

Accession Number: BLDG. 69-SMILE 6685
 File Code Number: 19-1-21
 Division/Department/Group: ICSD-ARCHIVES & RECORDS
 Series Title: ANNA BERGE'S HUMAN RADIATION EXPERIMENTS
 Box Number: 1/1 RECORD
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HUMAN RADIATION EXPERIMENT RESEARCH
ANNA BERGE RESEARCH NOTES

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Records Title Anna Berge's Human Radiation Experiment Records Search Project <u>Notes</u>		
Inclusive Dates of the Records 1994		Number of Records Boxes 1 folder in 1 small mss box
Brief Description of the Records These records consist of notes based on a review of the Human Subject Radiation Experiment records from a number of different records collections, including the E.O. Lawrence, Edwin MacMillan, John Lawrence, Cornelius Tobias, Robert Stone, Kenneth G. Scott, and D.C. Files. They were produced by Anna Berge, archivist in the Archives and Records Office (ARO) at the Lawrence Berkeley Laboratory, from January to March, 1994, as part of the ARO's response to Department of Energy Secretary Hazel O'Leary's directive to review all documents pertaining to human experimentation. They are arranged in the order in which they were produced.		
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PEOPLE

(20.1.94)

John Simpson--astrophysicist who worked on health and safety issues as a group leader on the Manhattan Project

on faculty of Division of Medical Physics, UCB:

nucleus:

John Lawrence
Joseph Hamilton
Paul Aebersold
Cornelius Tobias

important experimentalists:

Hardin Jones
Robert Arid
David Greenberg
C.L.A. Schmitt
Miller, Chaikoff, Anderson, Strait, Low-Beer, Althausen, and Soley

directors of Donner Lab:

John Lawrence
James Born
Edward Alpen
Paul Silverman

director of Crocker Lab:

Joseph Hamilton

people who worked with Hamilton:

Thomas Putnam (supervisor of 60" Cyclotron, don't think he knew of 48A)
Bernie Rossi (Operations, the supervisor of 60", don't think he knew)
L. Van Middleworth (1945-46 on the Plutonium Project)
Miss Axelrod (prepared monthly reports for proj. 48A)
Dr. Copp (prepared monthly reports for proj. 48A)
Kenneth Scott (1945 on; collected feces and urine samples from Stevens)
Dr. Earl R. Miller (analyzed CAL-II after injection)
Stephen P. Cobb Jr (Oak Ridge AEC)
Col. Stafford Warren (of UCLA re tests at Bikini Atoll, ie Operation Crossroads)
Dr. Overstreet (re Operation Crossroads)
Admiral Solberg (Operation Crossroads)
Patricia Durbin (1950's)

people to whom Hamilton's monthly reports were routed:

H.A. Fidler
R.S. Stone
R.S. Mulliken
E.O. Lawrence

other people aware or probably aware of Hamilton's efforts on 48A:

John Lawrence (worked on Uranium part of 48A along with Cornelius Tobias, Hardin Jones, P. Weymouth, L. Dobson, and Hal Anger)
Dr. Connick, Hanacker, Kosha, McVey, King, and Koch (mentioned in connection with urine samples checked by K. Scott)
Compton (told of plans to do limited studies of human subjects)

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ELEMENTS AND EXPERIMENTS

plans for experiments on humans using the following radioactive elements:

- Plutonium (aka Product; experiment known as the Project)
- Yttrium
- Cerium
- Zirconium
- Strontium
- Thorium
- Americium
- Curium
- Phosphorus
- Iodide
- Sodium
- Arsenic

(The following do not necessarily pertain to Hamilton)

types of people experimented on:

- prisoners
- hospital patients, most commonly those thought to be terminal
- elderly
- mentally incapacitated
- children

types of experiments:

- whole-body irradiation
- testes (Oregon, Washington prison inmates, 1963)
- thyroid (traces in milk led to exp. of dose of iodine absorbed by children)
- liver, kidneys, muscles, and skeleton (plutonium)

BREAKTHROUGHS

we have copies of Hamilton's notes (from Pat Durbin's files) which suggest that CAL-II was and was injected with plutonium AND two other substances, yttrium and cerium.

NOTES FROM MONTHLY REPORTS ON PROJECT 48A

May 1945: "difficulty in extrapolation from rat to man makes it desirable that some human studies be undertaken with a representative short-lived stand in for the various types of plutonium aerosols." (p. 3 text)
about rats: "Prolonged excretion studies have shown that the elimination of product from this body is very slow, even when the animals are subject to the type of treatment usually employed in lead and radium poisoning. After intramuscular injection, a large part of the absorbed material becomes fixed in the skeleton." (p. 4 text)

June 1945: "A patient suffering from carcinoma of the stomach, received, by intravenous injection, approximately 5 µgms of plutonium as $\text{Pu}^{238}\text{Pu}^{239}\text{Pu}^{240}$, enriched with Pu^{238} so that the activity was equivalent to 50 µgms of Pu^{239} . Four days later, as a result of surgery, specimens of bone, spleen, tumor, omentum, and skin were obtained. The distribution patterns of these tissues were very similar to that observed in rats." (p. 1, more details pp. 2 and 4)

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under Table V: "The fecal excretion in the patient was far less [than the rat] but perhaps is related to his operation and subsequent lack of fetal output. More specimens will have to be accumulated before any conclusive opinion can be reached in regard to the rate of fecal excretion of plutonium by this patient. It is planned to continue the daily collections of both urine and feces from this patient for an indefinite period. In addition there is enough Pu²³⁸ for another human study when a suitable patient is available. It should be pointed out that we feel the use of Pu²³⁸ as a tracer for a limited number of selected patients is desirable since it is possible to use from 1 to 5 µgms of plutonium, which is the range of dosage in man that is of greatest interest, due to the high specific activity of this material."

July 1945: p. 7, he claims there is enough Pu²³⁸ for another human tracer experiment, and the cyclotron will generate more for Col. Warren and Dr. Stone of the Health Division of the Metallurgical Project, so they will have "as much as 50 microcuries of Pu²³⁸ for both additional human tracer studies and small scale toxicity experiments".

January 1946: is named

March 1946 through March 1947: references to tests at Bikini Atoll and to Operation Crossroads

September 1946: p.3 "...to present an opportunity to study the effect of these two radio-elements [yttrium and cerium] in human subjects such as patients suffering from leukemia and allied diseases. We do not anticipate doing the actual human experiments but rather will make our techniques known to Doctor Stone and any other interested parties so that they can undertake such experiments that may appear to be in the interest of the Project."

(Notice! this is 5 months after they injected CAL-2, who was suffering from leukemia and allied diseases, with plutonium, yttrium, and cerium.)

October 1946: "The successful method of the preparations of solutions that are essentially carrier-free yttrium and cerium at the pH of blood have been developed. Metabolism of these radio-elements following intravenous administration in the rat is almost identical with their behavior following intramuscular administration. This opens the possibility of human experimentation with these radio-elements due to the fact that intramuscular studies using human subjects are not feasible as a result of the large fraction of these radio-elements that remain unabsorbed at the site of injection."

November 1946: more on the possibility of human tracer experiments with cerium

December 1946: "Materials are being made ready for human studies by intravenous administration. The radio-elements being prepared for this purpose include strontium, yttrium, zirconium, cerium, thorium, plutonium, americium, and curium."

January 1947: more on all the above and plans to investigate radio-arsenic in mammals including humans, p. 3

March 1947: human studies ready to start for uranium

MISCELLANEOUS NOTES:

(The following based on Hamilton correspondence in the E.O. Lawrence files)

As early as 1943, Hamilton and Stone were corresponding concerning health and the metabolism of Pu. In a June 1, 1943 letter, Stone expresses interest in the effects of contamination in people. In 1944, the issues of biological experimentation and the need for human protection are brought up. Early correspondence seems to be fairly open, and secrecy does not appear to be a central issue. Plutonium is referred to as the Product, but the real name does occasionally appear.

In 1945 and 1946, most correspondence pertinent to the Project is classified; most records still extant by Hamilton which pertain to the Project appear to date from this period.

There is very little of this nature from 1947 to 1957. Project 48 is referred to (possibly project 48A), which is the code for the project under which Plutonium studies were conducted, among other studies (including the Uranium tracer experiments, Operation Crossroads or the Bikini Atoll environmental studies, and radiation experiments on animals). There are lists of people who have access to classified reports.

In the 1950's, there are some direct references to the project. In October, 1952, L. Van Middleworth asks if the old material on Plutonium from 1945-1946 can be published. In June, 1956, Hamilton specifically mentions the man with the ulcer who was injected with Pu [i.e.].

The correspondence from the 50's also includes mention of quite a number of other human subject experiments, such as human studies and astatine, radio-sodium, radioactive iodide (in normal newborn infants), fluorine, and others (some on dying people). The Subcommittee on Human Applications is referred to several times. In 1955, The AEC, Hamilton, and Ferrebee exchange letters regarding the sources of accepted dosages, which Ferrebee would like to see published.

A number of reports are published regarding the history of nuclear medicine and radio-isotopes, in which human experiments are either not mentioned or are mentioned with respect to the 1930's and radio-sodium or iodine, and treatment for thyroid problems or leukemia.

Most of the Hamilton files in the E.O. Lawrence collection pertain to Hamilton's work as director of the Crocker Lab, and document the use of the 60" Cyclotron.

(I believe there must have been two separate series: the classified materials and the general files; the classified series is still missing. These may have been sent to Livermore in 1967 or so, as we have transmittals of Hamilton's classified correspondence).

Date: 24.1.94

KENNETH SCOTT'S ORAL HISTORY

The Crocker and Donner Labs

Martin Kamen was in charge of isotope production

Dorothy Axelrod Heller made radioautographs with plutonium (because it is an alpha emitter and gets good pictures). Aside from fission metabolism work, Hamilton shared a contract with Axelrod, on the radiography of fissionable products.

Dr. Robert Stone worked in the UC Medical Center Radiology; did neutron therapy with John Larkin; he later went to the Metallurgical Laboratory Project as director of medical research.

When Crocker was started, and Lawrence left, Hamilton was brought in from outside to direct it. John Lawrence moved to the new Donner Lab with Hardin Jones and Cornelius Tobias.

Hamilton had the support of E. Lawrence, although he was not so close with John Lawrence. He had enough physics knowledge to run the 60" Cyclotron, so the cyclotron was turned over to him. He was working on a secret project on fission metabolism when he became director. Scott was hired as a lab technician 1 at Crocker and was not part of the secret.

Earl Miller, the doctor who administered the injections to human subjects, became interested in treating thyroid diseases with I^{131} through Scott and moved to the lab at the UC Medical Center.

Everything at the Crocker lab was classified at least till Scott left in 1951.

Manhattan District and the Project years

Hamilton had influence with people in charge. The 60" and the facility at the University of Chicago could produce isotopes, which is why they became important in these circles.

Stafford Warren, one of Scott's bosses, was a full colonel in the Manhattan District. He supervised people who worked on the first plutonium to experiment with, to find out where it went in the body.

There was a relationship between Hamilton and Seaborg. Hamilton was responsible for making a decision to have plutonium set aside for biological research, through Seaborg. Stone was not in this part of it.

Roy Overstreet and Louis Jacobson were soil chemists; they later worked on the Operation Crossroads in Bikini.

Scott was the major tracer person for Hamilton's project and at the Crocker. He hired Pat Durbin, who worked for him and Hamilton. Joseph Crawley was hired as well.

The crew of the cyclotron was only responsible for scheduling and operating.

Scott in San Francisco

Scott left in 1951 to go to the Radioactivity Research Center in San Francisco (separate from the Radiology Department); he became its director. Hamilton wasn't worried about his safety or the safety of others, and he was doing what Scott considered morally wrong experiments on humans. Scott had helped Hamilton and Earl Miller with the first one. He knew about the Australian boy who received some fissionable product, but did not work on that one.

Scott was on the Human Use Committee when it was organized in 1948. The Committee didn't put a stop to the experiments. The members screened applications one by one. Through this committee, UC got permission from the Atomic Energy Commission for blanket authority on various and sundry radionuclides.

He picked out Dr. Glenh Sheline as a chairman. Sheline is now a radiotherapist in the Department of Radiology; he is on loan to the National Cancer Institute. Scott decided chairmen because he was the only one who could figure out what radiation doses would do to people.

He finally became uninvolved with Berkeley. One could find out more information on the problems Berkeley had with human experiments from Hardin Jones or Cornelius Tobias.

Bikini Atoll

Hamilton and Warren recruited the staff for that. Scott was made Major and set up the radiological laboratory on the hospital ship "Haven". He saw the Able and Baker bomb tests. He gave assays of samples and set up monitoring and detection instruments. One man he trained, Kermit Larson, went to UCLA (where Warren was).

NOTES FROM OTHER COLLECTIONS 31.1.1994

Hardin B. Jones

We have four boxes of Hardin Jones' papers; most are reprints. Interfiled among these are some manuscripts and correspondence. Some manuscripts are incomplete and refer to experiments with infusions of elliptocytic blood on pregnant women, or infusions of radioactive blood in pregnant women to prove leakage to the placenta. (box 2, shelf 6572)

Cornelius A. Tobias

a restricted document was found, the project report for project 48A

Some Tobias papers contain correspondence pertaining to Hamilton, but most concern other activities involving human subjects. Tobias worked with John Lawrence and Joseph Hamilton on the study of decompression sickness during the war years. During the 50's, he conducted human studies with respect to cancer research and radioactive tracers, including radiopotassium. References are found to studies of thyroid problems and mammary cancer. Tobias also has records from the Subcommittee on Human Applications and the Subcommittee on Radiobiological Research (or some such name).

Records in the boxes I looked at included the following:

In box 5, the Manhattan District Declassification Documents include papers on the morphological changes in the lymphocytes of persons exposed to ionizing radiations (by Annamae Dickie and L.H. Hempelmann, 1948, #1102) and the determination of plutonium in human feces (by Elizabeth Maxwell, Robert Fryxell, Wright H. Langham, of Los Alamos, declassified in 1947, #1167).

In box 6, the Atomic Energy Commission Documents include a paper on hematological studies on patients treated by total body exposure to X-rays (by Low-Beer and Stone at the Argonne Nat'l Lab, 1948).

In box 26, letters to and from Tobias include a letter from Earl D. Neslen from UC Med. (1954) on getting radiopotassium for investigations on human subjects approved by the Radiation Safety Committee. Names mentioned include San Souci and Low-Beer. In the next folder, a letter regarding Oppenheimer and experiments on marine uptake of radioactivity. In the folder for Aebersold, Paul, a letter from Aebersold to Low-Beer: Low-Beer will attend a meeting of the Subcommittee on Human Applications; Dr. Stone has appointed a committee consisting of Low-Beer, Scott, and Miller to develop proper training at Low-Beer's medical school. John Lawrence is sending his representative, Tobias.

In box 27, reference is made to human studies and Carbon 14.

In box 34, reference is made to human studies on cancer and radioactive tracers (see folder cancer research 1953).

Note: Tobias Records from 1945 to 1950 are largely missing.

John H. Lawrence

Box 1/25: contains a mostly complete set of records pertaining to the study of decompression sickness undertaken from about 1942 to 1944. Lawrence worked with Hamilton, Jones, and Tobias on this project. They were either part of or corresponded with the Subcommittee on Decompression Sickness, part of the Committee on Aviation Medicine of the National Research Council (John Fulton, Chairman).

Most records are correspondence, filed alphabetically by name of correspondent. Letters worth noting are:

H.S. Bazett re subcommittee's work; also in Captain Crawford (March 12, 1942) and Du Bois (Feb 10, 1942).

letter to Hastings (Jan 26, 1942), to Officer in Charge (Nov 27, 42) asking for volunteers for a metabolism test from among army or navy ROTC members between 17 and 27 years old.

letter to Lewis, Chairman of the Advisory Committee, re people on the team studying the problem of aeroembolism: Dr's J.C. Larkins, J.G. Hamilton, Farnsworth Loomis, J.H. Lawrence, H.B. Jones, Robert Smith, Martin Kamen, Paul Aebersold, Chieng Wu.

Jack Mohney's name also begins to appear somewhat prominently.

to Richards (Jun 15, 42): CMR-9 forms covering people working on the team.

letter to Dr. Neuburgh re Hamilton and iodine use for hyperactivity of the thyroid (Sept 30, 43).

and so on (if interested, let me know, and I will type up the rest of my notes).

Note: J.H. Lawrence records from 1945 to 1948 appear to be missing.

From 1949 to the early 1950's, Lawrence's correspondence pertains to multiple smaller projects to study cancers in humans. Experiments conducted or planned include: using human subjects for studies of radioactive stilbamidine for multiple myeloma; carbon-14 experiments; radiophosphorous in polycythemia vera charity cases; the search for an antileukemia factor by injecting human subjects with leukemic blood; red and yellow bone marrow and injections of phosphorous and sulfur; leukemia and the experimental use of ACTH and ammopteriu; red blood counts and pregnant women; blood conditions in Peruvian Indians; radioactive iodine and the treatment of Grave's disease; the localization of brain tumors with radioactive diiodofluorescein; and the effect of cortisone on leukemia.

Key people involved include: Shields Warren, bigwig in the AEC, to whom applications for permission to use human subjects were sent; in one instance, he refused permission because not enough animal studies had been done (folder U-Z 1949, box 3/25). Nathaniel Berlin, re C-14; Dr. Huff, re iron metabolism studies using P-32; John Gofman, Paul Aebersold, Charles Perry (Secretary for Subcommittee on Permissible Internal Doses), Low-Beer, and Merck.

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In his oral history (box 5/18), he states that in studies with injected substances, some patients may have been overdosed, but they were going to be terminal anyway.

NOTES FROM THE D.C. FILES

Date: 4 Feb. 1994

The restricted document I found last week, Hamilton's Report on 48A-1, was found again (I assume it is the same); the classification status was removed.

The D.C. Files generally contain information highly relevant to experiments on human subjects in the following folders:

- Projects and Building--Crocker Lab
- Accelerators--60" Cyclotron
- Medical Physics
- Chemistry

Key investigators represented in the files include:

- John Lawrence
- Joseph Hamilton
- Rex Huff
- Nathaniel Berlin
- John Gofman

Members of the Division of Medical Physics:

- John Lawrence
- John Gofman
- Hardin Jones
- Cornelius Tobias
- Nathaniel Berlin
- Rex Huff
- Nello Pace

Some experiments which seemed especially relevant to our searches:

1) John Lawrence's fieldwork in Lima, Peru, 1950 and 1952:

Lawrence seems to have been working with Professor Alberto Hurtado, of the University of Lima, Lima, Peru. Hurtado was one of the leading high altitude physiologists, and a new high altitude laboratory had just been completed in the Andes for him and his staff. Lawrence and other members of his group, including Nathaniel Berlin, were guests of Hurtado and were studying high altitude physiology and polycythemia. To do this, radioactive elements such as iron and phosphorus, and possibly carbon-14, were shipped to Peru, and experiments were carried out on native people of the high Andes. The relevant papers have been copied.

2) Lawrence apparently conducted some studies on convicts at San Quentin in 1949. It is unclear what this research actually was; a Dr. Leo Stanley was also involved. The relevant papers have been copied.

3) We have some project reports on research activities covering the time from the 1940's to 1951:

A Report of the Past, Present, and Future Research Activities for Project 48-A-1, by Joseph Hamilton. There is a concise summary of the nature of this project, as well as

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more detailed description of the the research and the results. It is apparent that Hamilton was covering up his later human subject experiments with plutonium. He and Dr. Stone were considering and already planning future tracer experiments with humans. There is a bibliography of reports written by members of project 48-A-1, as well as a list of students who worked on the project. (copied and filed in the Hamilton folder)

Program and Budget Estimate for 1948-49/Health and Biology Project/NDP 48C by Robert S. Stone, M.D. in Charge. There is a concise history of the project, which originally involved observing changes in blood counts of patients exposed to whole body X-rays; the history includes dates the researchers started using radioactive materials such as radiophosphorus. There is a list of reports which were submitted and a list of general conclusions.

The Activities of the Division of Medical Physics on Atomic Energy Supported Work Through February 1948; includes an outline and further description of the major fields of research endeavours. One of the fields was the biological effects of irradiation, done jointly with the Health Physics Division.

Proposal for continuation of studies on the distribution of gases, water and electrolytes in the human body, by Nello Pace, Project Supervisor. Studies were conducted on humans and included the use of radioisotopes, both by injection or by inhalation, in normal and ill subjects. The radioisotopes included sulfur, tritium, phosphorus, sodium, and calcium. Tissues studied included the heart, liver, lung, thigh muscle, and ankle bone. A list of participants includes Pace, San Souci, Lawrence, Jones, Siri, and others. It is possible, but I could be wrong, that the normal subjects used for this were the prisoners stated above. The project was originally called "carbon monoxide physiology".

Projects (under way in the Donner Lab). A list of 12 projects is followed by a description of each with goals and results where applicable. They include the following studies involving human subjects: studies with carbon 14 labeled stilbamidine, liver flow in leukemia, iron metabolism in hyperplastic and aplastic conditions of the bone marrow, blood volume measurements in leukemia, polycythemia, and cancer, carbon 14 labeled glycine studies and the life of the red cell in normal and neoplastic animals and patients, and others.

In addition to these records, there were others of a more general nature which seemed relevant. For example, there is correspondence pertaining to policy on human subjects, including copies of release forms used by the Donner Metabolic Unit. Lawrence was also working to establish a petty cash fund for studies on selected humans (1952-3), so that he could undertake blood studies without constantly seeking reimbursement. I also found correspondence from the AEC in which requests for uses of materials, including radioactive isotopes, were approved for use in human subjects; or correspondence in which requests were approved as long as no humans were used (some of these are addressed to Hamilton).

RESULTS OF THE EXAMINATION OF E.O. LAWRENCE RECORDS AT THE BANCROFT LIBRARY

Date: 11 February, 1994-28 February, 1994

Carton 5 60" Cyclotron Files: 1944

In May, Kenneth Scott informed Louis Hempleman how to ash human feces samples for "49" (I still am not sure what 49 is).

Hamilton's secret reports were routed to E.O. Lawrence, to the Area Engineer at Berkeley (in duplicate), to Robert Stone at Clinton Labs, and to Stone at Chicago; in some cases, also to Fidler. (see letter, Oct. 30, 1944)

Hamilton wanted to have human volunteers inhale briefly dust or smoke with tracer amounts of radioactive elements such as 3-day zirconium (Aug 10, 44). In a summary of activities of the Ber--- [illegible] Project from 1945, work planned included inhalation by human subjects of Zr^{89} as Zirconium Oxide, to determine the proportion of material retained in the lungs and upper respiratory tract.

Stone requested pieces of rib, liver, spleen, lymph nodes, and lung from a man with lymphatic leukemia (name of Donald Johnson) to be preserved in alcohol and sent to Hamilton; he wants both pre- and postmortem studies done. The request was made to Rochester. (Oct. 24, 44)

In December, Stafford Warren wrote a memo for the files concerning the Medical Experimentation Program on Radium and Product. There had been product experiments on rats since early 1944, and now they needed tracer experiments on humans. The rat injections were done by Dr. Cole in Chicago, Dr. Bale in Rochester, Dr. Hamilton, and Dr. Hemplemann. (Dec. 2, 44) In a summary of activities of the Ber--- [illegible] Project from 1945, work done included plutonium tracer studies in a human (Pu^{238}); the tracer studies were to be continued and initiated in a second human subject (with Pu^{238}). The Cyclotron correspondence also includes letters from Stone to Hamilton (Jul 30, 45) concerning payment to the first man for collections of feces and from Stone to B.H. Mackey and W.D. Norwood, MD, at Hanford, in reference to product determination in urine (Nov. 9, 45). There are also short notes to W.D. Douglass from Scott in 1946, informing him of the numbers of samples collected from _____ to date (name was mentioned). Scott also discussed an exchange of samples with Edwin R. Russell from patients injected with Pu (Ap. 15, 46).

1945

List of people in Hamilton's group as of January, 1945:

Chemists:

Dr. Roy Overstreet

Dr. Louis Jacobson

Physiologists:

Mr. Kenneth Scott

Miss Dorothy Axelrod

Mr. Henny Lanz

Mr. Robert Givens

Miss Josephine Crowley

Biochemists:

Dr. Douglas Copp

Dr. David Greenberg (consultant)

Technicians

Mr. Leo Herrera

Miss Marion Chace

Miss Elizabeth Cuthbertson

Miss Wylde Hammond

Mr. Lester Van Middlesworth

A memo from John Lawrence informed Hamilton that his patients were complaining of an adverse reaction to the new P³² injections; was there a heavy metal included in this preparation? (Aug 19, 45)

Hamilton sent a request to Captain Robert L. Miller, the Area Engineer in Berkeley. To survey the metabolic properties of the heavy elements, he wanted Ac²³⁷, Th²³⁰, Pu²³¹, 95²⁴¹, and 96²⁴⁶ to be made available to his group at Berkeley. These materials would be employed for a detailed investigation of their metabolic behavior in animals, and, if circumstances permitted, in man. (Dec. 27, 45) In 1946, he sent the Area Engineer, attention Russell Ball, a request for radioactive isotopes U²³², Pu²³⁸, and Ac²²⁷ for tracer research in man. Ac²³⁷ was part of the approved program for work on Project 48A-Div 1 (Nov 15, 46). Russel Ball, on behalf of AEC, sent notice in 1947 that approval for reports which deal with human experiments was being withheld for the time being (Feb 12, 47).

1946

Hamilton sent a summary of work accomplished and projected to Captain Joe W. Howland regarding the Pu projects and the inhalation experiments using oxides as well as soluble compounds of radioelements such as yttrium, zirconium, and columbium, ruthenium, cerium, and praseodymium. Also projected were tracer studies in humans using radium, actinium, uranium, americium, and curium, as well as tracer studies in humans using the most important of the long-lived fission products. The summary was routed to Col. E.B. Kelly, Prof. E.O. Lawrence, Col. S.L. Warren, Mr. K. Priestley, Dr. R.S. Stone, Dr. J.H. Lawrence, and the File. This list was crossed out and replaced with a handwritten one: Area Engineer, Prof. E.O. Lawrence, Dr. J.H. Lawrence, Mr. R.M. Underhill, and Mr. K. Priestley. (Apr 23, 46)

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1947

Many relevant papers from this year relate to Hamilton's attempts to get papers declassified, including those which dealt with human subject experiments. The rat and man paper was not declassified, but others were after minor changes and deletions. Many letters were exchanged between Hoyland D. Young, director of information division at Argonne, and Hamilton.

(1948 and 49--not much to note)

1950

There is correspondence between Wright H. Langham and Hamilton and between Langham and Harry Foreman at Crocker Lab concerning the patients who were once injected with plutonium in Rochester. Wright suggested he could get two patients to be treated with calcium ethylenediamine tetra-acetate (EDTA) as a therapeutic test. He was concerned about whether or not to experiment with versene (calcium versenate) on humans, and how he could avoid liability. He was thinking of starting up on Pu²³⁸ experiments again. (between Dec 12 and 18, 50). Foreman replied with a letter detailing who was involved in studies of various compounds on humans. For example Rubin had given EDTA to humans. (Dec. 20, 50). Joe Howland's role on the versene experiment was that he had contact with the patients; the patients were under the care of Dr. Waterhouse, who was associated with the Strong Memorial Hospital and with Howland's group. They had taken the urine samples (Dec. 23, 50). A letter to Hamilton from Thomas L. Shipman refuses approval for using versene clinically as yet, but to follow the lead (Dec. 27, 50). Versene is a chelating agent, and could be used for excreting Pu from the bones; but it was also very toxic. In 1951, there is a progress report on the Use of Chelating Agents for Accelerating Excretion of Radioelements, including EDTA and Fe³, by Foreman.

1953

The following studies on animals were under way:

- astatine studies, on the selective localization in the thyroid of astatine, for possible later thyroid carcinogenesis and pituitary tumors

- tracer studies with all sorts of radioelements (scandium, thulium, tungsten, iodine, astatine, versene)

- chelating studies on the effect of versene in diet by parenteral injection into animals with plutonium and curium, and on the use of berkelium or californium as tracers

- radioautography, to study the deposition and localization of either radioelements or radioactive particles, including astatine studies and plutonium inhalation studies

Scott informed Dr. L.K. Bustad that he had done no studies of versene and removal of lung aerosols, only of versene and the removal of Pu from soft tissue and intramuscular injection sites. (March 4, 53) A letter from Hamilton to F.G. Nicholls in answer to a query reveals that Hamilton had no experience in the USA of the effect of the

administration of EDTA on calcium blood levels, but lots on EDTA and its compounds on calcium blood level [almost sic] (May 21, 53)

A project report dated October 52-June 53 summarizes a study of two general techniques of labeling plasma proteins compared in a number of normal individuals. The first involved the simultaneous administration of I^{131} tagged albumin to determine turnover pattern of exogeneously labeled protein moiety, and the second involved the administration of S^{35} labeled cystine or methionine following incorporation and disappearance of S^{35} labeled albumin and globulin.

Project proposals of 1953 include descriptions of astatine studies, studies of the radiological effectiveness of injury produced by alpha-particles and beta-particles, and the effects of heavy nuclei in biological systems.

1954-1955

Hamilton took human thyroid slides from patients given tracer amounts of At^{211} ; two had thyroid carcinoma, the other 6 had different types of non-malignant, fibrotic tumors (letter to Hermann Lisco on March 25, 55). He had been doing studies at least since 1954 to see if he could treat hyperthyroidism and carcinoma of the thyroid gland.

1956

references to cases of skin-contamination from Pu at Hanford (Feb 3, 56, from _____ at Hanford to _____), and to Na^{22} experiments on humans (Feb 6, 56, from Harold Elnick of the Veterans Administrative Hospital).

Carton 8

In 1936, Hamilton and Dr. Stone conducted studies of 3 leukemia patients and NA^{24} . In 1937, he studied radioiodine and thyroid disorders; this was continued during the war by Dr. Soley and Dr. Miller. In 1938, he studied the rates of absorption of radioactive isotopes of sodium, potassium, chlorine, bromine, and iodine in normal human subjects. His bibliography should have more of this information. (In 1956, Aebersold requested information on when the first tests on humans were with irradiation at the cyclotron, with isotopes Na^{24} , P^{32} , and I^{130} . Isotopes in medicine were used at Berkeley, Chicago, Michigan, and Boston. Low-Beer and Erf did studies of phosphorus at Berkeley. Aebersold then wrote a history of this called "Development of Nuclear Medicine".)

Jan. 28, 1948, Hamilton sent Wensel a summary of OSRD contracts he worked under. These include:

- NDRC-8 OEMsr-456 (Feb 1, 1942 to Aug 31, 1944) Hamilton and Axelrod studied mustard gas and Levisite (?)
- NDRC-9 OEMsr-196 (June 1, 1942 to Dec 31, 1944) Hamilton and J. Lawrence
- NDRC-12 OEMsr-799 #9938 (Oct 1, 1942 to Apr 30, 1943) Scott, Axelrod, Copp, Fisher, Crowley, etc; this project became NDP-48-A-1
- NDRC-Research E-54 (Nov 1, 1942-Apr 30, 1943) Hamilton and Chaikoff (?) (strontium?)

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With respect to 48A, the records include an Oak Ridge Health Physics Division Organization Chart from 1953 (Nov 12, 53).

The cover letter for a report on Fission Product Warfare (July 7, 48) shows that it was routed to D.T. Briggs (Project Rand, Douglas Aircraft), E.O. Lawrence, Shields Warren, Gen. McCormack, R.S. Stone, and Kenneth Scott/J.G. Hamilton. With respect to radioactive warfare, the records include Hamilton's job description as a member of the test safety panel for the chemical corps (Sept 30, 52) and records with reference to Dugway (letter to Marquand, Oct 28, 52). He also sent Morgan (at Oak Ridge) a report on the progress on aerosol studies using uranium oxide to produce Pu²³⁹ (Nov. 6, 53).

The Subcommittee on Medical Instruction and Research, appointed by the Committee on Educational Policy, was concerned with the establishment of the Metabolic Unit at Cowell Hospital and with the employment of human subjects for clinical investigations. The Subcommittee wanted Hamilton to accept an appointment, to serve with John Lawrence, Stone, S.R. Mettier, and Chairman P.M. Barr (Jan. 12, 49).

The records include a curriculum vitae of L. Van Middlesworth (March 17, 54), as well as a copy of his paper "Radioactive Iodine Uptake of Normal Newborn Infants"; six of the infants were black, and one was white.

Carton 20

Among the records of the University of California--S.F. Medical School 1933-1943 is a "Proposed clinical investigation of activated sodium chloride" by Robert Stone, ca 1940; Stone also discusses the first clinical experiment of radioactive sodium chloride on humans. On April 2, 1946, he informed E. Lawrence that he was worried about treating human patients with neutrons, and that animals should be used instead. In communication with the Area Engineer (Apr 17, 46), he and Miller provided a report and proposed program on the effects of X-rays and radioactive elements on human subjects and animals (Exp. 48C). Since 1942, they had followed some 29 patients with blood studies from before, during, and after.

In the Administrative records 1943-1946 is a proposed plan for the Medical Physics Department and an organization plan for Medical Physics: points 2a, b, c, and d discuss recommendations on who will work for whom and what to do about human subjects (including the fact that all human subjects should be experimented on in San Francisco).

Carton 29

Manhattan District--Health Division Group 60" Cyclotron Monthly Reports 1943-1944

1943: tracer studies with Uranium-free fission products (zirconium, columbium, ruthenium, barium, etc.); decontamination studies on animals being undertaken by Drs. Copp and Greenberg.

1944: same as above, as well as intramuscular injections, emanation studies, radiative smoke and dust studies, and radioautographic studies. In the May report, the first mention of subject is included on the title page; it appears that two reports are filed from now on, one for Product studies, one for other 48A activities*. The focus on Pu had been

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increasing since March. Also, for the first time (I think), there is mention of humans under the heading "tracer studies": "it now appears that it will be feasible to use the intravenous route for human studies that should be reasonably quantitative from the interpretive point of view." Projected studies include the following: Dr. Copp and Dr. Greenberg within the next month will transfer most of their efforts from the decontamination studies with the fission products to the experimental program with plutonium. A large share of their work will, of course, be an attempt to evaluate possible methods of decontamination of individuals who have become infected with Product. However, at the same time the character of these studies with plutonium will serve to amplify the fundamental tracer studies now in progress."

The June special report, under subheading "tracer studies", includes: "...an attempt will be made to tie together all of the available information and interpret it in terms of what may reasonably be expected to take place in humans following the accidental introduction of plutonium into the body." (The June regular report contains the first mention I have come across in these reports of soil studies, with samples taken of drainage at White Oak Creek; studies were conducted by Drs. Overstreet and Jacobson, at the request of Dr. M.D. Whitaker.)

*(In fact, in carton 28, folder 41, there are instructions from Stone to Hamilton on Feb 24, 45, as to the procedure for the monthly reports: Hamilton was to make two reports, one for regular investigations, one for secret investigations. He was to send the reports to the Area Engineer, the Chicago Area Engineer, Stone, and his own files.)

1945: In April of 1945: (last page) "As a result of a misunderstanding, the sample of Pu²³⁸ which was in the possession of Dr. Latimer's group, contained less of this isotope than we had originally understood it to possess. Due to this fact, it will not be possible for us to employ this particular sample for a human metabolic study." Under projected studies: "For the last two months, radio-autographs, smokes, decontamination, and human studies will be continued." This is the first mention, to my knowledge, of human studies in these reports on plutonium.

(By the way, all reports are signed by Kenneth Priestly, business manager at the RadLab, and all are routed to Area Engineer M.J. Barnett. In carton 30, folder 16, there is a proposed standard distribution list for the Manhattan Engineer District reports from 1944 to 1945; under Health and Biology/Fissionable Materials, and also under Health, the routing would be as follows: 4 copies, 1 to Hamilton, 1 to Stone, and 2 for the files.)

May 10: "Puppies have been injected intramuscularly with plutonium to study overpayering of the plutonium deposits in an animal which closely resembles man with respect to bone metabolism." (p. 4)

1946: October 31: (p. 1) "The successful method of the preparation of solutions that are essentially carrier-free yttrium and cerium at the pH of blood have been developed. Metabolism of these radioelements following intravenous administration in the rat is almost identical with their behavior following intramuscular administration. This opens the possibility of human experimentation with these radio-elements due to the fact that intramuscular studies using human subjects are not feasible as a result of the large fraction of these radioelements that remain unabsorbed at the site of injection." On p. 5, he again mentions the possibility of experimenting with radio-⁹⁰yttrium and cerium on

humans suffering from leukemia and allied diseases. December: (p. 3, tracer studies)
"To date, it appears that satisfactory preparations of yttrium, zirconium, cerium, strontium, barium, and plutonium can be made for intravenous use in man."

monthly reports NDP 48A from July 43 to December 46 by JGH were declassified on 2/10/61.

Among papers found in the folder titled "Manhattan Engineer District--Health Division Group 1943-1944): a letter from Stone to Hamilton, dated June 1, 1943: "the idea is something like this--if you wished to raid a place and make everybody nauseated, vomiting and incapacitated within a period of 24 hours, how much radioactive material in either gamma-ray or beta-ray emitter type is needed?"

Carton 2

folder 30--Dec 46: Report of work during month of Dec., 1946, includes description of Total Body Irradiation with X-rays and P³², by B.V.A. Low-Beer. He had three patients started under a program of X-ray irradiation and followed with regard to bloodcount. Radioiodine studies were done under the leadership of Earl Miller; 12 people were given radioiodine in December to track the amount of iodine in the body. In January 10 resume of current work with radioactive materials in the Donner Lab of Medical Physics, it is mentioned that the short-lived isotopes of zirconium and yttrium can be made which would be useful immediately in clinical studies of circulation in man.

Carton 25, folder 10: Jan 9, 46: Stone asked Hamilton to help the University of Chicago again; Hamilton would be getting instructions from either Miller or Low-Beer. Lawrence had already agreed to help. It is not stated what the purpose of the help would be.

Carton 31 folder 3: E.O. Lawrence's Oct. 1, 1947 research program of the Radiation Lab. at UC for the coming four years report, p. 11, describes the biological and medical research program: Metabolism of fission products (under leadership of J.G. Hamilton)--projected plans call for continuing tracer studies of fission products and extend these to include rare earths; they will be studied in the body [but whose body is not specified]. Medical effects of radiation (under Stone)--the effects of radiation from internal and external sources will be studied; the program was started in 1942 as a study of the effects of total body X-ray treatments on the blood of patients and was expanded to include the effects originating internally from P³² and I¹³¹. Biological effects of radiation (under J.H. Lawrence)--the continuing study of the biological effects of radiation, with comparative studies of other forms of irradiation of tissue in situ for both research and health protection; it includes selective tissue irradiation with phosphorus, yttrium, zirconium, lanthanum, and uranium. Appendix I shows a summary of research and development work in progress or planned. p. 21 is copied below:

D. Biological and Medical Research

Biological and Medical Studies at "0"

1. Tracer studies using technetium, silver, indium, tin, antimony, samarium, europium, actinium
2. later tracer and autographic studies of gallium, germanium, selenium, rhodium, palladium, and cadmium
3. Investigate metabolic properties of the eight rare earths
4. deposition of lanthanides and actinides in the skeleton
5. treatment of poisoning from plutonium and trans-plutonium elements

Medical Research at U.C. Hospital

1. Effects of total body X-rays with lab as well as clinical work
2. study of effects of radiation originating internally from P³² and I¹³¹
3. use of animals to check effects seen in humans and to anticipate results in humans
4. study skin reaction to radiation from X-rays of all energies, gamma rays, beta rays, alpha rays, and neutrons
5. investigations in (4) extended to plants and animals
6. cause and cure of radiation sickness

Medical Research at Donner Lab and Elsewhere

1. selective tissue irradiation involving radioactive colloids of phosphorus, yttrium, zirconium, lanthanum, and uranium
2. biological effects of fission
3. biological effects of high energy neutrons
4. use of large animals in long range studies of item 3 with particular interest centered in carcinogenic and longevity studies

folder 19: 30 April, 1947 letter to Stafford Warren from Carroll Wilson, general manager: (second paragraph) "In any such clinical testing, the Commission continues to request that the same procedure be followed which was agreed upon early in March. That procedure contemplated that it should be susceptible of proof from official records that, prior to treatment, the individual patient, being in an understanding state of mind, was clearly informed of the nature of the treatment and its possible effects, and expressed his willingness to receive the treatment. In view of your recommendation, the Commission does not request that written releases be obtained in such cases, but it does request that in every case at least two doctors should certify in writing (made part of an official record) to the patient's understanding state of mind, to the explanation furnished him, and to his willingness to accept the treatment."

Nov. 21, 1947: letter to Hamilton from H.A. Fidler, chief declassification officer, states that it is touchy to declassify Hamilton's paper on the metabolism of polonium, plutonium, and radium, because Fidler does not want inferences to the Project to be known; plutonium technology must still not be revealed.

Oct. 21, 1949: letter to Charles C. Dunham, MD, Office of Director, Division of Biology and Medicine, AEC, from Kenneth G. Scott: summary of general plan of investigations under Project NDF48A1: "Studies upon the usefulness of radio-isotopes to humans with cancer are being conducted in collaboration with other members of the Divisions of

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Radiology and Medicine at the University of California Medical School in San Francisco. Owing to the fact that Doctor Hamilton and I hold staff appointments in the Medical School, it has been possible to set these studies up on a non-project basis. They are centered around facilities within the department of Radiology and at the Laboratory of Experimental Oncology at Laguna Honda Home. Those efforts do not receive A.E.C. financial support but are maintained on research grants (approximately \$50,000 yearly) from other sources. It is obvious, however, that data gained upon the fate of test doses of various fission products in man, is of interest to the Atomic Energy Commission." Non-project 48A-I personnel listed at the end of the letter are Harry Foreman, M.D. (Crocker Lab), and S.P. Masouredis, M.D. (Laguna Honda Home).

folder 21: Nov 28, 1950 letter to Shields Warren from Hamilton concern his ideas for the meeting on Dec. 8, which Hamilton will not be able to attend: (p. 2-3) "It seems to me that it is very desirable to determine in man the range of total body radiation required to induce an appreciable decrease in his capacity to execute intricate tasks for which physical well-being is essential. If this be done, it should in my estimation be not only total body radiation, but from gamma rays in the 1 to 2 MeV energy level. For both politic and scientific reasons, I think it would be advantageous to secure what data can be obtained by using large monkeys such as chimpanzees which are somewhat more responsive than the lower mammals. Scientifically, the use of such animals bears the disadvantage of the fact that they are considerably smaller than most adult humans and a critical evaluation of their subjective symptoms is infinitely more difficult. If this is to be done in humans, I feel that those concerned in the Atomic Energy commission would be subject to considerable criticism, as admittedly this would have a little of the Buchenwald touch. The volunteers should be on a freer basis than inmates of a prison. At this point, I haven't any very constructive ideas as to where one would turn for such volunteers should this plan be put into execution. There is much to recommend the use of adult males past the age of 50 in good physical status. However, one can't be certain that these people would respond in a similar manner to the 20 to 40 age group. In concluding, the picture as I see it is to ascertain what is the disabling range and factors which might influence it."

Carton 32

folder 21, Biomedical Research 50-51: There is some exchange between C.E. Andersen and Hamilton concerning the search for agents which might be useful in the removal of plutonium and fission products from the body. Hamilton sent Andersen a memo (March 14, 51), summarizing the activities of Harry Foreman, an AEC postdoc, doing work on this project (p. 6). He also mentioned his collaboration with Dr. Howard Myers at the UC School of Dentistry on the use of radiofluorine as a tag to determine the retention of this element on human teeth, to see if sodium fluoride did reduce cavities. in folder 22, Biomed. Research 51-52, Hamilton sent Andersen another report (May 3, 51) on the biological effects of heavy nuclei. He stated (p. 2): "The biological systems to be subjected to this type of radiation presently considered are the puch of the hamster, shaved skin of small laboratory animals, and transplantable tumor cells. If the results on animals show unusual interest, it might be desirable to explore the possibility of irradiation of small areas of human skin, notably that of the forearm. It is believed that this could be done quite safely since the general radiation level of the cyclotron under such conditions is quite small. Again, I should like to emphasize that any human

studies are purely speculative and would under any circumstances be undertaken with the full knowledge and agreement of the Director of the Division of Biology and Medicine and his associates."

Hamilton's 1952 project proposal includes the following:

- human studies and astatine
- chelating studies (Scott and Hamilton, Jan. 1952) of the calcium complex of Versene and Fe^{3+} ; studies in animals, with diagnostic use in people

a list of Hamilton's projects for 1952 includes the following:

- tracer studies (radio-scandium, radio-thallium, radio-tungsten)
- chelating studies (Ca EDTA)
- oral ingestion of fission products and plutonium in the monkey
- effects of heavy nuclei on biological systems
- radiation chemistry
- astatine studies
- radioautographic studies
- inhalation of tagged silicon dioxide

folder 23: a letter from Hamilton to Walter Claus, Director of Biology and Medicine, makes reference to the Sunshine Project. Hamilton is referring to reprints on the use of radio-strontium in human beings in the following: "Frankly, in looking over all these reprints including those of the University Press, there is not too much of value, inasmuch as these patients were not followed up in any great detail. However, I discussed the matter with Dr. Stone, explaining the need for obtaining this information and the available hospital records of these patients, the majority of which were treated at the University of California Medical Center, and he assured me that you would get all possible information pertaining to the matter and in particular to changes in the blood picture, and forward them to me as soon as possible. He is aware of the significance of this "Sunshine Project" and I told him that he should be the only person in the San Francisco area that would be aware of the importance of this particular project even though several members of his organization have "Q" clearances. As soon as the data that he can obtain is forwarded to me I will see that your office gets as much detail as can be gleaned from the hospital records of these patients." (Jan 28, 54) Another letter to Claus (Feb 3, 54) refers to the disaster at Chalk River, where several people inhaled or ingested Strontium 90; Hamilton suggested that a follow-up of these people and those in contact with the clean-up could be useful to the Sunshine Project. Strontium 90 becomes retained in the skeleton after a few weeks; but, he said, it has a 60 hour Yttrium 90 daughter. A letter from two days later to Stone from Charles Dunham, Chief of Medical Branch, Division of Biology and Medicine, asked for follow-up information on people given radiostrontium in 1942 to help set maximum permissible concentrations of a variety of radioisotopes in water supplies. This was also sent to Claus, Hamilton, and John Lawrence.

From 1941-1944, 8 patients received strontium lactate; 5 received radioactive strontium 88; and 3 received non-radioactive strontium lactate. There are charts among the records with information on these people (names, dates, dosages, etc.) The principle investigator on this project appears to have been Low-Beer.

a June 19, 54 letter from Hamilton to Claus (and routed to Dunham, Bugher, and the Hamilton file as well) reports that L. Van Middleworth stumbled onto something potentially touchy. He found radioactive iodine in beef thyroids in Memphis, and had asked Hamilton about beef thyroids in San Francisco. Hamilton tried to divert his attention (by claiming that it must have been from contamination from Oak Ridge). Middleworth went ahead and contacted beef companies in San Francisco and found radioactive iodine in their beef thyroids. Hamilton then got some himself, in a roundabout way so as not to attract attention, ostensibly for the further development of the isolation of non-radioactive iodine from the thyroid tissue. This was not really the truth, although it sort of was, since they were doing this sort of work for astatine experiments. Hamilton suggested that the animals were probably fed hay and alfalfa cut during 1953-54.

Sunshine and Gabriel code names were not classified, nor were the existence and purpose of the collection of samples, including human bones; but the results of the Sr⁹⁰ analyses and the comprehensive report were classified.

6 Nov, 56: a letter from Berlin to Hamilton contains a hand-written note saying "letter referred to destroyed"; a letter from Dunham (same date), however, refers to Hamilton's Nov 1 letter, with comments on the plutonium problem in Wright Langham's work. Nathaniel Berlin and Gordon Dunning are also mentioned.

A letter to C.B. Marquand, Director, Chemical Corps Advisory Council: Hamilton refers to Dugway and to the tests in the West of a similar nature, which will be continued.

Carton 28

Folder 40: a Feb 20, 1943 letter to Stone from Hamilton, in response to Stone's questions, described planned tracer studies: "...a procedure has been devised by which it is anticipated that both short lived and long lived active deposits arising from the slow neutron fusion of uranium can be suspended in the air and their distribution in the body determined following inhalation of these substances. In addition, it is planned to evaluate both the distribution and radiation effects of the raw fission mixture containing the long lifematerial upon human leukemia patients."

Jul 13, 1944: Stafford Warren wrote to Hamilton; he wanted Hamilton to accept the responsibility for directing the medical program at UC, to be the person who reports directly to the Area Engineer. Warren suggested that Hamilton could get Earl Miller to help.

Folder 41, Jan 30, 45: Stone wrote Hamilton with respect to human subjects injected with iodine. Hamilton was to do tests with Dr. Soley, without telling Soley the reasons for the studies being done at this time.

June 5, 45: Hamilton sent Fidler a proposed program for July 1, 45 to June 30, 46, including, in section 1b, "Plutonium studies: ingestion experiments with various compounds (including tracer studies on human subjects using 48)". It was approved by: C.A. Thomas on 8/3/45; A.H. Compton on 8/8/45; and Edgar J. Murphy of the U.S.

Engineers on 8/14/45. It was cc-ed to Norman Hilbern (assoc. project director for Metallurgical Project) and R.S. Stone. The following outline is taken from other sections of this proposal:

- I Plutonium
 - A metabolic behavior in tracer amounts
 - a) inhalation
 - b) injection
 - c) ingestion
 - B toxicity experiments
 - C decontamination studies
 - D fixation in soils
- II fission products
 - A metabolic behavior at tracer levels
 - B fixation studies on soils
- III other radioelements
- IV iodine studies using radio-iodine as a trace. object is to learn how best to block uptake of radioiodine by prophylactic means

June 18, 45: Hamilton wrote the following in a report on tracer studies, which were "needed for evaluation of health hazards which are related to nucleonics.

a. Expansion of knowledge concerning modes of entry, distribution within certain organs and tissues, and exact rates of excretion in man for polonium, uranium, and plutonium. Considerable information concerning the metabolism of plutonium in animals is available. Relatively little direct knowledge of the behavior of plutonium in man is at hand at the present moment. In the case of polonium and uranium both human and animal studies are far from complete. Thoroughly accurate quantitative values in the human for the distribution and excretion of these three substances are needed before reliable and realistic tolerance values can be established. The very probable large scale production of U^{233} suggests that this substance may approach in scope the problems of health protection already before us that have been the result of the preparation of plutonium in kilogram quantities. Moreover, the production of U^{235} containing up to several percent of U^{234} likewise emphasizes the desirability for very thorough study of the metabolic properties of this element.

b. The development of methods for treatment of individuals who have become infected with long lived radioactive materials such as fission products, plutonium, uranium²³³ and uranium²³⁴, etc. This work must first be initiated on the tracer level to permit a reasonably rapid survey of possible therapeutic procedures."

Jul 25, 45: William Bloom to Hamilton: "This is a fine experiment"

30 July, 45: Staffor Warren called for a review of the Manhattan District projects--only those directly related to the war effort were to be undertaken; longer term projects belonged to peace-time agencies.

Stone notified Stafford Warren (23 Jan, 46) that he was leaving the Metallurgical Project; he suggested, however, that work being done at the radiation Laboratory and at UC Med. be continued.

Hamilton sent a report on the research program from contract 48 to Col. E.B. Kelly (August 28, 46); the following excerpts are quoted:

"In addition to the animal experiments a very extensive study with plutonium 238 was undertaken employing a relatively normal human subject from whom several highly important tissue samples were secured including bone."

"The work planned for the coming fiscal year includes the following major items: First, we plan to perform more adequate inhalation studies with rats using the more important long-lived fission products; many of the earlier inhalation studies with fission products were unsatisfactory due to the unavailability at that time of what we now consider suitable technical methods. The projected experiments include the inhalation of oxides as well as soluble compounds of radio-elements such as yttrium, zirconium, and columbium, ruthenium, cerium, and praseodymium....it is planned to undertake inhalation studies with these agents using normal human subjects." (p. 4)

"Tracer studies will be initiated employing radium, actinium, uranium, americium, and curium in animals and humans using clinical materials available from the Medical School. In addition, tracer studies employing the most important of the long-lived fission products in such human subjects will be attempted if time is sufficient." (p. 5)

cc's of this report were sent to the Area Engineer, Prof. E.O. Lawrence, Dr. J.H. Lawrence, Mr. R.M. Underhill, Mr. K. Priestley, Col. S.L. Warren, Dr. R.S. Stone (this last name on 12-29-46).

Stone sent a letter to the Area Engineer referring to the therapeutic experiments being conducted; they included total-body radiation from external sources (X-ray), from internal sources (radioactive phosphorus), and he discussed observations of patients treated with radioactive iodine (Sept 12, 46). Hamilton sent the Area Engineer a letter (cc to E.O. Lawrence) with reference to the uranium, remarking that it deposits in bone, like Plutonium, as demonstrated in Chicago and here (Sept 16, 46).

(Nota Bene: Plutonium deposits in bone especially in humans; it will be remembered that the researchers were surprised at the high rate of bone deposition, since experiments with rats had shown other results.)

BANCROFT/MISC. COLLECTIONS

Date: Feb. 28-March 3, 1994

Robert S. Stone

Letters written to Stone A-K: A report, dated Dec. 7, 54, concerns the meeting of the AEC Subcommittee on Human Use of Radioisotopes. On Dec. 3, Low-Beer had expressed concern that there was no uniformity in the licensure for human use of radioisotopes. The committee recommended courses to train people in the use of radioisotopes.

Stone received a letter dated Oct. 20, 48, from Alan Gregg, a member of the Advisory committee on Medicine and Biology in the AEC. Gregg believed that X-ray treatment for arthritic patients was unjustified; he suggested that the committee did not want to collaborate in clinical investigations with physicians in whose judgement they did not have confidence. Some fairly sharp communications followed. (in folder "Letters written by Stone 1948-1954"): July 26, 48, Stone wrote Shields Warren in response to concerns about the treatment of arthritic patients. He claimed that the selection of patients, the choice of therapy, etc. had nothing to do with AEC; also, the radiation was given to patients with a reasonable expectation that it was therapeutic. He also sent a response (Nov. 4, 48) to Alan Gregg, slightly more scathing.

In response to a request by Shields Warren about patients' various reactions to radiation, Stone sent tables with information on people with hyperthyroidism who had been treated with radioiodine. The tables include patient names, total I¹³¹ dose, dates of first and last R_x, dates women became pregnant, etc. (May 26, 1950)

Shields Warren sent a note to Stone, from which the following is quoted: "I have delayed for some time answering your letter of May 27 because of the difficulty of clarifying in my own mind the problem of human experimentation. I am taking an increasingly dim view of it. I have talked with some of the people who were involved in the Illinois experiments and have learned something of the aftermath of one at the Massachusetts Prison Colony. The more I consider this problem, the more reluctant I am to go along with experiments of this type. record me as voting against human experimentation." (July 11, 1949)

Shields Warren (Oct 7, 49) suggested that the long-term/delayed effects of radiation on the human body of patients receiving radioiodine in therapeutic procedures could give a good opportunity to determine some effects of internally administered whole body radiation. He asked if Stone had noticed effects on 1) hematological picture, 2) fertility--menstruation or spermatogenesis, 3) electrolyte balance, 4) plasma proteins, 5) radiation sickness, 6) other abnormal responses.

Kenneth G. Scott

(folder: Reprints 1951-1952) excerpts from the Medical and Health Physics Quarterly Reports:

Jan-Mar 51: Hamilton's project included Astatine studies on the anterior chamber of the eye. Hamilton administered 500 mg potassium iodine for a week, then a shot of astatine, to see if it would break up a cyst in the cornea. There were no plans to repeat the experiment unless there was some improvement.

Also working on the thyroid and astatine studies were Scott, John Z. Bowers (formerly Assistant Director of the Division of Biology and Medicine, AEC), Dr. C.W. Asling (Assistant Professor of Anatomy), and Dr. Stuart Lindsay (Associate Professor of Pathology at U.C. Med.).

Tracer studies (being undertaken by Scott, H. Foreman, and J. Crowley) included studies of Ruthenium⁹⁷, Molybdenum⁹⁹, Palladium¹⁰³, Rhodium¹⁰⁵, Terbium¹⁶⁰, Rhenium^{183, 184}, Iridium^{190, 192}, and Lead²⁰³. They were trying to study the effects of versene on depositions of radioactive materials.

Jul-Sept 51: Tracer studies (Scott, Crowley, Patricia Wallace) of Tungsten¹⁸¹, Thallium^{200, 201, 202}, Gold¹⁹⁶, and Thulium¹⁷⁰.

Apr-June 51: Tracer studies (Scott, Crowley) of Platinum^{191, 193}, Iridium¹⁹², Mercury^{196, 197}, Bismuth²⁰⁶, and Rhodium¹⁰⁵.

folder Reprints 49-50 also has more quarterly reports, with more summaries of tracer studies by Scott, Crowley, Hamilton, and others.

Oct-Dec 52: Tracer studies--versene studies (Hamilton and Scott) to look for a procedure with results in the greater than normal elimination of radio-materials from the body; they were specifically looking at sodium and calcium salts of ethylene diamine tetraacetic acid, using Pu as the substance studied. Hamilton and Scott were also both involved in a study of inhalation effects of aerosols in monkeys using Pu oxide, and radiopotassium studies. Hamilton was also involved in rat astatine studies with Wallace, and Scott was conducting curium tracer studies with others.

misc. folder: There is a talk abstract from Scott and Henry F. Albronda of UC Med from Apr 19, 67: "A controlled study of Rb⁸⁶ Kinetics of erythrocytes from Schizophrenics". Blood samples were taken from 15 schizophrenic patients at Langley Porter Neuropsychiatric Institute and a control group of 19 members of the Medical Center academic staff; the blood was then treated with rubidium. A talk abstract from Apr. 14, 67 is entitled "A controlled study of Rb⁸⁶ erythrocyte kinetics of female patients with cancer of the reproductive system"; it was presented by Scott and Edmund W. Overstreet.

Stafford Leak Warren

Warren did his residency at Huntington Hospital in Boston; he had an appointment at the University of Rochester, where he did pioneer research at the Medical School on X-rays and cancer. His connection with Rochester is very early. During the war years, it was noted that the Rochester lab was the only one that could do animal work (p. 495, v. 2).

Stone's group was at the time working on fluorine, an offshoot of Dr. Harry Hedge's work at Rochester on fluorine in teeth. Stone and Warren knew each other quite early on.

Warren seems to have been responsible for worker safety at the different sites, especially with respect to the handling of radioactive substances, such as uranium. The Manhattan District's policy, according to him, was not to undertake contracts with firms which did not have adequate worker safety--for legal purposes. (This was however waved in the case of a Canadian firm, where the Manhattan District agreed to take unprocessed uranium).

Warren's recollection of Hamilton (p. 580, v. 2): "I didn't have much problem with the Berkeley people because Dr. John Lawrence, Ernest's brother, and Dr. Joseph Hamilton had already laid down the safety criteria for the cyclotron operation. John had gotten interested in some navy work so he didn't participate much in this [*use of uranium vs thorium**] but we relied on Dr. Joseph Hamilton. Dr. Hamilton had easy access to all the new fission products from the cyclotron group right there and then doing what we call quick and dirty experiments. First of all, they determined whether it was highly toxic material, whether it was a bone seeker that destroyed the bone marrow, how rapidly was it excreted, and so on. He was a beautiful experimenter, he did all of his on three points per dose level, which meant three rats. It was very cheap and very quick. And he could sacrifice his animals at intervals of days or weeks. He would come to a meeting every month and give day-to-day reports. We considered him a kind of explorer. He didn't want to do any of these long-term, big-scaled things. He was not that kind of an operator. He had a mind that was very quick and imaginative and he could take these small amounts from the cyclotron and in a very short time [finish the experiment]."

(* italics are my additional notes for comprehension)

DURBIN FILES
15-23 March, 1994

File drawer 1:

folder "RE-16 H" pertains to CAL-1 and includes the following records:
memo from DOE-SF, D.W. Pearman, Jr., noting the receipt of the list of 18 names, the paper titled "Update to 1977 Plutonium Injection Cases", another titled "Human Studies at the Crocker Laboratory", an abstract of paper titled "Survival, Causes of Death, and Estimated Tissue Doses in a Group of Human Beings Injected with Plutonium, and the publication titled "Plutonium in Man: A New Look at the Old Data".

Durbin's notes
graphs
draft of paper "Metabolism of Plutonium (Pu^{238}) in Man by Hamilton, Crowley, Lanz, and Scott
original notes and memos

folder "RE-16 H₂" pertains to CAL-2 and includes the following:
Durbin's notes, including name of patient, dates of birth and death, diagnosis, references to KGS's notebook and folder; mention of 14 children (one retarded); mass absorption on Ce graph; summaries of cartons Durbin looked at, of tissue samples; summary of activities around the injection of ; and pages from notebook

folder "Pu²³⁸" pertains to CAL-3 and includes the following:
Durbin's informational notes on Cal-3 (age, patient number, doctor attending--Dr. R. Mullen. These include the name of a witness to the tracer injection: Dr. B.V. Low-Beer.

Durbin's letter to Prof Oscar N. Ramabo, director of the Anatomy - Pathology Lab at UC Med Moffit Hospital, requesting information on the four people injected with Pu and Americium. She notes that some patients studied elsewhere were misdiagnosed. Durbin has the dates of injection and the descriptions of tissue specimens.

Letter to and from Doroth (Axelrod) Heller, who was working at the City of Hope Medical Center in Duarte, CA.

Letter to Howard G. Parker at Donner from Rambo: Rambo could easily help find slides and blocks from the patients who received plutonium, given the exact dates of operations and an indication of the tissues removed. UC Med has bound volumes of surgical reports in numerical order of acquisition which include date of procedures; and microscopic slides are stored forever. (Sept. 30, 68)

Correspondence with Argonne in regards to Cal-3 follow-up tests in 1973.
Notes

folder "Am [Cm?] H (95H) pertains to CAL-4 and includes the following:
Durbin's notes on Cal-4. Cal-4 had lung lesions and lesions in the knee and lower femur; he was diagnosed as having leukemia or sarcoma and admitted as patient #16244 on May 19, 1947 to UCMed?--he was a patient of the Chinese Hospital. He was injected (intramuscularly?) June 10, 1947 with Americium and underwent

PRIVACY ACT MATERIAL REMOVED

surgery on the 12th. He was monitored by Dr's Byron Hall and Dr. Lim. He was a 16 year old named _____ or _____ and he died on May 15, 1948.

Notes on tissue assays

Letter from Scott to Crowley re excreta from patient; they were to be brought to Crocker from UCSF.

folder "RE-19" pertains to the human experiments on inhaled zirconium and includes:

photographs

notes for JGH about procedures during the experiments; gas was inhaled through the left nostril and drawn into the lung, then exhaled through the mouth

assays from KGS

graph

A report was published pertaining to the inhaled zirconium, entitled "Studies on the Inhalation of Fissionable Materials and Fission Products and Their Subsequent Fate in Rats and Man" (K.G. Scott, H.C. Lanz, Dorothy Axelrod, Josephine Crowley, and J.G. Hamilton). The Zr^{89} aerosol was administered to one human subject and to rats. In the human, it was inhaled through a short rubber tube placed in the left nostril, and 100 cm³ of argon containing the aerosol was withdrawn for the assay. (p. 89 of report, found in file drawer three of Durbin's records.)

PRIVACY ACT MATERIAL REMOVED

Date: 25 March, 1994

NOTES FROM THE QUARTERLY REPORTS FROM PROJECT 48/48A

Medical and Health Divisions Quarterly Reports

October 1947-January 1948:

Hematological Effects of Total Body Irradiation from External and Internal Sources/B.V.A. Low-Beer: "The objective of this project has been to investigate the effect of therapeutic doses of ionizing radiations on the blood elements of human subjects. Patients selected for this study were those whose diseases required therapeutic irradiation of the entire body. The patients were selected for treatment with radiations and so treated by physicians on the staff of the University of California Medical School. Advantage was taken of the fact that they were being so treated to observe the effects on their blood picture. The clinical condition was followed by their physicians in the usual course of events and is not reported here. X-rays produced by electrical potentials of 100 kv, 200 kv, and 1000 kv were used for external radiation and radioactive phosphorus was used as a source of internal irradiation. From the inception of the project in October 1942 to June 1946 twenty-nine patients treated with external x-ray irradiation were studied. Two patients were treated with daily doses of 5 r; 5 patients with 10 r doses; 17 patients with 20 r doses; 2 patients with 15 r doses; 1 patient with 30 r and 1 patient with 50 r daily doses. All measurements were made on the skin... Studies included determinations of hemoglobin, red blood cell count, white blood cell count, platelet count, differential count, lobation index of polymorphonuclear neutrophils, sternal marrow studies, prothrombin time, sedimentation rate, hematocrit and icterus index. The observation period extended from one to three years following treatment." (p. 35)

Metabolism & Effects of Radio-Iodine (I^{131})/Earl R. Miller: "The purpose of the study of I^{131} in patients has been primarily to determine harmful effects of I^{131} , acutely and over a long period of time in humans. In order to know the amount of exposure of the patient to the radiation from the radio-iodine, it is important to study means of determining uptake of the I^{131} in the thyroid with the thyroid intact in the patient, and to study excretion of I^{131} .

Urinary excretion of I^{131} from patients has been measured in most cases in which thyroid uptake studies were made in order to determine what portion of the iodine could be accounted for by thyroid uptake and urinary excretion by our methods, what errors there were in the methods, and what fraction of the administered I^{131} was lost by other routes of excretion or was stored in other sites in the body.

Choice of Subjects. A few young doctors on the house staff of the University of California Hospital, fully cognizant of the dangers, volunteered to serve as normal controls. A series of patients were studied whose thyroid function was normal, but who were to have operations on the gland for nodules. This permitted study of the normally functioning gland as well as of the abnormal nodules. A number of patients were chosen for study whose primary disease was hyperthyroidism. The administration of relatively large doses of I^{131} to these patients, was warranted as a treatment of their disease. This was a particularly valuable group because of the interest of the patient in himself and his disease and because of the interest of the clinician in close laboratory and clinical follow-up. The last group of subjects were those in which carcinoma of the thyroid was suspected or proved. It was in this group that the largest number of tissue studies were

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made. In this group also, the administration of very large doses of I¹³¹ was warranted." (pp. 37-38)

Results on Patients, p. 41: no discernable results in most cases.

January-March, 1948:

Hematological Effects of Total Body Irradiation from External and Internal Sources/B.V.A. Low-Beer (R.S. Stone in charge, Project 48C) Objectives are same as those reported above. "The present report deals with the hematological changes observed in patients treated for arthritis with radioactive phosphorus administered intravenously." 21 patients were so treated; 4 men, 17 women, between 16 to 67 yrs old. (p. 41)

Metabolism & Effects of Radio-Iodine (I¹³¹)/Earl R. Miller: "From January 1 to March 31, 1948, 140 millicuries of I¹³¹ was received each month and was administered to 34 patients as follows: Tracer doses only (250 microcuries or less) ... 16, Test doses (up to 2000 microcuries per dose)... 5; Tracer and therapeutic doses ... 12; Therapeutic doses alone ... 1" (p. 46)

April-June, 1948:

Metabolism & Effects of Radio-Iodine (I¹³¹)/Earl R. Miller: tables with patient initials, date of injections, dose levels, and percent uptake; descriptions of some of the patients. 3 patients with carcinoma of the thyroid were given high doses of radioiodine; within two months, they had developed myxedema. (pp. 42-43)

July-September, 1948:

The Metabolic Properties of Plutonium and Allied Materials/J.G. Hamilton, Project 48A-I: Tracer Studies/Arsenic: "The site of deposition of arsenic in the red blood cells has been investigated. the major part of the arsenic is combined with the globin fraction of the hemoglobin of the red cell and this increases with the addition of arsenic carrier. These studies are being continued in order to determine if the same situation exists in the human as in the rat, since this method of labeling a red cell when combined with the radioautographic technique should enable one to determine the life of the red cell in the body in normal and abnormal conditions." (p. 5)

Biological Effects of Radiations From External and Internal Sources/R.S. Stone, Project 48C: Statement of the Program. "...the Arthritic Clinic of the University of California Hospital, composed of physicians from the Medical, Orthopedic and Radiological Divisions, became interested some years ago in the effects of total body irradiation on chronic arthritics, particularly those with ankylosing spondylitis. Such patients are therefore selected for this type of treatment by physicians having no connection whatever with the Atomic Energy Commission, and their treatment and follow-up is given by physicians in their capacities as members of the staff of the University of California. Project 48C, a hospital portion of the Radiation Laboratory, has taken advantage of the fact that these patients were being treated in this manner to study the effects of total body irradiation on the blood.

From the inception of the program in 1942 until October 1946, the patients were treated by exposure of their whole bodies to x-rays of various energies from 100 to 1000 kv. Starting in December 1946 radiophosphorus was used as the source of radiation, being given intravenously, and it has been used exclusively since that time. the last patient to be treated in this group received her final treatment on May 24, 1948." (p. 32)

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Hematological Effects of Total Body Irradiation from External and Internal Sources/**B.V.A. Low-Beer**: report on patients treated with S-ray and radiophosphorus. P³² obtained from Oak Ridge. 5 patients treated for arthritis, only one showed improvement, and one actually showed worsening; they will continue studies. (pp. 34-35)

Metabolism and Effects of Radio-Iodine (I¹³¹)/**Earl R Miller**: "In several patients with carcinoma of the thyroid, destruction of the thyroid has been achieved by radioiodine in doses on the order of 60 microcuries. Clinical and chemical myxedema has been produced. Destruction of the thyroid was carried out in order to see if the metastases would concentrate iodine when the normal thyroid ceased functioning. So far no success has been attained with this group of patients, most of whom has anaplastic growths. Studies are being continued on this." (p. 37)

Biological Studies of Radiation Effects/**J.H. Lawrence**, Project 48A-II Blood Coagulation in Polycythemia and Leukemia; Relation of Heparin and Platelets; Quantitative Measure of Clot Retraction and Heparin Clotting Time/**Robert L. Rosenthal**. A study of blood coagulation on 45 patients with polycythemia vera, 28 patients with leukemia, and 16 patients with other diseases. (p. 25)

Biological Effects of Radiation from External and Internal Sources/**Robert s. Stone**, Project 48C Hematological Effects of Total Body Irradiation/**B.V.A. Low-Beer**. "This report is concerned with hematological effects of radioiodine (I¹³¹) on patients. Two groups of patients have been observed. In one group, including eight individuals, seven had Graves' disease and one had chronic thyroiditis. A second group of eight individuals had carcinoma of the thyroid. Observations were made over periods from three months to one and a half years. Carrier-free I¹³¹ was administered orally. The doses varied from "test" doses to therapeutic doses. All total doses were given in multiple fractions of different size at different intervals. In the tables the individual doses are shown and the time of administration is given. Clinical management and radioiodine treatment of these patients including uptake and excretion studies are being carried on by Dr. Earl R. Miller." (p. 65)

1950 Publication:

Studies in Glycine 2-C¹⁴ Metabolism in Man 1/ The Pulmonary Excretion of C¹⁴O₂/**N.I. Berlin, B.M. Tolbert, and J.H. Lawrence** Sept. 1, 1950: concern about use of Carbon-14 in humans since it has such a long half-life; but animal experiments show most of it is excreted soon after intravenous injection. This study measured rate of pulmonary excretion of Carbon-14 as a C¹⁴O₂ when administered as glycine-2-C¹⁴ to four patients. Work supported in part by AEC. "The lack of hazard involved in the use of Carbon 14 in the manner described is discussed from the standpoints of excretion and possible retention in chemical compounds having a long turnover time." (p. 6)

October-December 1949:

Biological Studies of Radiation Effects/**J.H. Lawrence**, Project 48A-I Plasma and Red Cell Iron Turnover Studies in Normal Subjects and in Patients having Various Hematopoietic Disorders/**R.L. Huff, T.G. Hennessey, R.E. Austin, J.F. Garcia, B.M. Roberts, J.H. Lawrence**: "Iron tagged with iron 59 was injected intravenously into normal human subjects and patients having the following disorders: polycythemia vera, secondary polycythemia, lymphatic leukemia, myelogenous leukemia, pernicious anemia

[sic], hemolytic anemia, and refractory anemia. The concentration of the iron 59 in the plasma and the red blood cells was determined as a function of time. One or more total plasma iron analyses were made on each subject. In addition, clinical and laboratory studies were carried out.

The purpose of the studies was to determine the rates of turnover of plasma iron and red cell iron in order that comparisons might be made of the values in diseased subjects with those of normal subjects. This report concerns the comparison of the plasma iron and the red cell iron turnover constants with the clinical diagnosis." (p. 34)

April-June 1951:

The Influence of Heparin Upon Lipoprotein Metabolism/Dean Graham, John W.

Gofman, and Hardin Jones: there are certain classes of lipoprotein molecules associated with atherosclerosis in several experimental animal species and in the human developing or manifesting atherosclerosis. In this experiment, heparin is studied for its effect in changing the lipoprotein pattern. 20 patients were injected with heparin intravenously. (p. 49)