iron in the body) and seven normal, healthy volunteers.

Each subject was orally administered manganese-54 (Mn^{54}) as manganese chloride and measured for body retention with a whole-body counter two to three times a week. Eight subjects were counted for 3 weeks, and six subjects were counted for 60 days. Whole-body counting also was used to evaluate copper absorption and retention in the hemochromatosis patients who had been administered 20 to 25 microcuries of copper-67 (Cu^{67}).

These studies showed that Mn^{54} absorption ranged from 6 to 34 percent, with a mean of 13 percent. The Cu^{67} absorption ranged from 46 to 84 percent. Further study was needed to determine whether increased Mn^{54} absorption in two patients was associated with hemochromatosis or related to an iron deficiency produced by repeated phlebotomy (therapeutic bleeding). This research was funded by the U.S. Atomic Energy Commission.

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UCLA-16. Study of Inhaled Pollen-Associated Asthma Using Technetium-99m and Xenon-133

IN THE EARLY 1970s, researchers at the University of California Medical School, Los Angeles conducted a study of the distribution of inhaled grass pollen to understand how large pollen grains are able to induce bronchospasm reactions in sensitive subjects.

Four normal subjects and five asymptomatic allergic subjects inhaled pollen grains labeled with technetium-99m (Tc^{99m}). Gamma camera scintiphotos of their head, chest, and abdominal regions were then obtained. Standard lung function studies, which included administration of xenon-133 (Xe^{133}), were conducted before and after the pollen inhalation.

The results of the study indicated that the inhaled pollen grains were too large to reach the bronchial mucosa; and therefore the pollens deposited mostly in the mouth and pharynx and produced clinical asthma 4 to 8 hours later. This research was funded by the U.S. Atomic Energy Commission.

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UCLA-17. Liver Blood Flow Study Using Gold-198 and Technetium-99m

IN THE EARLY 1970s, researchers at the University of California, Los Angeles conducted studies on venous blood flow to the liver. The purpose of this study was to show that certain disease conditions tend to localize in the liver's right lobe.

Twelve volunteer patients without liver disease who were undergoing abdominal surgery participated as subjects. Each subject was administered 200 to 300 microcuries of gold-198 (Au^{198})–colloid intravenously. The uptake and retention of Au^{198} in lobes of the liver were then measured by scintiscan. Immediately thereafter, 2 to 5 millicuries of technetium-99m (Tc^{99m})–microaggregated albumin were injected into an arm vein and a second liver scan was performed. The distribution in blood flow of Au^{198} from the mesenteric vein was compared to the control injection using Tc^{99m}.

Results showed that streamlining to the right lobe did occur, but that it was dependent on which mesenteric vein (cecal, terminal ileal, midjejunal, or sigmoid) was injected. This experiment was funded by the U.S. Atomic Energy Commission.

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UCLA-18. Thrombophlebitis Scanning Using Technetium-99m and Iodine-125

IN THE EARLY 1970s, researchers at the Laboratory of Nuclear Medicine and Radiation Biology of the University of California, Los Angeles conducted studies using technetium-99m (Tc^{99m}) to diagnose and study thrombophlebitis (inflammation of a vein associated with clot formation) in veins of the legs. The purpose of this study was to see whether thrombophlebitis could cause pulmonary embolisms (obstructions caused by transported clots).

The subjects for the first study included 73 patients with thrombophlebitis (many of whom also had pulmonary emboli) and 90 control subjects without disease. This study involved injecting 1.5 millicuries of Tc^{99m}-albumin in the veins and measuring its accumulation. The results of this study showed that 80 percent of patients with pulmonary embolisms also had positive scans for thrombophlebitis.

In a related follow-on study involving additional normal subjects (10 or more) and hundreds of patients with actual or suspected thrombophlebitis, comparisons were made between two different diagnostic techniques. The first technique involved injection of 1.5 millicuries of Tc^{99m}-labeled albumin to detect areas of thrombophlebitis in 32 additional patients. The second technique involved injection of 100 microcuries of iodine-125 (I^{125})–labeled blood clotting factor (fibrinogen) in an additional 50 patients. Scans of the lower legs of each subject were then performed over a 7- to 30-day post-injection period to measure accumulation.

Both the Tc^{99m}-albumin and the I^{125}-fibrinogen uptake tests were found to be useful for detecting blood clots. This work was supported by the U.S. Atomic Energy Commission.

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UCLA-19. Studies of Liver Circulation and Metabolism in Normal and Diseased Subjects Using Technetium-99m Albumin Microaggregates

IN 1970 AND 1971, researchers at the Laboratory of Nuclear Medicine and Radiation Biology of the University of California, Los Angeles conducted gamma camera studies of the liver's dual circulation. The purpose of these studies was to investigate the utility of technetium-99m (Tc^{99m})–labeled albumin (a simple protein found throughout the body) aggregates for measuring the digestive capacity of the reticuloendothelial system.

Studies were conducted on an unspecified number of normal subjects, hospital patients with tumors, and patients with liver cirrhosis. Subjects underwent several tracer studies, each of which consisted of injection with unspecified amounts of Tc^{99m} microaggregates of albumin. Gamma camera images were then obtained to compare uptakes in the normal versus abnormal liver and in the liver versus heart.

A related study investigated the usefulness of Tc^{99m} albumin microaggregates for measuring the protein-digesting capability of the normal versus the diseased liver. Seventy-one studies were conducted on 47 patients with various liver and reticuloendothelial system disorders. Twelve hospital patients and one healthy volunteer with no known liver or infectious disorders were considered as the comparison group.

This study showed that diseased patients exhibited a more rapid excretion of Tc^{99m}-albumin via the biliary pathway and greater amounts of albumin degradation products in the intestines than comparison subjects. These studies were supported by the U.S. Atomic Energy Commission.

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UCLA-20. Studies of Hip Socket Vascularity Using Technetium-99m–Sulfur Colloid

IN 1971 AND 1972, researchers at the Laboratory of Nuclear Medicine and Radiation Biology of the University of California, Los Angeles conducted studies using technetium-99m (Tc^{99m}) sulfur colloid. The purpose of these studies was to gain information about the blood supply to the hip socket for use in treating hip diseases and fractures.

Subjects for these studies were an unspecified number of hospital patients with normal hips and patients with hip disease. Technetium-99m sulfur colloid was administered intravenously and

the pelvis was studied by gamma photoscan techniques. Scans were then correlated with pelvic x-rays for each patient.

These studies showed that uptake of Tc^{99m} sulfur colloid occurred symetrically in both hip sockets of patients with no known hip disease and that uptake was asymmetric in patients with hip disease. These studies were supported by the U.S. Atomic Energy Commission.

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UCLA-21. Test of Lung Scans in Normal Subjects Using Technetium-99m, Indium-113m, and Xenon-133

DURING THE PERIOD 1972 to 1973, researchers at the Laboratory of Nuclear Medicine and Radiation Biology of the University of California at Los Angeles conducted studies to learn more about abnormal lung scans from subjects with normal lung function. The study group consisted of 46 nonsmoking volunteers, aged 21 to 34 years, without history of asthma, emphysema, or other lung disease.

The subjects were administered an unstated amount of albumin macroaggregates labeled with technetium-99m (Tc^{99m}), either by inhalation or intravenous injection and were then given a chest image using a rectilinear scanner. The subjects also received pulmonary standard function tests. Thirteen percent of the scans indicated various perfusion defects such as pulmonary emboli, which were not present. It was concluded that these apparent anomalies could not be related to any pathologic origin.

In a later study, normal volunteer subjects and patients with suspected chronic bronchitis with normal results after pulmonary function testing were selected for gamma camera lung imaging using Tc^{99m}-albumin macroaggregates and albumin labeled with indium-113m (In^{113m}). In selected cases, the lung closing volumes were also measured with a xenon-133 (Xe^{133}) inhalation test. The number of subjects and amounts of radioisotope administered during these tests were not stated. This study showed a relation between abnormality of closing volume and the degree of unevenness of the inhalation scan, and indicated that the chest scan provided a more useful diagnostic tool than routine pulmonary function tests. These studies were supported by the U.S. Atomic Energy Commission.

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UCLA-22. Study of Cranial Developrnent Defects Using Fluorine-18

A STUDY IN 1973 was conducted at the Laboratory of Nuclear Medicine and Radiation Biology of the University of California, Los Angeles to determine the usefulness of fluorine-18 (F^{18}) in the study of cranial closure development in small children. Since x-ray and other clinical examinations can fail to detect the premature closing of the cranium in children, it was thought that cra-

nial imaging with F^{18} might provide a more effective diagnostic tool for early detection.

Subjects included 15 children with abnormal skulls, ages newborn to 4 years, and 7 children with normal skull development, ages 7 weeks to 16 years. Each subject was administered an unstated amount of F^{18} and then imaged in the nuclear medicine clinic.

The study provided an explanation for mechanisms involved in the premature closing of the cranium. This study was supported by the U.S. Atomic Energy Commission.

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UCLA-23. Study of Heart Chamber and Pulmonary Dilution Curves in Normal Subjects and Patients with Shunts Using Xenon-133 and Technetium-99m

A 1973 STUDY conducted by researchers at the Laboratory of Nuclear Medicine and Radiation Biology of the University of California, Los Angeles compared heart chamber dilution curves and dilution curves for blood vessels in the lungs in the diagnosis of congenital heart disease.

Thirteen normal patients (i.e., patients without heart disorders) and 33 patients with cardiac shunts were included in the study. The normal subjects ranged in age from 2 to 40 years and the patients with heart disease from 3 months to 48 years.

Unstated amounts of xenon-133 (Xe^{133}) in saline and technetium-99m (Tc^{99m}) sulfur colloid were intravenously administered. The flow of the isotopes was followed into the heart and blood vessels of the lungs, and images were made of Xe^{133} and Tc^{99m} uptake. Dilution curve measurements were also made using flow data. Differences between normal subjects and patients with shunts were observed. This study was funded by the U.S. Atomic Energy Commission.

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University of Chicago—Argonne Cancer Research Hospital

UC-1. Chromium-51 and Iron-59 Used to Study Red Blood-Cell Production

STUDIES WERE CARRIED OUT in the early 1950s at the Argonne Cancer Research Hospital to determine the rate of red cell production and destruction in healthy and anemic subjects. Two to 4 microcuries of iron-59 (Fe^{59}) were added to 20 milliliters of plasma and injected into the arms of the subjects. Several days after the administration of the Fe^{59}, the procedure was repeated using chromium-51 (Cr^{51})–labeled plasma. The subjects were six healthy individuals and two anemic individuals.

The combined use of Cr^{51} and Fe^{59} provided an indicator of red cell survival and total blood volume in humans. This work was carried out under a contract between the Office of the Surgeon General, the United States Army, and the Department of Medicine of the University of Chicago. The U.S. Atomic Energy Commission provided funding to the Argonne Cancer Research Hospital through the University of Chicago, its operating contractor. (Included in *The DOE Roadmap* of February 1995)

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UC-2. Studies on the Clinical Application of Yttrium-90

IN 1953, AT THE ARGONNE Cancer Research Hospital, preliminary studies were carried out with yttrium-90 (Y^{90}) to determine whether Y^{90} might be used for intracavitary therapy. A patient in the terminal stage of carcinomatosis was injected intrapleurally with a solution containing about 1.35 millicuries of Y^{90}.

Samples of fluid were drawn from the pleural cavity at 3, 24, and 48 hours and at autopsy, which was 7 days after the administration of Y^{90}.

The study found that Y^{90} had a biological retention half-time of 30 to 36 hours. The U.S. Atomic Energy Commission provided funding to the Argonne Cancer Research Hospital through the University of Chicago, its operating contractor. (Included in *The DOE Roadmap* of February 1995)

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UC-3. Chromium-51 Used to Study Primaquine Sensitivity

IN 1953, THE UNIVERSITY of Chicago and the Argonne Cancer Research Hospital conducted studies to determine the hemolytic defect that develops during primaquine administration. Primaquine is an antimalarial drug that induces an acute hemolytic anemia in some people, mainly members of heavily pigmented races.

The subjects for this study were healthy, male inmates from the Illinois State Penitentiary at Statesville. None of the inmates had ever had malaria. All of the primaquine-sensitive subjects were African-Americans and the primaquine-nonsensitive subjects included both African-American and Caucasian subjects. There was also one subject who was a student at the University of Chicago, who was included in the study because he had been splenectomized 2 years prior to the initiation of this research.

Blood labeled with 200 to 300 microcuries of chromium-51 as sodium chromate was injected into both the normal subjects and the group of primaquine-sensitive subjects. Subsequently, primaquine was administered to subjects in both groups. Blood samples showed that the primaquine-sensitive subjects developed a severe anemia, which was attributed to a unique susceptibility of their red blood cells. This study was carried out under a contract between the Department of Medicine at the University of Chicago and the Office of the Surgeon General for the United States Army. The radiochromium was obtained under an authorization from the Isotopes Division of the U.S. Atomic Energy Commission at Oak Ridge. The Argonne Cancer Research Hospital was operated by the University of Chicago, which was funded by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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UC-4. Chromium-51 Used to Measure Red Cell Survival Times in Subjects with Liver Diseases

IN 1953, at the Argonne Cancer Research Hospital, chromium-51 as sodium chromate was used to measure the red cell survival time of patients with liver disease. The subjects in this study were 19 patients with various types of liver disease. Liver biopsies were taken from all cases, except from four patients with bleeding tendencies.

The results indicated an abnormal red cell survival time in these patients. This study was supported in part by the Office of the Surgeon Gen-

eral, United States Army. The Argonne Cancer Research Hospital was operated by the University of Chicago, which was funded by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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UC-5. Radioactive Carbon in Studies of Cholesterol Metabolism in Humans Using Carbon-14

IN 1955, a study on the metabolism of cholesterol was reported by the Department of Medicine and the Argonne Cancer Research Hospital of the University of Chicago and the Los Alamos Scientific Laboratory. The objective of the study was to determine the rate at which cholesterol labeled with carbon-14 (C^{14}) appeared in the plasma and to determine how much of the C^{14} was incorporated. This study was conducted on patients admitted to the research wards of the Argonne Cancer Research Hospital. Thirty-four subjects with various forms of cancer were studied. Both male and female subjects were included; their ages ranged from 23 to 71 years.

Patients received 100 or 200 microcuries of C^{14}-labeled sodium acetate. The C^{14}-labeled acetate was administered either orally or intravenously, and in some cases by both routes. Larger amounts were given to patients having the shortest life expectancies. Blood was drawn from 30 minutes to several weeks after administering the C^{14} acetate. Some patients were subjected to additional tests to determine the amount of C^{14} lost from the body by respiration or excretion. This study was funded by the U.S. Atomic Energy Commission, the Damon Runyon Memorial Fund, and the American Cancer Society. (Previously described in #23 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

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UC-6. Study of the Origin of Steroid Hormones Using Tritium and Carbon-14–Labeled Compounds

IN 1955, a study was conducted at the Argonne Cancer Research Hospital, in collaboration with scientists at the Los Alamos Scientific Laboratory, to determine the relationship between dietary cholesterol and the synthesis of hormones in the body.

Seven patients who were to have their adrenal glands surgically removed or who were scheduled to have a therapeutic abortion, were fed 50 microcuries of tritium-labeled (H^3) cholesterol 7 days prior to surgery. An additional amount of 10 microcuries of H^3-labeled cholesterol was administered orally each succeeding day before surgery. During the surgery the patient was given 100 microcuries of acetate labeled with carbon-14 (C^{14}) by intravenous injection. The aborted fetuses, the removed adrenal gland, and other biopsy tissue samples were analyzed for C^{14}- and H^3-labeled cholesterol and steroid-based hormones.

This study showed that dietary cholesterol was rapidly converted to steroid hormones and that C^{14} from the acetate source was also incorporated into hormones. The research was supported by the U.S. Atomic Energy Commission. (Previously described in #23 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

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UC-7. Chromium-51 Used to Study Red Blood Cells

THIS RESEARCH was carried out at the Argonne Cancer Research Hospital in the mid 1950s. This study was the first to use the chromium-51 (Cr^{51}) labeling technique to study red cell survival in patients with abnormal hemoglobin syndrome.

The subjects were 11 black patients with various blood disorders including 4 with sickle cell anemia, as well as 2 healthy subjects. One hundred milliliters of blood were drawn from each patient, labeled with 200 microcuries of Cr^{51}, and reinjected. Samples of blood and feces were collected and analyzed to determine red cell survival times.

The study showed that there was a decreased survival of erythrocytes (red blood cells) in patients with sickle cell anemia. The U.S. Atomic Energy Commission provided funding to the Argonne Cancer Research Hospital through the University of Chicago, its operating contractor. (Included in *The DOE Roadmap* of February 1995, and since revised)

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UC-8. Digitoxin Metabolism Studies with Carbon-14 Digitoxin

IN THE MID-1950s, studies were conducted at the Argonne Cancer Research Hospital on the uptake and retention of digitoxin labeled with carbon-14 (C^{14}). Digitoxin is a drug used in the treatment of cardiac failure. This study sought to determine the rate of disappearance of unchanged digitoxin and to determine the conversion products arising from the parent drug.

Eight subjects with congestive heart failure were given an intravenous injection of 0.5 to 1.5 milligrams of digitoxin containing 0.36 to 0.65 microcurie per milligram of C^{14}. Digitalis medication had been withheld from 14 to 34 days prior to the injection and none was given after the injection. Subsequent to the injection, several 10 to 20 milliliter blood samples were drawn in a 96-hour period.

The same researchers conducted another study, using three terminal patients. The purpose of the second study was to determine the distribution of digitoxin in various tissues of the body and to determine the pathway by which the drug is removed from the body. The radioactive digitoxin was isolated from digitalis plants that had been grown in an atmosphere of C^{14}. The specific activity of the C^{14} ranged from 0.48 to 0.65 microcurie per milligram digitoxin. For three terminal patients, multiple doses were intravenously administered to maintain an adequate concentration in the tissues. Tissue samples were taken after the patients died. These tissues were analyzed for digitoxin content.

Further research was conducted where radioactive metabolites of digitoxin were studied following the administration of single intravenous doses of digitoxin labeled with C^{14} or with H^3. This research determined the reactions that digitoxin undergoes in humans. The Argonne Cancer Research Hospital was operated by the University of Chicago, which was funded by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995 and since revised.)

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UC-9. Carbon-14–Labeled Proteins in Multiple Myeloma

THIS RESEARCH WAS CARRIED OUT at the Argonne Cancer Research Hospital in the early to mid-1950s. A total of 5.41 grams of carbon-14 (C^{14})–labeled glycine were given orally in divided doses over an 11-hour period to a patient suffering from multiple myeloma, a malignant neoplasm that originates in the bone marrow and is characterized by abnormalities in formation of plasma protein. The myeloma cells produce abnormal proteins in the serum and urine. Blood samples were drawn and 24-hour urine collections were analyzed to determine the rate of synthesis and the possible precursor relationships of myeloma globulins and Bence-Jones proteins.

In a second experiment, the same researchers conducted further experiments with another patient who had different pathological proteins and graver clinical conditions. The subject of this experiment was a 70-year-old male with multiple myeloma. The patient was given 20 grams of stable nitrogen-15–labeled glycine. The results showed the direct interaction of the Bence -Jones proteins with the metabolic pool of nitrogen.

In a third experiment, a 64-year-old female patient was injected with C^{14}-labeled L-lysine to determine the rate of synthesis and excretion of the Bence-Jones protein. On the day of the experiment, a catheter was inserted and the patient was injected with 300 microcuries of L-lysine labeled with C^{14}. Urine and respiration were analyzed and two dialysis experiments were performed on the patient.

In a fourth experiment, a 67-year-old male patient at the Argonne Cancer Research Hospital, was injected with 450 microcuries of C^{14} glutamic acid. One reason for conducting this last experiment was to learn whether glutamic acid might be a better compound to use to study protein synthesis than L-lysine or glycine. This research was supported by grants from the National Cancer Institute, the National Institutes of Health, and the American Cancer Society. The Argonne Cancer Research Hospital was operated by the University of Chicago, which was funded by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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Reports of the Argonne Cancer Research Hospital. ❑

UC-10. Carbon-14–Labeled Digitoxin Administered to Pregnant Women to Determine Fetal Distribution

THIS STUDY WAS CONDUCTED at the Argonne Cancer Research Hospital in the mid-1950s. The purpose of the study was to investigate the transfer of digitoxin across the placental barrier of pregnant women and to determine the relative concentration of the unchanged drug and its metabolic products in various fetal organs.

The subjects were four pregnant women who were hospitalized at the Chicago Lying-In Hospital. Three of the women had abortions; the fourth delivered an anencephalic baby.

Three to 5 hours before hysterotomy, three of the women were intravenously given from 0.25 to 0.5 milligram of digitoxin labeled with carbon-14 (C^{14}) at a concentration of 0.25 to 0.5 microcurie per milligram. The fourth woman was given 0.5 milligram of the radioactive drug 2 to 3 hours before the expected time of delivery. The Argonne Cancer Research Hospital was operated by the University of Chicago, which was funded by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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UC-11. Human Tracer Studies Using Tritium- and Carbon-14–Labeled Cholesterol

IN 1957, an experiment was conducted at the Argonne Cancer Research Hospital using radioactively labeled cholesterol. A 60-year-old man with chronic arthritis was the subject of this study.

The subject received an intravenous injection containing 33.8 microcuries of tritium-labeled (H^3) cholesterol and 4.3 microcuries of cholesterol labeled with carbon-14 (C^{14}). Blood samples were drawn at various times, starting about 4 hours after injection and continuing periodically for 10 days. Urine samples were also collected and analyzed for C^{14}- and H^3-labeled cholesterol and steroid hormones.

This experiment showed the advantages of using H^3 and C^{14} as tracers for cholesterol metabolism studies in humans. It also showed the distribution of C^{14} and H^3 in hormones synthesized from cholesterol. This study was funded by the Damon Runyon Memorial Fund and the U.S. Atomic Energy Commission. (Previously described in #23 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

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UC-12. Study of Hormone Conversion During Human Pregnancy Using Carbon-14

THIS STUDY WAS CONDUCTED by the Argonne Cancer Research Hospital in the mid- to late 1950s. The purpose of the study was to determine whether acetate and cholesterol are precursors of estrone in pregnant women. The subject was a 36-year-old white woman who underwent a thyroidectomy prior to pregnancy. An intramuscular injection of 35.09 microcuries of testosterone-4-C^{14} was administered during the 7th week of pregnancy and an abortion was performed 4 days after the injection. About 55 percent of the radioactivity derived from the labeled testosterone was eliminated from the body by way of the kidney.

The results of this experiment demonstrated the conversion of testosterone to estrone during the course of human pregnancy. The U.S. Atomic Energy Commission provided funding to the Argonne Cancer Research Hospital through the University of Chicago, its operating contractor. (Included in *The DOE Roadmap* of February 1995)

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UC-13. Studies on Uric Acid Labeled with Carbon-14

IN THE LATE 1950s, studies were carried out at the Argonne Cancer Research Hospital to investigate the metabolism of uric acid in humans. Uric acid labeled with carbon-14 (C^{14}) was intravenously injected into five individuals: two healthy subjects, two gouty subjects, and one patient with arteriosclerotic heart disease. Urine samples were analyzed for C^{14} content. For three individuals, after the administration of the C^{14}-labeled uric acid, samples of expired air were collected and radioassayed for C^{14}-dioxide.

The expired air from all three patients showed that some of the injected uric acid had been degraded to carbon dioxide and ammonia. Saliva, gastric juice, and bile were also radioassayed to determine the amount of uric acid excreted into the intestine.

To verify the role of the intestinal flora on uricolysis, the degradation of intravenously administered uric acid C^{14} was studied before and after a high degree of intestinal bacteriostasis had developed. The subject was a healthy 57-year-old male who was kept on a diet during the study and for 10 days prior to the study. After intravenous administration of 33 milligrams of uric acid containing 35 microcuries of C^{14}, urine and expired-air samples were collected for 10 days. On the 11th day, three types of antibiotics were orally administered and after establishing the desired bacteria level in the intestinal tract, 35 microcuries of C^{14}-labeled uric acid were intravenously injected.

This research found that intestinal flora play a prominent role in the degradation of uric acid in humans. The Argonne Cancer Research Hospital was operated by the University of Chicago and supported by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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UC-14. Carbon-14 Study of the Carbon Dioxide Pool in Humans

THIS RESEARCH WAS CONDUCTED in the late 1950s at the Argonne Cancer Research Hospital. Since many materials labeled with carbon-14 (C^{14}) are oxidized to $C^{14}O_2$, this research sought to determine the metabolic pool of carbon dioxide in humans. A solution of sodium carbonate-hydrogen labeled with C^{14} was given intravenously at a constant rate for a period of 2 to 4 hours, while the one subject breathed continuously through a beta-particle chamber. The Argonne Cancer Research Hospital was operated by the University of Chicago, which was funded by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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UC-15. Metabolism, Retention, and Excretion of Molybdenum-99

IN THE LATE 1950s, the Argonne Cancer Research Hospital conducted studies on the absorption and excretion of molybdenum, using molybdenum-99 (Mo^{99}). The studies were carried out on healthy subjects to determine the role of molybdenum in the oxidation of hypoxanthine and xanthine (precursors of uric acid). The urinary excretion rate of molybdenum in normal subjects was determined. Molybdenum was readily absorbed from the gastrointestinal tract. Seventy-five percent of ingested Mo^{99} was recovered in the first 24-hour urine sample. The Argonne Cancer Research Hospital was operated by the University of Chicago, which was funded by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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UC-16. Metabolism of Strontium-85 and Calcium-47

IN 1960, at the Argonne Cancer Research Hospital, tracer amounts of strontium-85 (Sr^{85}) as strontium chloride, in amounts of 26 to 40 microcuries, were administered intravenously to seven adult subjects (six males and one female).

Measurements were made of Sr^{85} in blood specimens, urine specimens, and the total body. The subjects included a woman with moderate osteoporosis, a 66-year-old male with multiple myeloma, and two males in the 60-year age group. The research found that strontium is retained with greater avidity where there is deossification of the skeleton (skeletal disease). One other patient with metastatic parathyroid carcinoma was intravenously administered 50 microcuries of Sr^{85}, and total-body counting was performed over a 238-day period.

Studies on the metabolism of calcium were carried out using calcium-47 (Ca^{47}). Sixteen hospitalized patients were counted in the whole-body counting facility following a single 20-microcurie injection of Ca^{47}. The Argonne Cancer Research Hospital was operated by the University of Chicago, which was funded by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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UC-17. Development of Iodine-131–Labeled Fluorescein as a Brain Tumor Imaging Agent

THIS STUDY WAS CONDUCTED in 1960 at the Argonne Cancer Research Hospital. Fluorescein labeled with radioiodine (I^{131}) was developed to diagnose tumors of the central nervous system. Information obtained included the rate of disappearance from the blood, the rate of excretion, distribution in tissues, and comparison of concentrations in brain tumors and in normal brain tissue.

Patients suspected of having brain tumors were selected for studies on the localization and retention of I^{131}-fluorescein. The I^{131}-fluorescein was administered by intravenous injection. Urine and stool samples were also collected from six patients over a 48-hour period for I^{131} analysis. Two normal volunteers were also injected with 5.7 microcuries of I^{131}-fluorescein. A total of 102 patients were involved as subjects. This re-

search was supported in part by a grant from the American Cancer Society. The Argonne Cancer Research Hospital was operated by the University of Chicago, which was funded by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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UC-18. Studies Using Carbon-14–Labeled Compounds in Patients with Gout

STUDIES WERE CONDUCTED by the Argonne Cancer Research Hospital in the early 1960s on patients with gout, to determine the metabolism of uric acid in humans. This research was conducted to determine whether patients with various degrees and types of gout had an increased incorporation of glycine into uric acid. Gout is an inherited metabolic disorder characterized by chronic arthritis and usually by an elevated uric-acid blood level.

Twelve patients with gout were intravenously administered glycine labeled with carbon-14 (C^{14}) over a period of 60 minutes. The results of these experiments demonstrated that excessive incorporation of glycine into uric acid is usually confined to gouty subjects with abnormally high urinary outputs of uric acid.

Three of the subjects who were overproducers of uric acid were studied in detail to determine the pathway whereby glycine is incorporated into uric acid more promptly than in normal humans. Two of the healthy subjects and one other patient with gout, who did not overproduce uric acid, were also part of this study. These individuals were administered azathioprine, a cytotoxic and immunosuppressive agent, for 7 to 10 days prior to the intravenous administration of 100 microcuries of glycine labeled with C^{14}.

This research found that when azathioprine was given to subjects who overproduce uric acid, their urinary uric acid fell to normal values. The Argonne Cancer Research Hospital was operated by the University of Chicago, which was funded by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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UC-19. Use of Molybdenum-99 for Liver Scanning Studies

THE EARLY 1960S, the Argonne Cancer Research Hospital used molybdenum-99 (Mo^{99}) as a tracer agent to image the liver and to determine the disappearance from the blood of intravenously injected Mo^{99}. Both normal subjects and patients with liver disease were administered between 40 and 100 microcuries of Mo^{99} by intravenous injection. Liver scans were performed at the Argonne Cancer Research Hospital's whole-body counting facility.

Subjects included normal volunteers and one patient with viral hepatitis. Approximately 100 liver scans were performed using Mo^{99} as a tracer. The Argonne Cancer Research Hospital was operated under contract by the University of Chicago, which was funded by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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UC-20. Metabolism of Lithocholic Acid Labeled with Carbon-14

THESE STUDIES WERE carried out by the Argonne Cancer Research Hospital in the early 1960s to determine the metabolism of lithocholic acid. Lithocholic acid, a steroid produced by the human body, is found in human bile and feces.

A dose of 11 microcuries of lithocholic acid labeled with carbon-14 (C^{14}) was orally administered to four patients, 20 to 72 hours before they underwent elective gallbladder surgery for gallstones. Two other patients with functioning gallbladders were studied after oral administration of 50 microcuries of lithocholic acid labeled with C^{14}. Bile was obtained during their gallbladder operations and analyzed for C^{14}. The Argonne Cancer Research Hospital was operated under contract by the University of Chicago, which was funded by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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UC-21. Preliminary Tracer Studies Using Technetium-99m and Iodine-131

STUDIES WERE CONDUCTED in 1961 at the Argonne Cancer Research Hospital on the use of technetium-99m (Tc^{99m}) as a tracer and imaging agent for nuclear medicine. The purpose of this research was to determine the biological retention half-time, and suitability as an imaging agent, of Tc^{99m}.

Scans of subjects were made with a Picker Magnascanner 30 minutes after intravenous injection of Tc^{99m}. Overall, 86 patients were studied. Fifty-seven had normal thyroid function, 17 had overactive thyroids, 6 had underactive thyroids, and 6 had no thyroid function.

One white female received an intravenous injection of 1 millicurie of Tc^{99m}. Thyroid scans were conducted on a clinically normal white male, 30 minutes after intravenous injection of Tc^{99m}, and the results were compared with scans conducted after iodine-131 (I^{131}) administration. The urinary and fecal excretion of Tc^{99m} pertechnetate was studied in four patients. At least two normal subjects, including a healthy African-American male, were administered 440 microcuries of Tc^{99m}. Another male subject was administered 1 millicurie of Tc^{99m} and dose calculations were made for the total body, stomach, and thyroid.

With a biological retention half-time of 48 hours, Tc^{99m} was found to be a suitable imaging agent. It provided good scans with unmodified equipment, while providing a radiation dose to the thyroid of only 100 millirads, or one-thousandth of the dose from 50 microcuries of I^{131}. The Argonne Cancer Research Hospital was operated under contract by the University of Chicago, which was funded by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995, and since revised.)

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UC-22. Metabolism and Absorption of Skin Medications Labeled with Carbon-14

THIS RESEARCH WAS CONDUCTED by the Argonne Cancer Research Hospital in the mid-1960s. Eleven normal and nine psoriatic Caucasian volunteers served as subjects.

Palmitic acid containing 1 microcurie of carboxyl carbon (C^{14}) label dissolved in petroleum ether was dripped onto each of two demarcated areas of lesion-free skin on the back of each subject. After 2.5 hours, the skin was wiped with petroleum ether-soaked cotton and counted for C^{14} activity.

The entire study was repeated in four additional normal volunteers following the application of an ointment comparable to the standard treatment for psoriasis. The study was also repeated in one other normal volunteer and in two patients with minor eczema. The Argonne Cancer Research Hospital was operated under contract by the University of Chicago, which was funded by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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UC-23. Studies on the Use of Iodine-131 Antifibrinogen

THIS WAS A COLLABORATIVE study between the Argonne Cancer Research Hospital and the University of Rochester conducted in the mid-1960s. Its purpose was to determine the diagnostic and therapeutic potential of antifibrinogen labeled with iodine-131 (I^{131}), which was thought to combine with circulating fibrinogen and to localize in tumors.

In half of the tumors studied, localization allowed for clear visualization on scanning. The I^{131}-labeled antifibrinogen was intravenously administered. This procedure was carried out in two patients.

Although some tumors imaged, this study was not successful in treating cancer because of poor tumor localization of the I^{131} antifibrinogen. The Argonne Cancer Research Hospital was operated under contract by the University of Chicago, which was funded by the U.S. Atomic En-

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UC-24. Bone-Tissue Radiography Using an External Source of Iodine-125

A METHOD WAS DEVELOPED at the Argonne Cancer Research Hospital in Chicago to measure bone mineral content in animals or humans, using an external iodine-125 (I^{125}) source. Bone mineral was determined by transmitting a small beam of photon radiation from an I^{125} source through a single human finger bone, capturing an image of the finger on radiographic film. Mineral content was determined by analyzing the image density.

This technique was tested on a group of postmenopausal women (with ovaries removed) who were estrogen deficient to determine the beneficial effects of estrogen therapy on bone mineralization. Another group of postmenopausal women with ovaries and no hormone therapy was also studied, again using finger bone radiography. A group of premenopausal women served as controls. One hundred patients participated in this study.

The study showed that hormone therapy had a beneficial effect on bone mineral content in women. The Argonne Cancer Research Hospital was operated by the University of Chicago and supported by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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UC-25. Retention of Iron-59 in the Lungs

THIS STUDY WAS CONDUCTED at the Argonne Cancer Research Hospital in 1967. This study compared the amount of blood lost from the body to that retained from the lungs in a menopausal woman with pulmonary hemosiderosis, a disease characterized by expectoration of blood from the lungs or bronchial tubes. This was the first study in which linear profile scanning of iron-59 (Fe^{59}) was used for this purpose.

When the patient was in remission from the disease, 10 microcuries of Fe^{59} were injected intravenously. Analysis was done on plasma iron clearance, serial body surface counting rates, erythrocyte incorporation, and linear profile scanning of Fe^{59}. The Argonne Cancer Research Hospital was operated under contract by the University of Chicago, which was funded by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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UC-26. Studies on the Radiation Sensitivity of Tumors in Normal Tissues After Chemically Induced Hyperthyroidism

THIS RESEARCH WAS CONDUCTED by the Argonne Cancer Research Hospital in the late 1960s to determine whether induced hyperthyroidism increased the sensitivity of tumors to therapeutic x-rays. The subjects of this experiment were patients with advanced cancer who could tolerate an elevated metabolic rate caused by oral doses of triiodothyronine. X-rays were also administered in daily fractionated doses.

In two patients with bronchogenic carcinomas, after induction of the hyperthyroid condition, the metastases on one side were treated and the other side was treated only after the basal metabolic rate had been allowed to return to normal. At autopsy, 3 months after the treatment, the side treated with the drug and the x-rays showed only fibrosis while the tumor was still present in the side treated by x-rays alone.

Another patient with lung metastasis due to melanoma was subjected to the combined treatment with no response.

In two patients with adenocarcinoma brain metastases and unknown primary lesions, the combined therapy was effective on the brain lesions but not on the primary lesions. The U.S. Atomic Energy Commission provided funding to the Argonne Cancer Research Hospital through the University of Chicago, its operating contractor. (Included in *The DOE Roadmap* of February 1995, and since revised).

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UC-27. Metabolism and Retention Studies Using Selenium-75

THESE STUDIES WERE carried out in the late 1960s at the Argonne Cancer Research Hospital to determine the organ uptake of selenium-75 (Se^{75}). Four subjects were intravenously injected with Se^{75}. The first was a male with a varicose ulcer who was administered 100 microcuries. The second was a male with mild diabetes who was administered 200 microcuries on one occasion and was subsequently administered 220 microcuries. Subjects were followed by whole-body counting for up to 30 months.

The biological half-time was found to be about 80 days. The results of this study found that after a single injection of Se^{75}, one-half of the Se^{75} was eliminated from the body after 80 days. The Argonne Cancer Research Hospital was operated under contract by the University of Chicago, which was funded by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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UC-28. Comparison of Gallium-68, Technetium-99m, and Indium-113m for Diagnosis of Tumors

IN THE LATE 1960s, the Argonne Cancer Research Hospital conducted studies to determine the combination of radionuclide preparation and imaging system with the best lesion-detection capabilities per unit radiation dose.

Preparations of gallium-68 (Ga^{68}), technetium-99m (Tc^{99m}), and indium-113m (In^{113m}) were used to detect lesions in the brain, kidney, liver, and lung. Biological half-times in humans were compared with those in mice by measuring radioactivity in the excreta. The Argonne Cancer Research Hospital was operated under contract by the University of Chicago, which was funded by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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UC-29. Study of X-Ray Treatment of Gastric Ulcers

FROM 1937 TO 1954, researchers at the University of Chicago Department of Medicine conducted studies of the treatment of gastric (stomach) ulcers using radiation from x-rays. The purpose of the study was to evaluate the therapeutic benefits of x-rays in treating gastric ulcers.

The subjects were 116 patients with gastric ulcers; they ranged in age up to 70 years. All received x-ray therapy in addition to other therapy. The goal of the x-ray therapy was to reduce acid gastric secretions and to facilitate ulcer healing. The estimated total dose to stomach tissues ranged from 1,100 to 2,930 rads.

The researchers claimed that moderate irradiation of the stomach reduced acid secretion and served as a safe and valuable adjunct to conventional treatment of benign gastric ulcers. However, this form of therapy was discontinued as the risks were perceived to outweigh the benefits, and as nonradiation remedies for treating gastric ulcers were developed. Similar studies were conducted from 1936 to 1947 involving about 800 patients in an effort to reduce stomach acid secretions and allow healing of gastric ulcers. This work was supported by the U.S. Atomic Energy Commission.

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UC-30. Experimental Neurosurgery Using Palladium-109 and Silver-111 Implants in Parkinson's Disease Patients

IN THE 1950s, it was common for neurosurgeons to try to control the abnormal movements and rigidity of Parkinson's disease by creating cerebral lesions. The surgical methods then in use all had some type of disadvantage. Researchers at the Division of Neurological Surgery, Department of Radiology and at the Argonne Cancer Research Hospital collaboratively investigated the use of beta-ray source implants as an alternative method for creating similar lesions.

Eight patients with Parkinson's disease were treated using palladium-109 (Pd^{109}) to induce the desired lesions. A Pd^{109} needle was inserted through the skull under local anesthetic, using intensified fluoroscopic mapping to monitor the insertion and placement of the needle. Most patients had alleviation of rigidity or tremor or both upon placement of the needle. In others, the improvement progressed while the needle remained in place for up to 90 minutes.

If the Parkinson's disease symptoms returned, the procedure was repeated and another lesion was made. The radiation dose to the patient's skin during the fluoroscopic monitoring was estimated to be equivalent to a fluoroscopic examination of the gastrointestinal tract.

The researchers also investigated the use of silver-111 as an alternative, implanted bilaterally in two Parkinson's disease patients. This study showed that the radiation implants produced satisfactory relief of symptoms in the patients treated. This work was supported by the Simms Foundation. The Argonne Cancer Research Hospital was operated by the University of Chicago, under contract with the U.S. Atomic Energy Commission.

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UC-31. The Use of Yttrium-90 Pellets to Destroy the Pituitary Gland in Patients with Hormonally Influenced Cancers

BY THE EARLY 1950s, it was thought that inactivation of the pituitary gland might be effective for the long-term control of metastatic neoplasms of certain hormonally influenced tissues such as those in the breast and prostate. Some studies had shown that surgical removal of the pituitary gland had no significant effect on the tumors, and that residual pituitary tissue identified in these cases at autopsy was thought to have accounted for this lack of effect. Further research conducted at Argonne Cancer Research Hospital sought to determine whether total destruction of the pituitary gland could be accomplished by irradiation using yttrium-90 (Y^{90}) pellets implanted into the gland.

In 1954, following completion of preliminary animal experiments, pituitary gland irradiation was initiated in a series of patients with advanced metastatic cancers of hormonally influenced tissues with some hope of achieving a palliative effect. Initially, four pellets of Y^{90} containing 0.63 to 0.88 millicurie per Y^{90} pellet were inserted into the bony sella of the skull in each of six patients. One of these patients later had two additional pellets implanted.

On the basis of autopsy findings, it was determined that the radiation dose from four pellets was inadequate for total destruction of the pituitary, and that proper placement of the pellets in the pituitary was technically more difficult than had been anticipated. The protocol was modified and three additional patients were each implanted with six Y^{90} pellets. Subsequently, another eight patients were implanted with seven or eight pellets each that had an average total activity of 6 millicuries. In five of the later cases, the implantation procedure was performed under local rather than general anaesthesia because of the patients' poor preoperative condition. At least one patient experienced some palliative benefit following the treatment with Y^{90} pellets.

This study showed that irradiation of the pituitary gland using Y^{90} pellets was less risky to the patient than surgical excision. This research was supported by the U.S. Atomic Energy Commission.

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UC-32. Treatment of Pancreatic Cancer Using Implanted Iodine-131

IN THE EARLY 1950s, an established cancer treatment was adapted for use at the Argonne Cancer Research Hospital in patients with carcinoma of the pancreas. This procedure was used to treat carcinoma of the pancreas in seven patients. The subjects ranged in age from 42 to 66 years. In this procedure, fine polyethylene tubing filled with mercury was threaded through and around patients' abdominal tumors. The placement of the tubing was checked by x-ray imaging before closing the abdomen. Further x-ray images of the implant with stable mercury in the tubing were made, and from these, the volume of tissue to be irradiated was calculated. Subse-

quently, the contents of a centrifuge tube containing an isotope solution of iodine-131 (I^{131}) were drawn by suction into the tubing. Vulnerable organs were surgically moved a small distance away from the tubing. The amounts of I^{131} placed in the tubing ranged from 28 to 176 millicuries, and the calculated total radiation dose to the tumors ranged from 5,000 to 9,200 rads.

This method of treatment provided palliative (relief, not cure) benefit for four patients and appeared to extend the survival of one patient. The results indicated radiation could be delivered to intra-abdominal tumors in greater amounts than could be tolerated using external-beam radiation therapy, with less irradiation of normal tissues. The Argonne Cancer Research Hospital was operated by the University of Chicago, under contract with the U.S. Atomic Energy Commission.

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UC-33. Chicago Studies of the Metabolism of a Tuberculosis Drug Using Carbon-14

IN 1952, the University of Chicago conducted studies on the distribution and excretion of isoniazid, a new and clinically accepted antituberculosis drug, using isoniazid chloride labeled with carbon-14 (C^{14}). The study subjects were three patients being treated for tuberculosis at the University of Chicago Clinics, one male and two females, ages 23, 28, and 40 years, respectively.

The subjects were administered one or two intramuscular injections of 200 to 430 microcuries of C^{14}-labeled isoniazid chloride to determine its distribution and excretion from the body over time. Samples obtained from the subjects for C^{14}-isoniazid analysis included surgically removed tissues, whole blood, plasma, urine, saliva, gastric juice, spinal fluid, pleural fluid, and feces.

This study showed that peak levels of isoniazid in blood and plasma were reached within 1 hour after injection, that measurable quantities were found in blood and plasma 3 to 7 days after a single injection, and that the drug diffused freely throughout the body, with highest concentrations in the lung and skin tissues. This study contributed to the understanding of the metabolism of isoniazid, which became an important factor in the effective treatment of tuberculosis. It was supported by a grant from Motorola Inc., and by the Abbott Memorial Research Fund of the University of Chicago, the U.S. Public Health Service, and the U.S. Atomic Energy Commission.

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UC-34. Cholesterol Studies Using Carbon-14 and Tritium

DURING THE MID-1950s, researchers in the Department of Medicine, University of Chicago and the Argonne Cancer Research Hospital, in collaboration with Los Alamos Scientific Laboratory conducted studies on cholesterol synthesis using carbon-14 (C^{14})–labeled acetate and tritium (H^3)-labeled cholesterol tracers. The purpose of this study was to develop a double isotope labeling technique for investigating the metabolism of sterols and steroid hormones in man. Specifically, this work studied the conversion of acetate to cholesterol.

Four female hospital patients ranging in age from 36 to 60 years participated as subjects. Each subject was intravenously administered 100 to 200 microcuries of C^{14}-labeled acetate and orally administered 18.2 to 70.2 microcuries of H^3-labeled cholesterol. Carbon-14 activity was measured in exhaled breath as $C^{14}O_2$ and H^3 activity was measured in cholesterol that had been isolated from blood samples. Tissue biopsies were obtained from selected organs and tissues for C^{14} and H^3 analysis; these included the left ovary, tumor tissue (if present), right 12th

rib, right adrenal, peritoneal fat, muscle, and skin.

These studies verified the feasibility of the double tracer technique for investigating cholesterol metabolism in humans and showed cholesterol synthesis in the adrenals and ovaries. This work was supported by the Damon Runyon Memorial Fund, the American Cancer Society, the Chicago Lying-In Hospital, and the U.S. Atomic Energy Commission.

References

LeRoy, G.V., R.G. Gould, D.M. Bergenstal, H. Werbin, and J.J. Kabara. "Studies on Extrahepatic Cholesterol Synthesis and Equilibrium in Man Using a Double Labeling Technique." *The Journal of Laboratory and Clinical Medicine*. Vol. 49, January–June 1957, pp. 858–868. ❑

UC-35. Study of Glutamic Acid Metabolism Using Carbon-14 Tracer

DURING THE MID-1950s, researchers at the Argonne Cancer Research Hospital conducted studies on the metabolism of D-glutamic acid (an amino acid occurring in proteins) using carbon-14 (C^{14}) as a tracer. D-glutamic acid metabolism had not been fully explored in humans, although this acid was thought to be present in human and animal tumors, and thus was of interest in understanding tumor development.

A 67-year-old male terminal cancer patient served as the study subject. Approximately 450 microcuries of C^{14} DL-glutamic acid were given intravenously over a 15-minute interval to the fasting patient. Nineteen blood samples were obtained within the following 24 hours by intravenous catheter, and urine samples were collected by urethral catheter. Time curves were determined for the C^{14} activity of expiratory CO_2 and for blood and urine components.

This study showed that L-glutamic acid was metabolized rapidly, but was excreted apparently unchanged in the urine. It also was not incorporated in significant amounts into the Bence-Jones protein, thought to originate in tumor cells of multiple myeloma. Autopsy samples of tumor tissue obtained 2.5 months after administration of the labeled amino acid were devoid of detectable C^{14} activity. A diagnosis of multiple myeloma was confirmed at autopsy. This research was aided in part from grants from the National Cancer Institute, the National Institutes of Health, and the American Cancer Society. The Argonne Cancer Research Hospital was operated by the University of Chicago under a contract from the U.S. Atomic Energy Commission.

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Putnam, F.W., A. Miyake, and F. Meyer. "The Metabolism of DL-Glutamic Acid-1-C^{14} in Man." *Semiannual Reports to the U.S. Atomic Energy Commission. Vol. 2, Part 10, 1958.* Chicago: Argonne Cancer Research Hospital, pp. 35–43. The University of Chicago, Office of Legal Counsel, Semiannual Reports of the Argonne Cancer Research Hospital.

Putnam, F.W., A. Miyake, and F. Meyer. "The Metabolism of DL-Glutamic Acid-1-C^{14} in Man." *Journal of Biological Chemistry*. Vol. 231, 1958, p. 657. ❑

UC-36. Study of the Metabolism of Progesterone Using Carbon-14

IN THE MID-1950s, researchers in the Department of Obstetrics and Gynecology at the University of Chicago, and the Chicago Lying-In Hospital studied the metabolism of progesterone and its related compounds during the human reproductive cycle, and during pregnancy. The study groups were composed of 6 nonpregnant females, 5 subjects following interruption of pregnancy, and 11 pregnant subjects scheduled for therapeutic abortions.

All subjects received a single intramuscular injection of progesterone labeled with carbon-14 (C^{14}). Each injection contained about 25 to 30 microcuries of C^{14}. Five subjects received a second intramuscular injection of progesterone-C^{14}, 5 to 9 days after termination of pregnancy. Progesterone-C^{14} was also administered by intravenous injection to one subject during week 11 of pregnancy. Samples of plasma, urine, feces, expired air, and maternal and fetal tissue, obtained during surgical interruption of pregnancy, were collected for analysis. Progesterone-21-C^{14} (28.3 to 28.8 microcuries) was administered by intravenous injection to another subject during week 11 of pregnancy. Seventeen (α)-hydroxyproges-terone-4-C^{14}-caproate (25.9 to 28.8 microcuries) was administered by intramuscular injection to four other pregnant

subjects, followed by collection of urine specimens from each subject for a period of 7, 12, 14, and 15 days, respectively. Clearance, deposition, and excretion patterns were evaluated for the three compounds and their metabolites.

No relationship was found between the amount of radioactivity excreted and either the stage of pregnancy or the patient's clinical condition. There was no difference in the average urinary output of radioactivity before and after termination of early pregnancy or for the group of nonpregnant women. The work was supported by the May Cave Willet Research Fund, the Douglas Smith Foundation for Medical Research Fund, the Joseph Bolivar DeLee Memorial Fund, the University of Chicago, and the Argonne Cancer Research Hospital Fund. The Argonne Cancer Research Hospital was operated by the University of Chicago, under contract with the U.S. Atomic Energy Commission.

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Davis, M.E., E.J. Plotz, C.I. Lupu, and P.M. Ejarque. "The Metabolism of Progesterone and its Related Compounds in Human Pregnancy." *Fertility and Sterility.* Vol. 11, No. 1, 1960, pp. 18–48. ❑

UC-37. Influence of a Brain Extract on Cholesterol Metabolism Using Carbon-14 as a Tracer

IN THE MID-1950s, it was discovered that an extract of mammalian brain had hypocholesteremic properties (inducing abnormally small amounts of cholesterol in the blood) in humans. Research was conducted at the Argonne Cancer Research Hospital in collaboration with the Department of Medicine, University of Chicago, in the late 1950s to determine the mechanisms by which the brain extract had effects in humans.

Study subjects were three patients with coronary disease who were hospitalized in the metabolism ward. Two of these patients had an excess amount of cholesterol in their blood. All had normal basal metabolic rates and fasting blood glucose levels.

After 4 to 5 days of a low-fat, low-cholesterol hospital diet, 2 milliliters of a solution of carbon-14 (C^{14})–labeled sodium acetate containing 100 microcuries C^{14} per milliliter were injected intravenously into each subject. Blood was drawn twice in a 24-hour period and thereafter at 2- to 3-day intervals for cholesterol analysis. Two weeks after the initial injection, and 10 days after for one subject, 30 to 40 grams per day of the brain extract were administered orally to each subject for the rest of their hospitalization. After 2 weeks on this material, two of the subjects were again injected with 200 microcuries of C^{14}-labeled sodium acetate.

The research established that the brain extract acts by partially binding the intestinal cholesterol and its end products to enhance their excretion. This study was supported by grants from the American Heart Association and the U.S. Public Health Service. The Argonne Cancer Research Hospital was operated by the University of Chicago, under contract with the U.S. Atomic Energy Commission.

References

Jones, R.J., O.K. Reiss, and M.F. Golden. *Influence of a Brain Extract Upon Cholesterol Metabolism.* Chicago: Argonne Cancer Research Hospital, pp. 212–220. The University of Chicago, Office of Legal Counsel, Reprints of the Argonne Cancer Research Hospital, Vol. III, 1961. ❑

UC-38. Experimental Cancer Therapy Using Permanent Chromium-51 Implants

IN 1959, RESEARCHERS in the Departments of Radiology and Surgery at the University of Chicago and the Argonne Cancer Research Hospital, began a collaborative investigation of the use of implanted chromium-51 (Cr^{51}) gamma ray sources for interstitial (within tumor tissue) radiation therapy for cancer. The implants consisted of Cr^{51} wire in aluminum tubes, which were implanted within regions of tissue containing cancer cells.

The first cancer patient was treated in 1959 for metastatic squamous cell cancer of the anus. The next patient was not treated until approximately 1964 and, over a 2-year period, the researchers performed a total of 30 additional implants to treat 24 patients who had a variety of advanced cancers. Most of these patients had received previous external radiation and radium therapy, with or without surgery. Between 3 and 60 Cr^{51} seeds, each ranging in activity from 2 to

5 millicuries, were implanted through the skin into the tumor tissue in each patient. Five patients had multiple implants, up to a maximum of three in one patient.

Favorable responses were obtained in nine patients, including the first treated, who experienced no symptoms or cancer recurrence during the 7.5 years of follow-up. Seven others had good responses. Of the five remaining patients, four had questionable or unfavorable results and for one patient, follow-up was too short for adequate evaluation. Tissue destruction and hemorrhages occurred in three patients, all of whom had received radiation therapy prior to the implantation. Permanent Cr^{51} implants were generally well tolerated by the other previously irradiated patients. This work was supported in part by a Cancer Development Award from the National Institutes of Health. The Argonne Cancer Research Hospital was operated by the University of Chicago, under contract with the U.S. Atomic Energy Commission.

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Griem, M.L., P. Lazarovits, and P.V. Harper. "Preliminary Experience with Permanent Interstitial Implants Using Chromium-51 Sources." *Semiannual Reports to the U.S. Atomic Energy Commission. Vol. 6, Part 29, 1968.* Chicago: Argonne Cancer Research Hospital, pp. 30–37. The University of Chicago, Office of Legal Counsel, Semiannual Reports of the Argonne Cancer Research Hospital. ❑

UC-39. Treatment of Selected Tumors Using an Electron Beam

THIS RESEARCH at the Argonne Cancer Research Hospital involved development of a new technique for treating cancer using a high-energy electron pencil beam. An electron beam produced by a linear accelerator was directed into a scanning device positioned over the patients' tumor. Ninety-seven patients were treated between June 1959 and September 1962: 51 had malignancies of the head and neck, 8 had intrathoracic tumors, 5 had mycosis fungoides (a chronic, malignant disease of the lymphatic system), 1 had carcinoma of the thorax, 4 had urinary bladder carcinoma, 3 had benign lesions, and 25 had a variety of other cancerous lesions. Many of the procedures were performed for the alleviation of pain. The Argonne Cancer Research Hospital was operated by the University of Chicago, under contract with the U.S. Atomic Energy Commission.

References

Carpender, J.W.J., L.S. Skaggs, L.H. Lanzl, and M.L. Griem. "Radiation Therapy with High-Energy Electrons Using Pencil Beam Scanning." *Semiannual Reports to the U.S. Atomic Energy Commission. Vol. 4, Part 20, 1963.* Chicago: Argonne Cancer Research Hospital, pp. 47–56. The University of Chicago, Office of Legal Counsel, Semiannual Reports of the Argonne Cancer Research Hospital. ❑

UC-40. Human Ingestion of Real and Simulated Fallout

IN THE EARLY 1960s, the Argonne Cancer Research Hospital conducted studies on the human absorption and retention of radioactive materials (real or simulated fallout) taken into the body by ingestion. The purpose of these studies was to gain information that would be beneficial in civil defense planning. A total of 102 healthy, volunteer university students and hospital staff members participated as subjects.

During the study, 10 study subjects ingested 0.2 to 0.7 microcurie of real fallout from the Nevada test site. Simulated fallout particles or radioactive solutions that contained 0.4 to 2.5 microcuries of strontium-85 (Sr^{85}) were also ingested by 45 subjects, 4.0 to 13.5 microcuries of barium-133 were ingested by 15 subjects, and 0.5 to 14.0 microcuries of cesium-134 were ingested by 32 subjects. Whole-body counting was performed to determine the amount of activity remaining in the subjects at various intervals after ingestion. There were no reports of any gastrointestinal symptoms after the test materials were ingested.

These studies provided a basis for estimating the systemic uptake and internal radiation dose that could result from ingesting typical fallout soon after detonation of a nuclear weapon. This work was supported by the Office of Civil De-

fense and the U.S. Atomic Energy Commission. (This experiment was referenced in the Markey report.)

References

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UC-41. Use of an Experimental Strontium-90/Yttrium-90 Needle for Radiation Cordotomy Pain Relief

IN THE EARLY 1960s, researchers at the Department of Neurological Surgery and Roentgenology, University of Chicago Hospital and Clinics collaborated with the Argonne Cancer Research Hospital to explore an alternative approach to high-risk surgical cordotomy. Surgical cordotomy (division of the sensory nerve tracts of the spinal column) has been performed since the early 1900s to alleviate severe pain.

Sixty cordotomies, using strontium-90/yttrium-90 (Sr^{90}/Y^{90}) needles were performed by this method to relieve pain in a total of 42 patients (including both men and women) ranging in age from 3 to 71 years; of these, 37 had advanced malignant diseases of various types and 5 had benign conditions. Guided by x-ray pictures, a needle containing Sr^{90} and its decay product Y^{90} was inserted into the space between the first and second cervical vertebrae through the skin to divide the sensory nerve tracts of the spinal cord (cordotomy). The needle was held in place for 15 to 20 minutes in most cases, and up to 40 minutes in a few cases to deliver between 2,000 and 16,000 rads to the sensory tracts in the spinal cord.

The procedure resulted in some pain relief among 34 of the 42 patients and eliminated the mortality risk and the long convalescent period associated with the surgical approach. This work was supported by the Douglas S. Smith and Simms Foundations, and the U.S. Public Health Service. The Argonne Cancer Research Hospital was operated by the University of Chicago, under contract with the U.S. Atomic Energy Commission.

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Mullan, S., P.V. Harper, J. Hekmatpanah, H. Torres, and G. Dobbin. "Percutaneous Interruption of Spinal Pain Tracts by Means of a Strontium-90 Needle." *Journal of Neurosurgery.* Vol. 20, 1963, pp. 931–939.

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UC-42. Pharmacokinetics of Selenium-75–L-Selenomethionine

DURING THE EARLY 1970s, investigators at six institutions conducted collaborative studies on the pharmacokinetics of selenium-75 (Se^{75})–L-selenomethionine as a new radiopharmaceutical for imaging the pancreas in nuclear medicine diagnostic exams. The studies were conducted at Argonne Cancer Research Hospital; Veterans Administration Hospital, Hines, Illinois; Roswell Park Memorial Institute, Buffalo, New York; Danbury Hospital, Danbury, Connecticut; Sloan-Kettering Institute for Cancer Research, New York; and the National Center for Radiological Health and Radioisotope Laboratory, University of Cincinnati.

A total of 40 subjects, comprising 30 patients with various diseases, including unspecified types of cancer, and 10 normal comparison subjects, participated in the study at one of the above-mentioned institutions.

Each subject received a single intravenous injection of approximately 250 microcuries of Se^{75}. At varying intervals after Se^{75} administration, measurements of activity were made on samples of blood, urine, and feces collected from five subjects. Retained activity in the body was measured by whole-body counting of 24 sub-

jects at four institutions over a period ranging from 3 up to 923 days. Selenium-75 concentrations were later measured in tissues obtained at autopsy from a total of 23 subjects at four of the institutions. Other radioactivity measurements were obtained from hair, nails, and skin.

The biological data obtained in these studies were combined for analysis to determine the radiation absorbed dose to the total body and to individual organs from Se^{75}-L-selenomethionine. The information was needed in assessing the usefulness of Se^{75}-L-selenomethionine as a tumor imaging agent. This work was supported in part by the U.S. Atomic Energy Commission.

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"Summary of Current Radiation Dose Estimates to Humans from Se^{75}-L-Selenomethionine." *MIRD/Dose Estimate Report No. 1.* January 1973. ❑

UC-43. Experimental Use of Gallium-67 as a Scanning Agent in the Staging of Hodgkin's Disease

IN 1971, physicians in the Section of Nuclear Medicine, Departments of Radiology, Medicine, and Surgery at the University of Chicago Hospitals and Clinics, Pritzker School of Medicine, and the Argonne Cancer Research Hospital collaborated to review the clinical diagnoses of 20 patients with suspected Hodgkin's disease.

All 20 patients were evaluated using gallium-67 (Ga^{67}) as a scanning agent, followed by surgical exploration and tissue biopsies to confirm the diagnosis. Under the Ga^{67} scanning protocol, 1.5 to 3.0 millicuries of Ga^{67}-citrate (less than 2 milliliters) were administered intravenously to each patient. The scan was performed 72 hours after the administration of Ga^{67}. The scan results were compared with the extent of the disease as determined by pathological examination of tissue samples obtained during surgery, and by chest radiographs.

The researchers concluded that Ga^{67} was a useful supplement in Hodgkin's disease staging, particularly because of its non-invasive methodology. This work was supported by the U.S. Public Health Service, the Junior Auxiliary of the University of Chicago Cancer Research Foundation, and the Goldblatt Brothers Employees' Nathan Goldblatt Cancer Research Fund. The Argonne Cancer Research Hospital was operated by the University of Chicago, under contract with the U.S. Atomic Energy Commission.

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University of Rochester

UR-1. Polonium-210 Metabolism and Excretion Study

DURING THE EARLY 1940s, the University of Rochester in New York conducted studies on the retention, excretion, and gastrointestinal tract absorption of polonium-210 (Po^{210}) in humans, using patients at Strong Memorial Hospital in Rochester, as subjects. The purpose of the study was to determine occupational exposure limits for use in radiation protection programs.

Five patients with advanced lymphoma or leukemia participated. Four of the patients were administered an intravenous injection of 8 to 23 microcuries of Po^{210} and one patient was orally administered 18.5 microcuries of Po^{210} in tap water. Urine samples were subsequently collected and analyzed for Po^{210}.

All subjects died of preexisting ailments shortly after the administrations. Tissues were obtained at autopsy and examined for Po^{210} concentration. This research was supported by the Manhattan Engineer District. (This experiment was referenced in the Markey report and included in *The DOE Roadmap* of February 1995.)

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Stannard, J.N. *Radioactivity and Health: A History.* Office of Scientific and Technical Information. 1988, pp. 213–214. ❑

UR-2. Uranium Injections

FROM AUGUST 1946 TO JANUARY 1947, the University of Rochester conducted toxicity studies on uranium, using hospital patients as subjects. The purpose of the studies was to determine the dose level at which renal injury is first detectable, measure the rate at which uranium is eliminated from the body once it enters the bloodstream, and observe the effect of measures intended to alter the excretion rate.

Subjects included four males and two females, all with good kidney function, ranging in age from 24 to 61 years. All had medical conditions, such as undernutrition, alcoholism, or heart disease.

Highly enriched uranium (uranium-234 and uranium-235) was administered intravenously as uranyl nitrate in amounts ranging from 6.4 to 70.9 micrograms per kilogram of body weight. At levels approaching 50 micrograms per kilogram, the preparation was diluted with natural uranyl acetate to limit the potential radiotoxicity associated with systemic enriched uranium. Five subjects received a single injection and experienced no kidney damage. The sixth subject experienced slight kidney tissue toxicity at the 70.9 micrograms-per-kilogram level, suggesting that the human tolerance level had been reached. This patient was administered ammonium chloride to induce an acidosis condition (a decrease in alkali relative to acid in bodily fluids), then received a second injection of uranyl nitrate at a dose of 56.6 micrograms per kilogram.

These studies showed that the tolerance level for uranium in the human circulation was about 70 micrograms per kilogram of body weight, that uranium excretion occurred mainly through urine, that 70 to 85 percent was eliminated in the first 24 hours, and that acidosis decreased the rate of uranium excretion. This research was supported by the Manhattan Engineer District. (This experiment was referenced in the Markey report and included in *The DOE Roadmap* of February 1995.)

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UR-3. Ingestion of Milk Containing Iodine-131

THIS STUDY WAS CONDUCTED in 1963 by a graduate student at the University of Rochester to investigate the body's metabolism of radioiodine found in dairy products. The research sought to determine whether iodine found in milk was transferred to the thyroid in the same quantities as the inorganic iodide commonly used in medical studies. As much as 40 percent of the iodine found in milk was found to be protein bound. The study focused on the range of uptake percentages in children of various ages.

Subjects for the experiment were chosen with an emphasis on the younger age groups, since the majority of known research had been conducted on adults. The subjects ranged in age from 6 years to 50 years; seven were less than 21 years old. The milk used for this study was obtained from Cornell University's Department of Veterinary Medicine, where a cow had been fed iodine-131 (I^{131}) so as to produce 5 to 10 nanocuries per liter in its milk.

All subjects were put on an iodine-restricted diet prior to the study and then were fed the I^{131} milk for a minimum of 14 days. One of the children in this study subsequently developed a benign nodular hyperplasia of the thyroid, which was later surgically removed. The research was performed under a contract with the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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Correspondence. T.S. Ely to W. LeFurgy and D.R. Fisher. February 14, 1995. ❑

UR-4. The Fate of Radon Ingested by Humans

In 1964, the Department of Radiation Biology at the University of Rochester conducted a study on the fate of radon ingested by humans. Two male subjects, ages 36 and 56, participated.

On two occasions, each subject drank approximately 1 microcurie of radon-222 (Rn^{222}) in equilibrium with its decay products in 100 milliliters of water. On 3 separate days, the ingestions of radon were followed by a normal breakfast; the fourth followed a larger breakfast high in fat. The subject's respired air, blood, and urine were obtained and sampled for Rn^{222} activity.

This study provided rates at which the body loses radon and the impact of stomach contents on the rate of loss. The research was supported by the U.S. Atomic Energy Commission. (Previously described in #29 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

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UR-5. Excretion Studies Using Thorotrast Containing Thorium-232 and Decay Products

Between 1930 and 1945, researchers at the University of Rochester, New York and the National Naval Medical Center, Bethesda, Maryland, conducted studies on the human excretion of thorium, and its daughter isotopes of radium, using Thorotrast, a contrast medium containing thorium-232 (Th^{232}) and its radioactive decay products.

Five hospital patients (men and women) were administered 40 to 75 milliliters of Thorotrast by injection, equivalent in total alpha-particle activity to about 2.1 microcuries of radium-226. The activity of Th^{232} and its decay products: radium-228; thorium-228; and radium-224 was measured in body tissues, urine, and feces samples for up to 19 years post-injection.

These studies indicated that thorium is retained in the body with a biological retention half-time of about 400 years. This work facilitated the estimates of radiation absorbed dose to various organs (liver, spleen, bone marrow, and lung) from Thorotrast. This work was supported in part by the U.S. Atomic Energy Commission.

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UR-6. Radon-222 Inhalation Studies

In approximately 1956, radon inhalation studies were performed by researchers at the Department of Radiation Biology of the University of Rochester School of Medicine and Dentistry, New York. The purpose of these studies was to determine the radiation doses to various parts of the human respiratory system from inhaled radon and its decay products.

Radon-222 (Rn^{222}), obtained from a 50-microcurie radium chloride source, was introduced into an exposure chamber by water displacement. Two subjects breathed (by mouth only) air from the chamber containing about 0.025 microcurie of Rn^{222}. The air was typical of either normal room air (with normal dust loadings) or air filtered to remove normal dust. The radon daughter activity in the air exhaled by the subjects was compared to the radon daughter activity of the air in the chamber. Radon daughter product retention from normal dusty air was compared with retention from filtered air.

The average retention of the daughter products in air containing normal atmospheric dust was 25 percent, while the average retention in filtered air breathed by the subjects was 75 percent.

The radiation doses to the lungs of the subjects were calculated using the data obtained. The average radiation dose to lungs, as a whole, was estimated to be 4.9 millirads per week of 168 hours for normally dusty air. Data were insufficient to estimate the dose due to radon and its decay products in very clean (dust-free) air.

The investigators concluded that radiation exposure to the lungs from breathing an atmosphere

containing radon is usually due to radon daughters rather than radon itself. This work was supported by the U.S. Atomic Energy Commission.

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Shapiro, J. "Radiation Dosage from Breathing Radon and its Daughter Products." *A.M.A. Archives of Industrial Health*. Vol. 14, No. 2, August 1956, pp. 169–177. ❑

UR-7. Study of the Retention and Distribution of Thorium-232 Decay Products

BETWEEN 1960 AND 1964, a study was conducted at the University of Rochester, New York to determine the retention and biological distribution of thorium-232 (Th^{232}) and its decay products. Thorium-232 is the principal component of Thorotrast, a colloidal thorium oxide contrast agent used in diagnostic radiology. The purpose of this study was to learn more about the long-term retention and dosimetry of thorium decay products in patients who received thorotrast.

For this study, a group of four elderly volunteer subjects was chosen. Each of the subjects received an intravenous injection of 24 milliliters of Thorotrast. The amount of Th^{232} and daughter product activity administered was not stated. Each subject was then periodically monitored in a whole-body counter up to 4 years post-injection to determine the amounts of the Th^{232} decay products actinium-228 and thallium-208 remaining in their bodies.

Breath measurements for exhaled thoron (radon-220) were also made on two of the four subjects during the study period. These measurements provided estimates of the body contents of other Th^{232} decay products, including radium-228, thorium-228, and radium-224. Breath measurements showed that 9 percent of the thoron formed as a decay product in the body escaped in expired air. The lung dose to study participants was estimated to have been between 15 and 45 rems per year. This work was supported by the U.S. Atomic Energy Commission.

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UR-8. Study of the Metabolism of Natural Uranium in the Human Skeleton

BETWEEN 1960 AND 1964, scientists at the University of Rochester, New York conducted experiments on the metabolism of uranium in the human skeleton. Subjects for this study included 10 patients at the University's hospital metabolism ward. They included three patients with bone disease (osteoporosis or osteomalacia), one with Paget's disease of bone, one with hyperparathyroidism plus a parathyroid adenoma, and one with hypoparathyroidism. About 1.5 to 2.0 milligrams natural (not enriched) uranium were administered intravenously as the soluble uranyl ion (UO_2^{++}) to subjects following breakfast. Some of the subjects received multiple uranium injections over time. Measurements were later made to determine the rates of urinary uranium excretion by the subjects. Serum calcium was also measured to determine the effect of uranium on blood calcium levels.

These studies suggested that measurements of the uptake and release of uranium by bone, when compared to calcium uptake and release, could be a useful indicator of metabolic bone disease in man. This work was supported by the U.S. Atomic Energy Commission.

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Rochester, Atomic Energy Project, Brief Description of Most of the Research Programs Completed During 1964. Rochester, NY: University of Rochester, Atomic Energy Project, UR-668, September 1, 1965, pp. 92–94. ❑

UR-9. Use of Antibodies Labeled with Iodine-131 in the Diagnosis and Localization of Brain Tumors

IN 1962, the National Institute for Neurological Diseases and Blindness (NINDB) in Bethesda, Maryland, the Neurological Institute of Columbia University, New York, and the Strong Memorial Hospital (SMH) in Rochester, New York, under the direction of the Department of Radiation Biology at the University of Rochester, conducted a study of antibodies labeled with iodine-131 (I^{131}) for diagnosing and locating brain tumors.

A total of 28 patients were intravenously injected with I^{131} antibody. All patients had known extensive malignant disease or known or strongly suspected brain tumors. Most patients received 400 to 500 microcuries of I^{131} attached to antibody in a volume of 5 to15 milliliters of solution. Antibody content (rabbit gamma globulin) ranged from 0.15 to 0.8 milligram of protein per dose.

The investigators at NINDB found that, for sarcomas (18 patients), there was a good probability of a fairly specific uptake of I^{131}-labeled antibody compared with I^{131}-labeled human albumin. Analysis of blood samples from the five patients studied at SMH showed a biological half-time in blood of 4.3 days. External scanning and biopsy studies did not indicate localization of radioactivity in tumors outside the brain great enough to be of diagnostic or therapeutic significance. Scintillation scanning of the head of patients with brain tumors indicated that preparations of this type may be useful for diagnosis and delineation of these lesions. This work was performed under contract with the U.S. Atomic Energy Commission.

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UR-10. Skeletal Metabolism of Calcium-45 and Sodium-22

IN 1964, researchers at the University of Rochester, New York conducted a study on the kinetics of short-term blood disappearance and skeletal metabolism of calcium-45 (Ca^{45}) and sodium-22 (Na^{22}). The purpose of this study was to develop new approaches for studying the metabolism of calcium and sodium in the human skeleton.

Thirteen patients, some with bone disease, were admitted to the University's medical center metabolism ward for participation in this study. The amounts of Ca^{45} and Na^{22} administered to each subject were not stated. Measurements were made at frequent intervals after injection to determine the concentrations of Ca^{45} and Na^{22} in circulating blood. From these data, the size of the rapidly exchangeable calcium compartment involved in blood-to-bone mineral exchange was determined.

This study showed that Ca^{45} and Na^{22} tracers provided useful tools for evaluating and diagnosing diseases of the skeleton in man. This research was supported by the U.S. Atomic Energy Commission.

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UR-11. Lead-212 Absorption Studies

BETWEEN 1966 AND 1967, researchers in the Department of Radiation Biology and Biophysics at the University of Rochester School of Medicine and Dentistry, New York in collaboration with the Special Laboratories of Statens

Strålskyddsinstitut (the Swedish Radiation Protection Institute), Stockholm, studied the absorption of lead-212 (Pb^{212}) from the gastrointestinal tract. The purpose of the study was to determine the radiation hazard and chemical toxicity hazard of ingested lead.

Of the four Swedish volunteers, two received oral, one received intravenous, and one received both intravenous and oral administrations of Pb^{212}. The amounts of activity administered intravenously and orally were approximately 1 and 5 microcuries, respectively. The Pb^{212} excretion of these subjects was measured within 24 hours to determine Pb^{212} absorption from the gastrointestinal tract. The average absorption was 8 percent, which was equal to the value previously reported by the International Commission on Radiological Protection. In addition to absorption studies, Pb^{212} uptake by red blood cells also was determined.

The researchers concluded that lead might be released from the binding sites only when red cells die. This work was funded in part by the National Institute of Arthritic and Metabolic Diseases. The Department of Radiation Biology and Biophysics at the University of Rochester was supported, in part, by the U.S. Atomic Energy Commission.

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Other

OT-1. Study of Blood Volumes with Iodine-131–Tagged Plasma Protein

CASE WESTERN RESERVE UNIVERSITY conducted this study in 1950. Blood volume determinations were made on 76 ambulatory hospital patients who exhibited normal fluid and protein balance. The subjects were injected with plasma protein tagged with iodine-131 (I^{131}) while they were fasting. They were confined to bed until the experiment was completed.

Approximately 40 to 60 microcuries of I^{131} were intravenously injected. Twelve patients who were to receive spinal anesthesia were also given radioactive iodinated protein at various intervals, preceding the administration of the anesthesia. No radioactivity was detected in the spinal fluid of these patients.

The studies on the patients confined to bed showed that an average of 8 to 12 percent of the injected radioactive iodine was found in the urine within 24 hours of the injection. This research was partly supported by a U.S. Atomic Energy Commission contract. (Included in *The DOE Roadmap* of February 1995)

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OT-2. The Use of Iodine-131–Labeled Human Serum Albumin to Evaluate the Peripheral Circulation

THIS RESEARCH WAS carried out in 1952 at Case Western Reserve University. Human serum albumin labeled with iodine-131 was injected into 77 subjects and a scintillation counter was used to determine cardiac output and to observe peripheral vascular flow.

Approximately 150 microcuries of radioiodinated albumin were injected into the subjects. A series of these experiments were performed on young subjects with normal circulation. Four of the young subjects had one foot immersed in hot water for 20 minutes before the labeled albumin was injected into them. In two other subjects, the foot was immersed in ice water for 10 minutes before the test was performed. The study was carried out under contract with the U.S. Atomic

Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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OT-3. Use of Iodine-131–Labeled Protein in the Study of Protein Digestion and Absorption in Children With and Without Cystic Fibrosis of the Pancreas

THIS STUDY WAS PERFORMED in 1952 at Case Western Reserve University. During the two decades prior to the study, several studies of protein digestion and absorption had been carried out both in normal individuals and in patients with various diseases. This study describes a simple and accurate method to determine the efficiency of protein digestion and absorption, by measuring the isotope content of the feces after oral ingestion of protein labeled with iodine-131 (I^{131}).

The subjects were 10 children with diseases that did not specifically involve the gastrointestinal tract and 5 children with cystic fibrosis of the pancreas. The subjects ranged in age from 1.6 years to 9 years. These patients fasted for 12 hours before the experiment; then, a test meal containing I^{131} was given in place of breakfast. The test meal contained approximately 1 microcurie of labeled protein per kilogram of body weight. In the five children with cystic fibrosis of the pancreas, pancreatin was withheld for 3 days prior to and during the initial test.

The research demonstrated a diminished retention of dietary protein in cystic fibrosis of the pancreas. This research was supported by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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OT-4. Thyroidal Deposition of Iodine-131 in Humans, Rats, and Dogs, from Milk and Nonmilk Sources

IN 1963, Cornell University conducted studies on the comparative uptake of iodine from ingested water and milk, using human and animal subjects. Eleven healthy male volunteers ranging in age from 26 to 52 years participated and ingested 0.1 liter of milk containing iodine-131 (I^{131}). The study used milk obtained from cows that had been fed I^{131} 2 days prior to milk collection. The milk contained approximately 2.5 microcuries of I^{131} per liter. Inorganic I^{131} was administered with 100 milliliters of water containing about 0.26 microcurie of I^{131}.

Results of the study indicated that there was no significant difference in the uptake of iodine in humans when obtained through milk or water. This work was supported by the U.S. Atomic Energy Commission. (Previously described in #47 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

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OT-5. Plasma Volume Studies Using Chromium-51–Chloride

THIS RESEARCH WAS CONDUCTED at the Biophysical Laboratory and the Department of Medicine

at Harvard Medical School and the Medical Clinic at Peter Bent Brigham Hospital in Boston. Approximately 100 microcuries of chromium-51 as chromium chloride were intravenously injected into 26 normal adults (5 women and 21 men).

After allowing 5 minutes for mixing within the circulation, researchers drew four samples of blood and analyzed them in a gamma counter to determine plasma volumes. The plasma volumes were determined by this method. In some subjects, a second study was also performed. This method was further tested by measuring the plasma volume before and after transfusion or hemorrhage of between 250 and 500 milliliters of plasma in hospital patients and volunteer subjects. This research was supported in part by the U.S. Atomic Energy Commission and in part by the U.S. Public Health Service. (Included in *The DOE Roadmap* of February 1995)

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OT-6. Iodine-131 Uptake by the Human Embryo

IN 1953, studies were conducted at the University of Iowa, Iowa City on the uptake of iodine-131 (I^{131}) in thyroids of human embryos in utero. (The number of subjects is not known.)

Pregnant women scheduled for therapeutic abortions were given dosages of 100 to 200 microcuries of I^{131}. Some time later, the abortions were performed. The aborted embryos were sectioned and autoradiographed. The human embryos showed thyroid uptake at 4 weeks, nearly 1 month earlier than was previously known. This finding was useful in understanding the transfer of radioiodine across the placental barrier.

This study showed that it would not be prudent to administer I^{131} to pregnant women for diagnostic or therapeutic purposes. This work was funded by the U.S. Atomic Energy Commission. (Previously described in #5 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

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OT-7. Uptake of Iodine-131 in Normal Newborn Infants in Iowa City

IN 1963, the University of Iowa, Iowa City conducted studies on the uptake of iodine-131 (I^{131}) in newborn infants. Twelve male and 13 female infants were included in this study. All were less than 36 hours old, weighed between 5.5 and 8.5 pounds, and were considered to be healthy and normal.

Less than 1 microcurie of iodine-131 (I^{131}) was administered to each newborn. Eight received the radioiodine orally and 17 by intramuscular injection. The concentration of I^{131} in the thyroid was measured using a thyroid gamma probe. Measurements were continued at intervals of 2 to 8 hours for 3 to 4 days.

This study showed that I^{131} was taken up by the thyroid at a higher level and more rapidly when administered by injection rather then ingestion. This study was supported by the U.S. Atomic Energy Commission and the American Cancer Society. (Previously described in #4 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

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OT-8. Uptake of Iodine-131 in Normal Newborn Infants in Nebraska

THE THYROID FUNCTION of infants was studied jointly by the Veterans Administration Hospital, Omaha, Nebraska, and the Department of Radiology, University of Nebraska, College of Medicine, in 1960. Twenty-eight normal, healthy infants from the nursery at the College of Medicine, including 16 males and 12 females ranging

in age from 72 to 180 hours, were involved in the experiment.

Each of the newborn infants was given 5 microcuries of iodine-131 (I^{131}) through a gastric tube. The concentration of I^{131} in the thyroid was measured 24 hours later.

This study showed that the thyroid of a newborn functioned similarly to those of adult thyroids. The subject's sex and weight were not related to thyroid function. (Previously described in #4 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

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OT-9. Uptake of Iodine-131 in Normal Newborn Infants in Memphis

IODINE-131 WAS USED to study the uptake of iodine in normal, newborn infants at the University of Tennessee and at the John Gaston Hospital in Memphis, in approximately 1952 to 1954. Seven male infants (one white and six black) between 2 and 3 days old were injected intravenously with 1.0 to 1.5 microcuries of iodine-131 (I^{131}). The concentration of I^{131} in the thyroid was measured 24 hours after injection. Absorbed doses to the infant thyroids were estimated to be about 60 rads.

The I^{131} uptake of the thyroid of the subjects was found to lie within the range of values that would be found in hyperthyroid adults. This study was supported by a grant from the U.S. Atomic Energy Commission. (Previously described in #4 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

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OT-10. Radioactive Isotope Studies at Tulane

IN THE LATE 1940s and early 1950s, a series of metabolic experiments was conducted at Charity Hospital and Tulane University School of Medicine, New Orleans, LA. The focus of the experiments was to investigate the role of electrolytes in normal humans and in patients with congestive heart failure. The total number of subjects is not specified, but as many as 269 people could have been included in the study. Some of these subjects may have participated in more than one study.

The radioisotope studies examined retention times, excretion rates, biologic decay rates, and a variety of other physiological parameters. The radioisotopes used included mercury-203. One subject received only x-rays to determine the effects of radiation on humans. (Previously described in #8 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

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OT-11. Iron Metabolism in Human Pregnancy as Studied with Iron-59

FROM 1945 THROUGH 1949, Vanderbilt University Hospital conducted studies on iron absorption in pregnant women. Participants in the study were part of a larger nutrition survey conducted by the hospital.

In all, 829 normal, healthy, pregnant women ingested radioactive iron-59 (Fe^{59}) in an amount ranging from 1.8 to 120 milligrams. The Fe^{59} was administered at various times in the gestation period ranging from fewer than 10 to more than 35 weeks. Radioactivity in the blood was measured 2 weeks and, again, 3 weeks after administration.

The study showed that iron uptake is related to both dosage level and gestation period. The percentage of absorption decreased as the amount administered went up, while the actual amount of iron absorbed increased. Also, uptake increased later in the gestation period. At 30 weeks, three times as much iron was absorbed as at 15 weeks. This research was supported by the Nutrition Foundation, Inc., the Rockefeller Foundation, and the Tennessee State Department of Health.

From 1964 to 1967, Vanderbilt University School of Medicine conducted a follow-up study on the children born to these women. The study included 679 children of mothers who had been fed Fe^{59} and 705 children of mothers in the original study control population. One case of leukemia and two cases of sarcoma were discovered in the Fe^{59} population. There were no malignancies in the control population. Compared to an expected incidence of less than one, the three cases are statistically significant. There were no differences in malignancies among the mothers, congenital defects among the children, or congenital defects among subsequent children between the two populations. This follow-up work was supported by the U.S. Public Health Service and the U.S. Atomic Energy Commission. (Previously described in #1 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

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OT-12. Sodium-24 Used to Study Exchangeable Sodium in Relation to the Menstrual Cycle

THIS STUDY WAS CONDUCTED in 1969 at Vanderbilt University. Six healthy female volunteers, between the ages of 19 to 44 years, with no history of hypertension and with normal blood pressure, were fed a constant sodium diet for 30 to 45 days.

After administration of a 10 microcuries oral dosage of sodium-24 (Na^{24}), exchangeable sodium spaces were measured during the follicular phase and the luteal phase of the menstrual cycle. The subjects were followed daily at the Clinical Research Center for excretion of sodium, potassium and creatinine; urine volume; body weight; and basal body temperature. This research was funded by grants from the U.S. Public Health Service, the American Heart Association, and the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

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OT-13. Blood Volume Measurements Using Stable Chromium-50 and Radioactive Chromium-51

STUDIES WERE CONDUCTED at Vanderbilt University in Nashville during the period 1969 to1972 on methods for diagnosing intracranial hemorrhage in newborn infants suffering with respiratory distress. The red blood-cell volume and estimated time of intracranial hemorrhage was determined using chromium isotope labeling techniques. The purpose of this research was to develop tracer techniques for determining blood volumes in patients using the stable isotope chromium-50 (Cr^{50}).

After blood labeled with stable Cr^{50} was removed from the patient, it was irradiated with neutrons, and the activated products (chromium-51[Cr^{51}] and iron-59) were measured by gamma-ray analysis. To conduct this study, it was necessary to calibrate and compare with results previously obtained using standard Cr^{51} blood volume analysis. Therefore, at the start of the study, the total red blood-cell volume in one infant and three adult patients was measured using both Cr^{50} and Cr^{51} tracers as sodium chromate.

This study showed that stable Cr^{50} could be used in place of Cr^{51} in blood volume analyses to preclude the need to use a radioactive tracer in newborn infants. This study was supported in part by a U.S. Atomic Energy Commission contract and in part by a grant from the National Heart Institute. (Included in *The DOE Roadmap* of February 1995, and since revised)

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OT-14. Testicular Irradiation of Washington State Prison Inmates

FROM 1963 TO 1973, the University of Washington, Seattle conducted studies on the effects of radiation on human testicular function using inmates at the Washington State Prison in Walla Walla, as subjects. Initially, 232 healthy volunteers were accepted into the study program.

Sixty were subsequently irradiated with acute doses of x-rays, ranging from 7.5 to 400 rads to the testes. Four other participants went through an identical procedure, but received no radiation. Forty-three were released from the program for a variety of reasons. The remaining 125 inmates served as control subjects in the study. Each inmate selected for the study had expressed a desire to undergo a vasectomy at the conclusion of the study. Fifty-three subjects received post-study vasectomies. The other 11 subjects either declined the procedure or did not receive vasectomies. Tissue samples were analyzed at the Biology Division of Oak Ridge National Laboratory.

These studies showed that doses of 7.5 rads had no adverse effect on testicular function, that doses of 27 rads inhibited generation of sperm cells, that doses of 75 rads destroyed existing sperm cells, and that doses of 100 to 400 rads produced temporary sterility. All subjects of the study eventually recovered to their normal preirradiation condition prior to vasectomy.

Study results showed that adult males are very radiosensitive to temporary sterility, but also radioresistant to complete sterility. This work was supported by the U.S. Atomic Energy Commission. (This experiment was referenced in the

Markey report and included in *The DOE Roadmap* of February 1995.)

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OT-15. Iron-55 and Iron-59 Metabolism in Humans

A STUDY WAS CONDUCTED in 1956 by medical researchers at the University of Washington, Seattle to determine the effects of red blood-cell destruction and altered body iron stores on the amount of iron turnover in plasma. Study subjects comprised 14 normal male subjects, 12 patients with nonhematologic diseases, and 59 patients with various hematological diseases.

Red blood cells from donors were stored at cold temperatures (4 degrees Celsius to increase cell destruction. Iron-59 (Fe^{59}), as ferric chloride or ferric citrate, was incubated with fresh plasma and administered intravenously to the subjects. Subjects received between 1 and 15 microcuries of Fe^{59}. Samples of blood were later drawn and analyzed for plasma Fe^{59} activity. Unstated amounts of iron-55 were used in dual tracer experiments to determine clearance rates of iron administered in different ways.

The study showed that the plasma iron turnover is not affected by the rate of red cell destruction, and is affected, to a limited extent, by the increased body stores. This study provided new information on plasma iron turnover in both normal subjects and patients with hematological disorders. The research was supported by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995, and since revised)

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Bothwell, T.H., A.V. Hurtado, D.M. Donohue, and C.A. Finch. "Erythrokinetics. IV. The Plasma Iron Turnover as a Measure of Erythropoiesis." *Blood: The Journal of Hematology*. Vol. 12, 1957, pp. 409–427.

Letter. C.A. Finch to S. Marks. July 17, 1984. Pacific Northwest Laboratory General Human Subjects, Box Alan Rither, PNL-9055-DEL (CIC #701610, bate 8756). ❑

OT-16. Study of Blood Labeled with Chromium-51 in Normal Subjects

A STUDY WAS CONDUCTED in 1955 to1956 by medical scientists at the University of Washington using 19 normal subjects and 25 patients with anemia from the King County Hospital metabolic ward.

In this study, components of human blood from donors were labeled with chromium-51 (Cr^{51}), phosphorus-32 (P^{32}), iron-55 (Fe^{55}), or iron-59 (Fe^{59}) and infused into the circulating blood of study subjects. Blood samples for radioactive analysis were drawn before injection and at 10, 30, 60, 90, 120, and 180 minutes and 12 hours after injection. Iron-59 was counted in a scintillation well-counter. When Fe^{59} was employed to determine red cell utilization, P^{32} was used for the cell volume measurements. When Fe^{55} was used, Cr^{51} was employed for the red cell mass determination. The amount of each isotope administered to subjects is not known.

This study led to a new way of characterizing red cell formation (erythropoiesis) and helped explain the variation found in normal subjects. The research was supported by grants from the U.S. Atomic Energy Commission and the State of Washington Initiative 171 funds for research in Biology and Medicine. (Included in *The DOE Roadmap* of February 1995, and since revised)

References

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Letter. C.B. Finch to S. Marks. July 17, 1984. Pacific Northwest Laboratory General Human Subjects, Box Alan Rither, PNL-9055-DEL (CIC #701610, bate 8756). ❑

OT-17. Total-Body Neutron Activation Analysis

Between 1970 and 1973, studies on the potential usefulness of total-body neutron activation analysis as a diagnostic tool were conducted at University Hospital, University of Washington, Seattle.

In the first stage, 40 to 50 females were studied to develop the technique. All were over the age of 55 years and were afflicted with known bone-wasting diseases, such as osteoporosis. In the second stage, which used this new technique with subjects, 25 chronically ill adults suffering from kidney failure were studied to evaluate calcium balance. Females in the second stage were beyond childbearing years.

All subjects were exposed to uniform low-flux, high-energy neutrons. The total-body dose to study participants was estimated to be 2.1 rems. Initial subject were given a 1-year examination, but no longer-term follow-up was conducted. This study was funded by the U.S. Atomic Energy Commission and the Public Health Services. (Previously described in #38 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995, and since revised.)

References

Nelp, W.B., H.E. Palmer, R. Murano, K. Pailthorp, G.M. Hinn, C. Rich, J.I. Williams, T.G. Rudd, and J.D. Denney. "Measurement of Total-Body Calcium (Bone Mass) *In Vivo* with the Use of Total-Body Neutron Activation Analysis." *Journal of Laboratory and Clinical Medicine,* Vol. 76, 1970, pp. 151–162.

Letter. W.B. Nelp to S. Marks. August 30, 1984. Pacific Northwest Laboratory, General Human Subjects, Box Alan Rither, PNL 9055 DEL. ❑

OT-18. Utah Strontium-85 Metabolism Study

THE UNIVERSITY OF UTAH Radiobiology Laboratory conducted a strontium-85 (Sr^{85}) metabolism study on subjects in 1956 to determine the uptake, retention, and excretion of Sr^{85} in man. The study was conducted to learn more about the likely metabolism of strontium-90 (Sr^{90}) fallout from atomic testing.

Subjects consisted of seven male patients at the Salt Lake Veterans Administration Hospital and two male staff members. Five of the patients had normal bone metabolism and two had osteoporosis. After intravenous injection of approximately 5 microcuries of Sr^{85}, measurements were made over time to determine concentrations of Sr^{85} in plasma, urine, and feces. Bone tissue biopsy samples obtained from two osteoporotic patients and from two normal subjects were analyzed for Sr^{85} and calcium. In addition, several bone samples were obtained at autopsy from a tenth injected patient who was not bioassayed along with the other patients.

This work showed that strontium cleared more efficiently than calcium from the blood and was excreted primarily in urine rather than feces. This study was part of Project Sunshine and was supported by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995, and since revised)

References

Van Dilla, M.A., S. Wallach, and J.S. Arnold. "Sr^{85} Tracer Studies in Humans." *Semiannual Progress Report.* Salt Lake City: Radiobiology Laboratory, University of Utah, September 30, 1956. ❑

OT-19. Radioisotope Studies at the Fernald State School, Massachusetts

IN THE EARLY TO MID-1950s, various radiation-related studies were carried out at the Fernald State School in Waverly, Massachusetts, using students as subjects. In a study addressing calcium metabolism, nine adolescent males, institutionalized for mental inadequacy but otherwise physically normal, ranging in age from 10 to 15 years, and one 21-year-old male participated as subjects.

The adolescents received 0.7 microcurie of calcium-45 (Ca^{45}). The subjects were divided into two groups: one group was administered the Ca^{45} intravenously, the other received it orally. One month later, 0.74 microcurie was adminis-

tered, but the means of administration was reversed between the groups. Two years later, 2.02 microcuries of Ca^{45} were administered to the 21-year-old subject (who by then was 23). The studies showed that calcium is retained in the body for some time and that it is eventually excreted more through urine than feces.

A second study addressed thyroid function in Down's syndrome subjects and their parents. Twenty-one male and female Down's syndrome students ranging in age from 5 to 26 years participated, as did 5 female and 2 male normal parents of these students. The students were orally administered 70 microcuries of iodine-131 (I^{131}). The parents received 100 microcuries. Thyroid uptake, turnover, and urinary excretion were subsequently measured. Additionally, thyroxine metabolism was studied in two Down's syndrome students after intravenous injection of 55 microcuries of thyroxine labeled with I^{131}.

These studies showed that iodine uptake was in the low-normal range and did not differ significantly from normal values; that the iodine turnover rate was significantly faster than normal; that the thyroxine turnover rate was normal; and that the uptake, turnover, and excretion rates in parents of Down's syndrome children were normal. These studies were supported in part by the U.S. Atomic Energy Commission. (Included in *The DOE Roadmap* of February 1995)

References

Bronner, F., R.S. Harris, C.J. Maletskos, and C.E. Benda. "Studies in Calcium Metabolism. The Fate of Intravenously Injected Radiocalcium in Human Beings." *Journal of Clinical Investigation.* Vol. 35, 1956, pp. 78–88.

Kurland, G.S., J. Fishman, M.W. Hamolsky, and A.S. Freedberg. "Radioisotope Study of Thyroid Function in 21 Mongoloid Subjects Including Observations in 7 Parents." *Journal of Endocrinology and Metabolism.* Vol. 17, 1957, pp. 552–560. ❑

OT-20. Uptake of Iodine-131 by Premature Infants in Detroit

IN 1954, the Pediatric Division and the Radioisotope Laboratory of Harper Hospital in Detroit, Michigan, studied the uptake of iodine-131 (I^{131}) by the thyroid gland of premature infants. Sixty-five premature infants ranging in birth weight from 2.1 to 5.5 pounds were included in the study; seven full-term infants were used for the control group.

The premature infants were given 5 microcuries of I^{131} orally. Iodine-131 concentrations were then measured in the thyroid gland. It was found that the range of uptake of I^{131} in this series of infants was within the limits of normal as measured in studies of full-term children and adults. (Previously described in #4 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

References

Martmer, E.E., K.E. Corrigan, H.P. Charbeneau, and A. Sosin. "A Study of the Uptake of Iodine (I^{131}) by the Thyroid of Premature Infants." *AMA American Journal of Diseases of Children.* Vol. 17, 1955, pp. 503–509. ❑

OT-21. Testicular Irradiation of Oregon State Prison Inmates

FROM AUGUST 1963 to May 1971, the Pacific Northwest Research Foundation in Seattle, Washington, conducted studies on the effects of radiation on human testicular function using as subjects inmates at the Oregon State Prison in Salem. The purpose of the study was to determine the effects of ionizing radiation on sperm production and to determine minimum dose levels for initial effect and permanent damage.

Sixty-seven healthy volunteers ranging in age from 24 to 52 years were irradiated by x-rays at least once during the course of the study. Of these 67 subjects, 6 received a second irradiation, 1 received 3 irradiations, and 1 received a series of 11 weekly irradiations. Testicular absorbed doses ranged from 8 to 640 rads. Postirradiation studies included analysis of blood, urine, and seminal fluid, and biopsy of sperm-producing tissues.

Subjects were compensated for their participation and for each biopsy. All subjects who had not been previously vasectomized agreed to undergo a vasectomy at the conclusion of the study. All did so and received additional compensation for the procedure.

All subjects were volunteers and could withdraw from participation at any time. The study was

reviewed at 3-month intervals by a review board and three additional reviews were provided by a national ad hoc committee.

This study showed that a single testicular dose of 600 rads caused temporary disruption of testicular function. Recovery time was dose dependent; the higher the dose, the longer the time required for recovery. Subjects who were irradiated a second or third time had responses that were similar to their initial responses. This work was supported by the U.S. Atomic Energy Commission. (This experiment was referenced in the Markey report and included in *The DOE Roadmap* of February 1995.)

References

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Heller, C.G., D.E. Dilaconi, and M.J. Rowley. *Protection of the Rights and Welfare of Prison Volunteers: Policies Followed Throughout a 17-Year Medical Research Program.* Seattle: Pacific Northwest Research Foundation.

Rowley, M.J., D.R. Leach, G.A. Warner, and C.G. Heller. "Effect of Graded Doses of Ionizing Radiation on the Human Testis." *Radiation Research.* Vol. 59, 1974, pp. 665–678.

"Background Information on AEC Human Testicular Irradiation Projects in Oregon and Washington State Prisons." *Information from ERDA.* Washington, DC: U.S. Energy Research and Development Administration, March 1975. ❑

OT-22. Distribution of Zinc-65 in Blood and Organs of Humans

IN 1947, RESEARCHERS in Boston administered zinc-65 (Zn^{65}) to a 67-year-old male suffering from myelogenous leukemia and to a nonleukemic, healthy subject. The purpose of this study was to determine how the content and distribution of zinc in blood and organs of the normal subject compared with the zinc content and distribution in the leukemia patient.

Zinc-65 was injected intravenously as zinc chloride daily for several days and in amounts ranging from 2 milligrams per day to "far in excess of this amount." Analysis occurred over a long period of time to monitor Zn^{65} retention.

This experiment showed that zinc plays an important role in the metabolism of tissues and blood cells. The work was supported by the U.S. Atomic Energy Commission. (Previously described in #32 on the original list of 48 experiments released by DOE in June 1994 and included in *The DOE Roadmap* of February 1995)

References

Gibson, J.G., B.I. Vallee, R.G. Fluharty, and J.E. Nelson. *Studies of the Zinc Content of the Leucocytes in Myelogenous Leukemia.* Oak Ridge, TN: Oak Ridge Operations Office, 1947. (RHTG) Classified Docs 1944–1994, Records Holding Area-Bldg 2714-H Vault, Box RHA H108-5, 1 of 2, Folder "Advisory Committee."

Vallee, B.L., R.G. Fluharty, and J.G. Gibson. *Distribution of Zinc in Normal Blood and Organs Studied by Means of Zn^{65}.* Oak Ridge, TN: Oak Ridge Operations Office, 1947. (RHTG) Classified Docs 1944–1994, Records Holding Area-Bldg 2714-H Vault, Box RHA H108-5, 1 of 2, Folder "Advisory Committee." ❑

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OT-23. Thyroid Uptake and Urinary Excretion of Iodine-131 in Assessing Thyroid Function

IN THE 1950s, physicians in the Pediatric Department, University of Arkansas School of Medicine in Little Rock evaluated the use of measurements of iodine-131 (I^{131}) uptake by the thyroid and its excretion in urine as a means of assessing thyroid function in children. The study included 30 children, 25 with normal thyroid function (euthyroid), and 5 born either without a thyroid or with a thyroid that was virtually nonfunctional (congenital hypothyroidism). The euthyroid subjects consisted of 14 males and 11 females between the ages of 9 months and 15 years, of whom 11 were white and 14 were nonwhite.

Five microcuries of I^{131} with stable potassium iodide carrier were administered orally to subjects up to 6 years of age. Ten microcuries were administered to subjects, ages 7 to 15 years. The hypothyroid subjects also were given 65 milligrams of thyroid extract daily for an unreported period of time. Measurements of I^{131} activity in the thyroid were made and urine samples were obtained from the normal subjects 2, 4, 6, 48, 72, and 96 hours after administration.

Similar measurements were obtained frequently from the hypothyroid subjects during and after administration of thyroid extract.

Thyroid uptake of I^{131} was between 9 and 30 percent in the normal children, while the hypothyroid children absorbed between zero and 2.2 percent of the administered I^{131}. The rate of I^{131} excretion was much higher in hypothyroid children than in the normal controls. The researchers concluded that this method was reliable for assessing thyroid function. This study was approved by and appears to have been supported by the U.S. Atomic Energy Commission.

References

Reilly, W.A., and D. Bayer. "The Value of the Measurements of Thyroid Uptake and Urinary Excretion of I^{131} in Assessing Thyroid Function of Normal and Congenitally Hypothyroid Children." *Journal of Pediatrics.* Vol. 40, January–June 1952, pp. 714–721. ❑

OT-24. Short-Term Clearance Studies Using Iodine-131

DURING THE EARLY 1960s, researchers at the University of Arkansas Medical Center in Little Rock conducted studies on the accumulation of iodine-131(I^{131}) in the thyroid and elimination of iodine from subjects. In all, 40 healthy subjects participated. Each subject was injected with 10 microcuries of I^{131}. Measurements were made at various intervals of I131 activity in the thyroid and with samples of urine, plasma, and feces.

This study showed that the clearance of I^{131} through the kidneys decreased at night by a factor of 1.4 when compared to daytime clearance, while the clearance of I^{131} through the thyroid gland remained approximately constant over 24-hour periods. This information, together with other data on the loss of iodine through sweat, feces, and urine, improved the scientists' understanding of the metabolism of stable iodine in the body. This work was supported by the National Institutes of Health and the U.S. Atomic Energy Commission.

References

Oddie, T.H., D.A. Fisher, and J.M. Long. "Factors Affecting the Estimation of Iodine Entering the Normal Thyroid Gland Using Short-Term Clearance Studies." *Journal of Clinical Endocrinology.* Vol. 24, 1964, pp. 924–933. ❑

OT-25. Study of Iodine-131-Thyroxine Metabolism in Adolescent and Adult Human Subjects

A STUDY WAS CONDUCTED during 1961 to 1964 at the University of Arkansas Medical Center in Little Rock on the metabolism of iodine-131 (I^{131})–labeled thyroxine in 24 euthyroid (normal thyroid function) subjects. The purpose of this study was to measure the absorption and degradation rate of thyroxine in euthyroid subjects. The subjects ranged in age from 13 to 51 years. The adolescent subjects in the study were wards of the Arkansas Children's Colony and were physically normal with mild to moderate mental retardation. The adult participants were normal, healthy volunteers.

The subjects were administered thyroxine labeled with tracer amounts (about 15 microcuries) of I^{131} either by intravenous injection or orally. Radioiodine was measured by external counting of the subject's thyroid, by whole-body counting to determine extrathyroid thyroxine, and by analyzing fecal specimens.

Results of this study showed that 73 percent of orally administered thyroxine was absorbed, and that about 12 percent of the extrathyroid fraction of systemic thyroxine was excreted from the body per day. Iodine-131–labeled hormone was administered to evaluate the comparability of noninvasive *in vivo* (whole-body and thyroid) counting with the established invasive method. This method also involved administration of I^{131}-labeled thyroxine, but required the drawing of serial blood samples for plasma counting to evaluate thyroxine metabolism as a measure of thyroid function.

The investigators found that not only did the *in vivo* method give similar results to the plasma counting method, but it also required a smaller amount of I^{131}-labeled hormone and was more acceptable to the subject, thereby enabling measurements to be made more frequently or over a longer period of time. This work was supported by grants from the National Institutes of Health and the U.S. Atomic Energy Commission.

References

Oddie, T.H., D.A. Fisher, and C. Rogers. "Whole-Body Counting of I^{131}-Labeled Thyroxine." *Journal of Clinical Endocrinology*. Vol. 24, 1964, pp. 628–637. ❑

OT-26. Study of Iodine-131–Triiodothyronine Counting in Normal Subjects

A STUDY WAS CONDUCTED during the period 1961 to 1964 at the University of Arkansas Medical Center in Little Rock on the metabolism of iodine-131 (I^{131})–labeled triiodothyronine (T_3) in 18 healthy, adult volunteers with normal thyroid (euthyroid) function. The purpose of this study was to measure the absorption and degradation rate of triiodothyronine in subjects with normal thyroid function, and to develop noninvasive, whole-body counting techniques for this measurement.

The subjects were administered about 5 to 15 microcuries I^{131}-labeled thyroxine or triiodothyronine, either intravenously or orally. Radioiodine was measured by external counting of the subject's thyroid, by whole-body counting to determine extrathyroid hormone, and by analyzing fecal specimens.

Results of this study showed that T_3 is more rapidly excreted and degraded than thyroxine (T_4). Approximately 53 percent of extrathyroidal T_3 was degraded per day after intravenous administration. Approximately 85 percent of orally administered T_3 was absorbed. This study provided further explanation for observed T_4/T_3 ratios in plasma. This work was supported by grants from the National Institutes of Health and the U.S. Atomic Energy Commission.

References

Fisher, D.A., and T.H. Oddie. "Whole-Body Counting of I^{131}-Labeled Triiodothyronine." *Journal of Clinical Endocrinology*. Vol. 24, 1964, pp. 733–739. ❑

OT-27. Thyroid Hormone Secretion Studies Using Iodine-131

FROM 1963 TO 1964, the University of Arkansas Medical Center in Little Rock conducted studies in humans on iodine accumulation in the thyroid gland, iodine metabolism, and secretion of thyroxine hormone. In all, 152 subjects (including both men and women) ranging in age from 10 to 61 years and having normal thyroid function, participated. These subjects included volunteer hospital employees, students, and patients, as well as moderately mentally retarded children and young adult volunteers from the Arkansas Children's Colony.

Thyroid gland accumulation of iodine was measured in all subjects. Ten microcuries of iodine-131 (I^{131}) were injected intravenously into each subject to measure iodine uptake, retention, and clearance from the thyroid and urinary iodine excretion by the kidneys. In 29 subjects, the uptake of I^{131}-labeled thyroxine was measured by whole-body counting and compared with stable iodine accumulation.

These studies showed that thyroidal iodine increased progressively with increasing iodine uptake, while thyroxine secretion remained constant. This work was supported by the Institute of Arthritis and Metabolic Diseases, the U.S. Public Health Service, and the U.S. Atomic Energy Commission.

References

Fisher, D.A., and T.H. Oddie. "Comparison of Thyroidal Iodide Accumulation and Thyroxine Secretion in Euthyroid Subjects." *Journal of Clinical Endocrinology*. Vol. 24, 1964, pp. 1,143–1,154.

Oddie, T.H., D.A. Fisher, and J.M. Long. "Factors Affecting the Estimation of Iodine Entering the Normal Thyroid Gland Using Short-Term Clearance Studies." *Journal of Clinical Endocrinology*. Vol. 24, 1964, pp. 924–933. ❑

OT-28. Brain Scanning Studies Using Potassium-42

DURING THE LATE 1940s, researchers at the Neurosurgical and Surgical Services and Laboratories of Harvard Medical School, Children's Hospital, and Peter Bent Brigham Hospital in Boston, Massachusetts, conducted collaborative studies on brain tumor localization, using potassium-42 (K^{42}). A total of 15 normal, healthy volunteers (12 males and 3 females in their twenties) and 39 patients with known or suspected brain tumors, including 15 males and 22 females between the ages of 3 months and 66

years, participated as subjects. Adult subjects were administered 10 to 15 microcuries of K^{42} by intravenous injection. Subjects under 16 years of age were administered 2 to 3 microcuries of K^{42}. Activity in the brain was measured with an external counter.

The results of these studies showed that K^{42} was of limited value as a brain tumor scanning agent. Potassium is readily taken up by tumor tissue, but is taken up more rapidly by blood and muscle tissue—a difference which can cause a masking effect for tumor scanning. This work was supported by the American Cancer Society and the U.S. Atomic Energy Commission.

References

Susen, A.F., W.T. Small, and F.D. Moore. "Studies on the External Diagnostic Localization of Brain Lesions Using Radioactive Potassium." In *Surgical Forum Proceedings of the Forum Sessions*, Thirty-Sixth Clinical Congress of the American College of Surgeons, Boston, MA, October 1950, pp. 362–368. ❑

OT-29. Studies on Body Potassium Using Potassium-42

DURING THE LATE 1940s, researchers at Harvard Medical School and Peter Bent Brigham Hospital, Boston, Massachusetts, conducted studies on exchangeable potassium levels in humans using potassium-42 (K^{42}). The term "exchangeable" refers to that portion of total-body volume that is not stored in tissues.

Thirty healthy males, ranging in age from 21 to 32 years, participated as subjects. Each was administered about 100 microcuries of K^{42} by intravenous injection and activity was measured in urine samples collected over the next 40 hours. Blood samples from 16 of the subjects were also analyzed for activity.

The studies showed that exchangeable potassium accounts for approximately 95 percent of total-body potassium. This work was supported by the U.S. Atomic Energy Commission.

References

Cosra, L., Jr., J.M. Olney, Jr., R.W. Steenburg, M.R. Ball, and F.D. Moore. "The Measurement of Exchangeable Potassium in Man by Isotope Dilution." *The Journal of Clinical Investigation.* Vol. 29, 1950, pp. 1,280–1,295. ❑

OT-30. Serum Level of Protein Bound Iodine-131 in the Diagnosis of Hyperthyroidism

DURING THE LATE 1940s, scientists at the Medical Research Laboratories, Beth Israel Hospital, and the Department of Medicine, Harvard Medical School, Boston, Massachusetts, evaluated the effectiveness of iodine-131 (I^{131}) as a tool for diagnosis of hyperthyroidism. A total of 20 patients—10 with thyrotoxicosis (hyperthyroidism) and 10 normal controls—between 10 and 65 years of age, participated as subjects.

Sixteen of the 20 patients were female. Each subject received 150 microcuries of carrier-free I^{131} orally. Twenty-four hours after administration of the I^{131}, 10 milliliters of blood were drawn and measured for serum-protein bound I^{131}. It was found that the hyperthyroid patients had much higher levels of I^{131} in their serum protein than the normal controls.

The researchers concluded that I^{131} was a valuable diagnostic tool for investigating hyperthyroidism. This study was funded by the President and Fellows of Harvard College, the Office of Naval Research, and the U.S. Atomic Energy Commission.

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Freedburg, A., A. Urelis, and S. Hertz. "Serum Level of Protein Bound Radioactive Iodine (I^{131}) in the Diagnosis of Hyperthyroidism." In *Proceedings of the Society for Experimental Biology and Medicine.* Vol. 70, No. 4, April 1949, pp. 679–682. ❑

OT-31. Body Constituent Studies Using Sodium-24 and Potassium-42

BETWEEN 1946 AND 1951, researchers at Harvard Medical School and Peter Bent Brigham Hospital, Boston, Massachusetts, conducted studies of exchangeable sodium and potassium in humans using sodium-24 (Na^{24}) and potassium-42 (K^{42}). The term "exchangeable" refers to that portion of total-body volume that is not stored in tissues.

Fourteen normal young adults, both men and women, were administered Na^{24}, and 47 similar subjects were administered K^{42}. Amounts of body sodium and potassium were then calculated using standard dilution methods. One of the subjects had participated in a pilot study in 1946 and the earlier data were correlated with data from the present study.

These studies provided new information on sodium and potassium levels in both males and females, and indicated that the plasma was the best body fluid in which to measure this exchange. This work was supported by the U.S. Atomic Energy Commission.

References

Edelman, I.S., J.M. Olney, A.H. James, L. Brooks, and F.D. Moore. "Body Composition: Studies in the Human Being by the Dilution Principle." *Science.* Vol. 115, April 25, 1952, pp. 447–454.

Moore, F.D. "Determination of Total-Body Water and Solids with Isotopes." *Science.* Vol. 104, August 16, 1946, pp. 157–160. ❑

OT-32. Red Blood-Cell Volume Studies Using Chromium-51

IN 1949 AND 1950, scientists at the Biophysical Laboratory and the Department of Medicine of Harvard Medical School and the Medical Clinic at the Peter Bent Brigham Hospital, Boston, Massachusetts, conducted studies to determine red blood-cell volume using chromium-51 (Cr^{51}). Twenty-five healthy male volunteers participated as subjects.

A 50-milliliter blood sample was drawn from each subject, and the red cells were labeled with 40 to 200 microcuries of Cr^{51} as sodium chromate. After standing 1 hour at room temperature, the labeled blood sample was reinjected intravenously into the corresponding donor subject. Red blood-cell samples were obtained 10 minutes after injection and at three 10-minute intervals thereafter, and were measured for Cr^{51} activity. Blood volume was calculated using this information. The accuracy of this method was confirmed in five other hospitalized patients: three males ages 30, 36, and 38 years with cirrhosis of the liver or bronchiogenic cancer, and two females ages 53 and 69 years, with polycythemia vera. These subjects were given a second injection of Cr^{51}-labeled red cells after transfusion or recent hemorrhage of a known volume of red cells.

The study showed that Cr^{51} labeling was an effective tool in measuring red blood-cell volume. This work was supported in part by the Office of Naval Research, National Cancer Institute, and the U.S. Atomic Energy Commission.

References

Sterling, K., and S.J. Gray. "Determination of the Circulating Red Cell Volume in Man by Radioactive Chromium." *Journal of Clinical Investigation.* Vol. 29, 1950, pp. 1,614–1,619. ❑

OT-33. Studies on Body Sodium Using Sodium-24

DURING THE EARLY 1950s, researchers at the Harvard Medical School and Peter Bent Brigham Hospital, Boston, Massachusetts, conducted studies on exchangeable sodium levels in humans using sodium-24 (Na^{24}). Exchangeable sodium is that which is not stored in body tissue.

Twenty-seven healthy males or females, ranging in age from 22 to 61 years, participated as subjects. Between 100 and 200 microcuries of Na^{24} were administered to each subject by intravenous injection and the radioactivity was measured in blood and urine samples collected over the next 48 hours.

These studies showed that equilibrium in the body was reached 15 to 24 hours after injection and that total exchangeable sodium for both men and women is about 0.96 gram per kilogram of body weight. They also showed that Na^{24} was a convenient and accurate tool for estimating the exchangeable sodium content of the body. This work was supported by the Upjohn Company, Winthrop-Stearns, Inc., and the U.S. Atomic Energy Commission.

References

Edelman, I.S., A.H. James, L. Brooks, and F.D. Moore. "Body Sodium and Potassium IV. The Normal Total Exchangeable Sodium; Its Measurement and Magnitude." *Metabolism.* Vol. 3, 1954, pp. 530–538. ❑

OT-34. Bone Studies Using Sodium-24

DURING THE EARLY 1950s, researchers at Harvard Medical School and Peter Bent Brigham Hospital, Boston, Massachusetts, conducted studies of bone composition and sodium penetration using sodium-24 (Na^{24}). The subject was intravenously administered 100 microcuries of Na^{24}. A segment of rib and a blood sample were obtained and analyzed 26 hours after injection.

These studies provided data on human bone composition and indicated that about 45 percent of bone sodium was exchangeable in 4 hours. This work was supported by the American Heart Association, the Upjohn Company, Winthrop-Stearns, Inc., and the U.S. Atomic Energy Commission.

References

Edelman, I.S., A.H. James, H. Baden, and F.D. Moore. "Electrolyte Composition of Bone and the Penetration of Radiosodium and Deuterium Oxide Into Dog and Human Bone." *The Journal of Clinical Investigation.* Vol. 33, February 1954, pp. 122–131. ❑

OT-35. Studies of Calcium Metabolism and Thyroid Disease Using Calcium-45

DURING THE EARLY 1950s, researchers at Harvard Medical School, Boston, Massachusetts, conducted studies on the effect of thyroid disease on calcium metabolism in humans. Study participants included 11 patients, both male and female (with diagnoses of hyperthyroidism, myxedema, hypothyroidism, Paget's disease, and euthyroidism), at Massachusetts General Hospital in Boston, who ranged in age from 19 to 67 years.

Subjects received an intravenous injection of 5 to 7 microcuries of calcium-45 (Ca^{45}). After injection, samples of blood, urine, and feces were obtained over various time intervals and analyzed for Ca^{45} content.

The study indicated that bone formation and destruction occurred at increased rates in patients with thyroid disease. This work was supported by the U.S. Atomic Energy Commission.

References

Krane, S.M., G.L. Brownell, J.B. Stanbury, and H. Corrigan. "The Effect of Thyroid Disease on Calcium Metabolism in Man." *Journal of Clinical Investigation.* Vol. 35, 1956, pp. 874–887. ❑

OT-36. Analysis of Red Blood-Cell Survival in the Body Using Chromium-51

DURING 1950 TO 1953, researchers at Massachusetts Memorial Hospitals and the Boston University School of Medicine conducted studies on chromium-51 (Cr^{51})–labeling for red blood cells to determine the survival times of red blood cells in the body.

In the first experiment, donor blood was collected and tagged with Cr^{51} as sodium chromate, and injected into nine normal, healthy medical students. Approximately 500 milliliters of blood was drawn from each subject immediately prior to transfusion. In the second experiment, 10 hospitalized patients without hematologic abnormalities or other blood diseases received 50 milliliters blood tagged with Cr^{51} at weekly intervals. The amount of Cr^{51}-labeled red blood cells in circulating blood was then determined at various times after injection in each of the patients. The percent of donor cells surviving were determined for each time point. The excretion of Cr^{51} in subjects' urine was also determined.

This study showed that red blood cells rapidly combine with Cr^{51} in circulation and that the method is useful for determining red blood-cell survival times. This work also provided a simple, new method for evaluating the preservation of red blood cells. This work was supported by the American Cancer Society of Massachusetts, Inc., and the U.S. Atomic Energy Commission.

References

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OT-37. Blood Volume Studies Using Chromium-51

BETWEEN 1952 AND 1953, researchers at Harvard Medical School and the Peter Bent Brigham Hospital, Boston, Massachusetts, conducted studies on blood volume determination using chromium-51 (Cr^{51}). Nine normal males ranging in age from 23 to 57 years and 14 surgical patients ranging in age from 17 to 72 years participated as subjects.

Between 75 and 100 microcuries of Cr^{51} were administered as sodium chromate by intravenous injection to each subject. Activity was measured in blood samples drawn 20 to 40 minutes after injection and, in five cases, up to 100 days after injection. Eleven subjects participated in two separate studies.

The results of these studies showed that the radiochromium method was a valid, simplified procedure for blood volume measurement. This work was supported by the U.S. Atomic Energy Commission.

References

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OT-38. Studies of Stable Iodine Uptake Using Iodine-131 as a Tracer

IN 1952 AND 1953, researchers in the Radioisotope Unit at Boston Veterans Administration Hospital, the Massachusetts Memorial Hospitals, and the Department of Medicine at Boston University School of Medicine conducted studies of the uptake of iodine among three groups of patients that differed with respect to thyroid status. The purpose of these studies was to learn more about factors influencing the uptake of stable iodine in humans. Most of the 197 patients who served as study subjects had been referred for evaluation of possible thyroid disease. Of the 197, 85 either had tested negative for thyroid disease and were considered "normal" with respect to thyroid function (euthyroid) or had thyroid disease that remained untreated. The remaining 112 subjects had abnormally active thyroids (hyperthyroid) for which they had been treated previously (but not during the 3 months immediately prior to the study) with antithyroid drugs, radioiodine or surgery.

Iodine-131 (I^{131}), usually 50 microcuries, was administered as a tracer to each subject by intravenous injection 2 to 3 hours following breakfast. Blood samples were drawn at the time of monitoring to determine the serum protein-bound iodine concentrations. Urine samples were also collected from the subjects for I^{131} analysis.

The study showed a correlation between I^{131} uptake by the thyroid and serum protein-bound iodine concentration. Stable iodine uptake values associated with each protein-bound iodine level showed greater variation among the treated group than among the normal or untreated group. This study was supported by the U.S. Atomic Energy Commission.

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OT-39. Studies of Iron Metabolism, Anemia, and Cancer Using Iron-59 and Chromium-51

DURING THE MID-1950s, researchers at the Massachusetts Memorial Hospitals, Boston Veterans' Administration Hospital, and the Boston University School of Medicine conducted studies of the iron metabolism and causes of anemia in cancer patients, using iron-59 (Fe^{59}) and chromium-51 (Cr^{51}).

Thirty-eight cancer patients participated as subjects. Plasma was obtained from normal subjects, mixed with approximately 10 microcuries of Fe^{59} as ferric ammonium citrate, and intravenously administered to each patient. Iron-59 disappearance from plasma, plasma iron turnover, red cell utilization of Fe^{59}, red cell turnover, red cell iron renewal rate, and Fe^{59} localization were subsequently measured. Two patients also participated in a red cell survival study, which included administration of Cr^{51} and activity measurement in blood samples for 5 weeks.

These studies showed increased red cell destruction in the cancer patients and increased red cell production, which was insufficient to prevent anemia resulting from the red cell destruction. This work was supported by the U.S. Atomic Energy Commission.

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Miller, A., R.B. Chodos, C.P. Emerson, and J.F. Ross. "Studies of the Anemia and Iron Metabolism in Cancer." *Journal of Clinical Investigation*. Vol. 35, 1956, pp. 1,248–1,262. ❑

OT-40. Studies of Iron Metabolism, Anemia, and Rheumatoid Arthritis Using Iron-59

DURING THE MID-1950s, researchers at the Massachusetts Memorial Hospitals, Robert Breck Brigham Hospital, Boston University School of Medicine, and Harvard Medical School conducted studies of iron metabolism and anemia in patients with rheumatoid arthritis using iron-59 (Fe^{59}). Forty-two male or female patients ranging in age from 20 to 71 years, and 10 male or female controls (healthy volunteers) ranging in age from 30 to 65 years participated as subjects.

Plasma drawn from normal donors was mixed with Fe^{59} as ferric ammonium citrate and intravenously administered to each subject. The administered activity was approximately 5 to 10 microcuries. Plasma Fe^{59} removal rate, red cell uptake, serum iron concentration, red cell survival rate, red cell volume, plasma volume, and total blood volume were subsequently measured.

These studies showed that rheumatoid arthritis patients had normal utilization of plasma iron for red cell production, increased red cell destruction, and increased but insufficient red cell production. This work was supported by the U.S. Atomic Energy Commission.

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OT-41. Iron Absorption Studies Using Iron-59

DURING THE MID-1950s, researchers at the Boston Veterans Administration Hospital, Boston University School of Medicine, Harvard Medical School, and Tufts University School of Medicine conducted studies of the absorption of dietary iron using iron-59 (Fe^{59}). Thirty-two male patients with normal blood iron values, 15 patients with chronic blood loss, and 9 patients with idiopathic hemochromatosis (a disease characterized by excessive iron intake for unknown reasons) participated as subjects.

Red blood-cell indices were determined for each subject using a standard phosphorus-32 (P^{32}) labeling technique. The 56 subjects participated in a total of 84 individual studies involving the oral administration of 12 to 50 microcuries of Fe^{59} as ferric or ferrous chloride or the ingestion of 7 to 23 microcuries of Fe^{59} in labeled eggs or vegetables. Activity levels were measured in subsequently collected blood and stool samples.

These studies showed that iron administered as a chloride salt was more readily absorbed than dietary iron and that dietary iron was not absorbed in sufficient amounts to overcome increased loss or to respond to increased requirements. This work was supported by the U.S. Atomic Energy Commission.

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Halkett, J.A.E., R.B. Chodos, and J.F. Ross. "The Labeling of Human Foods with Radioactive Iron (Fe^{59})." *Journal of Laboratory and Clinical Medicine*. Vol. 53, January–June 1959, pp. 816–823. ❑

OT-42. The Effects of Whole-Body Radiation on Organ Transplant Survival

EXPERIMENTS WERE CONDUCTED at Harvard Medical School, Boston, Massachusetts, in the early 1960s to determine whether total-body radiation with x-rays (250 to 650 rads) would suppress

the natural rejection of organs and improve the success of organ transplantation. These studies were initiated after reports by French scientists that whole-body radiation might be helpful in suppressing the immune rejection response.

At least eight transplant recipients were known to have been involved in this study. These included six patients who received kidneys from identical twin donors. One patient was reported to be doing well 17 months after transplant. Additional radiation was prescribed to suppress the rejection response. Specific details on the survival times of transplant recipients and cause of death were not given, and some of the documentation is illegible. One patient, given 650 rads of x-ray radiation, accepted the kidney transplant, but died 28 days postirradiation. The death was ascribed to total-body radiation.

The study was terminated after it was determined that the deleterious effects of whole-body radiation were greater than their beneficial effects in suppressing the rejection of transplanted tissues. This work was supported by the U.S. Atomic Energy Commission.

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Factsheet. Human Experimentation-05 (SFS11.001) Project Name: Study of Transplantation of Bone Marrow Tissue and Whole Organs, etc., Department of Energy, Markey Files.

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OT-43. Blood-Cell Studies in Colorado Prisoners Using Iron-59, Phosphorus-32, and Chromium-51

A SERIES OF STUDIES were conducted between 1960 and 1968 by investigators at the University of Colorado Medical Center, Denver to determine rates of red blood-cell regeneration and hemoglobin recovery after excessive blood loss; and to determine the survival rates and characteristics of red cells formed during periods of rapid cell development and severe iron deficiency. The subjects were male prisoners from the Colorado State Penitentiary in Canon City, and local county jails in the Denver area, who had volunteered to be study subjects.

The subjects were phlebotomized (bled) regularly until a condition of iron deficiency was reached. The subjects were then administered about 5 millicuries of iron-59 and 0.2 or 0.4 millicurie of phosphorus-32 as diisopropylfluorophosphate to label newly formed blood-cells in circulation. Samples of the blood were then obtained at various times after injection and were counted to determine the isotope content or were autoradiographed to determine their histological characteristics and other parameters, such as rate of red cell formation. It appears that other studies were conducted using chromium-51 to determine red cell survival times.

According to one of the investigators, the results of most of these studies were not published in the open scientific literature at the request of the University of Colorado administration. The funding sources for these studies have not been identified, though the principal investigator had previously served as a Manhattan Project physician at Billings Hospital in Chicago and had close affiliations with the U.S. Atomic Energy Commission during his career.

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Personal communication. J. Franks to D.R. Fisher. May 24, 1995. ❑

OT-44. Tracer Studies of Arsenic Metabolism Using Arsenic-71 and Arsenic-74

IN APPROXIMATELY 1939 TO 1941, studies were conducted at the Massachusetts Institute of Technology (MIT) in collaboration with Massachusetts General Hospital and Harvard Medical School, Boston on the metabolism of arsenic in normal subjects and in hospital patients with leukemia. Small amounts of arsenic had previously been used in treatment of chronic myeloid leukemia. The purpose of this study was to evaluate the metabolism of arsenic using arsenic-71 (As^{71}) and arsenic-74 (As^{74}) produced at the MIT cyclotron.

After preliminary studies in rats, guinea pigs, and rabbits, two healthy human subjects were given As^{71} and As^{7} as potassium arsenite with a stable arsenic carrier (1.5 milligrams) by subcutaneous injection. Administered activities varied from 15 to 25 millicuries As^{71} or 2 to 3 millicuries As^{74}. Amounts of arsenic excreted in urine and stool samples were then determined at various times, postinjection. It was found that almost all of the arsenic was excreted in urine. Higher specific activity levels of As^{71} and As^{74} were administered to four leukemia patients to determine the rate of clearance of arsenic from blood. Bone marrow biopsies were obtained from two of the leukemia patients and spinal fluid was obtained from two patients to determine arsenic concentrations present.

One patient died of leukemia 4 days after injection and this provided an opportunity to measure arsenic concentrations in the patient's liver, spleen, kidney, lungs, marrow, skeletal muscles, and other soft tissues. The greatest arsenic concentrations were found in muscle tissue and other rapidly growing tissue. This work was supported by various sponsors, including the John and Mary R. Markle Foundation and the H.N.C. Gift of the Harvard Medical School. The MIT Radioactivity Center was supported in part by the Office of Scientific Research and Development beginning in 1941–1942. This function was later assumed by the U.S. Atomic Energy Commission.

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OT-45. Iodine Metabolism Studies in Graves' Disease Using Iodine-131

DURING THE EARLY 1940s, researchers at the Massachusetts Institute of Technology, Massachusetts General Hospital, and Boston City Hospital conducted studies on iodine uptake, retention, and excretion in hospital patients with Graves' disease using iodine-131 (I^{131}). Twenty-two patients and two normal individuals participated as subjects.

Each subject was orally administered I^{131} as sodium iodide. Activity was measured in the thyroid gland by external counting and in subsequently collected urine samples. This procedure was followed by routine iodine therapy and, in 19 cases, surgical removal of the thyroid.

These studies showed that the largest percentages of iodine uptake occur at low dosage levels, and that administration of clinical doses of iodine will cause a decrease in uptake of radioiodine administered later. This work was supported by private funding and a grant from Harvard University. The MIT Radioactivity Center was supported in part by the Office of Scientific Research and Development beginning in 1941–1942. This function was later assumed by the U.S. Atomic Energy Commission.

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OT-46. Early Studies of Iron Metabolism in Red Blood Cells Using Iron-55 and Iron-59

THE FIRST TRACER STUDIES using both iron-55 (Fe^{55}) and iron-59 (Fe^{59}) as tracers for red blood cells were conducted at the Radioactivity Center of the Massachusetts Institute of Technology (MIT) in collaboration with the Medical Clinic of the Peter Bent Brigham Hospital and the Department of Medicine, Harvard Medical School, during the period 1941 to 1946. The purpose of

these studies was to develop methods and demonstrate the usefulness of radioiron tracers for various physiological and clinical investigations on red blood-cell and iron metabolism in normal subjects, and hospital patients with various iron deficiency anemias.

These studies involved 48 human blood donors; 3 received intravenous injections of a mixture of Fe^{55} and Fe^{59} as ferric ammonium citrate: 6 received Fe^{59}, and 38 received Fe^{55}. Three of the latter also subsequently received injections of Fe^{59}. The calculated doses in these donors were estimated to have ranged from 0.05 to 0.2 roentgen per week. Residual Fe^{55} activity in blood was measured for as long as 4 years in some of the subjects. Red blood cells from these donors were later transfused into 160 subjects in amounts ranging from 50 to 250 milliliters. These subjects were all normal, young adult males with active daily routines. In addition, Fe^{55} or Fe^{59} was administered to 65 patients in the wards of the Peter Bent Brigham Hospital for evaluation of various blood anemia conditions.

Results of these studies showed that double-tracer radioiron studies were useful for clinical investigations, and that both normal subjects and hospital patients tolerated the radioiron injections or labeled blood transfusions without detrimental radiation effects. This work was done under a contract, recommended by the Committee on Medical Research, by the Office of Scientific Research and Development with the Massachusetts Institute of Technology, in collaboration with the Peter Bent Brigham Hospital.

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OT-47. Studies on Absorption of Insulin Labeled with Iodine-131 in Subjects

THIS STUDY WAS CONDUCTED in approximately 1943 as a joint effort of the New England Deaconess Hospital in Boston, the Massachusetts Institute of Technology (MIT), Wallace & Tiernan Products, Inc. of Belleville, New Jersey, and the Nutrition Laboratory of the Carnegie Institution of Washington in Boston. The purpose of this study was to investigate the rate of absorption of insulin. The study subjects comprised 5 normal subjects and 10 diabetic patients.

Each subject was administered 25 units of insulin-4–iodoazobenzene labeled with iodine-131 (I^{131}) by intravenous injection. The specific activity of the I^{131} and the total amount administered to each subject were not stated. The fraction of the administered activity in urine was measured 24 hours after injection. Blood-sugar levels were also determined in each subject.

Insulin absorption was found to occur at a similar rate in diabetics and normal subjects, although subjects with idiopathic (cause unknown) insulin resistance showed significant delay in insulin absorption due to prolonged residence of insulin in tissues. The MIT Radioactivity Center was supported in part by the Office of Scientific Research and Development beginning in 1941–1942. This function was later assumed by the U.S. Atomic Energy Commission.

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OT-48. Studies of the Effects of Thiouracil on the Thyroid Gland Using Iodine-131

STUDIES WERE CONDUCTED in approximately 1943 at the Massachusetts General Hospital, Boston, and at the Radioactivity Center of the Massachusetts Institute of Technology (MIT) to evaluate the effects of thiouracil treatment on thyroid glands among a group of 19 patients with Graves' disease, all of whom were scheduled for surgical excision of their thyroids (thyroidectomy). Thiouracil had been used to treat hypertension, but it was also known to decrease the basal metabolic rate. Of the 19 patients (14 females, ages 20 to 53 years; 5 males, ages 18 to 61 years), 4 had histories of previous treatment with stable iodine.

Thyroid biopsies were obtained from five of the patients prior to the start of thiouracil treatment. All patients were treated with thiouracil alone in

preparation for thyroidectomy. Thyroid uptake studies were conducted on 11 (9 females, 2 males) of the 19 patients. In these studies, iodine-131 (I^{131}) was administered to 10 of the 11 patients 24 to 48 hours before thyroidectomy. The 11th patient received tracer iodine 5 days before beginning thiouracil treatment, and again on days 1, 7, and 12 of the treatment. All urine excreted by the patients was collected and analyzed for I^{131} content, and the percent of the administered activity remaining in the excised thyroid gland tissue was determined after surgical removal.

Results of this study showed that I^{131} excretion decreased in patients receiving thiouracil prior to thyroidectomy, and that subjects' basal metabolic rate decreased, indicating that thiouracil blocked the synthesis of thyroid hormone. This work was supported by grants from the Josiah Macy, Jr. Foundation and the John and Mary R. Markle Foundation. The MIT Radioactivity Center was supported in part by the Office of Scientific Research and Development beginning in 1941–1942. This function was later assumed by the U.S. Atomic Energy Commission.

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OT-49. Studies on the Absorption of Ferrous and Ferric Iron Using Iron-59

A COLLABORATIVE STUDY involving researchers in the Department of Biochemistry and Medicine at Vanderbilt University Medical School in Tennessee, the University of Rochester School of Medicine in New York, the Louisiana State Medical School, and the Radioactivity Center of the Massachusetts Institute of Technology (MIT) was conducted between 1943 and 1944 to determine whether the ferrous or ferric salts of iron were better absorbed from the human gastrointestinal system. Nine patients (five white, four black) between the ages of 23 and 78 years, in various health conditions, were included in this study. The subjects included one male with an intestinal ulcer, one elderly woman with stomach cancer, and seven women with iron deficiency anemia or hemorrhagic iron deficiency.

Iron-59 (Fe^{59}) was administered with stable iron carrier as ferric ammonium citrate, ferric chloride, ferrous sulfate, or ferrous chloride. The amount of Fe^{59} tracer added to the iron was not described. Two different forms of Fe^{59}-tagged iron were administered to each patient at different times to compare absorption efficiencies and rates of iron utilization. Measurements were made on blood samples from the subjects to determine absorption efficiency as percent uptake of ingested iron.

This research showed that the ferrous iron salt was much more readily absorbed and subsequently utilized than the corresponding ferric salt or ferric ammonium citrate fed under the same conditions. This study preceded a larger study on nutrition in pregnancy at Vanderbilt University. This research was supported by a grant from the Nutrition Foundation. The MIT Radioactivity Center was supported in part by the Office of Scientific Research and Development beginning in 1941–1942. This function was later assumed by the U.S. Atomic Energy Commission.

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OT-50. Studies to Determine Red Blood-Cell Volumes in Human Subjects Using Iron-55 and Iron-59

STUDIES WERE CONDUCTED during 1943 to 1946 at the Radioactivity Center of the Massachusetts Institute of Technology (MIT) in collaboration with the Medical Clinic of Peter Bent Brigham Hospital, the Surgical Research Department of Beth Israel Hospital, and the Department of Medicine, Harvard Medical School, of methods using iron-55 (Fe^{55}) and iron-59 (Fe^{59}) to determine the circulating red blood-cell volume in humans. Blood volume estimates were important in the study of various blood anemias, heart diseases, thyroid disorders, renal diseases, and pregnancy. Donor blood was mixed with Fe^{55} and Fe^{59} and transfused into a patient to deter-

mine red cell volume. The method was developed using one hospital patient with emphysema and polycythemia vera and two patients with anemia, and was further tested using 40 normal male subjects who received Fe^{55}- and Fe^{59}-labeled blood and blood dye. Earlier methods using colored dyes provided estimates of total plasma volume, and red cell volumes had previously been determined using carbon monoxide.

Dual isotope studies using Fe^{55} and Fe^{59} proved to be advantageous over earlier methods. The dual-isotope method was also adapted to study the post-transfusion survival of red blood cells. This work was done under a contract, recommended by the Committee on Medical Research, by the Office of Scientific Research and Development with the Massachusetts Institute of Technology, in collaboration with the Peter Bent Brigham Hospital.

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OT-51. A Study of Red Blood-Cell Survival in Stored and Transfused Blood Using Iron-55

BETWEEN 1943 AND 1947, a study was conducted at Evans Memorial Hospital, Boston University School of Medicine, Harvard Medical School, and the Radioactivity Center of the Massachusetts Institute of Technology (MIT) to evaluate the effectiveness of certain selected preservatives in maintaining the viability of red cells in blood stored for transfusion and post-transfusion. The value of blood transfusion had been well established during World War II, but the survival times of red blood cells in blood stored in blood banks had not been determined. There was concern that nonviable red blood cells could be harmful to the recipient.

An accepted diagnostic technique of using iron labeled with tracer iron-55 (Fe^{55}) to monitor metabolism was used in determining red blood-cell survival times in 16 different preservative solutions, and in recipients' blood post-transfusion. Transfusion recipients were normal healthy adult male or female medical students, interns, or hospital technicians who volunteered for the study and were matched for compatible blood type.

To determine red blood-cell survival times, Fe^{55} as iron ammonium citrate was administered by intramuscular or intravenous injection to one of two selected healthy, young adult male donors. The second donor served as a source of blood for control studies. The first subject received two series of injections. In the first series, 4.68 milligrams of Fe^{55} were administered in 20 injections over 71 days. In the second series, 8 months later, 4.36 milligrams of Fe^{55} were administered by similar injections over 74 days. The amount of administered activity was not reported. Blood (400 to 500 milliliters) was then drawn from the donors into a preservative solution, and stored until use.

Transfusions of blood from the Fe^{55}-tagged donor were administered to 90 recipients; 88 recipients experienced no adverse effects of the transfusion, while 2 individuals developed mild fevers attributed to the dye solution used in the study. Each recipient received 100 milliliters of blood labeled with Fe^{55}. The specific activity of the donor's and recipient's whole blood, red cells, hemoglobin, and hemoglobin iron was determined by radioactivity measurements. The effectiveness of different techniques and preservation solutions to store whole blood was evaluated. The most effective preservative was an acid citrate-dextrose solution, and whole blood was found to have a satisfactory storage period of 21 days. This study was supported by the Office of Scientific Research and Development.

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Ross, J.F., C.A. Finch, W.C. Peacock, and M.E. Sammons. "The *In Vitro* Preservation and Post-transfusion Survival of Stored Blood." *The Journal of Clinical Investigation.* Vol. 26, 1947, pp. 687–703. ❑

OT-52. Studies on Red Blood-Cell Survival During Storage and After Transfusion Using Iron-55 and Iron-59 Tracers

DURING 1943 TO 1947, collaborative studies were conducted by researchers at the Peter Bent Brigham Hospital, Massachusetts General Hospital, and the Radioactivity Center of the Massachusetts Institute of Technology on methods for blood preservation and the post-transfusion survival of preserved red blood cells.

Donor red blood cells were tagged with iron-55 (Fe^{55}) by administering the activity intravenously and allowing the Fe^{55} to mix with donor blood. Pre-transfusion blood volumes in recipients were determined by transfusion of red cells tagged with iron-59 (Fe^{59}). The number of donors was not stated. All donors and most of the recipients were young male volunteers between 18 and 25 years of age with blood types from Groups O and A and free of disease or recent infections. Donors with Fe^{55}-labeled red blood cells were bled repeatedly, but not at less than 8-week intervals. Collected blood was cross-matched with recipient blood to ensure compatibility. Some of the recipients were hospital patients with various anemias, gastro-intestinal lesions, or cancer.

Each recipient received only one transfusion of labeled blood. Fifty-two subjects received transfusions of whole-blood tagged with Fe^{59} tracer and 81 subjects received transfusions of packed or resuspended red blood cells tagged with a tracer dose of Fe^{59}. Samples of blood from donors and recipients were later analyzed for Fe^{55} or Fe^{59} activity. The percent of cells surviving in stored blood and in recipient blood was determined at different times after labeling.

Experiments were conducted to determine the best of 11 preservative solutions and 12 electrolyte solutions for storing whole blood for maximum red-cell survival time. Methods were developed for storing whole blood for up to 21 days. This study showed that most of the nonviable transfused red cells were cleared from recipient blood within 2 hours of transfusion, and iron from nonviable red cells was reutilized by the body. This study was supported by the Office of Scientific Research and Development.

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OT-53. Effect of Phytate on the Absorption of Iron-59 and Iron-55

A STUDY WAS CONDUCTED in 1946 by the Departments of Food Technology and Physics of the Massachusetts Institute of Technology (MIT) and by the Fernald State School in Waverly, Massachusetts.

Fifteen boys, ages 12 to 17 years, living at the Fernald School, with I.Q.s ranging between 65 and 70, were fed breakfasts containing either iron-59 (Fe^{59}) or iron-55 (Fe^{55}) in the milk or water. The amount of radioiron received by each subject differed according to body weight. No food was eaten before or until 5 hours after the test meals, each of which contained differing amounts of phytates, a natural ingredient in rolled oats.

The experiment was done because there was concern that certain diets rich in cereal might affect iron absorption and thus result in malnutrition, especially in developing countries where iron-rich foods are not plentiful. These concerns were based upon earlier studies which showed that bread, which also contains phytates, could inhibit the uptake of dietary iron.

The general conclusion of this study was that iron supplements to the diet should not be given with meals. In addition, children living in institutions could continue to eat oatmeal without concern for negative effects, so far as iron uptake was concerned. In 1994, the Massachusetts Task Force investigation estimated that the absorbed dose to each of the participants in the study was approximately 300 millirems. The 1946 research was supported by a grant from

the Quaker Oats Company. The MIT Radioactivity Center was supported in part by the Office of Scientific Research and Development beginning in 1941–1942. This function was later assumed by the U.S. Atomic Energy Commission.

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The Task Force on Human Subject Research. "A Report on the Use of Radioactive Materials in Human Subject Research that Involved Residents of State-Operated Facilitates within the Commonwealth of Massachusetts from 1943 through 1973." April 1994. ❑

OT-54. Measurements of Radon-222 Absorption Through Skin

A JOINT STUDY WAS CONDUCTED in approximately 1946 by the New York Medical College (Metropolitan Hospital) and the Radioactivity Center of the Massachusetts Institute of Technology (MIT) to determine the scientific basis, if any, for contemporary claims of therapeutic effects on deep structures from topical application of ointment containing radon-222 (Rn^{222}).

The amounts of Rn^{222} in expired air were used as a measure of absorption of Rn^{222} into the bloodstream from the ointment applied to the body surface. The ointment, containing 49 micrograms of Rn^{222} per gram of lanolin, was applied in thicknesses varying between 2 and 3 millimeters to: a large varicose ulcer on the leg of one subject; intact skin on the legs of two subjects with other chronic diseases; and one normal subject. The applications were covered immediately with oil silk or glass and then sealed with layered adhesive.

In the first experiment, samples of exhaled air were taken after 20, 160, and 270 minutes and analyzed for Rn^{222} content. This study showed that 2.4 percent of radon applied to the leg ulcer, and about 0.08 to 0.13 percent of radon in the ointment applied to intact skin were exhaled after 270 minutes.

In a second experiment, the subject with the leg ulcer and the normal subject were monitored at intervals over a period of 23 hours following the application. They exhaled 10 and 4.5 percent, respectively, of the total Rn^{222} in the ointment application. This study demonstrated that Rn^{222} was absorbed into the blood from topically applied ointment and that absorption was greater through nonintact skin than through intact skin. The results indicated a potential for radiation effects to be induced in structures deeper than would have been predicted had Rn^{222} remained at the application site. The study did not, however, resolve the question of whether the amount of Rn^{222} made available to these structures by absorption and transportation was sufficient to induce effects of therapeutic value. The MIT Radioactivity Center was supported in part by the Office of Scientific Research and Development beginning in 1941–1942. This function was later assumed by the U.S. Atomic Energy Commission.

References

Lange, K., and R.D. Evans. "Absorption of Radon through the Skin and Its Exhalation through the Lungs." *Radiology*. Vol. 48, No. 5, 1947, pp. 514–516. ❑

OT-55. Studies of the Urinary Excretion of Iodine Using Iodine-131

RESEARCHERS IN THE THYROID CLINIC of the Massachusetts General Hospital and the Radioactivity Center of the Massachusetts Institute of Technology (MIT) collaborated on a study in approximately 1946 to 1948 of the rates of iodine excretion rates by subjects with normal thyroids and by hospital patients with thyroid disorders.

Three groups of subjects were involved, including 25 hospital patients with untreated thyrotoxicosis, 6 patients with myxedema, and 15 normal-thyroid patients who were hospitalized for illnesses not related to thyroid function.

Each subject was given 100 of microcuries iodine-131 (I^{131}) with 100 micrograms stable sodium iodide carrier orally, usually in the morning before breakfast. Urine samples were then collected from each subject either as 6-hour,

12-hour, or 24-hour specimens up to 48 hours after iodine ingestion. The amount of I^{131} in each urine specimen was determined and results for each group were compared.

The results of this study showed that the urinary excretion of iodine in the group of thyrotoxic patients was considerably less than in the group with normal thyroid function. However, patients with myxedema generally excreted more iodine than subjects with normal thyroid function. The sponsor of this research was not stated, although the author was a Rockefeller fellow during the study period. Funding for the MIT Radioactivity Center was provided by the U.S. Atomic Energy Commission.

Reference

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OT-56. Study of the Uptake of Iodine in Fetal Thyroids Using Iodine-131

A COLLABORATIVE STUDY was conducted in approximately 1947 by researchers at the Massachusetts General Hospital, the Boston Lying-In Hospital, and the Radioactivity Center of the Massachusetts Institute of Technology (MIT) to determine the age at which the human fetal thyroid begins to function and accumulate iodine.

Nine pregnant women with organic disease and scheduled for therapeutic abortions were injected with tracer amounts of iodine-131, 24 to 48 hours before an operation to remove the fetus. The intact fetus was obtained and measured for approximate age, fixed in formalin, and sectioned for histological analysis. The amount of administered activity was not reported. The radioactivity in the fetal thyroids was determined by direct counting.

Iodine-131 was not found in thyroids of fetuses ranging in age from 7 to 12 weeks, but amounts increasing with age were found in fetuses ranging in age from 14 to 32 weeks.

These studies showed that radioiodine could be therapeutically administered until the 4th month of pregnancy without concern for fetal uptake. Funding for the MIT Radioactivity Center was provided by the U.S. Atomic Energy Commission.

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Chapman, E.M., G.W. Corner, D. Robinson, and R.D. Evans. "The Collection of Radioactive Iodine by the Human Fetal Thyroid." *The Journal of Clinical Endocrinology*. Vol. 8, No. 9, 1948, pp. 717–720. ❑

OT-57. Red Blood-Cell Volumes and Hematocrit in Normal Pregnancy Using Iron-55

A COLLABORATIVE STUDY was conducted in approximately 1948 by researchers in the Department of Obstetrics and Gynecology at the Harvard Medical School, the Boston Lying-In Hospital, and the Radioactivity Center of the Massachusetts Institute of Technology (MIT) to determine the circulating red blood-cell mass in women during pregnancy and after childbirth. The subjects were 12 normal patients at the Boston Lying-In Hospital who were pregnant and near full-term.

Six to 12 separate studies were made on each patient to determine red cell volume, plasma volume, and extracellular space. Red cell volumes were determined by tagging blood donated by healthy male donors with iron-55 (Fe^{55}), administering the tagged blood to the female subjects, and obtaining 15 milliliters of blood from the subjects at various times during and after pregnancy. Blood samples were then counted for Fe^{55} content. The amount of Fe^{55} administered to each woman as Fe^{55}-labeled blood ranged from 2 to 12 microcuries.

This study showed that red blood-cell volume increased by 40 percent during normal pregnancy and continued to increase for 1 week after childbirth. Red blood-cell volumes returned to normal 60 days after delivery. Blood hematocrit decreased 8 to 15 percent during pregnancy. This study was supported by the Charles H. Hood Foundation, the Office of Naval Research, the National Institutes of Health, and the U.S. Atomic Energy Commission.

References

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perium." *American Journal of Obstetrics and Gynecology.* Vol. 57, 1949, p. 471–481.

Caton, W.L., C.C. Roby, D.E. Reid, R. Caswell, C.J. Maletskos, R.G. Fluharty, and J.G. Gibson II. "The Circulating Red Cell Volume and Body Hematocrit in Normal Pregnancy and the Puerperium." *American Journal of Obstetrics and Gynecology.* Vol. 61, No. 6, 1951, pp. 1,207–1,217. ❑

OT-58. Studies of Iron Storage and Utilization Using Iron-55 and Iron-59

STUDIES WERE CONDUCTED jointly by investigators at the Harvard Medical School and the Radioactivity Center of the Massachusetts Institute of Technology (MIT), in collaboration with Peter Bent Brigham Hospital during 1948 to 1949 on the dynamic relationship between stored iron and circulating iron in normal subjects and in patients with a variety of hematologic disorders.

The total number of subjects in these studies was 61; these included 9 normal male volunteers between the ages of 24 and 30 years, 6 patients with acute or chronic blood loss representing various degrees of iron-deficiency anemia, 3 subjects with other diseases not related to iron metabolism, and 49 subjects with either hemochromatosis; refractory anemia; uremia and other anemias; infection; malaria; cancer liver disease; endocrinological disease; and polycythemia vera.

Iron-55 (Fe^{55}) and iron-59 (Fe^{59}) from the MIT cyclotron were prepared as ferric chloride, ferric ammonium citrate, or ferrous ammonium sulfate with stable iron carrier. About 0.5 microcurie of Fe^{55} or Fe^{59} was administered to the subjects by intravenous injection. The radioactive iron then entered the hemoglobin cycle and red blood cells labeled with Fe^{55} or Fe^{59} began to appear in the circulation, reaching a plateau in 2 to 3 weeks. Samples of venous blood were drawn from the subjects at various time points after injection and counted for Fe^{55} or Fe^{59} activity to determine the utilization of radioiron over time, the labeled red cell population, and other blood-cell parameters.

This study showed that changes in iron utilization were due to alterations in body storage of iron and were affected by various disease conditions. This work was supported by a grant from the U.S. Public Health Service. Funding for the MIT Radioactivity Center was provided by the U.S. Atomic Energy Commission.

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OT-59. Study of Iron Turnover by Red Blood Cells Using Iron-55 and Iron-59

A STUDY WAS CONDUCTED at the Harvard Medical School and the Radioactivity Center of the Massachusetts Institute of Technology (MIT) during 1948 to 1949 on the disappearance of iron from red blood cells in circulation. Blood from donors was labeled with either iron-55 (Fe^{55}) or iron-59 (Fe^{59}) from the MIT cyclotron and was readministered to subjects. Blood from these subjects was later drawn, characterized, and readministered to other subjects to determine the lifetimes of the labeled red blood cells.

Recipients of the tagged donor blood included hospital patients with various blood disorders. These patients included one 6-year-old girl with aplastic anemia, a 4-year-old boy and a 4-year-old girl with Cooley's anemia, and a patient with hemochromatosis. These were subjects who required frequent blood transfusions.

In another series of observations, three normal male subjects were given Fe^{55} intravenously and 200 to 400 milligrams of stable iron as ferrous sulfate by mouth after meals. Blood was then drawn from the subjects and counted for Fe^{55} or Fe^{59} activity to determine the life span of red blood cells and the reutilization of iron.

This study showed that the reutilization of radioiron from broken-down red cells is blocked by the presence of enlarged iron stores and by bone marrow dysfunction in subjects. The life span of red blood cells was also determined. The iron turnover was found to be about 1 percent per day in man. This work was supported by a grant from the National Institutes of Health, the Office of Naval Research, the Charles P. Hood Foundation, and the U.S. Atomic Energy Commission.

References

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OT-60. Studies of the Metabolism of Maternal Iron in Newborn Infants Using Iron-55

A COLLABORATIVE STUDY was conducted during 1948 to 1950, by researchers in the Department of Pediatrics of Harvard Medical School, the Boston Lying-In Hospital, Children's Hospital, Peter Bent Brigham Hospital, Boston and the Radioactivity Center of the Massachusetts Institute of Technology. The purpose of this study was to determine the persistence and utilization of iron from maternal blood in newborn infants.

The study involved 11 females who had participated while pregnant in a previous blood study using iron-55 (Fe^{55}) (Caton et al., 1949, 1951), and the 16 infants born to them. The total activity of Fe^{55} administered as tagged red blood cells to each pregnant woman ranged from about 2 to 12 microcuries. The estimated doses to their infants were estimated to be 30 to 354 millirads.

Seven to 15 milliliters of maternal blood were obtained at time of delivery, and similar amounts of the infants' blood were obtained at delivery and at varying ages thereafter for up to 32 months. Each blood sample was analyzed for Fe^{55} cell count, total iron, and hemoglobin.

This study showed that all infant hemoglobin iron was maternal in origin and that dietary iron did not contribute to infant hemoglobin until 3 to 4 months after birth. At 1 year, maternal iron constituted 70 percent of total hemoglobin iron. This study was supported by the American Cancer Society, the Office of Naval Research, the National Institutes of Health, and the U.S. Atomic Energy Commission.

References

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OT-61. Thyroid Function Studies Using Iodine-131

DURING THE EARLY 1950s, researchers at the Fernald State School, Waverly, Massachusetts; the Harvard Medical School; the Tufts Medical School; and the Massachusetts Institute of Technology conducted studies on thyroid function in patients diagnosed with myotonia dystrophia (a genetic neuro-endocrine disorder associated with muscular dystrophy) using iodine-131 (I^{131}).

Six male patients were orally administered 54 microcuries of I^{131}. Activity was measured by external counting in urine samples during the next 24 hours, and in the thyroid over the next 8 days.

The results of these studies showed that although the thyroid gland was operating at a lower than normal capacity in the patients, iodine uptake by their thyroids, iodine excretion rates, and protein-bound iodine values appeared to be normal. This work was supported by the U.S. Atomic Energy Commission.

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OT-62. Interlaboratory Comparison of the Reliability of the Measurement of Cesium-137 in Humans

AN INTERCOMPARISON STUDY was conducted by the U.S. Atomic Energy Commission (AEC) during the period 1962 to 1966 to evaluate and compare the reliability of direct *in vivo* counting techniques for measurement of cesium-137 (Cs^{137}) in humans at AEC-affiliated research facilities. The purpose was to improve and assure comparability between the facilities' Cs^{137} measurements.

This intercomparison study was coordinated by an *ad hoc* committee appointed by the AEC Division of Biology and Medicine, with two of the committee members serving as volunteer subjects. Each was of medium body build. One subject was administered 0.2 to 0.3 microcurie of Cs^{137} by intravenous injection. The second subject was not given Cs^{137} or any other radionuclide; he served as the "normal" subject, representing an average member of the general population whose only exposure to Cs^{137} was from weapons-testing fallout directly or through the environment. The levels of radioactivity from Cs^{137} and potassium-40 (K^{40}, a natural component of human tissue) in the two subjects were measured using whole-body counters at 16 AEC or private laboratories nationwide. The results at individual laboratories were evaluated against national standards and compared across the laboratories.

Physiological rather than physical variables appeared to account for observed interlaboratory measurement differences. Study results indicated that the laboratories were capable of reliable measurements of Cs^{137} and K^{40} in humans and therefore were capable of accurately measuring changes in the levels of Cs^{137} to which their area populations were exposed as the result of nuclear weapons testing. This work was supported by the U.S. Atomic Energy Commission.

References

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Maletskos, C.J., P.N. Dean, S.A. Lough, and C.E. Miller. "Intercomparison of the Reliability of Body Cesium-137 Measurements on Human Beings." Washington, D.C.: U.S. Atomic Energy Commission, Division of Biology and Medicine, TID-23740, June 8, 1967. ❑

OT-63. Metabolic and Gastrointestinal Absorption Studies with Short-Lived Decay Products of Radium and Thorium

BETWEEN 1961 AND 1965, researchers at the Massachusetts Institute of Technology (MIT) conducted studies on the metabolism and gastrointestinal absorption of thorium and radium in normal human beings. The purpose of the studies was to determine the health impact of thorium-228 (Th^{228}), which was present in radium paint used and ingested by dial painters during the 1920s.

Seven females and 13 males ranging in age from 63 to 83 years, participated as subjects. During the study, subjects were housed at either the MIT Infirmary or the Sancta Maria Hospital adjacent to MIT. Six of the subjects received intravenous injections of radium-224 (Ra^{224}), while another six received intravenous injections of thorium-234 (Th^{234}). One received Ra^{224} orally, another received Th^{234} orally, and the remaining six received an oral mixture of Ra^{224} and Th^{234}. The purpose of injecting known amounts of Ra^{224} and Th^{234} was to calibrate the various measurements. Advantage was taken of the calibration period to provide information on the short-term metabolism of radium and thorium, nearly unknown at the time.

The administration of Ra^{224} for the calibration and absorption measurements ranged from 0.24 to 3.13 microcuries; that of Th^{234}, from 1.2 to 247 microcuries. The oral administration of these isotopes was in the form of simulated radium paint. Activity levels were subsequently measured in blood, urine, and feces samples. Further levels were measured in the breath and in various parts and the entire body.

The results showed that there was little Th^{228} absorption and therefore, the internal radiation dose from the initial Th^{228} was less than 5 percent of that of its parent Ra^{228}, and considerably less than the combined internal dose from Ra^{226} and Ra^{228}. Consequently, the dose from Th^{228}

could be ignored and the MIT subject group could remain intact for further dose-response and epidemiological studies. This work was supported by the U.S. Atomic Energy Commission. (This experiment was referenced in the Markey report.)

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OT-64. Comparison of Iodine-123 and Iodine-131 for Thyroid Uptake Studies

IN 1973, A STUDY was conducted at the Mayo Clinic, Rochester, Minnesota, to compare the suitability of iodine-123 (I^{123}) for measuring iodine uptake by the thyroid with that of iodine-131 (I^{131}). Forty-two patients were studied. The patients displayed a wide range of thyroid disorders, but were generally free from gastrointestinal and kidney disorders, and had been referred for an iodine uptake test.

Thirty-two patients ingested a gelatin capsule containing 100 microcuries of I^{123} and a capsule containing 2 to 5 microcuries of I^{131}. Six subjects ingested 5 microcuries of I^{131} in aqueous solution. Four other patients ingested a gelatin capsule containing 10 to 13 microcuries of I^{131}. The iodine activity in each subject was determined after 6 and 24 hours. In a few patients, uptakes were also measured at one or more additional times, such as 0.5, 1, 2, or 4 hours. Counts were obtained over the thighs of subjects to provide background information. The gel filler in one commercially available type of capsule inhibited absorption and uptake of the I^{131}; otherwise, the I^{123} and I^{131} were taken up by the thyroid at identical rates. This research was supported by the U.S. Atomic Energy Commission.

References

Robertson, J.S., M. Verhasselt, and H.W. Wahner. "The Use of Iodine-123 for Thyroid Uptake Measurement and Depress of the I^{131} Thyroid Uptake by Incomplete Dissolution of Capsule Filler." *Journal of Nuclear Medicine*. Vol. 15, No. 9, 1974, pp. 770–774. ❑

OT-65. Iodine-131 Localization

FROM APPROXIMATELY 1947 TO 1951, extensive clinical and postmortem studies were conducted on nine patients at the Memorial Center for Cancer and Allied Disease in New York to learn more about the localization and effects of iodine-131 (I^{131}). The subjects of this study were six women and three men between 37 and 80 years of age and near death with various diseases. Seven subjects had thyroid cancer with metastases. Of these, five had histories of prior therapeutic administrations of I^{131}. One subject had undergone a partial thyroidectomy for hyperthyroidism 30 years earlier. Another subject had a goiter.

In all cases, carrier-free I^{131} was administered in amounts varying from 1.9 to 250 millicuries in anticipation of postmortem studies. Two of the subjects received the I^{131} by injection; the remainder of the administrations were oral. The interval between the administration of the I^{131} for the purpose of postmortem studies and death, ranged from 8 hours to 35 days. Tissue samples were taken at autopsy and analyzed.

Study findings confirmed earlier reports that I^{131} localizes in the thyroid and in thyroid cancer metastases to levels that vary with histologic type. No significant localization was observed in other organs or tissues examined. The study showed that I^{131} localized exclusively in the thyroid and that no effects directly attributable to I^{131} were induced in other tissues. Because of the shot duration of the study, no conclusions were made on the potential long-term effect of I^{131}. This work was supported jointly by the Office of Naval Research and the U.S. Atomic Energy Commission.

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OT-66. Tolerance to Whole-Body Irradiation of Patients with Advanced Cancer

FROM 1942 TO 1944, researchers at Memorial Hospital in New York City (now known as the Memorial Sloan-Kettering Cancer Center), conducted studies to determine the clinical and hematological effects of prolonged daily exposure to whole-body high-voltage x-ray irradiation. Seven male and one female advanced cancer patients, ranging in age from 25 to 64 years, were selected as subjects. Each was exposed to filtered 180-kilovolt x-rays with exposure rates from 0.85 to 1.65 roentgens per hour for daily exposures of 10 to 15 roentgens. Six subjects received total exposures of 300 roentgens over 20 or 30 days. Treatment was discontinued for the other two subjects at 150 and 161 roentgens due to their deteriorating health. Three of the six subjects who received the total projected dose were followed for 7 to 19 months after exposure. The other three were followed for only 1 to 4 months because of declining health and death.

The results of these studies did not show any alterations in blood count or any stimulation of tumor growth that could be ascribed to radiation exposure, indicating that a whole-body exposure of 300 roentgens could be well-tolerated by healthy individuals. This work was supported by the Manhattan Engineer District.

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OT-67. Modification of the Distribution and Excretion of Lanthanum-140 by Chelating Agents

IN 1952, SCIENTISTS at Montefiore Hospital in New York conducted a study to investigate why so little lanthanum as the lanthanum-140 (La^{140})–complex with ethylenediaminetetraacetic acid (EDTA) was directly excreted in urine through the kidneys, compared to the urinary excretion of other metal-EDTA complexes. An unreported number of hospital patients participated as subjects of this study.

Each subject was administered 200 microcuries of La^{140} complexed with the chelating agent EDTA. The subject was catheterized to facilitate urine collection for La^{140} analysis. Urine and blood were collected at frequent intervals to determine the clearance and excretion of La^{140}-EDTA from the body. Calcium-EDTA was then administered to determine its enhancing effect on La^{140} clearance. Lanthanum-140–chloride was then administered (to the same or another subject) for comparison, and was then followed with calcium-EDTA.

This work showed that lanthanum was only slightly cleared (10 to 15 percent) using EDTA, due to exchange for calcium. The fact that the effectiveness of lanthanum-removal by the chelating agent EDTA decreases with time suggested its use as an investigative tool. This study was supported by the U.S. Atomic Energy Commission.

References

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OT-68. Metabolism Studies Using Strontium-85 and Calcium-45

DURING THE MID-1950s, researchers at Columbia University and Montefiore Hospital in New York City conducted metabolism studies using strontium-85 (Sr^{85}) and calcium-45 (Ca^{45}). The purpose of these studies was to obtain data that might be relevant to the metabolism of strontium-90, a product of nuclear fission.

Twelve hospital patients ranging in age from 49 to 72 years, including 10 terminally ill cancer patients, participated as subjects. The cancer patients received simultaneous intravenous injections of 1.5 microcuries of Sr^{85} and 0.4 microcurie of Ca^{45} per kilogram of body weight. The other two patients received only one injection of either Sr^{85} or Ca^{45}.

These studies showed that the isotopes were evenly divided between bone and soft tissue shortly after administration, but after 4 months, 99 percent of the Sr^{85} and Ca^{45} remaining in the body resided in bone. This work was supported by the U.S. Atomic Energy Commission. (This experiment was referenced in the Markey report.)

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OT-69. Strontium Metabolism Studies Using Strontium-85

DURING THE MID-1950s, researchers at Montefiore Hospital in New York City conducted studies on the human uptake, distribution, and excretion of strontium using strontium-85 (Sr^{85}). These studies arose from concerns about human hazards from strontium-90, a nuclear fission product.

Four hospital patients participated as subjects. Each subject received two intravenous injections of 0.1 to 0.4 microcurie of Sr^{85} per kilogram of body weight: one injection with stable calcium, and one without. Urine, feces, and plasma samples were analyzed over the next 48 hours for Sr^{85}. One subject underwent a second series of tests in which the injections were administered over a 5-hour period.

The results of these studies showed that strontium levels in plasma declined rapidly, that the kidneys are the main excretion route, that rate of excretion depends upon bone metabolism rate, and that simultaneous administration of calcium enhances strontium excretion. This work was supported by the U.S. Atomic Energy Commission.

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OT-70. Studies on EDTA and Strontium Excretion Using Strontium-85

DURING THE MID-1950s, researchers at Montefiore Hospital in New York City conducted studies on the effect of ethylenediaminetetraacetic acid (EDTA) on the excretion of strontium in humans using strontium-85 (Sr^{85}). One female and two male cancer patients ranging in age from 40 to 70 years participated as subjects.

Each subject received two intravenous injections of 0.1 to 0.4 microcurie of Sr^{85} per kilogram of body weight, accompanied by several intravenous injections of EDTA over several days. Strontium-85 activity was measured in plasma, urine, and fecal samples collected over the course of the study.

The results of these studies showed an inhibition of urinary excretion of Sr^{85} when EDTA was administered, followed by an excess excretion when the EDTA was discontinued. This work was supported by the U.S. Atomic Energy Commission.

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OT-71. Comparative Metabolism Studies Using Strontium-85 and Calcium-45

DURING THE MID-1950s, researchers at Montefiore Hospital in New York City conducted studies on the metabolism of strontium and calcium using strontium-85 (Sr^{85}) and calcium-45 (Ca^{45}). Six patients ranging in age from 54 to 72 years participated as subjects.

Each subject was orally administered 0.1 to 0.4 microcurie of Sr^{85} per kilogram of body weight. Activity was counted in blood, urine, and stool samples for 12 to 40 days. Two of these subjects received an oral administration of Ca^{45} prior to the Sr^{85} and activity was measured in a similar manner. At the completion of the oral administration studies, four of the subjects were intravenously administered another 0.1 to 0.4 microcurie of Sr^{85} per kilogram of body weight and activity was measured in plasma, urine, and stool samples for 14 to 16 days.

These studies showed that strontium was poorly absorbed in the gastrointestinal tract, that the main route of strontium excretion was through the kidneys to urine regardless of the means of administration, and that significantly less strontium than calcium was retained in the body. This work was supported by the U.S. Atomic Energy Commission.

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OT-72. Efforts to Increase the Rate of Strontium-85 Excretion

A STUDY WAS CONDUCTED in 1957 at the Montefiore Hospital in New York City to determine whether the natural excretion of radiostrontium by man could be accelerated by administering calcium and ammonium chloride. This study was conducted using three hospital patients: a 67-year-old female with breast cancer, a 74-year-old male with previous cancer of the larynx but no evidence of remaining disease and otherwise healthy, and a 58-year-old male with severe osteoarthritis of both hips.

Four separate tests with radiostrontium were conducted on each of the patients while they were maintained on a low-calcium diet. Strontium-85 (Sr^{85}) as strontium chloride was administered intravenously to each of the patients at the start of each of the four experiments. The amounts of Sr^{85} administered ranged from 0.1 to 0.4 microcurie per kilogram body weight of the patient for each injection. After injection, the patients were given calcium gluconate, ammonium chloride, or both to determine whether these agents had any effect on the skeletal retention of strontium.

The results of this study showed that urinary calcium and radiostrontium excretion increased markedly when calcium gluconate was administered intravenously or ammonium chloride was given orally to the patients. This study was supported by the National Cancer Institute and the U.S. Atomic Energy Commission.

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OT-73. Decontamination of Skin Contaminated with Carbon-14, Fission Products, Tantalum-182, and Alpha Emitters

DURING THE EARLY 1950s, researchers at Foster D. Snell, Inc., conducted studies for the U.S. Army on the effectiveness of various detergents and chemical agents to remove radioactive contamination from human skin surfaces and hair. The subjects for these studies ranged in age from 18 to 66 years.

The arms and hands of study participants were exposed to various media containing carbon-14, unspecified mixed-aged fission products in soil or synthetic soil, neutron-activated soil, samples of soil from the Nevada Test Site containing fallout, or liquid solutions of mixed-aged fission products or alpha-emitting radionuclides.

One of the studies involved placing a drop of liquid containing mixed fission products on subjects' forearms, allowing the contamination to dry, and then washing the skin with any of a long list of cleaning agents or chemical solutions. The radioactivity of the contaminated skin area was

measured before and after washing to determine decontamination effectiveness. Problems were experienced with test soils because the contamination often failed to adhere to skin.

A second study involved placing a drop of liquid containing zinc bromide, a radiological warfare agent containing a radioactive isotope of tantalum (presumably tantalum-182) on the subjects' palms, after which various decontamination agents were tested.

Another study conducted at Mound Laboratory in Miamisburg, Ohio, involved placing several drops of a solution containing unspecified alpha emitters (presumably polonium-210 and decay products) on the palms of four subjects, allowing the solution to dry, and then testing various detergents as decontamination agents. Measurements of radioactivity were made before and after washing to determine decontamination effectiveness.

These studies pointed to certain commercial products and chemical formulations that could be used for decontaminating human skin or hair. This research was sponsored by the U.S. Atomic Energy Commission.

References

Foster D. Snell, Inc. *Removal of Radioactive Contaminants from Human Skin.* Final Report, NP-4935, Department of Army, June 15, 1953. Technical Information Service, U.S. Atomic Energy Commission, Oak Ridge, Tennessee. ❑

OT-74. Effects of Radium-224 Applied to Skin

EXPERIMENTS WERE CONDUCTED in 1953 at the New York University Hospital and Medical School to evaluate the relative biological effectiveness of the alpha and beta-gamma rays from radium-224 (Ra^{224}, earlier known as "Thorium X") plaques applied directly to skin. Two types of plaques were studied: a very thin plaque that allowed alpha and beta/gamma radiation to irradiate skin, and a mica-windowed plaque that trapped alpha particles and only irradiated the skin with beta and gamma radiation.

Sealed plaques containing Ra^{224} were applied to arm skin surface of subjects selected from among patients being treated at the University Hospital. The plaques were taped to normal skin areas and allowed to remain in place for 48 hours, after which the skin was examined for visible biological effects.

During the study, 140 plaques were applied to 96 subjects. Seventy-five were alpha plaques and 65 were beta-gamma plaques, usually applied in matched pairs on a given subject. Sixty of the plaques leaked in place and the skin observations in these instances were not used to draw scientific conclusions. Usable observations were obtained from 58 subjects. The alpha plaques produced erythema in about 80 percent of the cases, whereas the beta/gamma plaques produced a discernible erythema in 64 percent of cases. This study was supported by the U.S. Atomic Energy Commission.

References

Witten, V.H., E.W. Brauer, V. Holmstrom, and R. Loevinger. "Studies of Thorium X Applied to Human Skin." *The Journal of Investigative Dermatology.* Vol. 21, No. 4, October 1953, pp. 249–257. ❑

OT-75. Effects of Strontium-90 and Yttrium-90 on Skin

EXPERIMENTS WERE CONDUCTED in 1954 at the New York University Hospital and Medical School on the biological effects of a pure beta emitter, strontium-90 (Sr^{90}), and its decay product, yttrium-90 (Y^{90}) when applied directly to skin. The purpose of these experiments was to investigate the dermatologic effects of Sr^{90}/Y^{90} beta particles, and to see whether they offered any practical medical advantages over phosphorus-32 (P^{32}).

Two Sr^{90} applicators of differing dose-rate were constructed using about 10 millicuries of Sr^{90} each on a ceramic disc, which was then covered by a thin (2 millimeters) stainless steel foil soft-soldered to the disc. One applicator was placed 9.5 millimeters from skin and the other was placed 3.2 millimeters from skin. The foil was sufficiently thin to allow the beta particles from Sr^{90} and Y^{90} to penetrate.

Nineteen subjects were identified among patients (mostly outpatients) attending the Hospital's Skin and Cancer Unit and the Radiotherapy Department. Each subject participated in at least one exposure series (four participated in two series) for a total of 23 series. A total of 195 dif-

ferent sites on normal skin of the subjects upper thighs and lateral buttocks were irradiated using the Sr^{90} application. Absorbed doses were estimated to range from about 85 to 1,540 rads to the local skin areas, although actual values were highly uncertain. The subjects were then observed at various times after irradiation for erythema.

Results showed that erythema occurred as early as 1 day following radiation, followed by pigmentation, and persisted for as long as 102 days. Pigmentation lasted as long as 504 days after irradiation. Other effects observed were papulation (formation of pimple-like skin lumps), induration (hardened portions of skin), and desquamation (shedding of scaly skin) at doses above 684 rads to skin surface. This study was supported by the U.S. Atomic Energy Commission.

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Witten, V.H., E.W. Brauer, V. Holstrom, and R. Loevinger. "Erythema Effects of a Pure Beta Emitter (Strontium-90) on Human Skin." *The Journal of Investigative Dermatology.* Vol. 23, No. 4, October 1954, pp. 271–285. ❑

OT-76. Topical Absorption Studies Using Radium-224

DURING THE MID-1950s, researchers at the New York University Hospital and Medical School conducted studies on the effect of an electrical current on the absorption of radium-224 (Ra^{224}) through the skin. Three volunteers participated as subjects. A 1.5-inch square of blotting paper saturated with 12 microcuries of Ra^{224} (also known as "thorium X") was applied to each forearm. One area was subjected to a small electrical current for 20 minutes. After the patches were removed, tissue was excised for analysis.

The results of these studies showed that introduction of an electrical current increased the level of absorption and the biological effect of topically applied Ra^{224}. The radiation dose to the skin was sufficient to produce erythema (reddening) and pigmentation. These effects were not seen in the absence of an applied electric current. It was believed that this technique could be used clinically in the treatment of various dermatologic lesions and skin cancers. This work was supported by the U.S. Atomic Energy Commission.

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OT-77. Effects of Polonium-210 on Skin

A SERIES OF EXPERIMENTS was conducted in 1956 to 1957 at the New York University Hospital and Medical School on the biological effects of a pure alpha emitter, polonium-210 (Po^{210}), applied directly to skin. Special polonium plaques were prepared by plating polonium on one side of a nickel disc and electroplating one micrometer of gold over the surface to seal it in place and yet allow alpha particles to freely pass through. The purpose of this study was to investigate further the early biological effects, such as reddening of the skin (erythema), of alpha particle radiation on human skin.

In the first experiment, four Po^{210} plaques of various intensities were each applied to the arm skin of five healthy white males between the ages of 23 and 39 years. Skin surface doses at points of contact were estimated to be 23, 55, 110, and 660 kilorads, respectively, to the layer of skin cells immediately beneath the plaques. Irradiated sites were examined at several times after removal of the plaques for appearance and intensity of skin erythemas.

A second experiment was conducted to determine the smallest dose of Po^{210} alpha radiation that produced a discernible erythema. Seven plaques producing skin surface doses of 12.5, 25, 50, 75, 100, 150, and 200 kilorads, respectively, were applied to arm skin of the same five subjects.

In a third experiment on the same subjects, the time to appearance of erythema was determined as a function of total skin dose.

A fourth experiment was conducted to determine whether the 5.3-MeV (million electron volt) Po^{210} alpha particles were capable of penetrating skin layers to the basement membrane and small blood vessels.

This study showed that a threshold dose for erythema was at 20 kilorads alpha radiation, that erythema appeared 2 to 8 hours after irradiation, that larger doses produced erythema in shorter times, and that erythema was transient. This study was supported by the U.S. Atomic Energy Commission.

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Witten, V.H., W.S. Wood, and R. Loevinger. "The Erythema Effects of a Polonium Plaque (An Alpha Emitter) on Human Skin." *The Journal of Investigative Dermatology*. Vol. 28, No. 3, March 1957, pp. 199–210. ❑

OT-78. Studies of the Transmission of Radioiodine to Infants Through Maternal Breast Milk

DURING THE EARLY 1950s, researchers in the Departments of Medicine, Medical Laboratories and Radiology, University of Tennessee College of Medicine, and the John Gaston Hospital, Memphis, studied the transmission of radioiodine in maternal breast milk to nursing infants. Two black females, ages 22 and 33 years, who were under routine medical surveillance for existing thyroid disease, and their 4-month-old infants, one male and one female, participated as subjects.

The mothers were given 100 microcuries of carrier-free iodine-131 (I^{131}) by oral administration as part of their routine medical follow-up to evaluate their thyroid function. Iodine-131 activity was measured subsequently in samples of their breast milk and over the thyroid glands of the mothers and infants. Clinical indications required the 22-year-old subject to have a repeat diagnostic thyroid function test 2 months later, for which she received another 100 microcuries of I^{131}. The infant was placed exclusively on formula, and lactation ceased 6 days later. Radioactivity in the mother's thyroid and breast milk was measured daily for 7 days after the more recent I^{131} administration.

The results of these measurements indicated that iodine concentration in maternal milk was high enough to allow significant uptake in the thyroids of nursing infants, and further indicated that iodine tracer studies in lactating women should be applied cautiously because of potential hazard to the nursing infants' thyroids. This work was supported by the U.S. Atomic Energy Commission.

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OT-79. Studies of Copper Metabolism Using Copper-64 in Healthy Subjects and Patients with Wilson's Disease

STUDIES WERE CONDUCTED at the University of Utah College of Medicine in Salt Lake City in approximately 1954 to 1955 on the behavior of elemental copper in normal subjects and in patients with liver disease (Wilson's disease and alcoholic cirrhosis). Wilson's disease is a condition involving abnormal metabolism of elemental copper and degeneration of hepatolenticular cells of the liver. The purpose of this study was to learn more about the metabolism and excretion of copper.

One millicurie of copper-64 (Cu^{64}) as cupric acetate was administered orally or intravenously to 11 normal, healthy males 25 to 30 years of age; to 4 patients with Wilson's disease; and to 2 patients with alcoholic cirrhosis of the liver. All individuals were hospitalized in the metabolic ward. A complete physical examination, urine analysis, fecal analysis, and determination of volume of packed red cells, leukocyte count, sedimentation rate, and total plasma copper were carried out on each subject. Urine and stools were collected and analyzed for Cu^{64} content at various times after administration.

This study showed that patients with Wilson's disease excreted 14 to 44 times more copper than normal subjects during the period of study. The uptake of Cu^{64} by the liver was determined by direct *in vivo* counting using a mobile body-surface scintillation counter placed over the liver. The uptake of copper in the liver of patients with Wilson's disease was significantly less than in normal subjects. This work was supported by the National Cancer Institute and the U.S. Atomic Energy Commission.

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OT-80. Studies on Copper Transfer Between Red Blood Cells and Plasma Using Copper-64

A STUDY WAS CONDUCTED in approximately 1955 at the University of Utah College of Medicine in Salt Lake City to determine the rate of movement of small amounts of copper into and out of red blood cells under various conditions.

Copper transfer was studied in one normal subject who was given about 1 millicurie of copper-64 (Cu^{64}) as cupric acetate orally, and in four normal male subjects given about 1 millicurie of Cu^{64} intravenously. Blood was drawn and the amount of Cu^{64} in plasma and red blood cells was determined at various times out to 36 or 48 hours after administration.

This study showed that copper bound to plasma albumin is taken up rapidly by red blood cells during circulation in the body. This work was supported by the National Cancer Institute and the U.S. Atomic Energy Commission.

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OT-81. White Blood-Cell Labeling Studies Using Phosphorus-32 in Utah Prisoners

DURING THE LATE 1950s, researchers at the University of Utah College of Medicine in Salt Lake City conducted studies on techniques for labeling white blood cells using phosphorus-32 (P^{32}). One hundred twenty healthy male inmates, 25 to 50 years old, at the Utah State Prison volunteered to be subjects.

Each subject was intravenously or intramuscularly administered up to 600 microcuries of P^{32}-labeled diisopropyl-fluorophosphate (DFP^{32}). A series of 26 blood samples were drawn from each subject over the 22 days following injection. Activity was measured in white blood cells isolated from the samples.

These studies showed that DFP^{32} was an effective label for counting white cells and validated the procedures used. The studies also showed that use of DFP^{32} did not produce toxic side effects and did not damage white cells. This work was supported by the U.S. Public Health Service. The assistance of the University of Utah Radiobiology Laboratory on this project was funded by the U.S. Atomic Energy Commission (AEC).

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OT-82. Granulocyte Studies Using Phosphorus-32 in Utah Prisoners

DURING THE LATE 1950s, researchers at the University of Utah College of Medicine in Salt Lake City conducted studies on the relationship between the distribution of granulocytes (a type of white blood cell) and the circulating pool of granulocytes.

The 45 healthy inmates, 20 to 50 years old, at Utah State Prison who volunteered for the granulocyte study, received diisopropylfluorophosphate (DFP^{32}) labeled with phosphorus-32 (P^{32}). After blood was drawn from the subjects, the granulocytes were labeled with DFP^{32} and infused into the original donor. Amounts of administered activity were not reported. Labeled granulocytes were counted and blood samples drawn after the infusion.

These studies showed that granulocytes were distributed in a total blood pool consisting of separate circulating and marginal pools. The study also provided estimates of the size of these pools. This work was supported by the U.S. Public Health Service. The University of Utah's

radiobiology studies were supported in part by the U.S. Atomic Energy Commission.

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Athens, J.W., S.O. Raab, O.P. Haab, A.M. Mauer, H. Ashenbrucker, G.E. Cartwright, and M.M. Wintrobe. "Leukokinetic Studies. III. The Distribution of Granulocytes in the Blood of Normal Subjects." *Journal of Clinical Investigation.* Vol. 40, 1961, pp. 159–164. ❑

OT-83. White Blood-Cell Production Studies Using Phosphorus-32

DURING THE EARLY 1960s, investigators at the University of Utah in Salt Lake City conducted studies to learn more about the production and fate of granular leukocytes (white blood cells) in humans. The subjects were 109 healthy, male inmates of the Utah State Prison between the ages of 19 and 54 years.

The study involved drawing 400 milliliters of blood from each study participant; labeling the granulocytes with the compound diisopropylfluorophosphate (DFP), which contained phosphorus-32 (P^{32}) tracer; and returning the blood to the donor. Alternatively, the DFP^{32} was intravenously injected directly into the subjects to label circulating granulocytes. At subsequent times, blood was drawn and counted for P^{32} activity to determine the production and kinetics of blood granulocytes.

The study was repeated on the same subjects about 1 month later to determine the biological variation between individuals or within the same individual over time. The amount of P^{32} tracer administered to each subject was not stated.

The study provided new information on the distribution of granulocytes and their rate of disappearance from circulation. Times required for granulocyte production and the rates of cell maturation were also determined. This work was supported by the National Institute of Arthritis and Metabolic Diseases. The University of Utah's radiobiology studies were supported in part by the U.S. Atomic Energy Commission.

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Wintrobe, M.M. *Hematology, the Blossoming of a Science.* Philadelphia: Lea and Febiger, 1985. ❑

OT-84. Study of Copper Metabolism Using Copper-64

DURING THE EARLY 1960s, basic studies on copper metabolism in normal subjects were conducted at the University of Utah College of Medicine in Salt Lake City. The purpose of these studies was to determine total serum copper (copper associated with red blood cells); copper in the liver, brain, kidneys, heart, spleen, and whole-body; and rate of copper excretion in urine and stool. The subjects consisted of 135 men and 100 women, including 72 normal pregnant women (in their third trimester). This study involved the analysis of stable copper as well as radioactive copper tracer in a few subjects.

Two or more of the subjects were administered copper-64 (Cu^{64}) either orally or intravenously, although the exact number given radioactive copper and the amounts ingested or injected is not known. Stable copper was determined using spectrophotometric methods; radioactive copper was determined by standard counting.

This study showed that about 0.33 of the 2 to 5 milligrams of copper ingested daily in the diet of the normal subjects was absorbed. Most copper was excreted in the bile to the bowel. Only a small fraction was excreted in urine. This work was supported by the National Institute of Arthritis and Metabolic Diseases. The University of Utah's radiobiology studies were supported in part by the U.S. Atomic Energy Commission.

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OT-85. Blister Studies Using Phosphorus-32 in Utah Prisoners

DURING THE EARLY 1960s, researchers at the University of Utah College of Medicine in Salt Lake City conducted studies on the cellular concentration of white blood cells in blisters using diisopropylfluorophosphate (DFP^{32}) labeled with phosphorus-32 (P^{32}).

Twenty-eight healthy male inmates of the Utah State Prison ranging in age from 20 to 44 years participated as subjects. Each was administered an unstated amount of DFP^{32} to label white blood cells in circulating blood. Blister formation was then induced on the subject's forearm and inflammation was generated by injecting a heat-killed culture of staphylococci bacteria into the blister. Fluid was drawn from the blister and DFP^{32}-labeled white cells were counted.

These studies showed extreme variation between subjects. The studies also showed that different types of white cells increased in the blister fluid at different rates. This work was supported by the U.S. Public Health Service. The University of Utah's radiobiology studies were supported in part by the U.S. Atomic Energy Commission.

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OT-86. Comparative Metabolism of Radium-226 and Strontium-85

DURING 1962 TO 1963, scientists at the Radiobiology Division of University of Utah in Salt Lake City conducted a study to determine the early retention and excretion of radium-226 (Ra^{226}) and strontium-85 (Sr^{85}) in man.

An 80-year-old man with an epidermoid carcinoma on his facial skin was given 10 microcuries of Sr^{85} and 1.5 microcuries of Ra^{226} in normal saline solution by intravenous injection. The radioactivity retained in the subject was counted periodically in the whole-body counter. Samples of blood, urine, and feces were collected and assayed for radioactivity.

Fifty-eight days after the injection, the subject retained 21 percent of the injected strontium (corrected for radioactive decay). Measurements made at the subject's time of death, 141 days postinjection, showed that Ra^{226} retention was only 6.5 percent of the administered activity, with 5.2 percent in bone plus 1.3 percent in soft tissue. This research was supported by the U.S. Atomic Energy Commission.

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OT-87. Total-Body Counter Calibration Using Cesium-132 and Potassium-42

FROM JANUARY TO OCTOBER 1963 researchers at the Radiobiology Division of University of Utah in Salt Lake City used subjects with known amounts of radioactivity in their bodies to calibrate the whole-body counter. After fasting, four female and six male healthy, fasting volunteers were given 0.1 microcurie of cesium-132–chloride ($Cs^{132}Cl$) orally. Two subjects were counted immediately after ingestion to establish a baseline by which the change in the counting rate could be determined. Counting was repeated periodically for an additional 50 hours. Total excreta collections were made and assayed for Cs^{132}. Nine months later, the same four females and six males (with one substitution) were orally administered 1 microcurie of potassium-42 (K^{42}), and the same protocol was followed.

This research helped calibrate the whole-body counter for later measurements of radioactive fallout in Utah residents from atomic weapons testing in Nevada. This research was sponsored in part by the Division of Radiological Health, Bureau of State Services of the U.S. Public Health Service. The assistance of the University of Utah Radiobiology Laboratory on this project was funded by the U.S. Atomic Energy Commission (AEC).

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OT-88. Study of Cortisone-Induced Granulocytosis Using Phosphorus-32–Labeled Diisopropylfluorophosphate in Utah Prisoners

RESEARCHERS AT the University of Utah College of Medicine in Salt Lake City conducted a study between 1964 and 1966 to find the mechanism by which steroids induce granulocytosis (a condition characterized by more than the normal number of white blood cells in the circulating blood).

Nine inmates between the ages of 23 and 40 from the Utah State Prison participated in this study. Each inmate had 300 to 500 milliliters of blood drawn and their granulocytes (a type of white blood cell) were then incubated with diisopropylfluorophosphate (DFP) labeled with phosphorus-32 (P^{32}) in tracer amounts. The cells were then returned to the corresponding donor. The amount of the P^{32} administered to each subject was not stated.

The participants were then injected intravenously with 200 milligrams of cortisol (a steroid) to induce granulocytosis. Inflammatory lesions were produced on the skin to assess the effect of the steroids on the flow of granulocytes to the skin. The accumulation of granulocytes in the inflammation was determined before and, at various times, after the administration of the steroid.

Results of this study helped researchers understand that granulocytosis is produced by an increased inflow of marrow granulocytes into the blood. This experiment was a continuation of an earlier study by the University of Utah that examined the production of granulocytes and was supported by the National Institute of Arthritis and Metabolic Diseases, and the National Institutes of Health. The University of Utah's radiobiology studies were supported in part by the U.S. Atomic Energy Commission.

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OT-89. Cesium-137 and Rubidium-83 Metabolism in Healthy Subjects and Subjects with Muscular Dystrophy

BETWEEN 1965 AND 1972, researchers in the Departments of Anatomy, Medicine, and Radiological Health at the University of Utah in Salt Lake City conducted a series of studies of the metabolism of cesium-137 (Cs^{137}) and rubidium-83 (Ru^{83}) in healthy individuals and in persons with muscular dystrophy. Estimates were made of the biological retention half-time of Cs^{137} from environmental radioactive fallout, based on measured body burdens and excretion rates.

Participating in this study were 39 healthy individuals: 5 infants, ages 17 to 143 days; 5 children, ages 5 to 10 years; 23 adults, ages 21 to 52 years, including 6 pregnant females; and 3 children, ages 4 to 11, with Duchenne muscular dystrophy.

The average values for Cs^{137} half-time in the healthy subjects was found to increase with age from 19 days in infants to 95 days in adults. The Cs^{137} half-time in the six pregnant females averaged 45 days, confirming earlier reports of increased Cs^{137} excretion during pregnancy. The average half-time for the dystrophic children was 18 days, about a third of that expected in healthy children.

Between 1968 and 1972, the initial investigation of Cs^{137} metabolism in persons with muscular

dystrophy was extended to (1) establish normal values for cesium and rubidium metabolism as a function of age for control subjects; (2) correlate observed metabolic differences between control and dystrophic subjects with the degree of disease severity; (3) compare Duchenne dystrophy with other muscle diseases; and (4) search for metabolic differences between female controls and female genetic carriers of Duchenne dystrophy. A total of 38 persons of various ages participated in the extended study. Seventeen subjects (14 males, 3 females; ages 5 to 61 years) had muscle disease, and 21 subjects (9 males, 12 females; ages 4 to 80 years, including at least 1 of the investigators) were normal volunteer subjects. About 1 microcurie Cs^{137} and 6 microcuries Ru^{83} as a double tracer were administered orally to each subject over 18 years of age. Younger subjects received half these amounts. Samples of blood, feces, and urine were collected for analysis, regularly from some subjects and intermittently from others. Cesium-137, and especially Ru^{83} retention, was notably lower among the dystrophic subjects than among the healthy volunteers, including the known or suspected carriers of the Duchenne gene.

The results supported the hypothesis that muscular dystrophy is associated with a cell membrane defect, resulting in altered permeability. These studies were supported by the National Institutes of Health and the U.S. Atomic Energy Commission.

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OT-90. Study of Granulocyte Kinetics During Endotoxin-Induced Granulocytosis Using Phosphorus-32

BETWEEN 1969 AND 1971, investigators at the University of Utah College of Medicine in Salt Lake City and the Salt Lake Veterans Administration Hospital conducted a study to determine whether endotoxins (bacteria toxins) liberated into surrounding medium produced granulocytosis (a condition characterized by more than the normal number of granulocytes, a type of white blood cell in the circulating blood).

Eighteen men from the Utah State Prison between the ages of 20 and 36 years volunteered as participants in this study. The subjects had 300 to 500 milliliters of blood drawn. The granulocytes were separated out and then incubated with diisopropylfluorophosphate (DFP) labeled with phosphorus-32 (P^{32}) tracer; the cells were then injected into the corresponding donor. The amount of P^{32} tracer administered to each subject was not stated. Granulocyte counts and specific activity measurements were made before and after bacterial endotoxin (Salmonella or Pseudomonas) was given intravenously to 12 subjects; in this study, both radioactive materials and biological toxins were administered to some subjects. The remaining six subjects served as controls and received DFP^{32}, but no endotoxin.

Results from this study showed that a moderate dose of bacterial endotoxin resulted in an increase in the granulocyte count. This experi-

ment was a continuation of an earlier University of Utah study that described the changes in granulocyte inflow and outflow rates before, during, and after steroid-induced granulocytosis. This study was supported by the National Institute of Arthritis and Metabolic Diseases and the National Institutes of Health. The University of Utah's radiobiology studies were supported in part by the U.S. Atomic Energy Commission.

References

Ostlund, R.E., C.R. Bishop, and J.W. Athens. "Evaluation of Non-Steady-State Neutrophil Kinetics During Endotoxin-Induced Granulocytosis." In *The Proceedings of the Society for Experimental and Biological Medicine.* Vol. 137, 1971, pp. 763–767. ❑

OT-91. Study of the Transfer of Iron-59 and Iodine-131 Between Mother and Fetus

RESEARCH WAS CONDUCTED during the period 1967 to 1968 at Vanderbilt University School of Medicine in Nashville, Tennessee, on the biological transfer and distribution of radionuclides between mother and fetus. The purpose of this study was to determine the magnitude of the hazard to the fetus from intakes of radionuclides by the mother. The five subjects chosen for this study were pregnant women already scheduled for therapeutic abortions. The gestational ages of the fetuses ranged from 11 to 22 weeks.

Each subject was administered 10 microcuries Fe^{59} intravenously as ferrous citrate and 50 microcuries of iodine-131 (I^{131}) orally as sodium iodide as tracers 18 hours prior to the scheduled abortion. The amounts of iron-59 (Fe^{59}) and I^{131} in the total aborted fetus were then determined. Samples of the fetal tissues were studied to determine the biological distributions of Fe^{59} and I^{131} among the different organs and tissues, the amniotic fluid, and the umbilical cord.

These data provided information about the fraction of activity passing from mother to fetus during the first 18 hours after radionuclide administration, and also the data on concentrations of I^{131} and Fe^{59} in fetal tissues. Eighty percent of the Fe^{59} was deposited in the fetal liver and 65 percent of the I^{131} was deposited in the fetal thyroid. This work was supported in part by the U.S. Atomic Energy Commission.

References

Dyer, N.D., A.B. Brill, S.R. Glasser, and D.A. Goss. "Maternal-fetal Transport and Distribution of Fe^{59} and I^{131} in Humans." *American Journal of Obstetrics and Gynecology.* Vol. 103, January 15, 1969, pp. 290–296.

Dyer, N.D., and A.B. Brill. "Fetal Radiation Dose from Maternally Administered Fe^{59} and I^{131}." In *Proceedings of the Ninth Annual Hanford Biology Symposium at Richland, Washington, May 5–8, 1969*, edited by M.R. Sikov and D.D. Mahlum, pp. 73–87. Sponsored by Battelle Memorial Institute Pacific Northwest Laboratory and the U.S. Atomic Energy Commission. December 1969. ❑

OT-92. Metabolism Studies Using Strontium-85 and Calcium-47

IN THE EARLY 1970s, researchers at the Veterans Administration Hospital, Hines, Illinois, conducted studies on the uptake, retention, and excretion of strontium using strontium-85 (Sr^{85}), strontium-90 (Sr^{90}), and calcium-47 (Ca^{47}). Ambulatory patients in the hospital metabolic research ward participated as subjects.

Each subject was orally or intravenously administered tracer amounts of Sr^{85} and Ca^{47}. Strontium-90 intake through normal diet was measured by low-level beta counting. Activity was measured in plasma, urine, and feces; the activity was then analyzed in conjunction with administration of stable strontium, stable calcium (high and low intake), phosphate (high intake), vitamin-D, aluminum phosphate gel, ammonium chloride, diuretics, magnesium, stable strontium, and various chelating agents.

The results of these studies provided considerable data on the metabolism of strontium in humans and on the effects of certain chemicals on strontium metabolism. This work was supported by the U.S. Atomic Energy Commission.

References

Spencer, H., L. Kramer, and J. Samachson. "Effect of Stable Strontium on Sr^{85} Absorption and Excretions in Man." *Radiation Research.* Vol. 47, 1971, p. 281.

Spencer, H., L. Kramer, and J. Samachson. "Metabolism and Removal of Radiostrontium in Man." In *Proceedings of the Symposium Bio-*

medical Implications of Radiostrontium Exposure. Berkeley, CA: University of California, Radiobiology Laboratory, April 1972, pp. 31–51. ❑

OT-93. Measuring Extracellular Fluid Using Sodium-24

DURING THE LATE 1940s AND IN 1950, researchers in the Department of Internal Medicine, Bowman Gray School of Medicine, Wake Forest University in Winston-Salem, North Carolina, conducted studies to measure extracellular fluid space using radioactive sodium-24 (Na^{24}).

Twenty patients with a variety of clinical conditions participated as subjects. Each received an intravenous injection of about 2 to 3 microcuries of Na^{24} per kilogram of body weight. Radioactivity measured in a subsequently drawn blood sample was used to determine fluid space. The results were compared with results obtained by similar measurements using nonradioactive thiocyanate.

These studies showed that radiosodium was a highly accurate means of measuring fluid space. However, the wide variation between Na^{24} and thiocyanate measurements in diseased individuals suggested that both methods should be applied in clinical investigations. This work was supported by the U.S. Atomic Energy Commission.

References

Aikawa, J.K. "The Significance of the Radiosodium Space in Human Disease." *Southern Medical Journal*. Vol. 44, No. 7, July 1951, pp. 654–661. ❑

OT-94. Potassium Studies in Diseased Patients Using Potassium-42

DURING THE EARLY 1950s, researchers at Wake Forest College and North Carolina Baptist Hospital in Winston-Salem, North Carolina, conducted studies to determine the total-body content of elemental potassium in diseased patients using potassium-42 (K^{42}) The subject pool consisted of 39 male and 30 female hospitalized patients ranging in age from 14 to 78 years, and 6 healthy individuals.

Each subject underwent up to three measurements of body potassium by intravenous administration of 100 microcuries of K^{42} and subsequent activity counting in urine samples.

These studies showed that the potassium levels in diseased subjects were similar to or lower than the levels in normal subjects. The lower levels in some patients suggested a potassium deficiency. This work was supported by the U.S. Atomic Energy Commission and partly by the American Heart Association.

References

Aikawa, J.K., J.H. Felts, Jr., M.P. Tyor, G.T. Harrell, and E.L. Rhoades. "The Exchangeable Potassium Content in Disease States." *The Journal of Clinical Investigation*. Vol. 31, July 1952, pp. 743–749. ❑

OT-95. Potassium Studies in Women Using Potassium-42

DURING THE EARLY 1950s, researchers at the Department of Internal Medicine, Bowman Gray School of Medicine, Wake Forest University in Winston-Salem, North Carolina, conducted studies on body potassium content in women using potassium-42 (K^{42}). The purpose of this study was to compare total-body potassium content in women compared to content in previously studied normal healthy men.

Twenty healthy females, comprising nurses, medical students, and laboratory technicians, ranging in age from 19 to 32 years participated as subjects. Each subject was intravenously administered 100 microcuries of K^{42} and activity was measured in subsequently collected urine samples.

The studies showed that the level of exchangeable potassium in the young female subjects was considerably lower than the levels observed in young men, apparently due to the relatively greater amount of fat in the women. This work was supported by the U.S. Atomic Energy Commission and partly by the American Heart Association.

References

Aikawa, J.K., G.T. Harrell, and B. Eisenberg "The Exchangeable Potassium Content of Normal Women." *Journal of Clinical Investigation*. Vol. 31, April 1952, pp. 367–369. ❑

OT-96. Sodium Volume Studies in Diseased Patients Using Sodium-24

DURING THE EARLY 1950s, researchers at the North Carolina Baptist Hospital and at the Bowman Gray School of Medicine at Wake Forest College in Winston-Salem, North Carolina, conducted research on body sodium in diseased patients using sodium-24 (Na^{24}). The purpose of the study was to compare the volumes of fluid available for dilution of thiocyanate and radiosodium ions in diseased individuals.

Twenty-six hospitalized patients and three normal medical students participated as subjects. Each was intravenously administered 150 microcuries of Na^{24} and activity was measured in subsequently drawn blood samples. Thiocyanate measurements were accomplished without administration of any radioactivity.

The studies showed almost identical thiocyanate and sodium volumes in normal subjects, but different volumes in diseased subjects. This work was supported by the U.S. Atomic Energy Commission.

References

Aikawa, J.K., and E. Rhoades. "Comparison of the Thiocyanate and Radiosodium Spaces in Disease States." *The American Journal of the Medical Sciences*. Vol. 224, 1952, pp. 632–637. ❑

OT-97. Study of Potassium Metabolism in Hyperthyroidism Using Potassium-42

DURING THE EARLY 1950s, researchers at the Department of Internal Medicine, Bowman Gray School of Medicine, Wake Forest University, Winston-Salem, North Carolina, conducted studies on the metabolism of potassium in subjects with untreated hyperthyroidism.

Thirteen hospitalized men and women ranging in age from 21 to 68 years participated in the study. Each subject received an intravenous injection of 100 microcuries of potassium-42 as potassium chloride. Urine samples were collected 24 hours after injection and the measured radioactivity was used to calculate body potassium content.

These studies showed that potassium levels were lower in untreated hypothyroid males than in normal males, but that the levels in untreated hyperthyroid females were similar to normal females. This gender difference was attributed to the dissimilarity in body composition and muscle mass normally found between males and females. This work was supported by the U.S. Atomic Energy Commission and by a grant from the American Heart Association.

References

Aikawa, J.K. "Isotopic Studies of the Body Potassium Content in Thyrotoxicosis." In *Proceedings of the Society for Experimental Biology and Medicine*. Vol. 84, No. 3, December 1953, pp. 594–596. ❑

OT-98. Studies of Potassium Metabolism in Diabetes Using Potassium-42 Tracer

DURING THE EARLY 1950s, researchers at Wake Forest College in Winston-Salem, North Carolina, and North Carolina Baptist Hospital conducted studies on potassium metabolism in diabetic patients. Forty-two male and female hospitalized patients ranging in age from 18 to 78 years participated as subjects.

One hundred microcuries of radioactive potassium-42 (K^{42}) were administered intravenously to the subjects. Twenty subjects received a single injection and 22 subjects received 2 to 4 injections. Measurements of K^{42} in urine specimens collected after each injection were used to calculate the exchangeable body content of potassium. Fifteen subjects who received multiple injections also received oral supplements of nonradioactive (stable) potassium beginning 1 week after the K^{42} injection.

The studies showed that potassium values were significantly lower in diabetic males compared to normal males, but not significantly different between diabetic and normal females. The studies also showed that a potassium deficit could be correlated with the relative adequacy of control of the disease and that a deficit could be regulated by administration of an oral potassium supplement. This work was supported by the American Heart Association and by the U.S. Atomic Energy Commission.

References

Aikawa, J.K., J.H. Felts, Jr., and G.T. Harrell, Jr. "Isotopic Studies of Potassium Metabolism in Diabetes." *Journal of Clinical Investigation.* Vol. 32, 1953, pp. 15–21. ❑

OT-99. Iron Absorption Studies Using Iron-55 and Iron-59 in Normal Subjects and Mental Patients

STUDIES CONDUCTED in the 1950s by medical scientists at the University of Washington, Seattle used a double isotope technique to improve the understanding of the way in which the human body absorbs and metabolizes iron.

The first in the related series of studies involved injections of iron-55 (Fe^{55}) and iron-59 (Fe^{59}) in various animals and 12 normal human subjects. In human subjects, the amount of Fe^{55} varied between 50 and 100 microcuries with stable iron carrier (100 and 500 milligrams). Approximately 1 microcurie of Fe^{59} was given intravenously as ferrous citrate. This study showed that both the size of iron stores and the rate at which red blood cells formed influenced iron absorption. The larger the iron stores, the less iron was absorbed, whereas the greater the red cell production, the greater the amount of iron was absorbed.

In another study, 20 patients with normal iron metabolism history, 19 anemic patients, 19 with abnormal red blood-cell counts, and 5 with iron storage disease were used as subjects to measure iron absorption. Some of the normal hematological subjects were mental patients. The absorption of iron was studied in patients who were given a test meal containing 50 microcuries Fe^{55} in the form of ferric chloride added halfway through the meal. After the meal, the subjects were also administered Fe^{55} as ferric chloride by intravenous injection to compare iron absorption after administration of iron by separate routes of intake. A double isotope technique using Fe^{55} and Fe^{59} was employed to measure absorption of iron from food. The absorption of iron from food by both normal and iron deficient subjects was slower than that seen when iron salts alone were given. Supplemental ascorbic acid diminished this difference.

The study also concluded that anemia was not an important factor in the regulation of iron absorption. Other observations were also reported with regard to iron absorption in cases of abnormal red blood-cell counts and anemia. This research was supported by the U.S. Atomic Energy Commission.

References

Bothwell, T.H., G. Pirzio-Biroli, and C.A. Finch. "Iron Absorption I. Factors Influencing Absorption." *The Journal of Laboratory and Clinical Medicine.* Vol. 51, No. 24, 1958, pp. 24–36.

Pirzio-Biroli, G., T.H. Bothwell, and C.A. Finch. "Iron Absorption II. The Absorption of Radioiron Administered with a Standard Meal in Man." *The Journal of Laboratory and Clinical Medicine.* Vol. 51, No. 1, 1958, pp. 37–48.

Letter. C.A. Finch to S. Marks. July 17, 1984. Pacific Northwest Laboratory General Human Subjects, Box Alan Rither, PNL-9055-DEL (CIC #701610, bate 8756). ❑

OT-100. Study of Iron Turnover Rates Using Iron-55 in Men, and Nonmenstruating and Menstruating Women

A STUDY WAS CONDUCTED between 1954 and 1958 by medical scientists at the University of Washington, Seattle, to investigate total-body iron turnover rates. The study involved 6 adult men, 12 adult nonmenstruating women, and 6 adult menstruating women.

All subjects were mental patients at the Northern State Hospital in Sedro-Woolley, Washington. The subjects were selected for study because of their good health, their normal hematologic values, and the absence of history of abnormal blood loss or anemia. Iron-55 (Fe^{55}) was injected intravenously to each patient as Fe^{55} citrate in dosages of 100 microcuries. Blood samples were drawn 2 months after injection, and at 4-month intervals thereafter over a period of 46 to 54 months, and analyzed for Fe^{55} activity.

This study showed that red cell iron turnover over a 4-year period is 0.61 milligram per day in men, 0.64 milligram per day in nonmenstruating women, and 1.22 milligrams per day in menstruating women. The research was supported by the and the U.S. Public Health Service and the U.S. Atomic Energy Commission.

References

Finch, C.A., and B. Loden. "Body Iron Exchange in Man." *The Journal of Clinical Investigation.* Vol. 38, No. 2, 1959, pp. 392–396.

Letter. C.A. Finch to S. Marks. July 17, 1984. Pacific Northwest Laboratory General Human Subjects, Box Alan Rither, PNL-9055-DEL (CIC #701610, bate 8756). ❑

OT-101. Study of Cooley's Anemia in Children Using Chromium-51 and Iron-59

A STUDY WAS CONDUCTED in 1955 by medical scientists at the University of Washington, Seattle and the Department of Research at Children's Hospital in Los Angeles on four children, two of whom were siblings, with Cooley's anemia, a genetic blood disorder.

The children, ages 4, 6, 9, and 13 were given iron-59 (Fe^{59}) and chromium-51 (Cr^{51}). About 20 microcuries, or 0.5 microcurie per estimated kilogram of body weight, of Fe^{59} as ferrous citrate were administered intravenously to the subjects to determine plasma iron turnover and red blood-cell utilization. Chromium-51 was administered intravenously to label red blood cells and to determine red cell survival times. The amount administered to each subject was not stated.

The study provided information on the underlying defects in children with the disease and showed that the severity of the anemia was largely related to a defect in the production of red cells, not in total hemoglobin synthesis. The research was supported by grants from the U.S. Public Health Service, the National Institutes of Health, and the U.S. Atomic Energy Commission.

References

Sturgeon, P., and C.A. Finch. "Erythrokinetics in Cooley's Anemia." *Blood: The Journal of Hematology.* Vol. 12, 1957, pp. 64–73.

Letter. C.A. Finch to S. Marks. July 17, 1984. Pacific Northwest Laboratory General Human Subjects, Box Alan Rither, PNL-9055-DEL (CIC #701610, bate 8756). ❑

OT-102. Study of Red Blood-Cell Production Using Iron-59

IN THE LATE 1960s, researchers at the University of Washington, Seattle and the Universidad Nacional Mayor de San Marcos in Lima, Peru, investigated the effects of altitude changes on erythropoiesis (red blood-cell formation), iron absorption, and oxygen binding at high altitudes.

Seven healthy male Lima residents, at sea level, between the ages of 18 and 30 years, were transported to Morococha (elevation 4,530 meters) for observation. Conversely, six healthy male Morococha residents, between the ages of 20 and 39 years, were transported to Lima for observation. While at the atypical altitude, each subject received an intravenous injection of 2 to 5 microcuries of iron-59 (Fe^{59}) citrate. Later, each subject received 15 microcuries of Fe^{59} intravenously. Blood and urine samples were taken to measure erythropoietin (a hormone that stimulates red blood-cell production), oxygen binding, and iron absorption levels.

The study found that erythropoiesis is stimulated by ascent to high altitudes and suppressed upon descent to lower altitudes. This study was supported by the U.S. Public Health Service and the U.S. Atomic Energy Commission.

References

Faura, J., J. Ramos, C. Reynafarje, E. English, P. Finne, and C. Finch. "Effect of Altitude on Erythropoiesis." *Blood: The Journal of Hematology.* Vol. 33, No. 5. 1969, pp. 668–676.

Lenfant, C., J. Torrance, E. English, C. Finch, C. Reynafarje, J. Ramos, and J. Faura. "Effect of Altitude on Oxygen Binding by Hemoglobin and on Organic Phosphate Levels." *The Journal of Clinical Investigation.* Vol. 47, No. 12, December 1968, pp. 2,652–2,656.

Cook, J.D. "Summary of Results—Peru Study." Seattle: University of Washington, 1969. Hanford Records Holding Area, DOE-RL Procurement Division Records, Box 024223, RLHTS94-0081, Contract AT (45-1) 2048. ❑

OT-103. Sodium Volume Studies in Children and Adults Using Sodium-24

BETWEEN 1949 AND 1951, researchers at Washington University in St. Louis; St. Louis Children's Hospital; and St. Louis Maternity Hospital conducted studies on sodium space in children and adults using sodium-24 (Na^{24}). The term "space" refers to the volume within which sodium is distributed in the body.

Thirty-seven male or female infants and children ranging in age from one day to 14 years, and 19 adult males ranging in age from 22 to 34 years participated as subjects. Each subject was intravenously administered 1.0 to 1.5 microcuries of Na^{24} per kilogram of body weight. Blood samples were drawn 1.75 to 4.5 hours after injection and analyzed for activity. The total estimated dose was between 0.11 and 0.17 roentgen equivalent physical in the adult. Urine samples were also collected and analyzed.

The results of these studies showed that the volume of fluid occupied by sodium declines in relation to body weight as growth proceeds. This work was supported by the Children's Research Foundation and the U.S. Atomic Energy Commission.

References

Perley, A., G.B. Forbes, and M.M. Pennoyer "Determination of Sodium 'Space' in Infants, Children, and Adults." *The Journal of Pediatrics.* Vol. 38, January–June 1951, pp. 299–305. ❑

OT-104. Estimates of Total-Body Sodium in Infants and Children Using Sodium-24

DURING THE EARLY 1950s, researchers at the Department of Pediatrics, Washington University School of Medicine in St. Louis, and St. Louis Children's Hospital conducted studies using sodium-24 (Na^{24}) to determine the amounts of total-body sodium in children and infants.

Twenty-one hospitalized patients ranging in age from 2 weeks to 14 years participated as subjects. Each subject was intravenously administered 1.0 to 1.5 microcuries of Na^{24} per kilogram of body weight. Activity was measured in subsequently collected urine and blood samples.

The results of these studies showed that sodium levels are high in infants and gradually decline with age until adult levels are reached. The studies also showed that sodium is related to body weight in a predictable way. This work was supported by the U.S. Atomic Energy Commission.

References

Forbes, G.B., and A. Perley. "Estimation of Total-Body Sodium by Isotopic Dilution: II. Studies on Infants and Children: An Example of a Constant Differential Growth Ratio." *Journal of Clinical Investigation.* Vol. 30, June 1951, pp. 566–574. ❑

OT-105. Total-Body Sodium Studies Using Sodium-24

DURING 1950 TO 1951, researchers at Washington University in St. Louis, and St. Louis Children's Hospital, St. Louis, Missouri, conducted studies to determine total-body sodium in adults using sodium-24 (Na^{24}). Thirty-four healthy male and female subjects ranging in age from 20 to 34 participated. These volunteer subjects included hospital staff members and medical students.

Thirty-two subjects were intravenously administered 1.0 to 1.5 microcuries of Na^{24} per kilogram of body weight. Two subjects received the Na^{24} orally. Four subjects received a second administration 4 to 22 months after the first injection. Blood and urine samples were subsequently obtained and analyzed. In addition to samples from the healthy volunteers, samples of normal bone and brain tissue and cerebrospinal fluid were obtained from patients at the time of regularly scheduled operations.

The results of these studies provided data on the levels of sodium in the subjects. The studies also showed that 82 percent of sodium in the body was exchangeable. This includes 40 percent of the sodium in bone that is considered to be exchangeable. This work was sponsored by the Children's Research Foundation and the U.S. Atomic Energy Commission.

References

Forbes, G.B., and A. Perley. "Estimation of Total-Body Sodium by Isotopic Dilution. I. Studies on Young Adults." *The Journal of Clinical Investigation.* Vol. 30, June 1951, pp. 558–565. ❑

Radiation Terms

DEFINED BELOW are some technical terms relating to radiation.

Radioactivity—the tendency of unstable atoms to undergo a spontaneous, energy-releasing change in their structure. The energy released is called radiation. It occurs at various energy levels. At a certain point, radiation energy is sufficient to strip electrons from the atoms in materials it strikes and is therefore called ionizing radiation. It is particularly dangerous for humans because these energy levels are such that they also can cause damage to living tissues. Ionizing radiation may involve alpha particles, beta particles, gamma rays, x-rays, or neutrons.

Alpha particles—a high-energy particle with a very short range. It does not pose an external hazard because it cannot penetrate human skin. It may be stopped by a single sheet of paper. However, if inhaled or ingested, the particles come in direct contact with tissue cells and can cause severe damage. Accordingly, alpha particles present a serious internal hazard. Uranium, radium, and plutonium all emit alpha particles.

Beta particles—exhibit a wide range of energy levels. Some have sufficient energy to penetrate human skin, and will cause skin burns. These particles can cause damage if inhaled or ingested. Beta particles can be stopped by plastic, aluminum, and wood. Tritium is one example of a beta emitter.

Gamma rays and x-rays—both are high-energy emissions that easily penetrate the human body. They are, therefore, dangerous in high amounts as external radiation hazards. They can be stopped by dense materials, such as lead, concrete, or steel. Gamma rays are produced by isotopes such as lanthanum-140, cesium-137, and cobalt-60. X-rays are produced by medical x-ray tubes and the x-ray machines used to examine carry-on baggage at airports.

Neutrons—a component of the nucleus of an atom. Neutron radiation can be harmful to living things. Neutrons are liberated in great numbers in a nuclear reactor, but they do not present a hazard to humans because they are absorbed by the heavy shielding that encloses the reactor. Neutrons are also emitted during the spontaneous decay of certain radionuclides such as californium-252. Amount of radiation is expressed in several ways.

A **curie** is a measure of activity, or the rate of disintegration of atoms undergoing change. This unit of measure is often expressed as millicuries (thousandths of a curie) or microcuries (millionths of a curie). A **roentgen** is a measure of the ionization of air by x-rays or gamma rays.

Exposure—refers to being placed in a field of radiation energy. Dose refers to energy imparted per unit mass of tissue. A **rad** is a measure of the absorbed dose to tissue from exposure to radiation; that is, the amount of energy deposited per unit mass of tissue. A **rem** is a measure of dose equivalent in man. It is the dose in rads multiplied by a weighting factor to account for the more damaging effects of alpha particles and neutron radiation.

Background radiation—refers to the natural radiation to which people are exposed in daily life. It differs for different locations and different circumstances. Brick and wood homes emit different levels of background radiation. Cities at different elevations have different levels of background cosmic radiation. For example, the average annual dose from all sources to U.S. residents is estimated to be 200 millirems per year. However, the average dose to residents of Los Alamos, New Mexico, a city at high elevation is 330 millirems per year. A transcontinental airplane flight will result in a dose of about 4 millirems to a passenger. A standard chest x-ray will result in a dose of about 10 millirems.

Occupational dose—refers to the dose that people receive in their workplace. To provide for the safety of workers, the International Commission on Radiological Protection (ICRP-60, 1990) has established certain standards to limit the dose received by workers. Standards for minors are 10 percent of the dose for adults. These annual dose limits for radiation workers are:

Whole body	2 rem
Skin or any extremities	50 rem
Eyes	15 rem
Embryo/fetus	0.2 rem

By comparison, the annual dose limit for the general public (not radiation workers) set by the Commission is 0.1 rem. ❐

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