

HUMAN RADIATION STUDIES: REMEMBERING THE EARLY YEARS

*Oral History of Radiologist
Hymer L. Friedell, M.D., Ph.D.*



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MASTER



FOREWORD

IN DECEMBER 1993, U.S. Secretary of Energy Hazel R. O'Leary announced her Openness Initiative. As part of this initiative, the Department of Energy undertook an effort to identify and catalog historical documents on radiation experiments that had used human subjects. The Office of Human Radiation Experiments coordinated the Department's search for records about these experiments. An enormous volume of historical records has been located. Many of these records were disorganized; often poorly cataloged, if at all; and scattered across the country in holding areas, archives, and records centers.

The Department has produced a roadmap to the large universe of pertinent information: *Human Radiation Experiments: The Department of Energy Roadmap to the Story and the Records* (DOE/EH-0445, February 1995). The collected documents are also accessible through the Internet World Wide Web under <http://www.ohre.doe.gov>. The passage of time, the state of existing records, and the fact that some decision-making processes were never documented in written form, caused the Department to consider other means to supplement the documentary record.

In September 1994, the Office of Human Radiation Experiments, in collaboration with Lawrence Berkeley Laboratory, began an oral history project to fulfill this goal. The project involved interviewing researchers and others with firsthand knowledge of either the human radiation experimentation that occurred during the Cold War or the institutional context in which such experimentation took place. The purpose of this project was to enrich the documentary record, provide missing information, and allow the researchers an opportunity to provide their perspective.

Thirty audiotaped interviews were conducted from September 1994 through January 1995. Interviewees were permitted to review the transcripts of their oral histories. Their comments were incorporated into the final version of the transcript if those comments supplemented, clarified, or corrected the contents of the interviews.

The Department of Energy is grateful to the scientists and researchers who agreed to participate in this project, many of whom were pioneers in the development of nuclear medicine. □

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DISCLAIMER

The opinions expressed by the interviewee are his own and do not necessarily reflect those of the U.S. Department of Energy. The Department neither endorses nor disagrees with such views. Moreover, the Department of Energy makes no representations as to the accuracy or completeness of the information provided by the interviewee.

ORAL HISTORY OF RADIOLOGIST HYMER LOUIS FRIEDELL, M.D., Ph.D.

Hymer Louis Friedell was interviewed on September 28, 1994 by Eleanor Melamed and Dr. Darrell Fisher of the Pacific Northwest Laboratory, on behalf of the Department of Energy Office of Human Radiation Experiments.

Dr. Friedell was selected for the oral history project because of his participation in the early stages of the medical use of radioisotopes, his important role in the Manhattan Engineer District Medical Division, and his distinguished medical career and his involvement in the distribution of isotopes and the approval for their use in humans.

Short Biography

Hymer Louis Friedell was [REDACTED] He was naturalized in Hennepin County, Minnesota, in 1915, and received his education in Minnesota, from grade school through his M.D. and his Ph.D in Radiology, at the University of Minnesota. He is married and has three children. Before World War II, Dr. Friedell held positions as a National Cancer Institute Fellow at Memorial Hospital (New York) from 1939 to 1940, and at the University of California Hospital (San Francisco) from 1940 to 1941. At both institutions, he participated in experiments involving humans.

Dr. Friedell enlisted in the U.S. Army in 1942, and was stationed at the University of Chicago Metallurgical Laboratory. In mid-1943, Friedell was transferred to Clinton Laboratories (now called Oak Ridge National Laboratory) in Oak Ridge, Tennessee, to be the Executive Officer of the Manhattan Engineer District (MED) Medical Division. As the ranking medical officer in the MED, Friedell assisted in the direction of experiments to determine dose tolerances for the new radioactive isotopes. He also was involved in the review of applications for use of isotopes. His executive experience led directly to his membership on the Atomic Energy Commission (AEC) Advisory Committee on Isotope Distribution, and its subcommittee, the Committee on the Allocation of Isotopes for Human Use.

After World War II, Dr. Friedell resumed his academic and research career with positions at Western Reserve University in Cleveland and at the University of California. He frequently published his research in the '50s and '60s, but published only a few articles in the '70s. Some of his personal research involves the use of isotopes in humans. Following his service to the MED and AEC, Dr. Friedell served as chairman of the University of California School of Medicine Department of Radiology until 1978. He is currently an emeritus faculty member of the Case Western Reserve University, Department of Radiation Biology.

Dr. Friedell has been associated with Case Western Reserve University from 1946 to the present. He has served as the Director of the Department of Radiology since 1946, and as the Director of the Atomic Energy Medical Research Project since 1947. Case Western is one of the participating institutions of Argonne National Laboratory, and Dr. Friedell was a member of the Executive Board of the Council of Participating Institutions of Argonne National Laboratory.

Dr. Friedell has received the following professional appointments:

- Member, Plowshare Advisory Committee, Atomic Energy Commission
- Member, Reactor Safeguard Committee, Atomic Energy Commission
- Chairman, Committee on Allocation of Isotopes for Human Use
- Member, Subcommittee on Permissible External Dose, National Bureau of Standards
- Member, Subcommittee on Toxicity of Internal Emitters (BEAR I Report), National Academy of Sciences
- Member, Subcommittee on Internal Emitters (BEAR II Report).

Early Training and Research

MELAMED: This is September 28, 1994. We are interviewing Dr. Hymer Friedell at Case Western Reserve University. The interviewers are Darrell Fisher from Pacific Northwest Laboratory, and Elly Melamed from the Department of Energy. Thank you very much for agreeing to spend time with us.

As we [mentioned] to you before, this is meant to be an informational interview as part of the general initiative that we're working on; directed by Hazel O'Leary, the Secretary of Energy, to try to make as much information available about research involving human subjects. Our role is simply to locate records and give descriptions of where they are. And to supplement that, we're trying to interview people like yourself, who are involved in this effort; and just get your perspective on what went on and how you look back on it, and so forth.

FISHER: It's a privilege to be able to meet with you now, fifty years after the Manhattan Project. Can you believe that that much time has gone by?

FRIEDEL: I think I can believe it.

FISHER: I had a chance to talk to you a little bit after your address to the Health Physics Society, which was very interesting and well attended. It was interesting to hear your perspectives on the work that you have done—both as a physician, as an officer in the Army [Medical] Corps—and then your perspectives on your work since then.

As we read your biography and looked at some of the papers you'd published, and as I listened to your talk at the Health Physics Society meeting, I noticed that you had an early interest in radiation and the effects of radiation. Your earliest papers dealt with analysis of the functioning of the heart, using x rays. Do you remember this research, and can you tell us a little about it?

FRIEDEL: Yes I do, as a matter of fact. After I graduated from the medical school [at the University of Minnesota], I decided that I would pursue some postgraduate approach. And as you may possibly know, I first entered the engineering school [there]. I was a good science student and good in mathematics, and I thought it would be interesting if I entered the engineering school. However, my family had already one physician, and there were others coming along, and they sort of felt that I could perhaps

pursue an academic career in medicine—in—well, I shouldn't say an academic career, but a career in medicine. So I finally decided to switch, and enter the medical.

So, I'd had a year of engineering, and I'd had a long interest in science. And I thought one of the things that would be interesting, and perhaps exciting because of the new things that were coming along, would be radiology.¹ So I applied for residence at the University of Minnesota, where I graduated. And I was granted a residency, and I proceeded to pursue the appropriate curriculum. I also wanted to get an advanced degree, which was offered. So I then made arrangements to do some work in physiology.² There I met Ansel Keyes, who was an associate of Dr. Vischer. Dr. Vischer was a professor of Physiology and also [was] interested in the heart. And naturally, they directed my interests into studying certain heart problems, that lent themselves possibly to x-ray examination. That's how I began my interest, and how I pursued research.

I was always interested in finding out something, so I didn't have the ordinary [clinical] residency. And they permitted me to do research as well. I did a lot of the research with Dr. Ansel Keyes. And our research really had to do with the physiological changes in the heart, particularly in athletes. Somewhere in the record, if you go back, you'll find Ansel Keyes's work. We, for example, examined all kinds of athletes who came to the University of Minnesota; especially those who were long-distance runners, or who were special athletes, of some sort, in the things that required strenuous activities.

I then decided to get a degree in which my minor was Physiology. So, under the guidance of Vischer and Ansel Keyes, I then proceeded to get an advanced degree; a Ph.D., as you may notice. So we did a lot of work on that. One of the interests we had is, we sort of devised a system whereby we could measure the heart—systole³ and diastole⁴—and then try to correlate it with the actual blood propulsion; in other words, cardiac output. You may notice, much later on we even did some studies with radioisotopes—trying to do some special studies. I'd had a fair amount of experience in looking into the literature, and so on.

FISHER: But those isotope studies would have come after.

FRIEDEL: Much later. They were related, in a way, to things I'd been observing and pursuing in these early studies.

FISHER: You published on the heart, both before the war and after the war.

¹ the diagnosis of disease, broken bones, and other physical conditions using x rays or other imaging techniques

² the branch of biology dealing with the functions and activities of living organisms and their parts

³ the normal rhythmical contraction of the heart, during which the blood in the chambers is forced onward

⁴ the normal rhythmical dilatation of the heart, during which the chambers are filling with blood

FRIEDEL: That's correct. That's how I got started. Naturally, when I got into radiology—in those days we also looked at radiation therapy.⁵ One of the intriguing things was: "How does this radiation really do its work?" Slowly, slowly, we began to elucidate the mechanism of how this would happen.

FISHER: Was this at the University of Minnesota?

FRIEDEL: All at the University of Minnesota. I would say that the work in radiation biology then was, I would say, preliminary, maybe even superficial. Because no real study was pursued then, that could be identified in any way as radiation biology, for example.

Pre-War Radiation Therapy

FISHER: What sources did you use back before World War II for radiation therapy? What type of radiation sources?

FRIEDEL: We used primarily x rays, usually around 200-kV⁶ machines, for treatment. We used interstitial⁷ radiation and radium⁸ needles and radium plaques [for cancer therapy].⁹

There were radium bombs, that they called them. We didn't have one, but I was aware that such existed. So I began to look into this more and more. I simply pursued the studies as they appeared. I found it very interesting, and I thought our cardiac output studies were very good. But they were a little laborious and cumbersome, and whether they could actually come to fruition in this way, from the point of view of being a practical application in the hospital, I think was uncertain. My main interest was to see if we could do it.

FISHER: Did you have a patient load for therapy of cancer?

FRIEDEL: Yes, we did. The chief of the service was then Dr. Wilhelm Stenstrum, who was under the general direction of Dr. Leo Rigler, who was the director of that department, and who was a well-known—in fact a towering figure in radiology, if you look into it. The main emphasis was on diagnostic radiology. Because, after all, it did make an important contribution in the management of disease.

Then, I got interested enough that someone, I think it may have been Dr. Vischer, who suggested that I might get a National Research Council Fellowship; because I ought to perhaps look around and see something

⁵ the treatment of disease, broken bones, and other physical conditions, using x rays or other radiological techniques

⁶ x-ray machines operating at 200 kilovolts (1 kilovolt = 1,000 volts) for therapy were called "ortho-voltage" x-ray units

⁷ administered between the interstices, or narrow spaces, within an organ

⁸ a radioactive, luminous white, metallic element that occurs in very small quantities in combination with minerals. Radium emits alpha particles and gamma rays to form radon gas. Radium has been used in luminous surface materials, such as the numbers on watch faces, and used in treating cancer.

⁹ thin, flat plates with a thin layer of radium

more than what might be provincial in Minnesota. I'd really never been away from Minnesota much. So I accepted this, and I spent roughly three years, and I spent a year at the Chicago Tumor Institute, in Chicago. I was intrigued by that, because the director had, on the staff, Henri Cutard. Henri Cutard was one of the pioneers in radiation therapy. He came from France and had been working on special studies; particularly on the larynx.¹⁰ That was an interesting year for me.

I thought that he had many oddities in his approach to radiation therapy. He had an idea that there was an indirect effect. But his concept of an indirect effect, as compared to our biochemical approach, was a little strange. What he would do, occasionally, is that he would block off the tumor¹¹ and treat the surrounding areas, which he considered possibly indirect.

Anyway, I observed this, and I thought that, after a bit, I'd learned what his general concepts were; and he was obviously a very dedicated individual. But I thought I ought to see what the citadel of cancer work was at that time, which was the Memorial Hospital;¹² and they still [are]. So I got a year over there.

FISHER: In New York City. So you spent a year in Chicago, at the Tumor Institute?

FRIEDEL: Roughly, and a year in New York.

FISHER: How successful was radium therapy, back in those years before 1940?

FRIEDEL: It was fairly successful, in the sense that, if you use interstitial¹³ radiation, certainly you could shrink down local tumors; without any question. You see, the problem was: first of all, to get the very last nubbin of the tumor—was somewhat uncertain. But, in many instances, if the lesion was reasonably sensitive enough, you could obtain cures. The laryngeal studies that Cutard did were very impressive. Indeed, what it did was save the larynx in many instances. Because surgeons then were pretty aggressive. And if you had a carcinoma¹⁴ of the larynx, you could consider this possibility.

Now, it turned out, there's an anecdotal bit here: one of the patients at the Chicago Tumor Institute is a fellow by the name of Spencer Penrose. Spencer Penrose was an interesting man because, first of all, he was the brother of Boyce Penrose, who was then Governor of Pennsylvania, or had been Governor. I don't know the exact relations. Spencer Penrose had decided, when he developed a carcinoma of the larynx (he was, incidentally, a resident of Colorado Springs), that he didn't want the

¹⁰ the muscular structure that houses the vocal cords

¹¹ an uncontrolled, abnormal, circumscribed growth of cells in any tissue; neoplasm

¹² now called Memorial Sloan-Kettering Cancer Center

¹³ administered between the interstices, or narrow spaces, within an organ

¹⁴ a malignant tumor composed of epithelial tissue—the tissue layer covering body surfaces or lining the internal surfaces of body cavities, tubes, and hollow organs

surgery. And had heard about Dr. Cutard. So he went to Paris, and was treated by Dr. Cutard. Dr. Cutard came to the United States, Spencer Penrose followed him, and he had a recurrence.

What happened then was that Spencer Penrose was a very wealthy man. Incidentally, he was the man who discovered the Crickle Creek gold mine. So, he owned about half of Colorado Springs. He was the man who built the Broadmore [Hotel] in Colorado Springs. In any event, he got tired of being in Chicago, so he bought a 400-kV [x-ray] machine from GE and had it put in his house. Somebody had to treat him, so they sent me there, because I had had some experience. I spent about a month, or three weeks, treating him.

In any event, it was an interesting side note in this history of how we did things in those days. But then, after that I left and went to New York, and I spent a year there. I was still interested in many things in New York, so I used to sneak off to the Neurological Institute and look at some of the things they were doing in regard to special studies in neural¹⁵ radiology. There I met Dr. Quimby and Dr. [Gioacchino] Failla, who were then on the staff.

FISHER: Edith Quimby?

FRIEDEL: Edith Quimby. And I got to know their approach to this. They were then interested in interstitial radiation, in part, but also radiation therapy. And that's where I discovered that they were using total-body irradiation for various lesions. As a matter of fact—

(pulls out a book from his briefcase)

I brought this book along—I happened to look through it, and I found something that we will discuss at the appropriate time—that I had a list of the patients there, or I believe it to be the list, because I didn't note it very well.

Because, when I got into the Manhattan Project,¹⁶ there was a question of what we could learn about patients and their responses to radiation, especially total-body [ir]radiation, because we knew quite a lot about selected areas. After all, there was a fairly long history, with Bergonie and Tribondeau, who had done radiation studies on the sensitivities of various tissues.¹⁷ This had been going on for some time. There was a fair amount of gross studies in radiation biology. It was interesting to see whether there was any particular utilization of this at the Memorial Hospital.

¹⁵ relating to nerves or the nervous system

¹⁶ the U.S. Government's secret project, launched December 28, 1942 by the U.S. Army Corps of Engineers' Manhattan Engineer District, to develop the atomic bomb. Headquartered in Washington, the Manhattan Project was the Office of Scientific Research and Development Section on Uranium and was codenamed S-1 (Section One of the Office of Scientific Research and Development).

¹⁷ J. Bergonie and L. Tribondeau, French scientists who in 1902 discovered that immature, rapidly dividing cells were more sensitive to the effects of radiation than slowly dividing, well-differentiated cells

FISHER: At Memorial, were tumors other than leukemia¹⁸ and lymphoma¹⁹ treated with whole-body radiation?

FRIEDEL: Yes, they were.

FISHER: Even solid tumors?²⁰

FRIEDEL: Oh, yes. Because it was really an experimental study. They abandoned the study, because they couldn't have any effect, usually. They couldn't give the patients enough radiation. Besides, they were terminal patients anyway. They selected some for terminal studies, and this became of interest to us, and we will discuss it a little later, since you've identified this in your letter to me. I can tell you something about this, and I'll give you some of the records that I have, or at least you can copy them if you like. They were interested in interstitial radiation. They didn't get a lot of it. They used to use a lot of what were known as radon seeds. Really, little fine tubes of gold tubing, which were sealed off at the ends, and contained radon. Then you measured them so you had an idea of the dose, and then you could insert them into the tumors.

FISHER: They didn't last very long. Why did they choose radon seeds over radium?

FRIEDEL: First of all, the radium had to be removed. The radon seeds could be left in there because they were decaying. The half-life²¹ of radon, what is it, three-point-eight days, or something?²² They calculated the dose, and that's where Quimby and Failla were very helpful, in making these decisions about how to treat them and the distribution, and could make studies about how they should be distributed. That was intriguing too.

FISHER: Do you remember which types of tumors, again, these capsules were used on?

FRIEDEL: They were primarily used on solid tumors. Head and neck lesions were often used with this. Any localized tumor which would be accessible would be used. I think, rarely they did some surgery and found lesions that they couldn't do anything about, so they would implant seeds in them, as well. In general, solid tumors were treated this way. A lot of these were really confined to metastases²³ in the head and neck.

FISHER: Was there any successful use of whole-body radiation in New York?

¹⁸ any of several cancers of the bone marrow characterized by an abnormal increase of white blood cells in the tissues, resulting in anemia, increased susceptibility to infection, and impaired blood clotting

¹⁹ a tumor arising from any of the cellular elements of lymph nodes

²⁰ tumors forming solid tissue masses, as compared to the highly diffuse, liquid tumors characteristic of leukemia and lymphoma

²¹ the time required for half the atoms of a radioactive substance to decay

²² Radon-222 has a half-life of 3.82 days.

²³ plural of *metastasis*, the spread of disease-producing organisms or of malignant or cancerous cells to other parts of the body by way of the blood or lymphatic vessels or membranous surfaces; or, the condition so produced

FRIEDEL: It depends on how you identify success. If you think of lymphomas or high-sensitive tumors or leukemia, there was no question that you could suppress the white count²⁴ and suppress the tumors even. But you couldn't give them enough dose from whole-body radiation, as we could tell. The treatment for solid tumors was abandoned. They didn't use it. The only ones that were probably retained, and I don't remember this, certainly, were probably for highly sensitive lumps like leukemia with widespread infiltration or with, certainly, very sensitive lymphatic²⁵ tumors.

FISHER: How did you overcome bone marrow²⁶ toxicity in these patients?

FRIEDEL: We didn't. We simply made very careful studies of the bone marrow suppression by peripheral blood counts. Those were the major indicators of how far you could go with this.

FISHER: Was the symmetry good enough to have a good estimate of the full-body dose?

FRIEDEL: I think it was fairly good. Because Quimby and Failla were looking at this, and I think they had a fairly good idea. I wouldn't say that they had made careful studies. Because, after all, they were really guided by clinical responses as to whether they knew that radiation could interfere with cell proliferation or cell division.

FISHER: Do you remember what some of the treatment protocols were at that time?

FRIEDEL: I can't really recall them, but I think they treated them several times a week. Maybe three times a week, or something of that order.

FISHER: What total dose did they want to achieve?

FRIEDEL: That was, in part—usually they went to about 150 or 200 rads²⁷ for a total dose. Something on that order, as I recall. But they were guided mainly by what the responses were. And the primary response was white cell depletion, and probably the way a patient felt. Because, after all, some of them would get nauseated. These were the indicators. They were primarily clinical indicators.

FISHER: Was the gamma radiation²⁸ from radium sources?

FRIEDEL: As a matter of fact, they were used very little. But at the Chicago Tumor Institute, which is affiliated with the University of Chicago—incidentally,

²⁴ the count of the number of white blood cells in a specific volume of blood

²⁵ of the lymphatic system, the system of glands, tissues, and passages involved in generating lymphocytes and circulating them through the body in the medium of lymph; it includes the lymph vessels, lymph nodes, thymus, and spleen.

²⁶ the soft, fatty vascular tissue in the cavities of bones; it is a major site of blood-cell production.

²⁷ a measure of the absorbed dose to tissue from exposure to radiation; one rad is 100 ergs per gram of tissue

²⁸ radiation from a highly penetrating photon of high frequency, usually 10^{19} Hz or more, emitted by an atomic nucleus

Dr. Arthur Compton²⁹ was the chairman of the Advisory Committee, which included Sir Lenthal Chettel, who had come from England; and Ludwig Hectom was a pathologist. So they had apparently decided that a radium bomb, which is really a large amount (I think it was 5 or 10 grams of radium), which was enclosed in a lead casing and shot when they used that.

FISHER: So they used radium sources for whole-body irradiation. Did they use radium?

FRIEDEL: I don't think we ever used it. I don't recall.

FISHER: What did they use at Memorial for whole-body radiation? What sources?

FRIEDEL: It was what they called a Heublein unit.

FISHER: An x-ray machine?

FRIEDEL: An x-ray machine. And I think it was at 200-kilovolt x-ray machine. And they simply used it elevated as high as possible, and the patients were essentially on the floor.

FISHER: That's interesting.

Pre-War Experience at the University of California

MELAMED: It was after *that* that you went to the University of California [at San Francisco] and worked with Dr. Stone?³⁰

FRIEDEL: Because about that time, we were beginning to hear about other artificial radioelements: radioiodine, radiophosphorus. So I thought: "I'd better," since I had this opportunity to find out about it, and I wrote to Dr. Stone and asked him if he would accept me. And he did. So I came and became a member of the staff.

FISHER: At the University of California.

²⁹ Dr. Arthur Compton, University of Chicago, a key member of the scientific team that established the Manhattan Project. Early in 1942, as part of the emerging effort to develop an atomic bomb, Dr. Vannevar Bush, head of the National Defense Research Committee, appointed Compton to be one of three program chiefs with responsibility to run chain reactions and develop weapons theory. As a result, under Arthur Compton the Metallurgical Laboratory at the University of Chicago became a critical research facility for the Manhattan Project.

³⁰ A pioneer in radiation therapy, Robert Stone, M.D., had conducted human radiation studies before World War II. He was an early researcher at the Lawrence Radiation Laboratory and became a major figure in radiobiology research. When Joseph Hamilton began operating his 60-inch cyclotron at Crocker Laboratory, Stone requested that fission products be made on the cyclotron and that their fate in mammals be systematically studied in small animals. That information would be used for radiation protection purposes. In 1942, while chairing the Department of Radiology at UC San Francisco's medical school, Stone was recruited to lead the Medical Division of the Manhattan Project, overseeing all biological, medical, and radiological protection research. Accordingly, he moved to the University of Chicago, where he served as Associate Director for Health under Arthur Compton. In the 1950s, after serving in the Atomic Energy Commission, Stone returned to his post at the UCSF as head of the Department of Radiology. Under Stone, UCSF acquired a 70-MeV synchrotron for conducting therapeutic research.

FRIEDEL: At the University of California. I think the hospital's name was then the Moffett Hospital, as I remember correctly. I used to go everyday across to Berkeley³¹ to work on the cyclotron.³² Then, there were a lot of people working on various things, and I sort of thought that maybe I could do something with radiophosphorus and patients.

FISHER: What did you do at the cyclotron? What was your work?

FRIEDEL: My work on the cyclotron was really, first of all, learning what the stuff did and how you produced it. And, secondly, I began to learn about how we could make appropriate measurements of the intensity of the element that we were working with. My interests at that time were primarily phosphorus and strontium-89, in radiophosphorus. I don't quite know how I got started in this.

Oh, I should add one more thing. One of the other things I observed is the treatment of neutron treatment in patients. We, [meaning] Dr. Stone and Dr. Larkin, actually treated, it's published—we were then pursuing studies on cancers. I think they were probably cancers that were difficult to cure, if I remember correctly. I think I recall abdominal tumors of various kinds, some chest tumors. And I don't believe they wanted to treat highly sensitive tumors, like lymphomas or things of that kind, with this; I can't be sure. I don't remember it that well. I was really not a part of the team. I was really an observer and occasionally I participated because Dr. Stone was away, or for some reason Larkin wasn't available, or something. I actually treated some of the patients.

FISHER: Did they bring patients to the cyclotron?

FRIEDEL: They brought patients to the cyclotron. Patients were treated at the cyclotron. I sort of was looking at radiostrontium. And what I did there was, first of all, study some distribution studies by injection of animals. I think we used a colony of mice and rats. Then we would simply assay³³ the studies. We didn't do much radioautographs at that time; which later we got to be well-developed. I don't recall myself doing any.

FISHER: Autoradiography?³⁴

FRIEDEL: But we did do studies on bone, and primarily other tissues, to see what the distribution was at various periods—and some of the stuff may have been published with others. But I never really got to publish the actual material that I did, because my interests were towards the clinical surface, [and] because I was really on the staff at the hospital. One of the things we found of interest was: to perhaps consider treating some of the diseases that hadn't been attacked previously with radioelements.

³¹ University of California, Berkeley, site of groundbreaking early research in nuclear science and location of Lawrence Berkeley Laboratory

³² an accelerator in which particles move in spiral paths in a constant magnetic field

³³ determine the amount of material present in tissue, urine or feces by any trial measurement

³⁴ a technique whereby photographic film is placed over thinly sliced tissue to record, in image form, the radiation tracks from the tissue that pass through the film's emulsion

First of all, radioelements theoretically had one important advantage. If you somehow had an element which had preferential deposition in tumors, or in the vicinity of tumors, it might be useful. And so it occurred to me, and others, that perhaps radiophosphorus might be very good. Because, first of all, phosphates are part of the DNA complex, and so they might be picked up in the tumor.

As a matter of fact, Dr. John Lawrence³⁵ was then busy treating various hematological³⁶ problems: leukemia and excessive red cell formation; the name escapes me. Anyway, he was treating patients with radiophosphorus. It occurred to me that maybe we could try this on widespread carcinoma-tosis,³⁷ particularly in carcinomas of the breast, because you would find—

FISHER: Polycythemia vera. Now did you participate in some of the first studies of phosphorus-32 in the treatment of polycythemia vera?³⁸

FRIEDEL: I participated with Dr. Lawrence, but I was not—he had already been doing this for some time. Oh, yes, you see, I treated that and leukemias as well.

FISHER: How successful was this?

FRIEDEL: It was very successful. Obviously, you could knock the hematopoietic system³⁹ down, and you at the same time suppressed the white cell count. And you had to be careful about how much suppression you did. We knew that you could suppress the hematopoietic system with relative ease. And one of the things we were thinking about is using radiostrontium, because radiostrontium [deposited] primarily in bone, and therefore, the energy was enough to get a fair amount in the hematopoietic⁴⁰ system.

FISHER: Why was radiostrontium preferred in the treatment of, say, bone tumors, over radioactive calcium?

FRIEDEL: I think—I don't know that there was any preference. I don't recall right now, but radiocalcium—I think there were problems in the preparation of radiocalcium. There were mechanical reasons. Theoretically, if you're going to get it into the bone, why not use calcium? I don't know. I've forgotten know what the energy was. It's been such a long time, I haven't

³⁵ Dr. John Lawrence, brother of Ernest O. Lawrence, was Director of the Division of Medical Physics at the University of California, Berkeley. He operated a clinic at Donner Laboratory, where he treated leukemia and polycythemia vera patients with radioactive phosphorus. For a colleague's recollection of Dr. Lawrence's clinic, see in the interview with Dr. John Gofman (DOE/EH-0457, June 1995), the sections "From Research to Laboratory Production of Plutonium," "Medical Treatments With Radioactive Phosphorus (³²P)," "Conflict Between University of California San Francisco and Berkeley," "Heparin and Lipoprotein Research With Human Subjects," and "Radiophosphorus Therapy for Polycythemia Vera." See also "Reflections on John Lawrence" in DOE/EH-0476, *Human Radiation Studies: Remembering the Early Years: Oral History of Physiologist Nello Pace, Ph.D.* (June 1995).

³⁶ relating to the study of the nature, function, and diseases of the blood and of blood-forming organs

³⁷ the condition of widespread dissemination of cancer throughout the body

³⁸ a disease characterized by overproduction of red blood cells

³⁹ the system involved with the formation of blood

⁴⁰ relating to the formation of blood

looked at it. There was a reason why radiostrontium had some advantages. First of all, it was a much longer half-life, if I remember. Do you know?

FISHER: [About] 50 days.

FRIEDEL: Radiostrontium was about 90 days. Strontium-89—what was it?

FISHER: I think it's about 50 days. Strontium-89—chloride has just been reapproved.

FRIEDEL: What was radiocalcium?

FISHER: I don't remember. I don't have that chart.⁴¹

FRIEDEL: It's not important. But anyway, for some reason, calcium could not—there were mechanical problems—otherwise they would have used that. We didn't really pursue radiostrontium with any weight.

FISHER: It could be produced in a cyclotron?

FRIEDEL: It could be produced in the cyclotron. So is radiocalcium, because there was a fellow by the name of Pashce who had sort of outlined that this area worked for him. If I remember correctly, he was a Frenchman and had been working in the Donner Lab⁴² before I was there, before I came. For reasons that are not clear to me . . . Anyway, radiostrontium really wasn't used very much. Actually, radiostrontium was done in a desultory sort of fashion, because it didn't look as if it was very promising, if all you got was radiostrontium all over the skeleton, which was troublesome.

FISHER: Because it didn't localize specifically in tumors?

FRIEDEL: No. And of course, the idea was tumors proliferating rapidly, It might indeed have some preferential uptake.⁴³ But the differences were very modest. And you had a long-lasting radioelement, reasonably long-lasting. You'd be irradiating bone marrow pretty vigorously.

FISHER: Do you recall, at that time—I've read your paper on the six cases that were injected with strontium-89, some prior to amputation—do you remember if strontium had been used previously to that, or prior to that, anywhere else in the country in studies of bone tumors?

FRIEDEL: First of all, there weren't too many places where they could have radiostrontium. They would have to have a cyclotron. I think there was one in Boston, and possibly one—this was in the very early '40s, maybe 1940, something like that, '40 or '41, just before [our entry into] the war. The [U.S. entry into the] war started in December of 1941 [with the bombing of Pearl Harbor on the 7th], so this must have been 1940, late '40 or early '41.

⁴¹ Calcium-45 has a half-life of 164 days; calcium-47, 4.9 days.

⁴² a laboratory set up at the UC Radiation Laboratory in Berkeley during the 1930s specifically to conduct experiments in medical physics. For an inside view of Donner Laboratory's role, programs, personalities, and day-to-day operations, see DOE/EH-0479, *Human Radiation Studies: Remembering the Early Years: Oral History of Donner Lab Administrator Baird G. Whaley* (September 1995).

⁴³ an excess assimilation of radioiodine in the thyroid, indicating abnormality

We were pretty vigorous. We were doing a lot of work that seemed impossible to me now, that I ever got involved in so many things. But we did it. The things that we pushed most were radiophosphorus and carcinomas of the breast. As I pointed out, one of the things that was intriguing about it was one: you could follow it, because you could take x rays of the skeleton and see what had happened.

FISHER: Were these with phosphorus plaques, or applicators, or was it injected?

FRIEDEL: No. It was intravenous radiophosphorus.

FISHER: It was administered intravenously [(into a vein)]?

FRIEDEL: Yes. I think it was sodium phosphate. We would prepare this. Of course, there was a system for preparing it already, because, as I pointed out, John Lawrence had used it a couple of years before. As soon as that cyclotron was operating, they were beginning to make radiophosphorus, and John Lawrence was already treating leukemia and polycythemia. The material was available. Of course, you could have done it through the alimentary tract,⁴⁴ but it was quicker and easier to do it intravenously. That's what we did. And so we actually showed many many patients—we would say, it probably didn't cure anybody. But I did have one patient that lived for 10 years with no metastases to the bone, identifiable by x ray.

FISHER: From breast cancer?

FRIEDEL: From breast cancer. The lesions calcified. That meant—the reason why there is desolation is because the tumor has interfered with bone deposition. As soon as the tumor disappears, bone deposition would occur. Sure enough, we had this in many patients, I would say in maybe 20 percent of the patients, maybe as many as 30.

The limiting thing was: how much phosphorus could we use, without suppressing the blood count severely? We had one patient in which we pushed the surrounding site count down to about 10,000 [white cells per microliter] from 300,000, and there was very little bleeding. We were surprised. Either our counting systems were no good, or for some reason the patient had no severe bleeding consequences.

In any event, we treated a lot of patients. It looked a rather promising, good-tallied approach and, as a matter of fact, when I came here after the war, we pursued this study and had the same kinds of responses then.

FISHER: At Case Western?

FRIEDEL: At Case Western Reserve University, then Western Reserve University.

MELAMED: One of the things we've seen in some of the documents is a kind of discussion of the line between treatment and experiment. All of this

⁴⁴ alimentary canal, a tubular passage functioning in the digestion and absorption of food and the elimination of food residue, beginning at the mouth and terminating at the anus; here, Friedell is referring to administration by ingestion.

work you did was really to treat patients. Or was some of it, once you determined a patient, to do some investigation as to effects?

FRIEDEL: Our investigation then, probably we did some investigation. That is, we could get postmortems on some of the patients, and then we would try to assay the tumors and the bone, and kind of correlate it with the dosage that the patient had received. We tried to do some distribution studies. But I would say that most of our studies were done on animals—because to control patients, it's extremely difficult.⁴⁵

Approaches then was that we were really responding to their clinical needs. After all, these patients were very ill. What we were doing was to see whether indeed we could renew, that we [could] produce serious changes in the tumors. We wanted to see whether indeed we could really prolong their lives a little and make them more comfortable. One of the things, one of the problems of course, is control of pain. All of these appeared. As a matter of fact, I think there is still a place for the use of radioelements, [although it] has now become rather awkward.

In a way, radiologists aren't the first line for the management of patients. The physicians, usually internists, who see them first are the ones who work with them. There is, of course, ample evidence that you can suppress tumor growth by various chemotherapeutic⁴⁶ elements. As a radiologist, my general observation is that I haven't got much faith in them. As a matter of fact, I don't have a terrible lot of faith in radioelements as well, unless you can make them specific. Because, they don't have specificity [(the ability to selectively kill cancerous cells while sparing normal cells)].

Chemotherapeutic [treatment of] patients, however, does it by interfering with it [or] by doing cross-linking nucleotides,⁴⁷ or by interfering with some protein—hasn't any way of selecting the tumors from other rapidly dividing cells. The chemotherapeutic agent usually goes around: in my facetious way I say, "Who's dividing today?" You see? Now if you don't have synchrony, you now have another problem and you're aware of that.

I'm frankly puzzled by how much credence is put in chemotherapeutic agents. I think they can suppress this all right, but why [they are] so effective is pretty hard for me to understand rationally. Because, unless you [have], say, normal cells, seriously depleted and great propensity for recovery . . . I also am uneasy about what you're doing to them, perhaps modifying them in such a way that they may show unusual growth in those tumors. It may be that I'm not cognizant enough of this. But, what it really meant was that the x ray or radiation approaches would gradually reduce in interest as the chemotherapeutic agents took over.

⁴⁵ Unlike humans, animals can be kept in cages and fed a prescribed diet.

⁴⁶ relating to chemotherapy, the treatment of disease by means of toxic chemicals that kill cells or inhibit their ability to grow and multiply

⁴⁷ Nucleotides are any of a group of molecules that, when linked together, form the building blocks of DNA or RNA.

FISHER: Did you ever use either phosphorus or strontium-89 for reduction of pain?

FRIEDEL: We never used radiostrontium. Because, in a way, that was abandoned pretty early.

FISHER: Why was that?

FRIEDEL: It didn't look very promising. We were uneasy about it. First of all, radiophosphorus—what is the half-life, 14 days or something like that?⁴⁸ That gave you a little bit better control. Secondly, radiostrontium wasn't the real thing. It was a substitute for calcium, if you will. It was an analog of calcium. I think that the results weren't terribly promising. So we said, "Why do this?" It seems to me, I recall correctly, "I do this and we stick with radiophosphorus."

Amount of Information Provided to Patients

FISHER: One of the questions that comes up in the 1990s about work done in the 1940s, has to do with: how much did the patient know about the procedures that were done on them? Can you kind of help us with this?

FRIEDEL: I would say that our approach at the present time is much more rigorous. We never really did any purely metabolic studies⁴⁹ on normal patients, for example. There may have been. But if we did, we would calculate the dose. At that time, there was kind of a, how shall I say, a level which was called the tolerance level; a sort of acceptable level, really based on radium standards. Therefore, if we used tracer⁵⁰ studies, we usually ignored the possible potential hazards, which obviously have to be very small.

When you look at it, the kinds of dosages that were used, even though they theoretically, by whatever means you use (if you're linear or the other one)⁵¹ have to be small, compared to all the other hazards that arise. If you assign, say, one rad to a potential cancer in one time in a thousand, something on that order, you could go another decade. Patients, primarily without any other impact, would have about [a] 20 percent chance of dying of cancer.

FISHER: Naturally.

FRIEDEL: That's the survival. The incidence is probably 30 percent. When you cure someone, if you look at the hard statistics, 20 percent. That means that, out of 10,000 patients, twenty [percent] will die, 2,000 will die. If you have 100,000 or something in that order, you see, you change the odds very little.

⁴⁸ Phosphorus-32 has a half-life of 14.22 days.

⁴⁹ studies related to metabolism, the rate at which chemical processes take place in the body

⁵⁰ radioactive tags on biomolecules, used to study a biological, chemical, or physical system

⁵¹ According to the "linear hypothesis," all ionizing radiation is harmful; the harm rises in direct proportion to the dose. Over time, some radiologists and health physicists came to find this assumption simplistic and proposed more complex models, most of them based on a linear quadratic equation.

FISHER: Did patients in the 1930s and 1940s have a difficult time understanding the concept of radiation?

FRIEDEL: I think they were much more receptive to the physicians' assurances. We would say, "This isn't going to be any problem to you, not at all." They would generally accept it. I think the whole approach to radiation has been inordinately . . . Nobody ever talks about radiation anymore, except they add a certain adjective. It's *lethal* radiation or *dangerous* radiation or *fatal* radiation. They never say it's a *lethal* Buick, or a *fatal* Chevrolet. The risks are somewhat simpler.

FISHER: You hear the word "deadly" radiation quite often in the news. "Deadly," that kind of thing.

FRIEDEL: Well, true. Radiation could be deadly. So now, the approach is very diffident. Once you mention radiation, never mind that radiation is streaming in here from cosmic rays.⁵² And never mind that you go up in the airplane and you receive a few millirads if you fly enough, there is a different approach. In those days, I think the patients relied more on the doctor's assurances. After all, there were no immediate responses. They could observe that themselves. If you gave radioiodine to patients,⁵³ and you gave it for diagnostic purposes usually, you would measure it over the thyroid;⁵⁴ and they had no problems.

Generally, people assign hazard to more-or-less immediate responses. Once it was established that radiation could produce oncological⁵⁵ impact at high enough doses, then you see there was a whole new examination of this; particularly the patients that didn't realize that their exposure was very high to cancer anyway. As I pointed out, 30 percent of the population is going to have some cancerous changes; and 20 percent of them, actually 18 percent, are going to die of cancer. That's the milieu in which you look at radiation now.

In those days that didn't occur. We probably were pretty sloppy, put on a little extra radiation here and there. It didn't impress us at all, because we did studies. And I am doing some of my studies, particularly in radiostrontium. [I] was looking for very sensitive counters, and Emilio Segrè,⁵⁶ who was then working at the lab—one of the best—I cajoled him into letting me use his [radiation detection equipment] because his

⁵² radiation of high penetrating power originating in outer space and consisting partly of high-energy atomic nuclei

⁵³ Radioiodine (¹³¹I) is widely used to diagnose thyroid function and also is a highly effective therapy for hyperthyroidism, Graves' disease, and thyroid cancer.

⁵⁴ an endocrine gland located at the base of the neck and secreting two hormones that regulate the rates of metabolism, growth, and development

⁵⁵ relating with tumors, including the origin, development, diagnosis, and treatment of cancer

⁵⁶ At Los Alamos Scientific Laboratory in early 1944, Segrè developed Little Boy, a lighter, smaller version of a uranium bomb that used a plutonium gun design. Little Boy was dropped, untested, at Hiroshima on August 6, 1945.

was the best. Of course, he was very careful about this, because he didn't want any contamination.

FISHER: He was at Berkeley?

FRIEDEL: He's a Nobel winner. I'm the guy that contaminated his counter. He will never forgive me. So I have this distinction.

FISHER: At Berkeley, you would have been about 29 or 30 years old? A young physician.

FRIEDEL: I was then about 29 or 30.

Prominent Researchers Working at Berkeley

FISHER: Who were the physicians of prominence that seemed to lead out and make the decisions on human studies at the University?

FRIEDEL: Joe Hamilton⁵⁷ was there. John Lawrence was there. Larkin was there, because he was working with the neutrons. There were other physicians who were actually working there. I think I was one of the few. I can't recall any; I'm trying to think of any. But the ones that come to mind—[Bert] Low-Beer was there.⁵⁸ But Low-Beer didn't do anything in radioelements until later.

FISHER: What did he do?

FRIEDEL: He was working in diagnostics. I'm not sure I got it straight. I may be wrong about this. Low-Beer came from either Czechoslovakia, or somewhere. Low-Beer may not have had a license to practice. He may have been working in research. He used to work with [and married] a girl by the name of Anne Treadwell, whose name appears in some of the studies. He may have been doing some research, but not on humans.

FISHER: At the cyclotron?

FRIEDEL: With the cyclotron. But I never saw him at the cyclotron. I only saw him over in the hospital in San Francisco.

FISHER: Did you recruit your patients mostly from the hospital in San Francisco, to come over?

FRIEDEL: No—except those that we were going to be treating with neutrons. We treated all our patients in the hospital. We had radiophosphorus and brought it over. All the patients were treated there. The other interesting

⁵⁷ Joseph Hamilton, an M.D., worked at Crocker Laboratory, then the site of a 60-inch cyclotron that he operated to produce radioisotopes in support of research and some medical diagnosis and treatment. Crocker was part of the Lawrence Radiation Laboratory, later renamed Lawrence Berkeley Laboratory, in Berkeley, California.

⁵⁸ a medical researcher at the University of California, San Francisco who died prematurely of leukemia, probably brought on by overexposure to radiation in the course of his career, which included work with radiophosphorus in England. Low-Beer, a physician, had been trained in his native Czechoslovakia. He served as an associate professor of Radiation Therapy before heading the Radiation Therapy Division of the Department of Radiology at UC San Francisco.

thing about the hospital was that they were the first ones to have a million-volt x-ray machine. One of the scientists, I've forgotten his name for the moment, built the machine.

FISHER: For therapy? Orthovoltage?

FRIEDEL: Supervoltage.

MELAMED: Were the patients you treated—was there any way to characterize them? Did they come from a very different kind of [stratum] and economic levels, or did you get more charity patients? Is there any theme there?

FRIEDEL: I think they came from all levels. Because the one patient that I recall so well, that had such a good response, sort of followed me over the United States. You may know that I came from Minnesota. She got in touch with me, and she discovered that I was visiting my family in Minnesota; and my uncle was a doctor. She arranged to come, and I examined her and saw her in Minneapolis. She was a fairly well-to-do patient.

There were all kinds of patients. We didn't make much distinction in those days;—that's not true: we did make distinctions. But we treated all of the patients. I would say that many of the patients that came to see Dr. Lawrence were well-to-do patients. They wouldn't come to see me in preference to Dr. Lawrence if they had leukemia or polycythemia.

MELAMED: And in the work Dr. Hamilton was doing, as well?

FRIEDEL: Dr. Hamilton's interest in patients was rather modest, clinically. He was doing research more than anything. But exactly what research he was doing, I wasn't particularly aware of. At that time, it was very interesting. There was real freedom, as we extol the virtues of freedom. Everybody did anything they wanted to do. There wasn't any real surveillance. The only surveillance that I had was from Dr. Stone. If I told him I wanted to do something and I outlined it in general, he would say, "Go ahead, do it." I don't think John Lawrence really had a kind of committee to take a look and see whether this was an appropriate approach as far as over here, for example.

Now, if you want to do something that hasn't been done before, there will be a committee that will approve—that will decide whether this is worthwhile. And there will be all kinds of elements in it. There were tremendous differences. I would say the further west you went, the less controls there were. I can't really characterize Joe [Hamilton]'s actual research, but I do know that he and Mayo Soley[, M.D.] were the first to use radioiodine. Mayo Soley was an endocrinologist. He was also dean of the medical school [at UC Berkeley, and later at the State University of Iowa].⁵⁹ I think they did some work together. Later on, I got to know Joe very well. I got to know him particularly well when I got into the Manhattan Project.

⁵⁹ For reminiscences of Dr. Soley's radioiodine treatment clinic, see DOE/EH-0465, *Human Radiation Studies: Remembering the Early Years; Oral History of Dr. Nadine Foreman, M.D.* (July 1995).

- FISHER:** What year would that have been when they first used radioiodine, as you recall?
- FRIEDEL:** I think it must have been late '30s.
- FISHER:** Were you ever involved with the teaching program at the university or over at Berkeley?
- FRIEDEL:** Theoretically, I maybe started out as a teaching fellow. But I would say that my teaching would be limited to house officers. I participated in conferences. There were regular conferences; and they were teaching exercises, if you will. The students attended, but it was not a rigorous or arranged curriculum. These were regular conferences that had to do with oncological approaches or certain diagnostic studies, and the students would be there. You could say that was my teaching experience.
- FISHER:** Dr. [Glenn T.] Seaborg⁶⁰ mentioned to us that he recalls incidences where either Dr. Lawrence or others, in demonstrating the principles of radioactivity, self-administer[ed] radiosodium to show its rapid uptake in the mucosa of the stomach [by holding a Geiger counter next to the palm of his hands to demonstrate activity in blood circulation]. Do you remember any of this?
- FRIEDEL:** I don't really recall this, but I think if anybody did it, it would be Joe Hamilton. I would guess it would be Joe to do it.⁶¹ I don't think it would be any of the other—well, it might be John Lawrence as well. But I never did it.
- FISHER:** Did you ever administer yourself with any radioactive solutions?
- FRIEDEL:** I think I probably took some radioiodine in my mouth for demonstration purposes.
- FISHER:** Uptake in the thyroid?
- FRIEDEL:** Right. I've taken the thyroid. I may even have done it after taking up doses of iodine to show that it didn't—I could block the radioiodine from appearing.
- FISHER:** Block it with some cold [(stable)] iodine?
- FRIEDEL:** Yes, potassium iodine or something.

⁶⁰ U.S. chemist, born 1912. A professor of Chemistry at the University of California, Berkeley, Seaborg discovered plutonium in 1940 and went on to play a key role in the discovery of more than half a dozen heavy elements through the 1950s, winning the Nobel Prize for Chemistry in 1952. Seaborg later served as Director of the Atomic Energy Commission.

⁶¹ Hamilton died prematurely of leukemia brought on, colleagues believe, by occupational exposure to radiation.

The Army Medical Corps and the Manhattan Project

MELAMED: Pick up what you were saying about getting to know Joe Hamilton and how you were working in the MED, in the Manhattan Engineer District.⁶² Were you working together at that time?

FRIEDEL: Afterwards, I got to know him very well. I suppose it's useful for me to tell you how I got into this. This is a little—some problems, here that should be look[ed] at if you want history completely. I was a reserve officer. And I had been a reserve officer for maybe four or five years, maybe six years, since I graduated from the University of Minnesota. I retained that reserve status for a long time. Then, when I got to California, the war was impending and they were beginning to call up reserve officers. And I thought, surely, they'd call me any day. When at Pearl Harbor, which was December 6 [(December 7, 1941)]—I thought—I hadn't received—

... As a matter of fact, I thought surely they were going to call me. I was saying that I lived in a house that I rented from an individual, who had been called up. So they were calling up everybody at that time. I expected that I would receive a call any minute. And I wondered about it. I kept saying to Dr. Stone, "You know, I'll be called anytime now." He didn't respond very well. I don't think he was evasive, but he didn't talk to me much about it.

Then I discovered that they had identified what they called an "essential list," which was being respected by the military forces for teaching purposes; so I wouldn't be called, as long as I remained on that essential list. I discovered that I was on this essential list. I thought about it after a bit, and I felt that I just couldn't continue on the list, even though it had been extremely desirable to stay out of the war. Because I'd been this reserve officer, all my friends were being called up, and I didn't think it was quite right. So I asked them to remove me from the essential list. And they treated this as a, somewhat, I would say—without serious attention.

MELAMED: Was it Dr. Stone who had seen that you got on this essential list, do you think?

FRIEDEL: After all, it was the dean's responsibility. I never had direct access to the dean; I usually went through Dr. Stone. I finally said, "I must be released. Otherwise, I'm going to have to resign and take my chances." As a matter of fact, I was already beginning to make contacts with some friends of mine who were in the Air Force. Because I thought if I'd go in, maybe I could get into the Air Force.

FISHER: Were you interested in joining?

⁶² the U.S. Army Corps of Engineers organization set up to administer the development of the atomic bomb under the secret Manhattan Project

Work at the Chicago Metallurgical Laboratory

FRIEDEL: I'm not sure I was interested in joining. I was just interested in making sure that I was discharging my obligation. I don't know that I looked upon it with great enthusiasm. But at the same time, I felt it was a responsibility of mine. They agreed, and then I received rather odd orders.

I received orders to appear at the Presidio for induction, which I did. Then I was given special orders to go to Chicago and respond to a Captain Craftan. I was to appear in civilian clothes at the MET Lab.⁶³ The address, I believe, was 5125 University Avenue in Chicago; I believe that's the address, if I remember correctly. Anyway, that was the MET Lab, and there I was received by Dr. Craftan, who immediately instructed me to go to New York and see a Colonel Marshall and a Major Blair, who would instruct me further. That simply explains to you how I got into this.

In August of 1942, I left the University of Chicago, and was a participant in what was then the Plutonium Project. Although we never really used that term. First of all, we [never] used the word plutonium. We used to talk about plutonium as "product"; and "uranium," I think, was called "tuballoy."

I then discovered that Dr. Stone had been going there at periodic intervals, and the decision was made, apparently, to transfer him to Chicago, as well—I guess a little before I got there. I think Dr. Stone felt that I would then be on his staff, as I did. Well, we began then to pursue certain activities; primarily with regard to [medical] surveillance of individuals to make sure that we knew something about their physical condition.

I examined a lot of people. One in particular was Edward Teller,⁶⁴ whom I got to know very well. I don't know whether you want this on the record or not, but Edward Teller—first of all, I discovered, had one leg. He lost his leg, and taking the history—I recorded it somewhere—taking the history, he lost his leg in apparently a streetcar accident in Berlin. At least, that is as I remember the history. He has a prosthesis, and he had lost part of the leg below the knee. I think it's the right leg, but I'm not sure now. He also had a hernia, a very large hernia, and I think to this day he might think I was a great diagnostician. But anybody could identify it. He had it correct[ed] at the [University of Chicago's] Billings hospital.

MELAMED: So you were doing [medical] surveillance of some of the scientists?

FRIEDEL: We were doing surveillance of the various people. I remember once examining Herbert Anderson, who was the assistant, that is well-known,

⁶³ Metallurgical Laboratory, the laboratory set up at the University of Chicago during World War II to lead the secret research and development of controlled nuclear fission under the Manhattan Project. Met Lab researchers had produced the first self-sustained nuclear chain reaction on December 2, 1942. Operating initially at one-half watt, it achieved 200 watts ten days later.

⁶⁴ (1908–) Hungarian-born refugee physicist and the "Father of the Hydrogen Bomb." Teller was one of a number of European scientists who had fled to the United States in the 1930s to escape Nazi and Fascist repression.

to [MET Lab director Enrico] Fermi. He didn't see what the hell I was doing there anyway. I was just cluttering up the place, and doing all these nonsensical sort of things. But we were doing surveillance, doing basic studies, making some estimates of how we would measure the radiation; then beginning to look at some of the agencies that were involved in radium and uranium.

I was assigned to go out and see a lot of these; partly because it was easier for me to do this as an officer. I could easily get orders to do this, whereas there were civilian personnel there, and they could have done it as well as I. But they probably thought I should do it. Besides, I had a little more experience with radioactive materials. As a matter of fact, I had had more experience than most, having come from, in effect, the citadel of radioelements [(the UC Radiation Laboratory)];⁶⁵ I knew quite a lot about it. In some ways I was more familiar with some of it than Dr. Stone was, because he was involved, really, in the broad administration of the department and wasn't doing direct research himself. But the Army—I should say this first: I believe that a lot of this was still under the Office of Scientific Research and Development.⁶⁶ It may have been in the OSRD still. But the Army was beginning to take over.

I discovered that there were grand plans when I went to New York, and was met by Colonel Marshall (no relation to the General Marshall). It was Colonel William Marshall, and a Major Robert Blair, I remember them very well, and some other officers.

I then discovered why it was called the Manhattan District—I'm sorry, it was never called the Manhattan Project—but it was called the Manhattan Engineer District of the Corps of Engineers. I think it was basically because a major office was in New York at that time. If I remember correct, their offices were on 29th and 5th [Streets]. I would go there not infrequently. So I began to learn that the program was going on. Before long, it became clear that they were going to go ahead and develop a program on their own.

MELAMED: Are you talking about a medical program, then?

FRIEDEL: A biomedical program of their own. Because they felt they had responsibility for the general surveillance in one way or another. It is my conjecture—and I want to make it clear that it's my conjecture—I believe that they wanted someone with considerable stature who had had experience with this to head the program. I believe they asked Dr. Stone to do it. I'm not sure that is the case, but I believe it to be so. I think that he was importuned not to do it and to remain with what was then the Plutonium Project.

⁶⁵ founded by Ernest Lawrence in 1936; now Lawrence Berkeley Laboratory, a National Laboratory under the U.S. Department of Energy

⁶⁶ established by an executive order June 28, 1941—six days after German troops invaded the Soviet Union. The OSRD's Director reported directly to the President and could invoke the prestige of the White House when dealing with other Federal agencies. The National Defense Research Committee, at the time headed by Harvard President James Conant, became an advisory body responsible for making research and development recommendations to the OSRD.

The Army then decided, then conferred with me a little bit, because they thought I could make some suggestions. I really had no real suggestions to make. If I remember, I thought there were various superior individuals in radiology, that they might contact. I believe I may have even mentioned Dr. [Stafford] Warren⁶⁷ in Rochester. But the only reason I would have done it—I didn't know him at all—it was only because he was a recognized leader in the general field of radiology. I felt that I was too young to take on this august responsibility, and I didn't know where it would lead to.

This created some minor problems for me, because here Dr. Stone had refused to accept this, if he indeed did. Now they were intent upon identifying someone, and about late December, or something on that order, they asked Dr. Warren to come on as a civilian consultant. That's when I first met Dr. Warren. Here I was, pursuing my activities as part of the Manhattan Engineer District, but Dr. Warren was my immediate consultant, and I knew that eventually he would become the director. They decided then that he should become—have a commission in the Army. And later arranged—there are some interesting anecdotes with this. But in any event, he became the director sometime in March of 1943.

FISHER: Had you already moved? Where were you living at this time?

FRIEDEL: At this time, I had already moved. As soon as I was detached—that is, as soon as I had been ordered to Chicago—I arranged to have my family go back to Minneapolis. And then, I tried to find a place for us to live in Chicago. Now recall, I had already lived in Chicago when I was at the Tumor Institute, so I knew something about the arrangements. Actually, I had lived in the vicinity of the university. I lived somewhere off University Avenue. When I was transferred there, I finally found a place. I believe I lived in Cornell Towers in Chicago. I moved my family there. At that time, my family consisted of my wife and a daughter about four or five years of age.

FISHER: Then you moved to Oak Ridge,⁶⁸ when?

FRIEDEL: I moved to Oak Ridge—it must have been in the middle of '43 or something of that order. We'd lived in Chicago a little over a year, and then moved to Oak Ridge in '43, and then continued there until 1946.

MELAMED: Can you generally characterize your responsibilities, what you did in this whole period, as part of the MED?

⁶⁷ a professor of Radiology at the University of Rochester (Rochester, New York), site of research involving plutonium and human subjects. Dr. Warren worked on the Manhattan Project in Oak Ridge as head of the medical section and headed an Intramedical Advisory Committee. After World War II, Dr. Warren became dean of the University of California, Los Angeles Medical School.

⁶⁸ During World War II, the Manhattan Project had built a vast complex of highly classified facilities in and near Oak Ridge, Tennessee, to process uranium for use in atomic bombs. The Atomic Energy Commission assumed control of these facilities upon its creation. Today they belong to the Department of Energy.

Inspection of Manhattan Project Facilities and Proposed Sites

FRIEDEL: Until Warren actually came onto the scene, I was really under Dr. Stone's direction. And I was pursuing activities that Dr. Stone determined were appropriate, which were generally surveillance. I visited various activities [(sites)]. I visited Harshaw Chemical,⁶⁹ which was involved in the process, and to see what hazards I could identify. I went to places near Boston who were involved in these activities.

One of the things that I did that is of interest to you, is that in our conferences we were discussing how indeed we would assign whatever we learned about animals, to humans. Then we began to think, "Where are there any places where there are any human studies that would be useful?" Then, of course it occurred to me, it came like a flash, that Memorial Hospital [in New York City] had a group of patients that had been treated with total-body [irradiation], and there might be a source of information that could be used.

The idea of doing any work on humans was not seriously considered. Because first of all, the problems of secrecy. We didn't want anybody to know that we were working on radiation. Work on animals was secret, because we didn't want anyone to be aware of this. As a matter of fact, publications in the literature, once they came into our office, were stamped "SECRET." Throughout the literature—it wasn't to be discovered by anybody that we were looking at data in the literature. All of this, then, had to be handled in a secret fashion. That was obvious. Secrecy probably made a big difference.

The other reason was that it was necessary to do some control: how were you going to do it? The more we examined it, the more it seemed that we would somehow learn to do some extrapolation from the data that we did [have] on animals. There is something to be said here about this that I got from Norman Hillberry, who was Dr. Arthur Compton's right-hand man, who was really his executive officer. You'd probably get to see Dr. Compton if you wanted anything done in the lab. Norm Hillberry would be the man to see. You probably know his history. Later on, he left Chicago and went to Tucson at the University of Arizona. It's not called University of Tucson.

FISHER: University of Arizona.

FRIEDEL: There isn't a University of Tucson—the University of Arizona. As a matter of fact, when I was later-on looking at the history, he confided in me something rather interesting that might be useful. It's an anecdote. I'm quoting, really relaying it from what Dr. Hillberry said. He [(Hillberry)] said, in a facetious way, he said that they were concerned

⁶⁹ E.I. du Pont de Nemours and Company constructed and operated the Hanford site in Washington state from 1943 to 1946 for the Manhattan Project. Du Pont and the Harshaw Chemical Company of Cleveland produced uranium hexafluoride on a scale sufficient to keep the vital isotope-separation research going.

about the pile⁷⁰ that they were going to build and the enormous amount of radioactivity that would be produced.

FISHER: At Hanford?⁷¹

FRIEDEL: No, in their experimental piles [at the Met Lab, in Chicago], and their other studies. They said, "Well, doctors don't know much about this stuff, so we've got to get a good biophysicist." So they got a hold of Dr. Kenneth Cole. Kenneth Cole is really the first individual who was assigned any responsibility in this. Then he said, after reflection—they said, "What will we do if something serious happens? We don't have anybody who has medical credentials. So we better get somebody who has medical credentials." That's when they contacted Dr. Stone, who came on as a consultant and who would visit on-and-off.

Now it always puzzled me that Chicago [—which] was going to be the seat of the plutonium project for a while—would not have contacted their own Departments of Radiology. Perhaps they did. And it may be that they suggested Dr. Stone. I don't know. But anyway, they were not involved in any way, as far as I know.

FISHER: Maybe to maintain secrecy, perhaps?

FRIEDEL: Possibly to maintain secrecy. But Leon Jacobsen⁷² was involved immediately because he was a hematologist. And, as you know, one of the ways we use for monitoring was blood cell counts,⁷³ which are obviously a pretty crude way of doing it, but nevertheless was one of the ways that we used. So, he became involved in the project.

FISHER: What was your understanding of the project when you were working that one year at Chicago?

FRIEDEL: I don't know that. Because of secrecy, there was a considerable compartmentalization. Often, we weren't told everything. But my understanding was: that they were going to see whether they could build an experimental pile. Then we knew that they needed a moderator.⁷⁴ We learned a lot about the nuclear science by the fact that they looked at moderators, and they decided that carbon [(graphite)] was a very good one. And we used to see carbon blocks around there and machining of carbon blocks. There was already some talk about—

⁷⁰ an early form of a nuclear reactor, an apparatus in which a nuclear-fission chain reaction is sustained and controlled

⁷¹ the DOE's 570-square-mile former site for plutonium production, located near Richland, Washington

⁷² Leon O. Jacobsen, M.D. (born 1911), specialized in internal medicine. He served as Director of Health, Plutonium Project of the Manhattan Engineer District at the University of Chicago. Jacobsen specialized in hematology, radiation biology, and the effects of chemotherapy and isotopes on leukemia and lymphoma. Jacobsen served as the first director of the Argonne Cancer Research Hospital.

⁷³ the count of the number of red and white blood cells and platelets in a specific volume of blood

⁷⁴ a substance that slows (moderates) or thermalizes neutrons coming from the fission reaction, increasing the probability of their causing additional fissions in sustaining the chain reaction. In modern reactors, water is used as the neutron moderator.

MELAMED: *(smiling)* I could shut the door.

FRIEDEL: Did somebody open it?

FISHER: *(smiling)* We didn't ever close the door.

FRIEDEL: It's no secret. So we knew that they were going to do this. We were discussing—we saw reports. I have them somewhere in my files, as you do. You have everything I had, as a matter of fact, but you probably can't find them.

(laughter)

You see, I have much smaller files. And so, the presidential commission,⁷⁵ when they came along, copied a lot of this stuff and they have it.

In any event—so we got to know what the approach would be. I seem to recall that they must have been studying this approach for a long time, because I recall when I was in Chicago, that Du Pont⁷⁶ was sending its representatives regularly to visit various people at Chicago (which was later called the Plutonium Project). We never called it the Plutonium Project. We said, "the metal MED project," or whatever it was.

I do recall a weather expert who was looking at the possible kinds of discharges from tall columns, under various conditions; which he called wind roses. They must have already been looking at some kind of chemical plants in Hanford. Of course, I didn't know the exact approach. After all, you didn't ask too many questions; it wasn't your business. But I knew that some things were going on. As I said, we learned a lot by osmosis. The fellow who was really the original biophysicist was a fellow by the name of Ernest Wallen. He was the first one who [was] a biophysicist interested in radiation hazard assessments and surveillance, and so on—of course, the group [leader] later on.

Even before it really gelled, it seemed to me that they had already on the drawing boards, had an approach to this. I can tell you that for some reason, General Groves⁷⁷ asked me to go to Hanford even before it was built—maybe I've pointed it out in some of my collections of material—to review the possible hazards that might occur if they had some kind of a nuclear pile there. He didn't really go into any details. He just asked me whether, indeed, I could identify any conditions that would prohibit any kind of operation at that time.

Actually, I went all over the place, walked over some of it, flew over most of it, and reported back to him that I could not identify anything that was unusual. My guess would be, simply looking back, that I must

⁷⁵ Friedell is referring to the presidential Advisory Committee on Human Radiation, formed in 1994 and chaired by Dr. Ruth Faden, a bioethicist from Johns Hopkins University.

⁷⁶ For Du Pont's role in the Manhattan Project, see the footnote on Harshaw Chemical Company, earlier in this section.

⁷⁷ General Leslie R. Groves, of the U.S. Army, assumed command of the Manhattan Engineer District in 1942 and led it to completion of the Manhattan Project.

have done it very early, because it would have been more appropriate for Stafford Warren to go there than I. So it must have been before Stafford Warren came on the scene.

[Groves] also asked me to go to Oak Ridge, before it was built, partly to examine whether there were medical facilities in Knoxville that could handle the growth of, what were then called the Clinton Engineer Works. I had a chance to survey these areas, long before they ever got well-developed.

FISHER: Was this while you were assigned to Chicago?

FRIEDEL: This was still while I was in Chicago. I'd never heard of the Clinton Engineer Works, and I had never been to Knoxville. Obviously, if I were, the only places I would have been would have been at Chicago and Oak Ridge. It was when I was at Chicago.

FISHER: When you went to Hanford, was the site construction activity quite intense?

FRIEDEL: No, as far as I could make out, there were none.

FISHER: This was before construction, then?

Search for Data on Human Exposure to Radiation

FRIEDEL: Before construction. They must have looked at this for a long time, because they wouldn't suddenly send me off there. That's, as I surmise, the situation. My then somewhat oblique analysis is: that they must have been planning this for some time, with the Du Pont people coming there regularly, with my visiting there. An expert on environment and wind shifts [was] doing studies there. We got a chance to look at them. This must have been planned, even in the OSRD⁷⁸ days before the Army took over.

One of the things that I did was, when we talked about human studies—and that's something you want to learn about, as I recall—here was a possibility to get some information. So I was instructed by Dr. Stone, and I got privileges. I had to always find someone, since I wasn't the director and chief. In order for me to travel anyplace, I had to receive orders.

I got orders to go there to Memorial Hospital. I didn't go to Memorial Hospital alone. As I recall, I went to some of the places around Boston, and then came back to the Memorial Hospital, and then spent several days in New York; possibly visiting the headquarters there. But in any event, working with the records. As I said, when I was looking over some of this

⁷⁸ Office of Scientific Research and Development. Established by an executive order June 28, 1941—six days after German troops invaded the Soviet Union. The OSRD's Director reported directly to the President and could invoke the prestige of the White House when dealing with other Federal agencies. The National Defense Research Committee, at the time headed by Harvard President James Conant, became an advisory body responsible for making research and development recommendations to the OSRD.

data, I suddenly discovered that I had a list of patients that I must have gotten from the Memorial Hospital. I brought them along with me.

Incidentally, I didn't fill this [oral history agreement form] out. I'm glad to fill it out, but it requires some little decision making on your part. You have to tell me whom I'm—the way this comes out. I'll sign it.

FISHER: We'll help you with it.

FRIEDEL: There's no question about this in any way, but [tell me] how exactly would you like it filled out and I'll fill it out. But we can leave that for later.

MELAMED: No problem.

FISHER: We'll do that. We can't forget to do this. These are notebooks that you're showing us now from that visit to—

FRIEDEL: Right. I don't know what this is, right there.

FISHER: That one says, "Beverly, Mass."

FRIEDEL: That's one of the places. I don't understand how I got this. This would be secret. So this must have been enclosed in some "SECRET" envelope and put away; and when it was declassified I got it back. What I want to show you is this. You see. Here is the list. I must have gotten it.

FISHER: It's a list of people's names with dates. It would be from 75 to 225.

MELAMED: We're discussing the papers Dr. Friedell is showing Darrell.

FISHER: Then there are two numbers: maybe a first blood number, a second blood number, and a time period.

FRIEDEL: Let me see what I think they are.

MELAMED: Dr. Friedell is examining the papers for us.

FRIEDEL: This is the period of treatment, I think. And these are the white counts: 10,000, 4,400, 50. This must be the rads that were delivered.

FISHER: Then the reduction in blood cell count.

FRIEDEL: Right. But the main point . . . Then there are these.⁷⁹ These are patients with solid tumors, I believe. Carcinoma of the tonsil, carcinoma of the breast, endothelioma.⁸⁰ These, I think, are [the] studies. Then, later on, Dr. Stone made contact with Dr. Lloyd [F.] Craver, who had been my immediate supervisor when I was at the Memorial Hospital.⁸¹ So I got these from the records there, and I brought them back, and I gave them to Dr. Stone,

⁷⁹ Dr. Friedell is discussing some of his papers on the Craver study.

⁸⁰ a tumor that originates from the layer of smooth tissue that lines the blood vessels

⁸¹ From 1942 to 1944, researchers under Dr. Craver at Memorial Hospital conducted studies to determine the clinical and hematological effects of prolonged daily exposure to whole-body, high-voltage x-ray irradiation. The work was sponsored by the Manhattan Engineer District. For a summary and list of references, see OT-66, "Tolerance to Whole-Body Irradiation of Patients with Advanced Cancer," in *Human Radiation Experiments Associated with the U.S. Department of Energy and Its Predecessors*, DOE/EH-0491, July 1995.

I believe. Then there was, at some appropriate time, I guess—they put them in the records, or they decided not to pursue it any further. But in effect, this was material that was being used for some kind of assessment of what happened to patients, who had been exposed to whole-body radiation. So I have these here, and I suppose they can be reproduced.

FISHER: I think they would be of interest.

MELAMED: Maybe we could copy them when we're done.

FRIEDEL: I think we can probably reproduce them here, and I'll get you a copy.

MELAMED: Thank you.

FRIEDEL: That is my—since you specifically asked about my experience—that was my experience with regard to the Memorial Hospital data, as I recall. In my discussion with Dr. Craver—I don't know how I did this—because obviously, there was a matter of secrecy. That may be that Dr. Craver had already been clear[ed]. However I did this, there was—I had access to the data. And this may be the basis for whatever studies we were thinking about, in regard to humans.

But what kind of human studies you could do wasn't clear. Obviously, you couldn't do total-body radiation with normal subjects [as it was not medically ethical]. That was out of the question. No such decision was really ever seriously considered; partly because of the secrecy. If they had decided to do it, they probably would have made a contract with somebody in a hospital someplace, and they would have sent these patients over. Then again, to send a normal patient over, no way it could be done. There was no question.

Then, all the studies were essentially directed towards doing animal studies. These were done ad infinitum. In some ways, it was probably overdone, probably a lot of redundancy. But it was a fairly new problem. They didn't quite know how to handle this thing, and so a number of agencies were involved.

I should say something about the University of California and how I got to know Dr. Hamilton better, and his group. First of all, I was a little astonished that Dr. Lawrence hadn't been involved in the Manhattan Project. The reason was, that he had worked with radioelements and [had been] learning about the metabolism longer than anybody, probably. He was considered an authority in at least therapeutic uses of this. It turned out later, I discovered that he had made a commitment to the Air Force to study oxygen tensions at various altitudes. And they needed radioactive materials, primarily. I think oxygen could be obtained. So he was involved in that program, and made this commitment.

Then, what also was interesting in retrospect, and it seemed a little odd at first, was that Dr. Hamilton made all his reports to the University of Chicago; possibly because it was considered the plutonium project. But nevertheless, all other groups like [the University of] Rochester, and so on, always reported directly: made their own reports and submitted them

somewhere to the Manhattan Project someplace. It wasn't known as the Manhattan Project, so it came to the Manhattan Corps of Engineers. And then, the reports from the University of Chicago all then came to us, once it was organized.

It was always interesting that the reports came under the general [(General Groves)]. First of all, it always identified Compton as the director, Stone as the director of the biomedical studies, and then Dr. Hamilton as the director of the studies which were being done on fission products.⁸² It was an illogical, in a way, thing to do. And it was obviously the best place to do it because they had the cyclotron working there. They would then go ahead and do these studies. The reports were always made through Chicago, and then, in turn, we would receive it.

FISHER: In Oak Ridge?

FRIEDEL: Oak Ridge. For a while, while I was in Chicago, I would receive it.

FISHER: Was Colonel Warren in Oak Ridge when you arrived?

FRIEDEL: Yes. He was not in Oak Ridge. But when it was decided that the headquarters would be in Oak Ridge, we made plans to move, and he made plans to move from Rochester to Oak Ridge. So we came simultaneously, and I was already visiting with him and communicating with him.

FISHER: You mean the headquarters of the Manhattan Engineer District was moved from New York to Oak Ridge?

FRIEDEL: It was moved from New York to Oak Ridge, correct.⁸³ The new director was Colonel Kenneth Nichols.⁸⁴

FISHER: Up in Chicago?

FRIEDEL: No, in Oak Ridge.

FISHER: The new Manhattan Engineer District's office.

Purchase of a Cyclotron; the Manhattan Engineer District's Early Biomedical Program

FRIEDEL: Obviously, all of the shots were really being called by General Groves from Washington. Often, General Groves would call on me to do things. One of the anecdotes is that—I have written it up—was that he asked me to go to Boston to Harvard [University] to buy their cyclotron. The reason for asking me to do it—and I was still at Chicago—the reason for asking me to do it was: they wanted to camouflage the idea that the

⁸² products such as the elements strontium and cesium that are formed during the splitting of uranium atoms in a nuclear reactor

⁸³ Originally headquartered in New York, the MED was moved to Washington, D.C., and finally to Oak Ridge in the summer of 1943.

⁸⁴ Colonel Kenneth D. Nichols, U.S. Army, was General Groves's chief aide and troubleshooter for the Manhattan Project.

Army was buying a cyclotron—well, that the Manhattan Engineer District was buying a cyclotron.

Ostensibly, the cyclotron—actually—the cyclotron was being purchased for Los Alamos.⁸⁵ We used the facade of my representing the [Army's] Medical Corps, which wasn't true, and that I wanted it for medical purposes. We were going to treat lots of leukemia, some polycythemias, and use it for the usual medical reasons: iodine preparation for possible therapeutic studies and iodine for diagnostic studies, and so on. I made this pitch as best I could. I'm not sure that they really believed it. But nevertheless, we adhered to it, and they finally agreed to it.

What isn't known—if you look through the records, you'll find that Robert Wilson, who later became director of the Fermi Lab [National Accelerator in Batavia, Illinois], had written up this. But one of the things he didn't realize, didn't know, was that [Harvard President] James [Bryant] Conant had written a letter, a handwritten letter, to General Groves, saying, "We will transfer this to you for one dollar," or something like that. The reason I know about it is that General Groves asked me to come to Washington first. And then he explained to me what he wanted done. In fact, he didn't explain it to me, he directed me. He gave me this letter to read, which outlined what was going to happen. We were going to get the cyclotron, no matter what. We wanted to purchase it.

He told me, "When it comes to money, ignore that. Whatever they [(Harvard's negotiators)] want, you agree to, because they're not going to get it, anyway." Then they apparently had Robert Wilson, [in] the group was a finance officer, a legal officer, Robert Wilson; and myself. I did most of the talking because I was trying to convince them that this was going to the Medical Corps. I think—I've forgotten the name of the chairman of the Department of Physics, who was a well-known, towering individual in physics—he must have had an inkling of what was going on, because some of his staff had already disappeared to Los Alamos, Ken Bainbridge,⁸⁶ for example—so he may have been aware of this, but he didn't dare say anything. I think he wasn't the chairman; the chairman was a professor of History or Administration. The names are there someplace.

In any event, we finally agreed that it would be done. Robert Wilson was an expert on [the] cyclotron, and he knew how to dismantle it and put it together; and he was going on to Los Alamos anyway. I think they shipped it to the medical depot to further obscure what was happening, and then got it from there on.

⁸⁵ Los Alamos Scientific Laboratory was a key research and development center for the Manhattan Project. Nuclear bombs were assembled there before and during the Cold War. It has been a research and development center for nuclear weapon designs. Renamed Los Alamos National Laboratory, it is now a part of the U.S. Department of Energy, operated by the University of California.

⁸⁶ Bainbridge was a professor at Harvard who taught courses in physics in the 1930s.

MELAMED: It would seem from the story that General Groves was pretty closely involved in the biomedical program. He kept a close eye on it and he oversaw it.

FRIEDEL: He was involved, because I'm sure that he had to make some decisions about these various things. He was involved, as a matter of fact, in the fishery study. The reason the fishery study, I think, was done at the University of Washington [(Seattle)] (it was a logical place, anyway) was: I think that General Groves had done some studies there, or may even have been a graduate of the University of Washington, and then a program was created. I didn't really know about it until it was full-fledged, because I think it was handled primarily by Dr. Warren and General Groves. In any event, he was interested, and he would often contact me or General Groves about various problems.

One of the issues that I think we need to discuss—on your list there may be some other things you wanted to ask about—is the studies that were done at—the human studies with plutonium. We ought to get into that at the appropriate time. Are there any other?

FISHER: Just leading in to that. Can you briefly describe Colonel [Stafford] Warren, his personality, and your relationship with him?

FRIEDEL: Colonel Warren was, I think, a very easily approachable man. People liked him. He was very likable. He was very enthusiastic. I would say that he was very interested in research, and had a lot of contact with research. As a matter of fact, I discovered later that one of the reasons they considered him very seriously, was that he had contracts with the Office of [Scientific] Research and Development. I discovered from a member of the staff here, who had one Jack Coy, who was on the staff of the OSRD, who recalls that his contracts with the University of Rochester for Stafford [Warren] were abruptly canceled. Then he didn't know why, but afterwards, he discovered that [(Warren's appointment to Oak Ridge)] was the reason.

He was a very affable sort of person. People liked him. He delegated responsibility easily. I think he got along very well; people liked him. I think, though, that I wouldn't have said he was a superior scientist. I thought that some of the physicists, for example, were more rigorous in their approaches to scientific problems. But he was pretty good. He was interested. I would say he wasn't quite at their level. He would often turn to me with problems. The truth of the matter is that I knew more about radioactivity than he did at the time, because I had been involved in it at great extent. He leaned on me very extensively and gave me many opportunities to pursue my own approaches. As in the Army, I always did it under his authority.

Plutonium Injection Studies

FISHER: You mentioned to me at San Francisco that he was ill, I think in 1944, during the planning era.

FRIEDEL: Oh, yes. That explains one of the reasons why I went to Los Alamos. Actually, he was a pretty robust person, and I don't quite understand why he was ill; because he wasn't ill very often. But apparently, this trip to Los Alamos had been planned. I think it should be clear that of all the places that we used to visit, this one was sharply circumscribed. We never went there, except under direction.

For example, if I wanted to know something about the program at the University of California, I had no hesitation in going to the University of California and talking with Hamilton or Chakoff or Greenberg, or somebody. And some of the other people were learning some of the methods that they wanted to use, for example, in autoradiography. There was a gal by the name of Dorothy Axelwright who got to be pretty expert at this, and I remember visiting and seeing how this was done, and so forth.

Paul Aebersold⁸⁷ was a part of the program, and I got to know him very well. Although I knew them from before, from my period before. But the main point was: we never went to Los Alamos unless we were instructed to go to Los Alamos. It was sort of somewhat surprising, that I was then instructed to go to Los Alamos to pursue this program, to examine this program. Obviously, this program had been under discussion for some time; otherwise, it wouldn't have been developed to this level, with presumably Dr. Hempelmann⁸⁸ and Wright Langham.⁸⁹

MELAMED: You're discussing the plutonium injections now? That's the program?

FRIEDEL: In humans. Remember, they were doing animal work. They had already been doing lots of animal work. Animal work with plutonium was being done all over the place. I shouldn't say all over the place, but being done in California [(at Berkeley's Crocker Laboratory)], primarily, and also at Los Alamos and some in Chicago. Probably, some of it was done at Oak Ridge under what is known as [the] X-10 [graphite reactor] (that division of the Chicago project which then moved down there where the

⁸⁷ Dr. Paul Aebersold established the administrative system for distribution of radioactive isotopes. After working on the Manhattan Project at Los Alamos and Oak Ridge from 1942 to 1946, he served as director of the Atomic Energy Commission's Isotopes Division at Oak Ridge from 1947 to 1957. He retired as the Director of the AEC's Office of Isotopes Development in 1965. Two-and-a-half years later, he committed suicide. For additional information on Dr. Aebersold, see "Safety of the Nuclear Industry" in the interview with Merrill Eisenbud (DOE/EH-0456, May 1995); "Remembrances of Personalities" in the interview with Earl Miller (DOE/EH-0474, June 1995); and "Oak Ridge Committees (Isotope Distribution, Human Use, et al.)" and "Vanderbilt University Study of Pregnant Women and Iron-59" in the interview with Karl Morgan (DOE/EH-0475, June 1995).

⁸⁸ Hempelmann was a group leader in the Health Division at Los Alamos Scientific Laboratory from 1943 to 1947 and led the division from 1946 to 1948. An expert in radiology and radiobiology, he served in the Atomic Energy Commission from 1948 to 1950, then joined the faculty of the University of Rochester.

⁸⁹ At Los Alamos, Langham led the Health Division's Radiobiology group from 1947 until his death in 1972.

experimental pile was). This program must have been under considerable discussion.

I can't recall exactly my conversations. Because, very frankly, when Eileen Welsome,⁹⁰ who brought this to my attention first, said [that] I had gone there and approved it, I was nonplussed—because I didn't remember it. When she sent me the letter, then I began to cajole my brain and I remembered it.

I remembered—here's some of the instances: For example, Louis Hempelmann came out to meet me. I'd met Louis Hempelmann before. I knew him not well, but I knew him pretty well. Louis Hempelmann came out to pick me up at Albuquerque, I believe, maybe at Santa Fe; I've forgotten. Probably Santa Fe. He drove me and we got a flat tire on the way, and we had to fix it. So I remember that. I remember the conversation, and I remember Dr. Oppenheimer⁹¹ coming in occasionally.

Now my own recollection is that Dr. Hempelmann was in favor of the program, but he wasn't wildly enthusiastic. I would say that the one that was more enthusiastic, was pushing this more, was Wright Langham; because he felt that the work was coming in showing that there was a special distribution of the material in the endosteal⁹² areas, and where the primary bone marrow is more likely to be affected. They were concerned about that.

Besides that, they'd had an accident in which some of the—there was a minor explosion, and some of the material [(plutonium)] had been impacted into one of the individuals. They felt that some studies should be done in humans. This must have been approved by Stafford Warren. I shouldn't say, "approved." It must have been reviewed by Stafford Warren before I went.

MELAMED: What was the date that you went, do you remember, or the time?

FRIEDEL: I don't know the date, but there is a letter. I saw the letter, but I can't put my hands on it right now. There's a letter that indicates when it was done. Because the letter was written to Colonel Warren, stating who was present at the meeting; the date, of course; and was written by Oppenheimer and not by Hempelmann, asking that it be approved.

So the approval formally was to be given by Stafford Warren, I believe. But in the letter, it said I had reviewed the program—I had seen no objections to their pursuing it. But what was not in there was some conditions that we talked about. Those are useful because it's understood that that's what we would do.

⁹⁰ a reporter for the *Albuquerque Tribune* who in 1993 wrote a lengthy series on the AEC-sponsored plutonium injections. Her series was awarded a Pulitzer Prize.

⁹¹ J. Robert Oppenheimer, U.S. nuclear physicist (1904–67) who was chosen by General Leslie Groves to direct the development and construction of the atomic bombs at Los Alamos.

⁹² pertaining to the endosteum, the inner cavity of a bone, lining the marrow cavities

FISHER: What were those conditions?

FRIEDEL: One, it should not be done at Los Alamos; because it required sophisticated studies where patients could be handled properly. Two, it should be done in patients where you could get real data. One of the ways in which you could get real data, besides excretory data, would be where you could get some postmortems. So we used terminal patients, where there was a chance of getting data. And three, that we ought to use the doses that were in the vicinity of what were considered body burdens, from calculations from radium.

So those were the general conditions that we felt ought to be pursued. We saw no reason that appropriate patients couldn't be gotten for these studies. I personally was not terribly enthusiastic about the program. I said, "We've got to do it." The reason is that it was fairly late in the game.⁹³ Secondly, the real problem was interdiction. The real way to handle a problem where they don't know anything about it, but suspect, is make sure that you can't come in contact with it [(the radioactive material)] in various ways.

On the other hand, you couldn't argue that there couldn't be accidents. And therefore, you ought to know something more about it. So my enthusiasm wasn't wild, but I certainly couldn't object to the studies. Therefore, they seemed to be earnest, wanted to do it. They had enough background, and understanding of the problem, *both* from their own studies. If I remember correctly, Wright Langham and Louis showed some of the data, and we were aware of the data that was already coming out from Joe Hamilton's place [(Crocker Laboratory)].

FISHER: So you reviewed the excretion data from the worker with impacted plutonium.

FRIEDEL: Yes, but more than that, excretion data in animals, which was quite voluminous.

FISHER: Was there some discussion about the lack of agreement; the animal excretion rates with the human excretion rates?

FRIEDEL: That I can't recall. But there was some discussion, yes, because that was one of the arguments for doing it in humans. There was a discrepancy, they felt, in what they observed in this [in] man and [in] the animals.⁹⁴

⁹³ The race to build the atomic bomb would soon result in a working bomb and possibly large-scale production. There was an imminent need to understand the relationship between plutonium intake and rate of excretion, so that workers could be properly monitored by urine bioassay.

⁹⁴ Animals had been suspected, and were later confirmed, to metabolize and excrete radionuclides at rates that differed, often substantially, from the rates in humans; animal metabolic rates are usually higher than man's.

FISHER: Was there any connection drawn between your experience before the war, or early in the '40s, with injection of strontium, and the contemporary injection of plutonium? Was there any connection drawn?

FRIEDEL: No, none. The only thing that occurred was: there was some discussion of radiostrontium, and something that I don't remember. But Dr. Hamilton wrote a letter much later, somewhere in the '50s I think, to Shields Warren⁹⁵ about radiostrontium; in which he apparently got ahold of the data that I had done before I was ever involved in the Manhattan Project. And [the letter] indicated that I had injected so much strontium into a patient that, apparently, I considered such-and-such a dose lethal. Exactly why I considered it, and how, I [couldn't begin to] recall unless I was confronted with the data and had a chance to study it for a month. My experience was of this nature.

However, I do not recall whether we did—I shouldn't say "we," but a patient was injected with plutonium at Oak Ridge, Tennessee, when I was there. I didn't know the patients. I'd never had any contact with them. I know who injected it. It was a young man by the name of—I'll think of it. It was done under Dr. Warren's auspices, because obviously [someone] could not obtain plutonium, unless they got it from a formal source. They couldn't get the plutonium and have it properly prepared to inject into this patient.

The individual who did it, I have somewhere in my notes. I can find it. It's in Eileen Welsome's records because I gave her the name. I looked it up. I'll think of it. I can't recall it for the moment.

MELAMED: Joe Holland?

FRIEDEL: No, it wasn't Joe Holland. It was someone who had very little contact with it. He'd come from Chicago. He's a surgeon. Let me think for a moment. It's odd that I don't remember it. Anyway, it's in the record someplace. He injected it.

FISHER: Your description of that event—

FRIEDEL: He injected an individual that was about 60 years of age. He had been in a fearful accident in which he smashed up all kinds of bones. One of the reasons he was injected with this is: there was some vague report that it increased endosteal bone rapidly in animals. They thought, "Here was a chance of giving somebody some plutonium, which might possibly be useful in the healing process, and yet would give them some information on something about the distribution." He was the first individual that I

⁹⁵ Shields Warren, M.D., was Chief Pathologist at New England Deaconess Hospital and Professor of Pathology at Harvard Medical School. He joined the U.S. Navy Medical Department in 1939 and wrote with others on what was then known about radiation during World War II. Dr. Warren served on the first U.S. team to visit Hiroshima and Nagasaki after they were bombed with atomic weapons and was involved in creating what became the Atomic Bomb Casualty Commission. He was the first director of the AEC's Division of Biology and Medicine and, later, established his own cancer research institute at New England Deaconess Hospital. See "Recollections of Shields Warren" in DOE/EH-0471, *Human Radiation Studies: Remembering the Early Years; Oral History of Radiologist Henry I. Kohn, M.D., Ph.D.* (June 1995).

know of that received plutonium. It was really done in part for some obscure therapeutic reason, but also, presumably, to collect some data.

MELAMED: Did General Groves approve this? Do you know if he gave his approval and knew about it?

FRIEDEL: That, I don't know. But he would not have interfered.⁹⁶ It's possible that Dr. Warren had discussed this with General Groves. I don't know of it, but it's possible. General Groves liked Stafford Warren and maybe, indirectly, liked me too. General Groves was a pretty gruff sort of fellow.⁹⁷ I can tell you this: when he asked me to appear—I remember this very vividly—he asked me to appear, to go to Boston and buy the cyclotron. I got there promptly before he got there. I was to be there at eight o'clock so I was there at quarter-to-eight.

There was a long line of officers waiting to see him, and he came in and he didn't say hello to them. He was either preoccupied or very gruff. And then he very nicely asked me to come in before all the rest of them. All of them outranked me. Then he gave me this letter and I read it. And it was a handwritten letter, as I said earlier, from James Conant to him about transferring the cyclotron. He was a rough-and-ready individual. But I think he left Stafford Warren pretty much on his own unless there was some serious conflict.

FISHER: You mentioned to me in San Francisco, when we talked the last time, that these meetings in Los Alamos and the discussions with Oppenheimer got back to General Groves; and he was pretty well aware of the plan to test plutonium in human subjects.

FRIEDEL: I think he was. I think he would be. But I don't know if from the record. If I recall correctly, I never communicated with him. But Stafford Warren almost certainly did.

FISHER: In the acknowledgments section of the Rochester report on the two or three plutonium injection cases (the report that was classified and secret for some time and was declassified)—it's a nice, printed report; I noticed it was well-typeset. In the acknowledgments of this report, Stafford Warren was acknowledged as: "primarily responsible for the initiation of the program under the MED."

FRIEDEL: I think probably that's right.

⁹⁶ Karl Morgan recalls: "I don't think it would be any problem in getting the plutonium. Probably—my guess would be that Hymer Friedell or Stafford [Warren] were brought intimately into the earlier stages of [this study]. I say that without any great knowledge, but only because I knew both parties quite well at the time and knew what their interest[s] were and what one of their main goals was: to get information on the risks of plutonium [and uranium]. —from "Plutonium Injection Studies at an Oak Ridge Military Hospital (1945)" in DOE/EH-0475, *Human Radiation Studies: Remembering the Early Years; Oral History of Health Physicist Karl Z. Morgan, Ph.D.* (June 1995).

⁹⁷ Groves was portrayed by Brian Dennehy in a 1989 movie (*Day One*).

FISHER: That was report *LA-1151*,⁹⁸ dated September 20, 1950. I wondered if that would be your recollection.

FRIEDEL: I wouldn't know whether exactly he did it, but I wouldn't be surprised that he did. I wouldn't be surprised that this particular notation might not be after any research they did for this reason. I don't think I'm telling anything that is necessarily conjectural, but I think that President Vallentine, who was then in charge of the University of Rochester, probably made a hard bargain with the Army, saying, "You can have Stafford Warren." Remember Stafford Warren was also on the essential list, although he was overage. I think he's about 10, 12, maybe 15 years older than I.

They probably made an agreement to have a research program going on in Rochester, and to build the building then for them to do it. That was, I don't think, a [hard] bargain, but it was a bargain: "You can have Warren if you'll do this." I think the Army probably felt that we needed the research program anyway, and so, they did it. Undoubtedly, in the contract someplace, it probably outlined some of the studies that could be done—I know that I visited many times there before the building was built—and what the general program might be like.

FISHER: At Rochester?

FRIEDEL: At Rochester.

FISHER: What was your involvement in the analysis of the results from the plutonium injection studies?

FRIEDEL: As a matter of fact, I never really had an opportunity to analyze them. First of all, almost all the studies were done after 1946. Do you know the exact dates?

MELAMED: They were '45 and '46. I can get you the exact dates.

FISHER: The dates were compiled by Dr. Durbin; starting in April 9 or 10, of 1945 and continuing on to about January of '46, I think. Something on that order.

FRIEDEL: I would say that probably.

MELAMED: Here's a document we picked up from one of the records, that just listed all of the injections by code and the dates. They skip around. Here's the Oak Ridge one in 4-10-45. You see, you've got one down in '47.

FISHER: One as late as June and July of 1947, in San Francisco.

FRIEDEL: In a way, I'm surprised that 11 of them were done at Rochester.

MELAMED: There were quite a few at Rochester.

⁹⁸ the short title for a Los Alamos report on results of research involving injection of plutonium into human subjects: W.H. Langham, S.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, 1950; reprinted in *Health Physics*. Vol. 38, No. 6, 1980, pp. 1031-60.

FRIEDEL: I don't remember that. I have to confess that I don't really know anything about the results. I should have, probably. I don't recall any report that outlined what. There probably wouldn't be. It's fairly early. First of all, they'd probably be doing excretion data primarily. After all, what else could they do. They would do all kinds of metabolic studies: what happened to the white count, and what happened to kidney function, and what happened to various other studies. It wouldn't be surprising that the first reports weren't made until somewhere in '46.

So about that time, I was leaving the Army. I may not have even seen any of the reports. The obvious reports would have to be, first of all, what observations were made. There would have to be excretory data. There would have to be peripheral metabolic studies of various kinds: hematopoietic system, maybe bone marrow studies. Maybe—I'm sure they looked at the bones and got x rays before, and were going to do periodic x rays. As a matter of fact, Dr. Hempelmann at one time, some time in the late '50s when he went to Rochester, asked me to examine a patient and do some x ray studies on him; which I did.

They must have been looking at some of these patients and just doing a general surveillance. I'm sure they must have been hoping to get postmortem studies, because those are the ones that would really tell them something about the distribution [of plutonium within the body]. They may even have done some peripheral radioisotope studies, like: "What happens to the thyroid function?" for example, or, "Could we identify their kidneys by using appropriate radioisotopes?" All of these studies probably would have been done. But to get the reports—after they injected, which was late '45 and '46—I don't know when the first report came out. It was probably—well, I would guess, either early in '47 or late in '46.

FISHER: That raises a couple of other questions. Nichols, who was the chief in Oak Ridge—what was his outlook on this experimentation, do you remember?

FRIEDEL: He may not even have been aware of it, if it was reviewed. After all, it originated from Los Alamos. Therefore, it may even be that Nichols didn't know what was going on in Los Alamos; because General Groves kept this thing very tightly under control.

FISHER: Do you feel in anyway that your work with the plutonium injection study was misrepresented by anyone?

FRIEDEL: No, I don't think so. They say I had approved it, and in fact I'm the one closest to this and I had approved it. I can't deny it. The records indicate that I did. The records indicate that I visited. But after that, I had no contact with it.

FISHER: Were these experiments delayed, pending the development of radioanalytical methods by Wright Langham at Los Alamos?

FRIEDEL: You mean the human experiments?

FISHER: Yes. As he developed—

FRIEDEL: I don't think so, for this reason. First of all, you didn't know when you could get tissue to examine this; sporadically spread through long periods of time. So they must have taken whatever patients they could.

Patient Consent in the Plutonium Injections

MELAMED: Do you remember any discussions at all, that you were party to in any way, involving consent issues, or what you would tell the patients who were going to be injected—given the secrecy of what was going on?

FRIEDEL: I never saw any of the patients, never had contact with any of them, wouldn't know them. It may be that this was tightly compartmentalized, again for secrecy, because plutonium was involved.

MELAMED: You never heard any discussion, by people who were involved in planning, of how you would treat the actual contact?

FRIEDEL: No. I think Stafford Warren must have done this; because the program sort of came out of the blue. I'll say this off-the-record. I think one of the reasons this program was pushed—this will be off-the-record.

MELAMED: You can excise it later, if that would be all right. I'll just leave it on the tape, and when you get the transcript.

FRIEDEL: Will it come on the tape? I'm holding my hand over this thing.

MELAMED: I don't know. Do you want me to turn off the tape?

FRIEDEL: Turn it off.

(tape interrupted)

FRIEDEL: —when we get into controversy about this. In a way, it's conjecture. I don't really, can't, read their minds, and so on. One could argue that the very fact that I bring this up shows that I have that kind of devious approach to this, and I don't. I can't help feeling that it lingered there.

FISHER: Because so few people are still alive who can remember. Maybe you're the only one; I don't know. But in those planning meetings in Los Alamos in 1944, or was it 1945? It would have been early 1945, March or so. Was there any concern about "What do we tell either the patient, or his family, about injecting with plutonium?"

FRIEDEL: I have to be honest and say, "I do not recall any discussion." But Louis [Hempelmann] was a very, very sound, in my opinion, careful individual. He, I don't think, would subject patients to any unusual risk. And remember, in those days when we said, "Here we're thinking of using terminal patients," we're going to use what would be considered doses on the order of a body burden. Therefore, there should be very little hazard.

It [has] got all kinds of hazards they're already involved with. If we generally considered it was minimal hazard, and the thing would ordinarily not have been discussed at great length. Because the limitation of

doses, we were talking about doses at what was then considered the body burden level.

FISHER: *(to Melamed)* Do you want to move beyond the plutonium studies, or did you have any more questions?

MELAMED: I have just one more question in this area. Do you know of any other human experimentation that Dr. Hamilton might have been involved in in this period, other than this specifically, any involvement he might have had?

FRIEDEL: The only human experimentation, I would say, were these. Of course, before the Manhattan Project, I think he did a fair amount of work in metabolic studies with iodine; possibly even with radiophosphorus. He may have done it with Dr. Lawrence. It's conceivable. He probably did some work with some of the other biochemists and biophysicists who were also interested in certain metabolic studies. They may have done some studies of that kind in humans.

I'm sure they did studies which they considered to be trivial in hazard. They wouldn't cavalierly do this. I can't believe that. Although Dr. Hamilton is accused of being very cavalier in this. I think it was—if there is any such element in it—it could be due to the fact that we generally considered these tracer doses of no real consequence. That's how it might occur. When you look at it and look at the doses, it's true that they had an added risk. But the added risk, compared to the natural risks that existed, say in oncological diseases, was trivial.

What if your chances were increased from 1,800 per 10,000 to 1,810 or 1,820 per 10,000? That's not the kind of risk that is of real consequence. Generally, it would be ignored. Nobody made such calculations. These are the kinds of calculations we make now. When we do the linear quadratic (that's the term I was looking for earlier) or the linear extrapolations, you can come to some decisions about the kinds of risks. When you put it into the general risks, in those days, it didn't look very serious.

FISHER: After the end of the war and after your return from Hiroshima, Japan,⁹⁹ you went back to Western Reserve University?

FRIEDEL: I was never [previously] there. They offered me this position. I decided to accept it.

⁹⁹ the city onto which the first atomic bomb was dropped by a U.S. bomber on August 6, 1945, killing tens of thousands and helping to end World War II

Advisory Role in the Early AEC Biomedical Program

FISHER: You continued to serve the AEC¹⁰⁰ as an advisor and consultant?

FRIEDEL: I did. And I served on a number of committees. If you look through the record, you'll find my name scattered—all kinds of things I didn't know I did.

FISHER: One of the things that I'm curious about, and you'll have to forgive my insatiable curiosity—the *1947 Biology and Medicine Research Plan of the Atomic Energy Commission* outlines the next five to ten years of essential radiation research, and divides up responsibilities among the laboratories and universities that were affiliated with AEC. The mission identified for you and for Western Reserve University was work on the toxicity of thorium.

FRIEDEL: Yes, we never did it.

FISHER: Was it not funded?

FRIEDEL: I don't know why, but we never really pursued the program. It may have been that the University of Chicago was working on the thorotrast¹⁰¹ problem, as you may know. It may be that we decided we had plenty of other things to do first, and finally dropped it.

FISHER: What was your major radiation-related research with isotopes?

FRIEDEL: First of all, what we wanted to do was to see if we could develop some new approaches to the utilization of radioelements for diagnostic purposes, and perhaps therapeutic purposes. We did a number of studies. First of all, we did—most of our work was done on animals. We really did real studies on biological effects. Because it became intriguing to see if we could find special ways in which we could identify the mechanism, and maybe interdict it by various agents.

In the process, we began to look at some new approaches. One of the things that was of interest to us, was the fact that we were able to prepare—we had a biochemist, I think it was [G.W.] Buckaloo. We had a biochemist, who was able to prepare (under the direction of Dr. Lavette, who was a biochemist also, who came on our staff before Dr. Nygard, as a matter of fact), in which we could make [radiologically] tagged [(labeled)] protein. One of the intriguing things with tagged protein was that if we could get a tagged albumen,¹⁰² we could then study blood volume very easily. Because all we would do is put something mixed in the blood volume and then take a sample, know what we put in, and

¹⁰⁰ the U.S. Atomic Energy Commission, predecessor agency to the U.S. Department of Energy and Nuclear Regulatory Commission (NRC); established January 1, 1947

¹⁰¹ a contrast agent containing ²³²thorium oxide, used in radiology to highlight certain parts of the body in x-ray images

¹⁰² a protein found in nearly every animal and in many vegetable tissues, and characterized by being soluble in water and coagulable by heat. Serum albumen is the chief protein of human blood plasma.

what the dilution was on the blood volume. We did all this in animals, and then we came to our clinical staff.

I need to point out that the radiologists didn't have a pool, or patients, on its own. We would go to the clinical staff, show them our data, and say, "Wouldn't this be a very useful thing for you to do in your clinical study? Because now you can measure blood volumes. After all, what are you doing now when you assess the amount of any element in blood? You don't know whether his blood volume is low or high. You ought to be doing it at the same time."

It seemed rational. So we did some patients in which we used, in effect, tracer studies of albumen to study blood volumes. At the same time, somebody was doing something elsewhere and using tagged red cells. I think we may have done some studies to see which one was better. I think they tagged it with phosphorus. Again, it was the same kind of study. These are the only kind of studies. We never did any biological effect studies on humans.

FISHER: Do you recall any radionuclide¹⁰³ metabolism studies at Case Western?

FRIEDEL: Actual metabolism?

FISHER: Radionuclide metabolism studies?

FRIEDEL: You mean excretory studies?

FISHER: Sure.

FRIEDEL: Well the only studies we did—yes, we probably did some studies on thyroid patients, in which we wanted to measure the excreta and we wanted to see whether the data that was on the literature compared to our own, or whether we could develop special measures. We undoubtedly did some of that.

AEC Isotope Distribution Committee

FISHER: You served as an advisor to Paul Aebersold and his isotope distribution efforts. Can you recall that work?

FRIEDEL: I thought I was the chairman for a while. As a matter of fact, I do. I and Dr. Quimby, I believe were the committee. I think it may have been that Robley Evans¹⁰⁴ was also on the committee.

¹⁰³ atomic species in which the atoms all have the same atomic number but different mass numbers according to the number of neutrons in the nucleus

¹⁰⁴ In the early '30s at MIT, Evans investigated the bioeffects of radium on dial painters in New Jersey and Connecticut. By 1941, Evans with others had set the first standards for a tolerance level for radium in the human body. The first "tolerance level" for radium was set at 0.1 microgram body burden: Evans judged that there would be no bone cancers below 0.1 microgram ²²⁶Ra in the skeleton. Later he served on the AEC's Committee on Isotope Distribution. At a 1967 symposium, he proposed that the AEC establish a National Center for Human Radiobiology so the AEC could follow up and combine all the radium cases being studied at MIT, Argonne National Laboratory, and elsewhere. On September 1, 1969, the center

(continued...)

MELAMED: This is the Committee on Isotope Distribution [of the AEC]?

FRIEDEL: Isotope Distribution. It may have been Paul Aebersold that we responded to. If you say that, I believe it to be so.

FISHER: I'm recalling from my memory, which may not be as good as yours.

FRIEDEL: All I remember is that I served as the chairman and we received requests, which were sent to the AEC. The AEC, in turn, would send them to us for approval. I think I met once or twice with Edith Quimby. But the way we did it was: she would get a copy and I would get a copy, and then we would review this. And it may be that Robley Evans was involved as well, but I'm not sure about that.

In any event, we would then decide: yea or nay. And our usual decisions were generally [based upon], what kind of experience did they have? What kind of facilities were available for them to do what they said they would do? Generally, if there [were] no obvious objections, we would approve it.

It [be]came, before long, [a] somewhat onerous duty. And so we thought that perhaps they ought to do it formally, on their own. And if they needed an advisory committee, maybe we could form an advisory committee to see where the overall program was going. But for us to decide on each individual one, didn't appeal to us. Because it meant so much work. It was beginning to burgeon.

FISHER: As more and more of these studies proposed human injections of radioactive materials, what was the committee's viewpoint toward this? More and more of these applications proposed the use of radioactive materials in patients for studies where there was no diagnosis or treatment of a condition.

FRIEDEL: Generally we didn't approve them unless they were done for, "What are you going to do with it?" "We're going to try to study something to do this." One of the things that I recall is they wanted to see if they could identify the pancreas¹⁰⁵ by appropriate tagging of certain proteins. We said, "That's a good idea; it's hard to see the pancreas." If the doses were reasonable, we would approve it. Obviously those were a kind of metabolic general experimental background, so that we would approve it. Otherwise, it would look as if we were—after we were doing it, other people were doing it that were associated with the Manhattan Project—it would look as if we were keeping this all to ourselves, and we don't [want] anybody else to have anything to do with it. Generally, we were ready to approve any program that looked reasonable.

MELAMED: I guess underneath the Advisory Committee on Isotope Distribution, there was a special Committee on the Allocation of Isotopes for Human

¹⁰⁴ (...continued)

opened at Argonne, headed by Robert E. Rowland; Evans maintained a satellite office at MIT. In the early 1990s, Evans's pioneering basic research earned him the Department of Energy's Fermi Award.

¹⁰⁵ a large, elongated gland behind the stomach. Its secretions are concerned in digestion.

Use. Was that the same people that you just mentioned, who were involved with you on that?

FRIEDEL: I suspect that was special. Otherwise, we didn't want to be involved in somebody using carbon-14¹⁰⁶ for studying whatever it—fossils. So it must have been for humans.

MELAMED: Human use was what you focused on?

FRIEDEL: One of the questions that we started on was: "What do we do here in which we use humans?" The major ones we did was, first of all, we pursued that ³²P [(phosphorus-32)] study that we started in California.

FISHER: Intravenous ³²P?

FRIEDEL: Intravenous ³²P. And we found some successes here in which we were able to ablate,¹⁰⁷ or in effect, eliminate some of the metastases to bone. We used radiophosphorus, and it's published.

The other thing that we did—we thought was interesting. I still think it's interesting. I had worked with the heart originally, way back a million years early-on. One of the things that we thought was interesting was: a man by the name of Tinsley Harrison had introduced a system for measuring cardiac output by using a dye, in which he cannulated¹⁰⁸ an artery and then just took samples at periodic intervals, and then determined the dilution characteristics, and then could measure the cardiac output, which was something like what we wanted to do originally with x rays.

We got the idea using the iodinated protein, albumen, which was injected. Then we could study in some isolated arterial area, the dilution characteristics, which would do the same thing; and therefore [was] a simple way of, in effect, sampling really what was kind of awkward if you did it by doses. And you wouldn't have to cannulate the artery. If you could isolate it, then you could look at it, and you could see the dilution curve. We published that, and it's in the reports. That dilution curve now told you what the cardiac output was. It was kind of clever. Because if you used iodinated protein, presumably it eventually came into equilibrium. Then, you see, you've got a fixed level which represented the final dilution level.

We looked at the curve of dilution and the period of time at which it was obtained. By integrating this curve and comparing it with the final level, you could now determine the amount of the blood volume that had flowed during that interval of time. And therefore, you had the cardiac output. Now, if you wanted it in cc's [(cubic centimeters)], you just took a sample of the venous blood. So we thought it was great stuff. The problem with it was that isolation of an arterial pool was very difficult.

¹⁰⁶ a radioactive isotope of carbon having a half-life of about 5,730 years: widely used in the dating of organic materials; also called *radiocarbon*

¹⁰⁷ to remove or destroy by radiation

¹⁰⁸ installed a cannula, a metal tube inserted into the body to draw off fluid or introduce medication

We finally decided, by looking at a certain part of the aorta, we thought that would minimize venous pools. That's what we had to do. You had to look at an artery, the same pool all the time, and not seek after pools. Then, later on, we discovered that a good way to do it would be to arteri-¹⁰⁹alize the ear. You do that by heat. You warm it up. You get the circulation going. Anyway, we did that in patients. Of course, we went to the clinical staff and they thought it was great stuff, or at least they thought it was good to do in patients.

We did that and we also did arterial interference. That is, we found patients who had obstructions to flow. And now, that was a very good way of immediately identifying it; by simply putting counters¹¹⁰ over the feet.

We thought we were doing a lot, but other [(pharmaceutical)]¹¹¹ systems came along and the use of radioisotopes required more and more care and management. So eventually it petered out. That's what we did.

FISHER: Was there, associated with these studies, concern for radiation side effects, irradiation of the thyroid?

FRIEDEL: The doses were so small that you would have no chance in finding anything. The only side effects we ever looked at were those which we use in phosphorus, and widespread bone metastases from breast, primarily; in which we looked at the hematopoietic system. There, we monitored this very carefully in order to make sure that we didn't do more harm than we did good. That's the kind of studies we did. But we never pursued the patients for a long period. They were terminal patients, so it was really an approach for effective amelioration.

FISHER: Were terminally ill patients normally selected to participate in tracer studies, or did you use—

FRIEDEL: Well, we really didn't do tracer studies just to be doing them. By then, the literature was replete with all kinds of studies. We wanted to do something that was different. So we did these studies with the albumen. We did one other thing. We pancreatized some dogs, and fed them this albumen, and found, of course, that they couldn't metabolize it. And we thought that was a great thing for possibly looking at enzyme deficiencies and gastrointestinal studies. We introduced this to one of the clinicians who wanted to do it. So we fed some of it to patients and made some studies. This is the kind of work we did in humans here.

FISHER: I [can] think of one more question.

MELAMED: I have one more.

FISHER: *(to Melamed)* Why don't you go ahead, and then I'll ask one?

¹⁰⁹ the provision or supplying of oxygenated blood instead of venous blood

¹¹⁰ devices used to count the rate of radiation emissions from radionuclides inside a subject's body, using radiation detection instruments or a whole-body counter

¹¹¹ drugs approved for human use

MELAMED: I just have a curiosity. This isn't an area that in any way shows up in the material that we've read of your involvement. But, after the war, there was a lot of discussion about the potential for developing radiological warfare¹¹² weapons, using these new procedures. Did you have any knowledge of what was going on in that area?

FRIEDEL: The only knowledge I had was during the war. You may possibly know that there were reports that came out of the University of Chicago, in which there was a report which identified the possibility of using massive doses of fission products to occupy certain areas, or make areas uninhabitable. At the same time it said, "We must look at this because we don't know that the enemy may not be considering the same thing." That report came out, and then I never saw any report again.

The question came up and I do remember the man, I don't remember his name. If I looked at the records, I would remember. I do remember the man who wrote the report. He was one of the physicists who was looking in general at these problems. Afterwards, I knew of no such program. The only thing that I was involved with was the Project Plowshare.¹¹³ The Project Plowshare, which was then being considered, the idea was to use nuclear explosions as excavation elements across someplace, maybe Honduras or someplace like that, to build another canal. The AEC director who was involved in this was a fellow by the name of Spoffard English. You may come across his name; if you go back and look at the records, you will find that he was the director. We probably met for a couple of years.

There were military officers. As a matter of fact, one of the officers was the fellow who led the raid on Tokyo, the air officer. What was his name? Jimmy Doolittle was a member of the committee. There was another Army officer, who I think was an engineer, who was a member of the committee. Then we had other members of the committee who were interested in marine activities. And the two biomedical people who were involved were Louis Hempelmann and I.

Before long, it became clear that it wasn't a tenable thing to do, and it disappeared.

The other possible thing having to do with warfare, was the fact that there was a committee formed, I think in Cincinnati, but under the auspices of the AEC, with regard to considering flight by nuclear energy.¹¹⁴

¹¹² the conceptual use of fission-product radiation to kill enemy troops

¹¹³ a program initiated by President Dwight D. Eisenhower to identify and demonstrate uses for peaceful nuclear explosives (PNEs), such as civil engineering projects. For a variety of reasons, no such peaceful nuclear explosions ever were conducted by the United States as anything other than tests. Before its breakup, the Soviet Union reportedly used PNEs in several massive civil works projects.

¹¹⁴ In the late 1950s and early '60s, several contractors worked on the development of nuclear-reactor-powered jet engines for long-range military aircraft. The projects were funded by the AEC and the Department of Defense, and the contractors included General Electric, Pratt & Whitney, and others. Engines were built in Connecticut (Pratt & Whitney) and Ohio (GE), and some were tested at the National

(continued...)

The question came up, "Can you fly this great big thing and shield it? How would you do it?" so on and so forth. After a little study, it became pretty clear that it was a very difficult problem. It petered out, the way it should.

FISHER: Did you have any involvement in the assessment of potential biological risk from this nuclear energy propulsion in the space project, or in aircraft?

FRIEDEL: No. The only contact I ever had, surprisingly, was: One day one of our professors of Neurology came to me and he said, "We're going to go to the moon." I said, "What else is new?" It was years before we did it. He said, "They're going to the moon." I said, "What are you talking about?" He said they were going to have a program that they were going to moon.

Apparently, there were some neurological studies that were being involved, and he was involved with it. He said, "Who do you know that would be free to work on space radiation?" I gave him the name of Cornelius Tobias.¹¹⁵ There were several others, but they liked Tobias. I think they contacted him, and I think he did work on it.

FISHER: He's made a career out of studying interactions of high-energy particles with tissue.

FRIEDEL: Right, I know that. I knew Toby very well and I kind of liked him. I felt he was a very sincere, honest, reliable individual.

FISHER: I don't remember what year you first started working with the NCRP,¹¹⁶ the National Council on Radiation—

FRIEDEL: It must have been in the '60s.

FISHER: Was it?

FRIEDEL: I served on their radiation study section. Wait a minute. The NCRP—I must have been about—I can tell you exactly when it was. It was about the middle, early '70s. That's not quite right. I was put on their board, or made a member; I've forgotten. I may have been a member before. I guess I [had] better retract. Maybe it was early as the '60s. But in the '70s, I was put on the board, and that's when I became more intimately involved.

And I was on the board of the NCRP until I became its vice president. Then I was vice president for about six or seven years. I resigned be-

¹¹⁴ (...continued)

Reactor Testing Station in Idaho. Also known as the NEPA (Nuclear Engine for the Propulsion of Aircraft) program, the nuclear aircraft program was cancelled by President Kennedy because problems with engine weight and crew shielding, as well as design philosophy disagreements, were halting progress.

¹¹⁵ Tobias was a professor of medical physics and radiology at the Donner Laboratory and the University of California at Berkeley. Dr. Tobias's main research focused on the biological effects of radiation; cancer research; and space medicine. For the transcript of the interview with Tobias, see DOE/EH-0480, *Human Radiation Studies: Remembering the Early Years; Oral History of Biophysicist Cornelius A. Tobias*, Ph.D. (July 1995).

¹¹⁶ National Council on Radiation Protection. Although the words "and Measurements" were later appended to the name, the council's initials remain NCRP.

cause they said they wanted younger people. They said, "Anybody over 65 ought to be out." I was already 72 at the time. I felt, at 72, to show the flag, the proper approach. I resigned at 72.

FISHER: Now in 1955, a report from the University of Chicago described incidence of thyroid cancers in children treated earlier in the '30s and '40s with radium tubes and radium applicators. Do you recall this report coming out, and what was your response to it? How did you feel?

FRIEDEL: First of all, I think it was due to radiation. You say "radium." I think it was due to x rays. Michael Reese, the radiotherapist [after whom the Michael Reese Hospital and Medical Center in Chicago is named], I think was [originally] a European; and they were, in a way, even more cavalier than we might have been in the use of radiation. They treated a lot of conditions around the head and neck for relatively benign conditions. Patients that would likely have long survival rates [if left untreated], not for carcinoma or anything of that kind. I think also they treated patients for fungus diseases in children.

Reports came out in which they reported tumors of the thyroid. I don't know whether it was carcinoma of the thyroid. I must confess, I was a little skeptical because I felt the doses—I think most of these were kids and the treatment for kids would have been on the skull, and they were usually 100-kilovolt x rays, which really were quite superficial. I was skeptical, but as the reports came on, I said, "It may well be that the thyroid is susceptible in some way." I felt sort of strongly about some of this, anyway. Because here, when I came here to the university, they used to make a practice of treating newborns with 25 to 50 rads over the thymus,¹¹⁷ because they thought that thymic deaths occurred. Because they would see enlarged thymus, and of course they had nothing to do with it. Here they were delivering pretty serious doses.

FISHER: What years were those: in late '40s?

FRIEDEL: No, they were done in the late '30s and early '40s, during the war and maybe during the '30s. When I found out about it, I stopped it. I think they muttered and fussed. I kind of wielded a lot of authority because they hadn't encountered radiation the way I had, and they thought I must surely know what I'm talking about. So they demurred, but they didn't always listen.

FISHER: There was concern that enlarged thymus would inhibit breathing.

FRIEDEL: They found crib deaths and they would often attribute it to the enlarged thymus, which wasn't correct at all. Children often have enlarged thymus normally. And they would see this by x ray, and say, "Yes, we have a treatment." So they did it routinely. I'm glad I had this impact.

FISHER: Was that at this university?

¹¹⁷ a ductless gland lying at the base of the neck, formed mostly of lymphatic tissue and aiding in the production of T cells of the immune system

FRIEDEL: And probably done at other places. It may have been done at Michael Reese, as well.

I've been interviewed by NBC, when the Eileen Welsome report got started [in 1993]. I have been interviewed also by a couple of Japanese outfits. More recently, who else? I think a German outfit wanted to interview me, but we never did make the arrangements, thank goodness.

On two different occasions, Japanese came to interview me; TV broadcasting agents. They came once to my house and once, I have a place in California and they came there. They asked me questions. They were really interviewing me. The recent one interviewed me because they were going to have some kind of special program in 1995, which is 50 years after Hiroshima, and they prefaced this by saying, "One of the reasons we're conducting these interviews with you and others"—they had fellows like Phil[lip] Morrison¹¹⁸ on the program and [nuclear physicist] Hans Bethe.¹¹⁹

They used some others that are still around. They said that the reason was that the Japanese people feel that Hiroshima nuclear explosion was really a demonstration; that the war was over, that the Japanese could no longer resist, and the Americans either knew it, or sensed it. And we did it only to show that we could accomplish it. I pointed out to them—as I think you know, I went to Hiroshima and I was involved in various things—in any event, I pointed out to them that I had been stationed with the Third Marine Division, and for some of us to go into Japan after the war. But the Third Marine Division was all ready to invade. We would have had enormous casualties, and *they* would have had enormous casualties. Even though a tremendous number of casualties occurred, perhaps even more would have happened if we had invaded. From everything I knew, which is really—I had no special responsibility or authority—it looked to me that the end of the war was a desirable thing. We left it there. But then they asked me other questions.

FISHER: What's the most remarkable memory you have of the Manhattan Engineering Project?

FRIEDEL: I guess I would have to say my trip to Alamogordo, just before the explosion.¹²⁰ But a close second is my trip to Hiroshima, and the period I spent there. I think one of the remarkable things—also from a broad general point of view, it had little impact—was the idea that this enormous project was going to go forward with determination and earnestness when I got to Chicago. I said to myself, "Good heavens, are we really going to do all that?" And we did it.

¹¹⁸ physicist, group leader at the Met Lab in Chicago (1943–44), and subsequently of Los Alamos Scientific Laboratory (1944–46), and Cornell University (1946–); recipient of numerous prizes in physics and astronomy

¹¹⁹ Nobel Laureate for discovery of the energy processes of the sun

¹²⁰ Alamogordo, a city in New Mexico, is located 50 miles southeast of the first atomic bomb explosion (July 16, 1945); Dr. Friedell was in Albuquerque during the test.

- FISHER:** There's few people who live today who have had these experiences that you have had. Certainly *I* missed out by a few years. We appreciate the opportunity to obtain an oral history with someone [with] as remarkable career as you had and so much to share. We want to thank you for it.
- FRIEDEL:** I'm glad to do it. I think I probably should have written *my* memoirs at some time. I always feel that somebody else should write it.
- FISHER:** Maybe in conclusion I could mention that you gave a paper just after the war to a small medical society in Pennsylvania on radiation and cancer. I don't know if you remember that?
- FRIEDEL:** Yes, I did. The reason I remember it is that I had some slides that had to be specially protected because they were made of flammable materials. They had to encase the projector with all kinds of things. Yes, I remember it.
- FISHER:** That was a very good paper, and as I read it now, almost everything you said was right-on with forty more years of experience. I want to congratulate you for that.
- MELAMED:** Thank you very much. Can you think of anything that you would like to share with us that we haven't covered, that might be good to have on this tape about your experiences?
- FRIEDEL:** The only thing that was interesting in a way was the Hiroshima experience. But I don't know whether this is germane to the interests you have. If you want me to, I can tell you something about it, because it was kind of interesting as the way it was conducted and what we did, and what the problems were. It's just an interesting episode. Whether it had significant impacts, I doubt.
- MELAMED:** I guess we're worried about time.
- FISHER:** We're worried about time.
- FRIEDEL:** We have to get out of here.
- FISHER:** We could move to another place.
- FRIEDEL:** What about lunch? Do you want to have lunch?
- MELAMED:** Why don't we stop for now.
- FISHER:** Can we take you to lunch?
- MELAMED:** Thank you very much. □