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ON
Human Radiation Experiments

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Experiments with Plutonium, Uranium, and Polonium

IN August 1944, at the secret Los Alamos Laboratory in New Mexico, a twenty-three-year-old chemist was trying to learn what he could about the properties of a radioactive metal. One year later, the new "product"—one of several code words for this three-year-old element with a classified name—would power the bomb dropped on Nagasaki. That day the young scientist, Don Mastick, was working with the entire Los Alamos supply of the material, 10 milligrams. It was sealed in a glass vial several inches long and about a quarter inch in diameter. Unknown to Mastick, a chemical reaction was causing pressure to build up inside the vial. Suddenly it burst, firing an acidic solution against the wall from where it splattered into Mastick's face, some of it entering his mouth.[1]

Realizing the importance to the war effort of the plutonium he had just ingested, Mastick hurried directly to the office of Louis Hempelmann, the health director at Los Alamos. Hempelmann pumped Mastick's stomach and instructed the young scientist to retrieve the plutonium from the expelled contents. Hempelmann expressed a concern related to worker safety: there was no way available to determine how much plutonium remained in Mastick's body. He immediately pressed the lab's director, J. Robert Oppenheimer, for authorization to conduct studies to develop ways of detecting plutonium in the lungs, and in urine and feces, and of estimating the level of plutonium in the body from the amount found in excreta.[2]

Looming over Mastick's accident was the well-known tragedy of the radium dial workers more than a decade earlier. Like Mastick, they had ingested radioactive material through their mouths, as they licked the brushes they used to apply radium paint to watch dials. As time passed, many suffered from a gruesome bone disease localized in the jaw, and some bone cancers developed. Could plutonium cause a similar tragedy? If so, how much plutonium needed to be ingested before harmful effects might arise? How could one tell how much plutonium a person had already ingested? The answers to these questions were crucial, not only in the case of accidents such as Mastick's, but also, in the long run, to establish occupational health standards for the hundreds of workers who would soon be mass-producing plutonium for atomic bombs. Several pounds of radium, handled without recognition of the dangers, had led to dozens of deaths; what might plutonium cause?

A starting point was to examine the available data on radium poisoning, compare the characteristics of the radiation emitted by radium and plutonium, and try to extrapolate from radium to plutonium. However, plutonium had already revealed unexpected physical properties, which

were posing problems for the bomb designers. Could plutonium also have unexpected biochemical properties? Extrapolation from radium was a good starting point, but could never be as reliable as data on plutonium itself.

Oppenheimer agreed that this research was critical. In an August 16, 1944, memorandum to Hempelmann, Oppenheimer authorized separate programs to develop methods to detect plutonium in the excreta and in the lung. With respect to biological studies, which Oppenheimer speculated might involve human experimentation, he wrote: "I feel that it is desirable if these can in any way be handled elsewhere not to undertake them here."[3] The reason Oppenheimer did not want these experiments conducted at Los Alamos remains obscure. Nine days later, Hempelmann met with Colonel Stafford L. Warren, medical director of the Manhattan Project, and others. They agreed to conduct a research program using both animal and human subjects.[4]

Mastick, who reported no ill effects from the accident when Advisory Committee staff interviewed him in 1995,[5] was not the first alert to the potential hazards of plutonium. Human experiments to study the metabolism and retention of plutonium in the body had been contemplated from the earliest days of the Manhattan Project. On January 5, 1944, Glenn Seaborg, who in 1941 was the first to recognize that plutonium had been created in the cyclotron at the University of California at Berkeley, wrote to Dr. Robert Stone, health director of the Metallurgical Laboratory in Chicago (a Manhattan Project contractor) and a central figure in efforts to understand the health effects of plutonium:

> It has occurred to me that the physiological hazards of working with plutonium and its compounds may be very great. Due to its alpha radiation and long life it may be that the permanent location in the body of even very small amounts, say one milligram or less, may be very harmful. The ingestion of such extraordinarily small amounts as some few tens of micrograms might be unpleasant, if it locates itself in a permanent position.[6]

Seaborg urged that a safety program be set up. In addition, "I would like to suggest that a program to trace the course of plutonium in the body be initiated as soon as possible. In my opinion such a program should have the very highest priority."[7] Stone reassured Seaborg that human tracer studies "have long since been planned. . . . although never mentioned in official descriptions of the program."[8] The work began at Berkeley with studies on rats conducted by Dr. Joseph Hamilton.[9]

Even as these studies on the biological effects of plutonium were beginning, the amount of plutonium being produced was dramatically increasing. Most of the effort at Oak Ridge was devoted to the separation of isotopes of uranium. However, the X-10 plant at Oak Ridge was a larger version of the very small plutonium-producing reactor developed at the University of Chicago. The X-10 plant began operating on November 4, 1943, and by the summer of 1944 was sending small amounts of plutonium to Los Alamos.[10] By December 1944 large-scale production of plutonium began at the Hanford, Washington, reactor complex.[11]

By late 1944, in the wake of the Mastick accident, the need to devise a means of estimating the amount of plutonium in the body became acute. It seemed that the only way to estimate how much plutonium remained in a worker's body would be to measure over time the amount excreted after a known dose and, from this, estimate the relationship between the amount excreted and the amount retained in the body.[12]

MAXIMUM PERMISSIBLE BODY BURDEN (MPBB) FOR PLUTONIUM

The plutonium injections were part of a larger research project intended to provide data for an occupational safety program riddled with uncertainty. Not only was there a need for ways to monitor the exposure of personnel—the driving force behind the plutonium injections—but the maximum permissible body burden (MPBB) for plutonium,

the maximum amount of plutonium that would be permitted in the bodies of workers, was still under debate.

The concept of "maximum permissible body burden" had begun to develop before the war in light of the known hazards of radium. Just prior to the war, primarily at the request of the Navy, a committee of experts was formed to establish occupational health standards for the factories producing dials illuminated by radium paint. After examining the data on radium dial painters, this committee agreed that 0.1 microgram fixed in the body should be the "tolerance level" for radium: an amount that, in the words of the committee chairman, Robley Evans, would be "at such a level that we would feel comfortable if our own wife or daughter were the subject."[a] After the war the term *maximum permissible body burden* was adopted and defined more precisely as the amount of a radioisotope that, when continuously present inside the body, would produce a dose equivalent to the allowable occupational exposure (the maximum permissible dose). For radioisotopes that, like radium, primarily reside in bone, biological data and mathematical models were used to determine how much of another bone seeker would produce the same dose as the original 0.1-microgram radium standard.

Between 1943 and the spring of 1945, based on the body burden for radium and preliminary results of animal experiments, a tentative MPBB for plutonium of 5 micrograms was adopted by the Manhattan District.[b] This level was derived by direct comparison of the relative energies of plutonium and radium.

By the spring of 1945, differences between the deposition of radium and plutonium in the body were becoming clearer. Animal data indicated that plutonium deposited in what was called at the time the "organic matrix" of the bone—the part of the bone most associated with bone growth. This was different from radium, which seemed to deposit instead in the mineralized bone. Wright Langham wrote to Hymer Friedell supporting the choice of 1 microgram as an operating limit in lieu of a more formal policy. Langham wrote that with the adoption of this lower limit "the medico-legal aspect will have been taken care of and of still greater importance, we will have taken a relatively small chance of poisoning someone in case the material proves to be more toxic than one would normally expect."[c] This level was adopted and held until the Tripartite Permissible Dose Conference at Chalk River, Canada, in September 1949.

At this conference, representatives from the United States, United Kingdom, and Canada agreed on tolerance doses for many radioactive isotopes, including a maximum body burden of 0.1 microgram for plutonium. This reduced by a factor of 10 the value under which Los Alamos production had been operating. This reduction was based on the results of acute toxicological experiments with animals, which indicated that plutonium was as much as fifteen times more toxic than radium.

On January 20, 1950, Wright Langham wrote to Shields Warren, then the director of the AEC's Division of Biology and Medicine, alerting him to the problems caused by the Chalk River Conference's new "extremely conservative tolerances [which] may have a drastic effect on the efficiency and productivity of the Los Alamos Laboratory. Their official adoption will undoubtedly force major alteration in both present and future laboratory facilities and may add millions of dollars to the cost of construction of the permanent building program now in the

a. Robley Evans, "Inception of Standards for Internal Emitters, Radon and Radium," *Health Physics* 41 (September 1981): 437–448.

b. W. H. Langham et al., "The Los Alamos Scientific Laboratory's Experience with Plutonium in Man," *Health Physics* 8 (1962): 753.

c. Wright Langham, Los Alamos Scientific Laboratory Health Division, to Hymer Friedell, 21 May 1945 ("Since the Chicago Meeting, I am somewhat lost as to what our program should be in the future . . .") (ACHRE No. DOE-113094-B-7), 1.

planning phases."[d] Langham continued with reasons for regarding the Chalk River value of 0.1 micrograms of plutonium as "unnecessarily low." He cited, among other things, differences between acute and chronic toxicity and new analysis of data from the radium watch dial painters.

On January 24, 1950, Shields Warren, Austin Brues of Argonne National Laboratory, Robley Evans, Karl Morgan, and Wright Langham met in Washington. Langham wrote later: "As a result of this meeting, Dr. Shields Warren of the Division of Biology and Medicine authorized 0.5 ug (0.033 uc) of Pu^{239} as the AEC's official operating maximum permissible body burden."[e] There were no minutes or transcripts taken of this meeting. The calculation of this level was again based on the body burden for radium, this time modified by the 1/15 toxicity factor (since experiments had indicated that plutonium was up to fifteen times more toxic than radium), by the relative retention of plutonium and radium in rodents, and by the energy ratios modified by radon retention.

Thus far, the entire debate had occurred behind the closed doors of the AEC. Consideration of all the complex issues applied in setting a permissible body burden had been within a small circle of scientists and administrators. While the MPBB for plutonium accepted at the January 1950 meeting has held until today, its derivation has changed over the years.

By March 1945, there was disturbing news that urine samples from Los Alamos workers were indicating, based on models developed from animal experimentation, that some might be approaching or had exceeded a body burden of 1 microgram.[13] A March 25 meeting led to Hempelmann's recommendation that the Project "help make arrangements for a human tracer experiment to determine the percentage of plutonium excreted daily in the urine and feces. It is suggested that a hospital patient at either Rochester or Chicago be chosen for injection of from one to ten micrograms of material and that the excreta be sent to the laboratory for analysis."[14] The overall program, as it was envisioned by Dr. Hymer Friedell, deputy medical director of the Manhattan Engineer District, Oppenheimer, and Hempelmann, consisted of three parts: improvement of methods to protect personnel from exposure to plutonium; development of methods for diagnosing overexposure of personnel; and study of methods of treatment for overexposed personnel. On March 29, Oppenheimer forwarded the recommendation to Stafford Warren, with his "personal endorsement."[15]

The accident at Los Alamos was part of the prelude to experiments conducted between 1945 and 1947 in which eighteen hospital patients were injected with plutonium to determine how excreta (urine and feces) could be used to estimate the amount of plutonium that remained in an exposed worker's body. One patient was injected at Oak Ridge Hospital in Oak Ridge, Tennessee; eleven were injected at the University of Rochester, three at the University of Chicago, and three at the University of California.

The results of these experiments contributed to the development of a monitoring method that, with small changes, is still used today. The experimental data were used to develop a model relating body burden to short-term excretion rate. Known as the "Langham model," it was based on short-term excretion data, long-term

d. The letter went on to say that "operations of the Los Alamos Laboratory would be curtailed or stopped if such action were necessary to the reasonable and sensible protection of the personnel. The seriousness of this action, however, seems to be adequate reason for requesting that official adoption of the tolerances by the AEC be postponed until they have been carefully reviewed in order to make certain that the values are not unnecessarily conservative." Wright Langham, Los Alamos Laboratory Health Division, to Shields Warren, Director of AEC Division of Biology and Medicine, 20 January 1950 ("Radiation Tolerances Proposed by the Chalk River Permissible Dose Conference of September 29-30, 1949") (ACHRE No. DOE-020795-D-6), 1.

e. W. H. Langham et al., "The Los Alamos Scientific Laboratory's Experience with Plutonium in Man," *Health Physics* 8 (1962): 754.

excretion data that were collected in 1950 from two injection subjects, and worker excretion data. This model has been used almost universally to monitor plutonium workers since 1950, although it has been modified over the years as longer-term and more extensive data were accumulated. While now, fifty years later, not every question concerning the quality of the science or the basis for estimating risk can be answered with precision, there is general agreement among radiation scientists that the experiments were useful.

Although this would be the first time that plutonium would be injected into human beings, the plutonium experiments were not viewed at the time as being extremely risky, and for good reason. Based on experience with other bone-seeking radioisotopes such as radium, the investigators had firm basis for believing, even in the 1940s, that the amount of material to be injected was likely too small to produce any immediate side effects or reactions. No one was expected to feel ill or have any negative reaction to the injection, and apparently no one did. Because acute effects were not expected, the plutonium injections were viewed as posing no short-term risks to human subjects. There was concern, however, about long-term risk. A draft report, written by one of the primary investigators within a few years of the injections, records that "acute toxic effects from the small dose of pu [plutonium] administered were neither expected nor observed." The document also recognized that "with regard to ultimate effects, it is too early to predict what may occur."[16] Based largely on the experience of the radium dial painters, it was recognized that exposure to plutonium could result, perhaps ten or twenty years later, in the development of cancer in a human subject. This was viewed as a significant risk but also as a risk that could be minimized by the use of small doses and wholly avoided if the subjects were expected to die well before a cancer had a chance to materialize.

Even if the plutonium injections had been entirely risk free, an impossibility in human experimentation, they could still be morally problematic. As we discussed in chapter 2, it was not uncommon in the 1940s for physicians to use patients as subjects in experiments without their knowledge or consent. This occurred frequently in research involving potential new therapies, where there was at least a chance that the patient-subjects might benefit medically from being in an experiment. But it also occurred even in experiments—like the plutonium injections—where there was never any expectation and no chance that the experiment might be of benefit to the subjects.

The conduct of the plutonium experiments raises a number of difficult ethics and policy questions: Who should have been the subjects of an experiment designed to protect workers vital to bomb production in wartime? What should the subjects have been told about the risks of the secret substance with which they were being injected? What should they have been told about the purpose of the experiment? What were the subjects told? Did they know they were part of an experiment in which there was no expectation that they would benefit medically?

An inquiry initiated by the AEC commissioners in 1974 investigated some of these questions. That inquiry focused on whether consent was obtained from the subjects, either at the time of the plutonium injections or during 1973 follow-up studies funded by the AEC's Argonne National Laboratory in Chicago, designed to determine the long-term effects of the injections. Sixteen patient charts were examined for evidence of consent at the time of injection; the other two charts had been either lost or destroyed. Of the sixteen charts examined, only one chart—that of the only subject injected after the April 1947 directive of AEC General Manager Carroll Wilson (discussed in chapter 1) that required documented consent—contained evidence of some form of consent. The other fifteen contained no record of consent.[17] According to AEC investigators, oral testimony pointed to failure to obtain consent in the case of the Oak Ridge injection and to some form of disclosure to patients for the California and Chicago experiments. The AEC concluded that testimony was inconclusive for the Rochester experiments.[18] With regard to the follow-up studies conducted with three surviving subjects in 1973, the investigation concluded that two subjects had deliberately not been informed of the purpose of the follow-up and that one

subject had actually been misled about the purpose.[19]

As we will see later in this chapter, the AEC's conclusion that consent was not obtained from the surviving subjects for the 1973 follow-up studies was correct. Moreover, additional documentary evidence and testimony suggests that patient-subjects at the Universities of Rochester and California were never told that the injections were part of a medical experiment for which there was no expectation that they would benefit, and they never consented to this use of their bodies.

The rest of this chapter provides a chronological account of the plutonium injection experiments and follow-up studies conducted over the course of many years, assesses the influence of secrecy on the conduct of the experiments, and examines the motivating factors behind the prolonged secrecy of the experiments and the continued deception of surviving subjects. We also consider the conduct of experimentation with uranium and polonium. Finally, we render judgments where we can about the ethical conduct of these experiments.

THE MANHATTAN DISTRICT EXPERIMENTS

The First Injection

A few days after Hempelmann's March 26, 1945, recommendation that a hospital patient be injected with plutonium, Wright Langham, of the Los Alamos Laboratory's Health Division, sent 5 micrograms of plutonium to Dr. Friedell, with instructions for their use on a human subject.[20] The subject, as it turned out, was already in the Oak Ridge Army hospital, a victim of an auto accident that had occurred on March 24, 1945.[21] He was a fifty-three-year-old "colored male"[22] named Ebb Cade,[23] who was employed by an Oak Ridge construction company as a cement mixer. The subject had serious fractures in his arm and leg, but was otherwise "well developed [and] well nourished."[24] The patient was able to tell his doctors that he had always been in good health.[25]

Mr. Cade had been hospitalized since his accident, but the plutonium injection did not take place until April 10. On this date, "HP-12" (the code name HP—"human product"[26]—was later assigned to this patient and to patients at the University of Rochester) was reportedly injected with 4.7 micrograms of plutonium. (It is important here to distinguish between *administered* dose and *retained* dose; not all of the injected dose would remain fixed in the body. It was not known with certainty, however, how much of the 4.7 micrograms of plutonium would remain in his body.)

The small amount of material injected into Mr. Cade would not be expected to produce any acute effects, and there is no indication that any were experienced. However, except for his fractures, Mr. Cade was apparently in good health and at age fifty-three could reasonably have been expected to live for another ten to twenty years. Thus, in Mr. Cade's case, the risk of a plutonium-induced cancer could not be ruled out.

Dr. Joseph Howland, an Army doctor stationed at Oak Ridge, told AEC investigators in 1974 that he had administered the injection. There was, he recalled, no consent from the patient. He acted, he testified, only after his objections were met with a written order to proceed from his superior, Dr. Friedell.[27] Dr. Friedell told Advisory Committee staff in an interview that he did not order the injection and that it was administered by a physician named Dwight Clark, not Dr. Howland.[28] The Committee has not been able to resolve this contradiction.

Measurements were to be taken from samples of Mr. Cade's blood after four hours, his bone tissue after ninety-six hours, and his bodily excretions for forty to sixty days thereafter.[29] His broken bones were not set until April 15—five days after the injection—when bone samples were taken in a biopsy.[30] Although this was several weeks after his injury, during this era when antibiotics were only beginning to become available, it was common practice to delay surgery if there was any sign of possible infection. One document records that Mr. Cade had "marked" tooth decay and gum inflammation,[31] and fifteen of his teeth were extracted and sampled for plutonium. The Committee has not been able to determine whether the teeth were extracted primarily for medical reasons or for the purpose of sampling for plutonium. In a September 1945

letter, Captain David Goldring at Oak Ridge informed Langham that "more bone specimens and extracted teeth will be shipped to you very soon for analysis."[32] It remains unclear whether these additional bone specimens were extracted at the time of the April 15 operation or later.

According to one account, Mr. Cade departed suddenly from the hospital on his own initiative; one morning the nurse opened his door, and he was gone.[33] Later it was learned that he moved out of state and died of heart failure on April 13, 1953, in Greensboro, North Carolina.[34]

The experiment at Oak Ridge did not proceed as planned. "Before" and "after" urine samples were mistakenly commingled, so no baseline data on kidney function was available.[35] Thus, the subject's kidney function would be difficult to assess. In May 1945,[36] Dr. Stone convened a "Conference on Plutonium" in Chicago to discuss health issues related to plutonium, including the relationship between dose and excretion rate, the permissible body burden, and potential therapy and protective measures.[37] Wright Langham spoke about the Oak Ridge injection at the conference, carefully qualifying the reliability of the excretion data obtained from Mr. Cade. Langham observed that "the patient might not have been an ideal subject in that his kidney function may not have been completely normal at the time of injection"[38] as indicated by protein tests of his urine.

The Chicago Experiments

On April 11, the day after the Oak Ridge injection, Hymer Friedell transmitted the protocol describing the experiment on Mr. Cade to Louis Hempelmann at Los Alamos. "Everything went very smoothly," he wrote, "and I think that we will have some very valuable information for you."[39] He then went on to discuss the injection of more patients: "I think that we will have access to considerable clinical material here, and we hope to do a number of subjects. At such time as we line up several patients I think we will make an effort to have Mr. Langham here to review our setup."[40]

Subsequently, between late April and late December of 1945, three cancer patients, codenamed CHI-1, 2, and 3, were injected with plutonium. At least two and possibly all three were injected at the Billings Hospital of the University of Chicago. The doses to subjects CHI-2 and CHI-3 were the highest doses administered to any of the eighteen injection subjects—approximately 95 micrograms.[41] However, the amount of material injected was still below what would be expected to produce acute effects. Moreover, unlike Mr. Cade, all three of these patients were seriously ill and at least two of them died within ten months of receiving the injection. That the selection of seriously ill patients was an intentional strategy to contain risk is indicated in a 1946 report on CHI-1 and CHI-2: "Some human studies were needed to see how to apply the animal data to the human problems. Hence, two people were selected whose life expectancy was such that they could not be endangered by injections of plutonium."[42] It remains a mystery why CHI-3 was not included in this report.

On April 26, 1945, CHI-1, a sixty-eight-year-old man who had been admitted to Billings Hospital in March, was injected with 6.5 micrograms of plutonium. At the time of injection he was suffering from cancer of the mouth and lung. The patient reportedly "remained in fair condition until August 1945, when he complained of pain in the chest."[43] His lung cancer had apparently spread, and he died on October 3, 1945.[44]

The next injection took place eight months later. CHI-2 was a fifty-five-year-old woman with breast cancer who had been admitted to Billings Hospital in December 1945 after the cancer had already spread throughout her body. The 1946 report recorded that "the patient's general condition was poor at the time of admission and deteriorated steadily throughout the period of hospitalization."[45] She was injected with 95 micrograms of plutonium on December 27 and died on January 13, 1946.[46]

There is little known about the condition of CHI-3, the other subject who was injected with approximately 95 micrograms. He was a young man suffering from Hodgkin's disease, reportedly injected on the same date as CHI-2.[47] His condition at the time of injection remains unknown, as does his date of death. There is some question whether he was injected at Billings hospital or at another hospital in the Chicago area.[48]

There was no discussion of consent in the original reports on the Chicago experiments. However, a draft report on an interview conducted with E. R. Russell for the 1974 AEC investigation into the experiments (Russell was coauthor of the 1946 report on the Chicago experiments) summarized Russell's description of consent as follows: "[H]e prepared the plutonium solutions for injection and acted together with a nurse as witness to the fact that the patient was or had been informed that a radioactive substance was going to be injected. The administration of this substance, according to what was said in obtaining consent, was not necessarily for the benefit of the patients but might help other people."[49] To say that the injection was "not necessarily" for the benefit of the patient implies that there was some chance these patients might benefit; in fact, there was no expectation that this would occur.

Russell's account was obtained in the context of an official inquiry into his conduct and the conduct of the other investigators and officials involved in the plutonium injections, an inquiry that focused on whether consent was obtained from the subjects. We have no way of corroborating this account or of assessing what Dr. Russell's motivations were in explaining the plutonium injections to the subjects in the way claimed.

The Rochester Experiments

By the time the war began, the University of Rochester, which had a cyclotron, had assembled a group of first-rate physicists and medical researchers who were pioneering the new radiation research. Following the selection of the university's Stafford Warren to head its medical division, the Manhattan Project turned to Rochester for an increasing share of its biomedical research—including, in particular, research needed to set standards for worker safety.[50]

The university's metabolism ward, at what is now the Strong Memorial Hospital, became the central Manhattan District site for the administration of isotopes to human subjects. The two-bed ward, headed by Dr. Samuel Bassett, was part of the Manhattan District's "Special Problems Division," which worked on the health monitoring of production plants, the development of monitoring instruments, and research on the metabolism and toxicology of long-lived radioactive elements.[51] An experimental plan called for fifty subjects altogether, in five groups of ten subjects each. Each group would receive plutonium, radium, polonium, uranium, or lead.[52] Although the exact number of subjects remains unknown, at least twenty-two patients were administered long-lived isotopes in experiments with plutonium (eleven subjects), polonium (five subjects), and uranium (six subjects).

At the time the experiment was being designed, the main selection criterion for the subjects chosen at Rochester for the plutonium experiment was that they have a metabolism similar to healthy Manhattan Engineer District workers. In a work plan for the plutonium study based on a September 1945 meeting with a representative of Colonel Warren's office and the Rochester doctors, Langham wrote:

> The selection of subjects is entirely up to the Rochester group. At the meeting it seemed to be more or less agreed that the subjects might be chronic arthritics [patients with serious collagen vascular diseases, such as scleroderma] or carcinoma patients without primary involvement of bone, liver, blood or kidneys.
>
> It is of primary importance that the subjects have relatively normal kidney and liver function, as it is desirable to obtain a metabolic picture comparable to that of an active worker.
>
> Undoubtedly the selection of subjects will be greatly influenced by what is available. The above points, however, should be kept in mind.[53]

Although this protocol specifies cancer patients as potential subjects, evidently the deliberate choice was made later by the experimenters to select patients without malignant diseases in the hope of ensuring normal metabolism.[54] Thus no cancer patients were included among the plutonium subjects at Rochester. Preference appears to have been given to patients the doctors believed would benefit from additional time in the hospital.[55]

An additional perspective on the selection of subjects for the plutonium experiments is pro-

vided in three retrospective reports written by Wright Langham. In a 1950 report on the plutonium project, including the experiments conducted at Rochester, Langham wrote that "as a rule, the subjects chosen were past forty-five years of age and suffering from chronic disorders such that survival for ten years was highly improbable."[56] In subsequent reports, Langham refers to the plutonium subjects as having been "hopelessly sick"[57] and "terminal."[58]

Documents retrieved for the Advisory Committee show that all but one of the plutonium subjects at Rochester suffered from chronic disorders such as severe hemorrhaging secondary to duodenal ulcers, heart disease, Addison's disease, cirrhosis, and scleroderma.[59] One subject, Eda Schultz Charlton, did not have any such condition. According to the draft of the 1950 report, she was misdiagnosed: "a woman aged 49 years may have a greater life expectancy than originally anticipated due to an error in the provisional diagnosis."[60]

Most of the subjects at Rochester were not terminally ill, and at least some of them had the potential to live more than ten years. Three of the Rochester subjects were known to still be living at the time of the 1974 AEC investigation into the plutonium experiments. Whether the inclusion of subjects at Rochester with the potential to live more than ten years is an indication that the investigators were not using Langham's criterion to select subjects or that they erred in their predictions is unclear. Judgments about the life expectancy of the chronically ill are difficult to make and often in error, even today.

The likelihood that long-term risks can be altogether eliminated does exist, however, if the subject is in the terminal stages of an illness and death is imminent. This was recognized by the plutonium investigators, and it led to the observation that the use of a terminal patient permitted a larger dose, which would make analysis easier. The first terminal patient at Rochester was injected toward the end of that series, and the possibility of further injections into terminal patients was discussed explicitly. In a March 1946 letter, Wright Langham wrote to Dr. Bassett, the primary physician-investigator at Rochester:

> In case you should decide to do another terminal case, I suggest you do 50 micrograms instead of 5. This would permit the analysis of much smaller samples and would make my work considerably easier. . . . I feel reasonably certain there would be no harm in using larger amounts of material if you are sure the case is a terminal one [as was done in two of the three Chicago injections].[61]

As was the case at Oak Ridge and Chicago, there was no expectation that the patient-subjects at Rochester would benefit medically from the plutonium injections. The Advisory Committee found no documents that bear directly on what, if anything, the subjects were told about the injections and whether they consented. The recollections of at least some of those intimately involved have survived, however, and these recollections all suggest that the patients did not know they had been injected with radioactive material or even that they were subjects of an experiment.

Milton Stadt, the son of a Rochester subject, told the Advisory Committee the following at a meeting in Santa Fe, New Mexico, on January 30, 1995:

> My mother, Jan Stadt, had a number, HP-8. She was injected with plutonium on March 9th, 1946. She was forty-one years old, and I was eleven years old at the time. My mother and father were never told or asked for any kind of consent to have this done to them.
>
> My mother went in [to the hospital] for scleroderma . . . and a duodenal ulcer, and somehow she got pushed over into this lab where these monsters were.

Dr. Hempelmann, in an interview for the 1974 AEC investigation, said he believed that the patients injected with plutonium were deliberately not informed about the contents of the injections.[62] Dr. Patricia Durbin, a University of California researcher who in 1968 undertook a scientific reanalysis of the experiments, reported on a visit with Dr. Christine Waterhouse in 1971. Dr. Waterhouse was a medical resident at Rochester at the time of the plutonium injections. Durbin wrote the following regarding the Rochester subjects who were still alive:

> She [Dr. Waterhouse] believes that all three persons would be agreeable to providing excretion samples and

perhaps blood samples, but they are all quite old—in their middle or late 70's and cannot travel far. More important, they do not know that they received any radioactive material.[63]

In notes on a 1971 telephone conversation with Wright Langham, Dr. Durbin wrote: "He is, I believe, distressed by . . . the fact that the injected people in the HP series were unaware that they were the subjects of an experiment."[64] This recollection is even more troubling than the recollections of Drs. Waterhouse and Hempelmann, as it indicates not only that the subjects did not know that they were being injected with plutonium or a radioactive substance, but also that they did not know even that they were subjects of an experiment.

Even the doctors in charge of some of the injections at Rochester may not have known what they were injecting into patients. In 1974, Dr. Hempelmann suggested that the physician who actually injected the solution quite possibly did not know of its contents.[65]

Further evidence suggesting that the patient-subjects were never told what was done to them comes from 1950 correspondence between Langham and the physicians at Rochester. These physician-investigators were looking for signs of long-term skeletal effects in follow-up studies with two of the subjects at Rochester. Langham wrote to Rochester that he was "very glad to hear that you will manage to get follow-ups on the two subjects. The x-rays seem to be the all-important thing, but please get them in a completely routine manner. Do not make the examination look unusual in any way."[66]

Moreover, a letter from Langham to Dr. Bassett discussed the undesirability of recording plutonium data in the Rochester subjects' hospital records:

> I talked to Col. [Stafford] Warren on the phone yesterday and he recommended that I send copies of all my data to Dr. [Andrew] Dowdy where it would be available to you and Dr. [Robert M.] Fink to observe. He thought it best that I not send it to you because he wanted it to remain in the Manhattan Project files, instead of taking a chance on it finding its way into the hospital records. I think this is probably a sensible suggestion.[67]

Uranium Injections at Rochester

Under the Manhattan Engineer District program, physicians at the Rochester metabolism ward also injected six patients with uranium (in the form of uranyl nitrate enriched in the isotopes uranium 234 and uranium 235) to establish the minimum dose that would produce detectable kidney damage due to the chemical toxicity of uranium metal, and to measure the rate at which uranium was excreted from the body. To achieve the first objective, the experimenters used a higher dose with each new subject until the first sign of minimal kidney damage occurred. Damage occurred in the sixth and last subject (at a calculated amount of radioactivity of 0.03 microcuries), indicated by protein tests of his urine. Unlike the plutonium injections, this was an experiment that evidently was designed not only to obtain excretion data but to cause actual physical harm, however minimal. Thus, although the investigators could reasonably view the plutonium injections as an experiment that was extremely unlikely to produce acute effects, this was not true of the uranium experiment, which was intended to produce acute effects. As with the plutonium injections, the uranium injections also posed a long-term risk of the development of cancer. The Committee does not know in this case how long subjects survived after injection; there is no documentation of follow-up with these subjects as there is for some of the subjects of the plutonium injections.

The subjects of this experiment, like some of the plutonium-injection subjects, were not at risk of imminent death, but did suffer from chronic medical conditions such as rheumatoid arthritis, alcoholism, malnutrition, cirrhosis, and tuberculosis. According to Dr. Bassett, again the primary investigator, the subjects "were chosen from a large group of hospital patients. Criteria of importance in making the selection were reasonably good kidney function with urine free from protein and with a normal sediment on clinical examination. The probability that the patient would benefit from continued hospitalization and medical care was also a factor in the choice."[68]

The 1948 report on the experiment did not discuss the question of consent. We were not able to locate any documents that bear on what, if anything, the subjects were told about the uranium injections, nor have any relevant recollections about the experiment survived. Two 1946 documents, however, discussing whether Dr. Bassett should be permitted to give a departmental seminar on the excretion rate of uranium in humans, illustrate the secrecy that surrounded these injections and suggest that the subjects were not informed of the experiment. By the time of this correspondence, the uranium research with animals at Rochester had been declassified. The first document, a letter written by Andrew Dowdy, the director of the Manhattan Department at the University of Rochester, to a Manhattan District Area engineer requesting permission for Bassett to give the seminar, included the following: "I feel that there is no reason why he should not discuss this matter, and I believe that the fact that this information was actually obtained on his own patients is of more concern to himself than to the District."[69] In the second document, an intraoffice memorandum, the area engineer discussed this point, and more:

> Dr. Dowdy states that the patients were Dr. Bassett's, but it should be borne in mind that all the work performed by Dr. Bassett was performed at the request of the Manhattan District Medical Section. This seminar is to be conducted for persons who are all Doctors of Medicine and it is doubtful if this information would get out to any of the families of the patients or the patients on whom the experiments were performed. . . .
>
> At the time these experiments were started, this office was given strict orders that the information should not be released to any but authorized persons. Almost all the correspondence and result of experiments were exchanged between Dr. Wright Langham at Santa Fe and Dr. Bassett of the University of Rochester. This rule is still in effect on some of the material that Dr. Bassett is using and knowledge of the experiments is kept from personnel at the Rochester Area.[70]

Polonium Injections at Rochester

In addition to the subjects injected with plutonium and uranium at Rochester, five subjects were chosen for an experiment with polonium. The purpose of the experiment was to determine the excretion rate of polonium after a known dose, as well as to analyze the uptake of polonium in various tissues. The primary investigator for these experiments was Dr. Robert M. Fink, assistant professor of radiology and biophysics at the University of Rochester. Four patients were injected with the element, and one ingested it.[71] All five patients selected for this study were suffering from terminal forms of cancer: lymphosarcoma, acute lymphatic leukemia, or chronic myeloid leukemia. It is unclear why patients with malignant diseases were chosen as subjects in this experiment but excluded from the subject pools for the plutonium and uranium experiments. There is no discussion in the 1950 final report on the polonium experiments of the possibility that patients with malignant diseases might have abnormal metabolism, and the excretion data were employed right away in the establishment of occupational safety standards.[72]

The final report, unlike other reports on the Manhattan District metabolism studies, briefly discusses the question of consent: "the general problem was outlined to a number of hospital patients with no previous or probable future contact with polonium. Of the group that volunteered as subjects, four men and one woman were selected for the excretion studies outlined below."[73] This statement leaves no clear impression of what the subjects actually were told; like the experiments with plutonium and uranium, the human polonium experiment was a classified component of the metabolism program. Still, this report provides a contrast to the contemporaneous reports on the Manhattan District plutonium and uranium experiments, which make no mention of consent and which do not refer to the patient-subjects as "volunteers."

The California Experiments

While the University of Rochester had been conducting experiments for the Manhattan Engineer District, a related effort was under way at the University of California at Berkeley.[74] Before the war, Drs. Joseph Hamilton and Robert Stone had been exploring medical applications of radioisotopes with the aid of the University

of California's cyclotron. Hamilton and his colleagues had pioneered in using radioisotopes to treat cancer, in particular iodine 131 in the 1930s. At the time the United States entered the war, they were investigating another isotope for cancer therapy, strontium 89. Indeed, it was this area of Hamilton's expertise that attracted the interest of the Manhattan Project. While Stone moved to the Chicago Metallurgical Laboratory during the war, Hamilton remained at the University of California's Radiation Laboratory, or "Rad Lab," at Berkeley. A colleague of both men, Dr. Earl Miller, a radiologist at the University of California, reported regularly to Stone on the progress of the Berkeley plutonium project.

Under the Manhattan District contract, Hamilton's studies originally had involved exposing rats to plutonium in an effort to determine its metabolic fate and thereby project the risk to workers at atomic plants. Toward the end of the war, Hamilton began to conduct plutonium studies on humans for the government.[75] Experiments with humans could be handled expeditiously, Hamilton wrote, because of the close relationship between the Rad Lab and the medical school at the University of California at San Francisco.[76] In January 1945, Hamilton confirmed to the Manhattan District that he planned "to undertake, on a limited scale, a series of metabolic studies with [plutonium] using human subjects."[77] The purpose of this work, Hamilton wrote, "was to evaluate the possible hazards . . . to humans who might be exposed to them, either in the course of the operation of the [Chicago] pile, or in the event of possible enemy action against the military and civilian population."[78]

Subsequently, three subjects, two adults and one child (known as CAL-1, 2, and 3), were injected with plutonium. In addition, in April 1947 a teenage boy (CAL-A) was injected with americium, and in January 1948 a fifty-five-year-old female cancer patient (CAL-Z) was injected with zirconium.[79]

On May 10, 1945, Hamilton reported he was awaiting "a suitable patient" for the plutonium experiment.[80] Four days later, fifty-eight-year-old Albert Stevens, designated CAL-1, was injected with plutonium, becoming the first human subject in the California portion of the project.[81] Albert Stevens was chosen in the belief that he was suffering from advanced stomach cancer.[82] Shortly after the injection, however, a biopsy revealed a benign gastric ulcer instead of the suspected cancer. The researchers collected excreta daily for almost one year, analyzing them for plutonium content.[83] Evidently, by two months after the injection, Mr. Stevens was considering moving out of the Berkeley area; this would have prevented further collection of excretion specimens. Dr. Hamilton proposed to Drs. Stone and Stafford Warren that he be permitted to "pay the man fifty dollars per month" in order to keep Mr. Stevens in the area. Hamilton recognized, however, that there were "possible legal and security situations which may present insurmountable obstacles."[84] In response to this request, Dr. Joe Howland (who was reportedly involved with the Oak Ridge plutonium injection) wrote the following to the California area engineer:

> Possible solutions to this problem could be:
>
> a. Pay for his care in a hospital or nursing home as a service.
> b. Place this individual on Dr. Hamilton's payroll in some minor capacity without release of any classified information.
>
> It is not recommended that he be paid as an experimental subject only.[85]

According to a 1979 oral history of Kenneth Scott, an investigator at Berkeley who evidently was responsible for the analysis of Mr. Stevens's excretion specimens, the patient was paid some amount each month to keep him in the area. However, Dr. Scott also recalled that he never told Mr. Stevens what had happened to him: "His sister was a nurse and she was very suspicious of me. But to my knowledge he never found out."[86]

In addition, an April 1946 report on the experiment records that "several highly important tissue samples were secured including bone."[87] It appears that these tissue specimens, which included specimens of rib and spleen, were removed four days after the injection in an operation for the patient's suspected stomach cancer.[88]

Four months after Mr. Stevens was injected, Dr. Hamilton told the Manhattan District that

the next subject would be injected "along with Pu238 [plutonium], small quantities of radio-yttrium, radio-strontium, and radio-cerium." The purpose of this experiment was to "compare in man the behavior of these three representative long-lived Fission Products with their metabolic properties in the rat, and second, a comparison can be made of the differences in their behavior from that of Plutonium."[89] This research would provide data to improve extrapolation from higher-dose animal experiments.

Despite Hamilton's hope to have a second patient by the fall, CAL-2 was not selected until April 1946. Simeon Shaw was a four-year-old Australian boy suffering from osteogenic sarcoma, a rare form of bone cancer, who was flown from Australia to the University of California for treatment. According to newspaper articles at the time, Simeon's family had been advised by an Australian physician to seek treatment at the University of California.[90] Arrangements then were made by the Red Cross and the U.S. Army for Simeon and his mother to fly by Army aircraft to San Francisco. Within days, he had been injected with a solution containing plutonium, yttrium, and cerium by physicians at the university.[91]

Following his discharge on May 25, about a month after his injection, the boy returned to Australia, and no follow-up was conducted. He died in January 1947. In February 1995 an ad hoc committee at the University of California at San Francisco (UCSF) concluded that probably at least part of the motivation for this experiment was to gather scientific data on the disposition of bone-seeking radionuclides with bone cancers.[92]

One piece of evidence indicating that there was a secondary research purpose for the injection of CAL-2 was a handwritten note in the boy's medical record saying that the surgeons removed a section of the bone tumor for pathology and for "studies to determine the rate of uptake of radioactive materials that had been injected prior to surgery, in comparison to normal tissues."[93]

It is likely that the CAL-2 experiment was designed both to acquire data for the Manhattan District and also to further the physicians' own search for radioisotopes that might treat cancer in future patients. The California researchers themselves noted the dual purpose of their research at the time. Hamilton wrote in a report to the Army in the fall of 1945 that there were "military considerations which can be significantly aided by the results of properly planned tracer research."[94]

As the February 1995 UCSF report on the experiments concluded, however, the "injections of plutonium were not expected to be, nor were they, therapeutic or of medical benefit to the patients."[95] This corresponds with the evidence of a letter, written by Hamilton in July 1946, three months after the injection of CAL-2, to the author of an article on the peacetime implications of wartime medical discoveries:

> To date no fission products, aside from radioactive iodine, have been employed for any therapeutic purposes. There is a possibility that one or more of the long list of radioactive elements produced by uranium fission may be of practical therapeutic value. At the present time, however, we can do no more than speculate.[96]

Documentary evidence suggests that consent for the injections likely was not obtained from at least some of the subjects at the University of California. A 1946 letter from T. S. Chapman, with the Manhattan District's Research Division, said the following regarding preparations for injections:

> . . . preparations were being made for injection in humans by Drs. [Robert] Stone and [Earl] Miller. These doctors state that the injections would probably be made without the knowledge of the patient and that the physicians assumed full responsibility. Such injections were not divergent from the normal experimental method in the hospital and the patient signed no release. A release was held to be invalid.
>
> The Medical Division of the District Office has referred "P" reports for project 48A to Colonel Cooney for review and approval is withheld pending his opinion.[97]

Chapman does not specify whether the "injections" referred to in this letter were injections of plutonium or of some other substance. It is unclear whether "'P' reports" refers to Hamilton's overall progress reports on his tracer research, which had reported mostly on research with plutonium (but also on research with

cerium and yttrium), or whether "P" referred specifically to reports on work with plutonium. As we noted at the outset of this chapter, Chapman's claim that it was commonplace at the time to use patients in experiments without their knowledge and without asking them to sign a "release" is correct.

In the case of Albert Stevens (CAL-1), no documentary evidence that bears on disclosure or consent has been found. Simeon Shaw's (CAL-2's) medical file contains a standard form "Consent for Operation and/or Administration of Anaesthetic." This form, however, was signed by a witness attesting to consent of Simeon's mother one week after the injection and therefore probably applies to a biopsy done a week after the injection, not to the injection itself.[98]

On December 24, 1946, at the prompting of Major Birchard M. Brundage, who was chief of the Manhattan District's Medical Division, Colonel K. D. Nichols, commander of the Manhattan District, ordered a halt to injections of "certain radioactive substances" into human subjects at the University of California.[99] "Such work," Nichols wrote, "does not come under the scope of the Manhattan District Programs and should not be made a part of its research plan. It is therefore deemed advisable by this office not only to recommend against work on human subjects but also to deny authority for such work under the terms of the Manhattan contract." The following week, the civilian AEC took over responsibility for all Manhattan District research and temporarily reaffirmed the Manhattan District's suspension of human experimentation at the University of California.[100] It is unclear why this action was taken.

THE AEC'S REACTION: PRESERVING SECRECY WHILE REQUIRING DISCLOSURE

When the civilian Atomic Energy Commission took over for the Manhattan District on January 1, 1947, the plutonium injections provoked a strong reaction at the highest levels. One immediate result was the decision to keep information on the plutonium injections secret, evidently for reasons not directly related to national security, but because of public relations and legal liability concerns. The other immediate result, as we saw in chapter 1, was the issuing of requirements for future human subjects research as articulated in letters by the AEC's general manager, Carroll Wilson.

In December 1946, as the civilian AEC was about to open its doors, Hymer Friedell, who had been deputy medical director of the Manhattan Engineer District, recommended the declassification of one of the plutonium reports, "CH [Chicago]-3607—The Distribution and Excretion of Plutonium in Two Human Subjects." The report, Friedell argued, "will not in my opinion result in the release of information beyond that authorized for disclosure by the current Declassification Guide."[101]

Friedell's recommendation was soon reversed. Officials with the new AEC had learned of the human injection experiments, and on February 28, 1947, an AEC declassification officer concluded that declassification was out of the question. The reasons are revealed in a previously classified document recently found at Oak Ridge:

> The document [CH-3607] appears to be the most dangerous since it describes experiments performed on human subjects, including the actual injection of the metal plutonium into the body. The locations of these experiments are given and the results, even to the autopsy findings in the two cases. It is unlikely that these tests were made without the consent of the subjects, but no statement is made to that effect and the coldly scientific manner in which the results are tabulated and discussed would have a very poor effect on the public. Unless, of course, the legal aspects were covered by the necessary documents, the experimenters and the employing agencies, including the U.S., have been laid open to a devastating lawsuit which would, through its attendant publicity, have far reaching results.[102]

It is not clear to the Advisory Committee on what basis the declassification officer who wrote this comment concluded that it was unlikely that consent was not obtained from the Chicago subjects. This statement could be read as careful bureaucratic language, intended to leave an appropriate paper trail in the event of subsequent legal problems. On the other hand, the state-

ment does support the claim, noted earlier, made by one of the Chicago doctors in 1974 that some form of oral consent for the injections had been obtained from the Chicago subjects. It is clear that there was no documentation of disclosure or consent on which the AEC could rely. As a consequence, secrecy was to be maintained, not as a defense against foreign powers, but to avoid a "devastating lawsuit" and "attendant publicity." Upon further review the report was "reclassified 'Restricted' on 3/31/47."[103] In a March 19, 1947, memorandum, Major Brundage, by that time chief of the AEC's Medical Division, explained:

> The Medical Division also agrees with Public Relations that it would be unwise to release the paper 'Distribution and Excretion of Plutonium' primarily because of medical legal aspects in the use of plutonium in human beings and secondly because of the objections of Dr. Warren and Colonel Cooney that plutonium is not available for extra Commission experimental work, and thus this paper's distribution is not essential to off Project[104] experimental procedures.[105]

In July 1947, Argonne National Laboratory's declassification officer, Hoylande D. Young, inquired about possible declassification of this report as well as Hamilton's report on the CAL-1 injection. She stated that the directors of Argonne's Biology and Health Divisions (including J. J. Nickson, one of the authors of the Chicago report on the injections) believed that declassification of these reports would not be "prejudicial to the national interests."[106] The AEC continued to withhold declassification of these reports, however, on the grounds that they involved "experimentation on human subjects where the material was not given for therapeutic reasons."[107] Thus, there was clearly no expectation at the time that the plutonium injections would benefit the patient-subjects but some expectation that the general public might be disturbed by human experimentation in the absence of a prospect of offsetting benefit.

In 1950, Wright Langham and the Rochester doctors undertook to prepare a "Plutonium Report"[108] that would be "the last word on the plutonium situation."[109] It would be the "last word" to only a select few. In 1947, Rochester's Andrew Dowdy had urged Los Alamos to give advance notice of declassification of the Rochester part of the experiment "because of possible unfavorable public relations and in an attempt to protect Dr. [Samuel] Bassett from any possible legal entanglements."[110] This is likely a reference to the same concern raised in the discussion of Dr. Bassett's seminar about his having experimented upon his own patients, except in this case the context is the plutonium rather than the uranium injections. "We think," Langham wrote to Stafford Warren, "the classification will be 'Secret,' and the circulation limited, depending on Dr. Shields Warren's [the head of AEC's Division of Biology and Medicine] wishes."[111] In August, Shields Warren approved the report for "CONFIDENTIAL classification and limited circulation as [Dr. Langham] requested."[112]

Even though its data and analysis were the basis for widespread plutonium safety procedures, the report remained unavailable to the public until 1971 when, at the urging of Dr. Patricia Durbin, it was downgraded to "Official Use Only."[113] (This categorization means that while the document was not likely to be released to the public absent specific request, it could be disclosed.)

What was it that was so potentially embarrassing about the plutonium experiments? The answer appears to lie in the 1947 letters from General Manager Wilson, discussed in detail in chapter 1. These letters state rules for both the conduct of human experiments and the declassification of previously conducted secret experiments.[114]

In his April 1947 letter, Wilson stated the requirements that there be expectation that research "may have therapeutic effect" and that at least two doctors "certify in writing (made part of an official record) to the patient's understanding state of mind, to the explanation furnished him, and to his willingness to accept the treatment."[115] In his November 1947 letter, Wilson reiterated these terms for human experiments, again calling for "reasonable hope . . . that the administration of such a substance will improve the condition of patient" and this time calling for "informed consent in writing" by the patient.[116] All of the seventeen plutonium injec-

tions conducted prior to the letters violated both these terms. As a consequence, they would have to stay secret. The only secret experiments that could be declassified were those that satisfied these requirements; to do otherwise was to risk adverse public reaction. Thus, the decision to keep the plutonium reports secret was itself an example of the way in which the AEC's assertion of conditions for human experimentation was coupled with the decision to keep secret those experiments that evidently did not adhere to these conditions (see chapter 13).

HUMAN EXPERIMENTATION CONTINUES

In March 1947, just as he was declaring that "public relations" required the reclassification of plutonium data, Medical Division chief Major Brundage approved a 1947–48 "Research Program and Budget" for Rochester that provided for metabolism studies with polonium, plutonium, uranium, thorium, radiolead, and radium.[117] The program was put on hold by the AEC soon after.[118]

The future of the metabolism work at Rochester apparently was decided when Shields Warren was named the first chief of the AEC's Division of Biology and Medicine in fall 1947. In his private diary for December 30, 1947, Warren tersely noted: "Ordered abandonment of human isotope program at Rochester."[119] The program at the University of California at Berkeley, however, continued. On December 4, 1947, Shields Warren had met with Hamilton and Stone;[120] the decision to allow the program to continue clearly was not a hasty one. A 1974 recollection of Shields Warren indicates that his decision to allow the program to continue may have been due to Hamilton's assertion in December 1947 that it had been the University of California's practice to obtain some form of (undocumented) consent.[121]

According to Warren, Hamilton had said that subjects were told "they would receive an injection of a new substance that was too new to say what it might do but that it had some properties like other substances that had been used to control growth processes in patients, or something of that general sort."[122] Warren went on to observe that "you could not call it informed consent because they did not know what it was, but they knew that it was a new and to them unknown substance."[123] Warren's observation does not go far enough, however. If Warren's secondhand account is accurate and this is indeed what the patient-subjects at the University of California were told, then they were more misled than informed. Analogizing plutonium to substances that "control growth processes in patients," even in prospect, might reasonably lead patients to believe that they would be receiving a substance with some hope of treating their cancer. Certainly such a remark would not communicate to patients that the experiment to be performed was not for their own benefit. It would have been appropriate that these patients be told that their participation might benefit future patients with the same conditions. It would have been crucial to distinguish, however, between this legitimate explanation of potential benefit to future cancer patients and misleading the patient into believing the experiment might benefit him or her.

Human Experimentation Continues at the University of California

By the summer of 1947, human experimentation had resumed at the University of California under AEC contract. In June, "CAL-A," a teenage Asian-American bone cancer patient at Chinese Hospital in San Francisco, was injected with americium. An instruction in the patient's file by one of Hamilton's assistants specifies that "we will use the same procedure as with Mr. S,"[124] evidently a reference to Albert Stevens. Dr. Durbin, Hamilton's associate, believes that CAL-A's guardian was informed of the procedure followed in that case.[125] The Advisory Committee received incomplete records for CAL-A that contained no evidence of disclosure or consent; UCSF has told the Committee that records at Chinese Hospital from the 1950s and earlier have been destroyed.[126]

A thirty-six-year-old African-American railroad porter named Elmer Allen, code-named CAL-3, was believed to be suffering from bone cancer and was injected with plutonium at the

University of California in July 1947. His left leg was amputated shortly thereafter. There is a note in his medical chart signed by two physicians, stating that the experimental nature was "explained to the patient, who agreed to the procedure" and that "the patient was in fully oriented and in sane mind."[127] It is likely that this note was intended to fulfill one of the April 1947 conditions for human experimentation, which allowed for such a procedure as documentation of having obtained the patient-subject's consent. It is not clear from the note, however, whether in explaining about the experimental nature of the procedure the physicians told the patient about the potential effects of the injection, as required by the Wilson letter, or that the injection was not intended to be of medical benefit to the patient. On this second point, the injection was *in violation* of the Wilson letter, which also required that there be an "expectation that it may have therapeutic effect."[128] As acknowledged by the February 1995 UCSF report, there was never any expectation on the part of the experimenters that the injection would be of therapeutic benefit to Mr. Allen.

Mr. Allen lived until 1991. According to UCSF's 1995 review of patient-subjects' medical charts, upon biopsy of his tumor a pathologic diagnosis was made of chondrosarcoma, a type of malignant bone tumor. UCSF reported that patients with this type of tumor "frequently surviv[e] many years beyond diagnosis if there is complete excision of the primary tumor."[129] This pathology finding suggests that Mr. Allen was a long-term cancer survivor. A note in his patient chart recorded that the tumor was "malignant but slow growing and late to metastasize. Prognosis therefore moderately good."[130]

On March 15, 1995, Elmerine Whitfield Bell, the daughter of Elmer Allen, told the Advisory Committee in Washington, D.C., that she

> continue[s] to be appalled by the apparent attempts at cover-ups, the inferences that the nature of the times, the 1940s, allowed scientists to conduct experiments without getting a patient's consent or without mentioning risks. We contend that my father was not an informed participant in the plutonium experiment. He was asked to sign his name several times while a patient at the University of California hospital in San Francisco. Why was he not asked to sign his name permitting scientists to inject him with plutonium? Why was his wife, who was college trained, not consulted in this matter?

On January 5, 1948, a fifty-five-year-old woman with cancer was injected with zirconium at the University of California.[131] The patient record for this case has not yet been located, nor have any other documents that might bear on whether this experiment was conducted in compliance with the consent requirements of the Wilson letters. We do know that the injection of zirconium was not expected to benefit the subject herself.[132]

A secret report on the zirconium injection was reviewed by the AEC in light of public relations and liability concerns. In August of that year, the report was denied declassification with the approval of Shields Warren, who wrote, "This document should not be declassified for general medical publication [and] it would be very difficult to rewrite it in an acceptable manner."[133] Warren was responding to a memorandum from Albert H. Holland, Jr., medical adviser at Oak Ridge, which specified that the concern about rewriting had to do with public relations and the fact that the report "specifically involves experimental human therapeutics."[134]

Follow-up of the Patient-Subjects at Rochester

The investigators at Rochester and the AEC were interested in obtaining long-term data from surviving subjects on excretion levels and the distribution of plutonium in various tissues. Follow-up studies at Rochester continued at least through 1953 with two of the subjects in the HP series, Eda Charlton and John Mousso. We have already noted Wright Langham's 1950 instruction to the physicians at Rochester suggesting that they were not to give these patients any indication of the true purpose of the follow-up studies.[135] In addition, Langham sought help in early 1950 to locate Ebb Cade (the man injected at Oak Ridge Hospital) for follow-up excretion studies. Langham asked Dr. Albert Holland at Oak Ridge to try to locate Mr. Cade and to keep his "eyes open for a possible autopsy."[136] It is

unclear to the Committee whether follow-up of any kind was ever done with Mr. Cade.

On June 8, 1953, Eda Charlton's rib was removed during exploratory surgery for cancer and analyzed for plutonium. Louis Hempelmann, who by that time had moved from Los Alamos to Strong Memorial Hospital at Rochester, wrote to Charles Dunham of the AEC's Division of Biology and Medicine in advance of the procedure:

> The patient in question was brought in for a skeletal survey, and turned out to have a 'coin-like' lesion inside the chest wall. . . . It is undoubtedly an incidental finding, but she must be explored by the chest surgeon here at Strong. In the course of the operation, he will remove a rib which we can analyze. Her films show the same type of minimal indefinite change in the bone that the others have had.[137]

It was standard practice at the time to remove a section of rib incidental to lung surgery. It is clear that the patient was still being followed for long-term effects of plutonium and that some subclinical bone changes of unclear significance had already been observed by this time. Therefore, the examination of this rib segment would have included special tests to determine whether plutonium was present.

On August 31, 1950, an internal DBM memorandum recorded the understanding of some AEC officials that Wright Langham and Rochester doctors were engaged in follow-up studies.[138] In a 1974 interview, however, Shields Warren recalled that he had no knowledge that the patients were the subjects of follow-up studies: "I did not learn of this continuing contact while I was in office at AEC. . . . I had assumed because I had been told that they were incurable patients that they all had died by the time we talked."[139]

Additional Follow-up Studies and the Argonne Exhumation Project

In 1968 Dr. Patricia Durbin undertook an investigation of the plutonium-injection subjects, which included a reevaluation of the original plutonium data. Her goal was to pursue "some elusive information on Pu in man and the information or assumptions about physiology needed to create a believable Pu model for man." She "decided to look at all the old Pu patients as individuals rather than in a lump. . . ."[140] Durbin was surprised to find in her search for the original experimental data that the University of California data were drawn from three subjects who received plutonium and one who received americium; the data from only *one* plutonium subject from California had previously been reported in the open scientific literature.[141] Durbin asked the original researchers why these data had not been analyzed. She wrote: "I understand from Wright Langham that this problem has been discussed before and discarded as too messy."[142]

In 1972, after the classified report on the experiments had been downgraded to "Official Use Only," she went on to publish "Plutonium in Man: A New Look at the Old Data," a landmark paper in the plutonium story.[143] This was the first review in the open literature to analyze Langham's results in light of the actual medical conditions of the patient-subjects. Because of the prolonged secrecy surrounding the experiments, it was generally not known that two of the three University of California cases had been omitted from the 1950 analysis. The report also revealed in retrospect that all the patients were not hopelessly or terminally ill, as had been suggested in Langham's later public references, that some were still alive, and that some had been misdiagnosed.

In December 1972, Argonne National Laboratory's Center for Human Radiobiology (CHR), to whom Durbin had provided the names of surviving subjects, began a review of the data from all eighteen people who were injected with plutonium between 1945 and 1947. CHR was the national center designated by the AEC to do long-term follow-up of individuals with internally deposited radionuclides, primarily the radium dial painters. Argonne's follow-up plan for the plutonium experiments was to uncover the postinjection medical histories of all the subjects, obtain biological material from those still living, and exhume and study the bodies of those deceased in order to "provide data on the organ contents at long times after acquisition of plutonium."[144]

In 1973, three patients—Eda Charlton, John Mousso, and Elmer Allen—were admitted to the University of Rochester's metabolic ward for

more excretion studies paid for by CHR. Elmer Allen had first been brought to Argonne, where an unsuccessful attempt had been made to detect plutonium by external counting techniques. In the course of his examination, however, CHR found subclinical bone "changes" that an Argonne radiologist characterized as "suggestive of damage due to radiation."[145]

Again there was no disclosure to the subjects that they were now being followed because they had been subjects of an experiment that had been unrelated to their medical care, an experiment in which there was continuing scientific interest. The 1974 AEC investigation concluded that, in the case of the surviving Rochester subjects, Dr. Waterhouse, who conducted the follow-up studies with these patients for Argonne, had not told them the purpose of the studies in 1973 because she believed "that disclosure might be harmful to them in view of their advanced age and ill health."[146] This suggests that Dr. Waterhouse had well-intentioned motivations for not being straightforward with the Rochester subjects. It also suggests that these subjects had not been told the truth about the experiments at the time the injections occurred, or that they had forgotten. According to Dr. Waterhouse, the studies were feasible without the subjects' knowledge of the true purpose of the research since these two patients "were accustomed to participating in clinical studies, unrelated to this matter, involving the collection of excretion specimens."[147] Elmer Allen's physician was told by CHR that the purpose of bringing Mr. Allen to Argonne's CHR and the University of Rochester for follow-up was interest in the treatment he received at the University of California in 1947 for his cancer.[148] This use of the term *treatment* in the information provided Mr. Allen's physician, which he presumably relayed to Mr. Allen and his family, was deceptive and manipulative; it implied that the injection Mr. Allen received had been given as therapy for his benefit.

The second component of this follow-up study was research on the exhumed bodies of deceased subjects. The 1974 AEC investigation concluded that the families were not informed that plutonium had been injected. Instead, they were told that "the purpose of exhumation was to examine the remains in order to determine the microscopic distribution of residual radioactivity from past medical treatment" and that the subjects had received an "unknown" mixture of radioactive isotopes.[149] The investigation concluded that such disclosure "could be judged misleading in that the radioactive isotopes were represented as having been injected as an experimental treatment for the patient's disease."[150] Thus, the families of the deceased subjects as well as those subjects still surviving were deceived by officials of the AEC.

A December 1972 intralaboratory memorandum, written by an Argonne investigator, instructs that "outside of CHR we will *never* use the word *plutonium* in regard to these cases. 'These individuals are of interest to us because they may have received a radioactive material at some time' is the kind of statement to be made, if we need to say anything at all."[151] Robert E. Rowland, the author of this memorandum, told Advisory Committee staff in 1995 that he had written this after he had been instructed earlier that month by Dr. James Liverman, director of the AEC's Division of Biomedical and Environmental Research, that "I could not tell the individuals that they were given plutonium. I protested that they must be given a reason for our interest in them, and I was told to tell them that they had received an unknown mixture of radioisotopes in the past, and that we wanted to determine if it was still in their bodies. Further, we were not to divulge the names of the institutions where they received this unknown mixture."[152] Dr. Rowland said he had received these instructions during a trip to Washington, D.C., to obtain approval and funding for the study.[153] Dr. Liverman told Advisory Committee staff that he has "no recollection of discussions with anyone in which some stricture would have been placed on what could be discussed with the patients. That is a medical ethics issue which would have been left to the physicians."[154]

This study was not brought to the attention of the Argonne Human Use Committee until November 1973, even though it had been established in January 1973. (See chapter 6 for a discussion of human use committees.) In a briefing for the 1974 AEC investigation, Dr. Liverman attributed this failure to bring the study

before the Human Use Committee to the following factors: "(1) [Argonne's] opinion that the studies came under the scope of a protocol approved by that Committee in 1971. (2) The nature of the studies was to be suppressed to avoid embarrassing publicity for AEC."[155]

In 1974 the AEC informed at least two of the four living subjects—Eda Charlton and John Mousso—of the plutonium injections and had them sign documents to this effect. These documents did not provide any information on possible effects of the injections, although they did describe the purpose as having been "to determine how plutonium, a man-made radioactive material, is deposited and excreted in the human body."[156] One living patient, Jan Stadt, was not told, because it was her attending physician's opinion that her condition was precarious and that disclosure in this case would be "medically indefensible."[157] This judgment, like that of Dr. Waterhouse's, exemplifies how physicians of the time commonly managed the information they shared with their patients. Physicians typically told patients only what they thought it was helpful for them to know; if in the physician's judgment information might cause the patient to become upset or distressed, this was often considered reason enough to withhold it.[158] The judgment also suggests that Ms. Stadt, like Ms. Charlton and Mr. Mousso, had not been told the truth about the experiments at the time the injections occurred or that she had forgotten.

The AEC recommended that exhumations continue, but only with full disclosure to the subjects' next of kin.

The Boston Project Uranium Injections

Human experiments conducted to measure the excretion and distribution of atomic weapons materials did not stop with the last of the injections at the University of California. The Boston Project human uranium-injection experiments were conducted from 1953 to 1957 at Massachusetts General Hospital (MGH) as part of a cooperative project between the hospital and the Health Physics Division of Oak Ridge National Laboratory. Eleven patients with terminal conditions were injected with uranium, although data obtained from three of these subjects were never published.[159] The ORNL and the AEC undertook the Boston Project to obtain better data for the development of worker safety standards. One of the investigators wrote that the Boston Project would provide "a wonderful opportunity to secure 'human data' for the analysis and interpretation of industrial exposures."[160] The occupational standards for uranium at the time were based on animal data and on the experiment conducted at Rochester in the 1940s. No autopsy data were obtained from this earlier experiment at Rochester, however, since none of the patients had terminal diseases. Thus, wrote a Boston Project investigator, "the uncertainty, in so far as the distribution of uranium was concerned, was not reduced [by the Rochester experiment] or could not even be determined."[161]

The Boston Project involved a second purpose—the search for a radioisotope that would localize in a certain type of brain tumor—called glioblastomas—and destroy them when activated by a beam of neutrons. This had long been the research interest of Dr. William Sweet at MGH; at the time, these tumors were clearly diagnosable and 100 percent fatal, and there was no effective treatment. This research involved many radioisotopes over the years, most notably isotopes of boron and phosphorus. It is unclear whether Dr. Sweet would have tested uranium without ORNL's involvement—or whether it would have been made available to him by the AEC. Dr. Sweet has indicated to the Committee that he was interested in the potential of uranium as a therapeutic agent prior to being approached by the AEC about the possibility of conducting a joint project.[162]

The Boston Project produced data on the distribution of uranium in the human body that the earlier Manhattan District uranium studies had not provided. The data obtained indicated that uranium, at least at the dose levels used in the Boston Project, localized in the human kidney at higher concentrations than small animal data had predicted and that therefore the maximum permissible levels for uranium in water and air might be unsafe. Recommendations made by the investigators of the Boston Project for more conservative occupational standards were apparently not heeded, however. The accepted occupational

levels for uranium became less rather than more conservative over the years, despite the findings of the Boston Project.[163]

Hopes that uranium would localize sufficiently in brain tumors to be of potential therapeutic use were unfulfilled. In a 1979 interview, Robert Bernard, one of the health physicists at ORNL most intimately involved with the study, was asked if during the experiment uranium was showing any promise as a treatment. "No, it concentrated in the kidney just like Rochester said back in the '40's. . . . They got brain tumor samples. There was very little uranium present, but Sweet was still wondering: maybe [it was] not a high enough dose."[164]

In a 1995 interview, Karl Morgan, head of the Health Physics Division of ORNL at the time of the Boston Project, indicated that the project was ultimately discontinued in 1957[165] because of the concerns of an ORNL health physicist:

> He felt that the patients were given very large doses of uranium which our data had indicated—that is, the data we collected [at ORNL] in setting permissible doses—would be very harmful. . . . I immediately cancelled our participation in the program. Apparently, they were given doses that were many times the . . . permissible body burden.[166]

In their application to their radioisotope committee, MGH investigators clearly recorded that the proposed dose of 2.12 rem per week "exceeds maximum permissible exposure rate of 0.3 rem/week but [patients] are terminal."[167]

At least one of the subjects was selected for the distribution part of the study only. Reports describe the patients as "virtually all" having malignant brain tumors; newly available documents indicate that at least one patient injected with uranium did not have a brain tumor at all. An unidentified male, identity and age still unknown at the time of his death, became Boston Project subject VI when he "was brought to the Emergency Ward after being found unconscious. . . . No other information was obtainable."[168] According to his autopsy report, this patient was suffering from a subdural hematoma—a severe hemorrhage—on his brain. There was clearly no benefit intended for this patient from the injection of uranium, but there is evidence of harm attributable to the injection. His autopsy report records clinical evidence of mild kidney failure[169] and pathological evidence of kidney nephrosis (damage to the kidney tubules) from the chemical toxicity of uranium metal.[170] The report also records that "the liver, spleen, kidneys and bone marrow showed evidence of radiation."[171]

Even for the patient-subjects with brain cancer, there was no expectation on the part of investigators that the experiment would benefit the subjects themselves. The object of the experiment was to test whether uranium would localize sufficiently in brain tumors to be of therapeutic value in the future. In order for uranium to have had therapeutic potential for patient-subjects, exposure to a reactor's neutron beam would have been necessary to then activate the uranium, *if* it had localized sufficiently in the tumors, which it did not. There was, however, no plan to expose these particular patient-subjects to a neutron beam; the goal was to see whether the concentration would justify further research that would involve exposure to a neutron beam. Most of the subjects were already comatose and "in the terminal phase of severe irreversible central nervous system disease."[172]

The doses used in the Boston Project were high; the lowest dose was comparable to the highest used in the earlier Rochester uranium experiment—a dose that had caused detectable kidney damage in one of the Rochester subjects. One document records that at least two Boston Project subjects, in addition to subject VI, had kidney damage at the time of death, although this document does not directly link this damage to the uranium injections.[173]

There is no discussion of consent in any of the Boston Project reports. It appears that ORNL left such considerations to Dr. Sweet and MGH. In an interim report, ORNL discusses the division of responsibility in the experiment: "It was agreed that the Y-12 Health Physics Department [at Oak Ridge] would prepare injection solutions and perform the analytical work associated with this joint effort. Massachusetts General Hospital agreed to select the patients, perform the injections, and care for the patients during the period of study."[174]

Dr. Sweet told the Advisory Committee in 1995 that it was his practice to obtain consent from patients or from their families and "scrupulously to give a patient all the information we

had ourselves."[175] The Committee has not been able to locate any documents that bear on questions of disclosure or consent for this experiment.[176] The case of the Boston Project subject who was brought into the hospital after being found unconscious, and who, according to his autopsy report, was never identified and never regained consciousness, indicates that this rule was not applied universally.

CONCLUSION

From 1945 through 1947 Manhattan Project researchers injected eighteen human subjects with plutonium, five human subjects with polonium, and six human subjects with uranium to obtain metabolic data related to the safety of those working on the production of nuclear weapons. All of these subjects were patients hospitalized at facilities affiliated with the Universities of Rochester, California, and Chicago or at Oak Ridge. Another set of experiments took place between 1953 and 1957 at Massachusetts General Hospital, in which human subjects were injected with uranium. In no case was there any expectation that these patient-subjects would benefit medically from the injections.

At fifty years' remove, it is in some respects remarkable that so much information has survived that bears on the question of what the patient-subjects and their families were told. Particularly for the Manhattan Project plutonium experiments information is available, in large part because of the 1974 AEC inquiry in which interviews with principals of these experiments were conducted and records of these interviews maintained. At the same time, however, there are *significant* gaps in the record for all the experiments. Particularly where the evidence is skimpy, it is possible that some of the patient-subjects agreed to be used in nontherapeutic experiments. But the picture that emerges suggests otherwise. This picture is bolstered by the historical context. As we discussed in chapter 2, it was not uncommon in the 1940s and 1950s for physician-investigators to experiment on patients without their knowledge or consent, even where the patients could not benefit medically from the experimental procedures. This context is referenced in a 1946 letter about the University of California injections: "These doctors state that the injections would probably be made without the knowledge of the patient. . . . Such injections were not divergent from the normal experimental method in the hospital. . . ."[177]

Here we present our conclusions about the ethics of these experiments, first for the set of experiments conducted between 1945 and 1947 and then for the experiment conducted from 1953 to 1957. Because the facts appear to be different in the different institutions at which these experiments took place, we summarize what we have learned about risk, disclosure, and consent at each location. We also analyze the ethical issues the experiments raise in common. In our analysis, we focus on whether the subjects consented to being used in experiments *from which they could not benefit medically,* and the extent to which the subjects were exposed to risk of harm. We also focus on the particular ethical considerations raised when research is conducted on patients at the end of their lives. All but one member of the Advisory Committee believe that what follows is the most plausible interpretation of the available evidence in light of the historical context.

With one exception, the historical record suggests that these patients-subjects were not told that they were to be used in experiments for which there was no expectation they would benefit medically, and as a consequence, it is unlikely they consented to this use of their person.

In the case of the plutonium experiments, there was no reason to think that the injections would cause any acute effects in the subjects. This was not true, however, in the case of the Rochester uranium experiments. Both the plutonium and the Rochester uranium experiments put the subjects at risk of developing cancer in ten or twenty years' time. In some cases, this risk was eliminated by the selection of subjects who were likely to die in the near future. The selection of subjects with chronic illnesses was also an apparent strategy to contain this long-term risk of cancer. However, some of these subjects lived for far longer than ten years, and some were misdiagnosed altogether. On the basis of available evidence, we could not conclude that any individual was or was not physically harmed as

a result of the plutonium injections. There is some evidence that there were observable, subclinical bone changes of unclear significance in at least two surviving subjects who were followed up in 1953 and 1973 and in one deceased subject who was exhumed in 1973. The uranium injections at Rochester were designed to produce minimal detectable harm—that was the endpoint of the experiment. Such minimal damage is reported to have occurred in the sixth patient of the series.

In the case of Mr. Cade at Oak Ridge, a physician claiming to have injected Mr. Cade reported that his consent was not obtained. An apparently healthy man in his early fifties, Mr. Cade was put at some (probably small) risk of cancer by the plutonium injection.

At the University of Chicago, the only evidence that bears on disclosure and consent comes from an interview with a Chicago investigator conducted as part of the AEC's 1974 inquiry. The investigator was recorded as saying that in obtaining consent patients were told that the radioactive substance to be injected "was not necessarily for the benefit of the patients but might help other people."[178] This statement is misleading. It suggests that there was some chance these patient-subjects might benefit when there was no such expectation. At the same time, however, this statement suggests that the subjects at Chicago were told something. These subjects also were all apparently terminally ill and thus at no risk of developing plutonium-induced cancer; at least two of the three were known to have died within one year of the injection.

Misleading language was purportedly also used with subjects at the University of California, where a secondhand account suggests that subjects were told they were to be injected with a new substance that "had some properties like other substances that had been used to control growth processes in patients."[179] Language in a 1946 letter suggests that at least some of the injections at the University of California may have occurred altogether without the knowledge of the patients. In the case of Mr. Allen, one of the California subjects, two physicians attested that the experimental nature of the procedure had been explained to Mr. Allen and that he had consented. And yet Mr. Allen's physician was subsequently informed that the follow-up studies were in relation to *treatment* Mr. Allen had received at the University of California. This suggests that, while Mr. Allen may have been told the procedure was experimental, it is not likely that he was told that the procedure was part of an experiment in which there was no expectation that he would benefit medically. Both Mr. Allen and Mr. Stevens survived long enough after injection to be at risk of plutonium-induced cancer.

All the available evidence suggests that none of the subjects injected with either plutonium or uranium at Rochester knew or consented to their being used as subjects in experiments from which they could not benefit. This evidence comes from recollections of some of the individuals who were involved with the plutonium injections, as well as documents about seminars and follow-up studies in the early 1950s suggesting that information about the experiments should be concealed from the subjects. Most of the subjects at Rochester had serious chronic illnesses. It is unclear how likely it was at the time that these patients would not survive more than ten years. A few of these subjects were still alive more than twenty years after the injections. None of the plutonium subjects but all of the uranium subjects were put at risk of acute effects from the experiment.

The purpose of the 1973 follow-up studies was withheld from two surviving subjects. Also, both Elmer Allen's physician and family members of deceased subjects were misled by AEC officials about the purpose of the follow-up studies. They were told that the follow-up was in relation to past medical treatment, which was not true.

It is unlikely that AEC officials would have lied about or otherwise attempted to conceal the purpose of the follow-up studies if at the outset the subjects had known and agreed to their being used as subjects in nontherapeutic experiments. It is also relevant that when the Atomic Energy Commission succeeded the Manhattan Project on January 1, 1947, officials decided to keep the plutonium injections secret. It appears that this decision was based on concerns about legal liability and adverse public reaction, not national security. The documents show that the AEC

responded to the possibility that consent was not obtained in the plutonium experiments, as well as their lack of therapeutic benefit, by stating requirements for informed consent and therapeutic benefit for future research, while still keeping the experiments secret. As a result of the decision to keep the injections secret, the subjects and their families, as well as the general public, were denied information about these experiments until the 1970s.

The one likely exception to this picture of patients not knowing that they were used as subjects in experiments that would not benefit them is the polonium experiment conducted at Rochester. This is the one instance in which the patient-subjects are said to have volunteered after being told about "the general problem." Although there is no direct evidence that these subjects were told that the experiment was not for their benefit, the language of volunteering suggests a more forthright disclosure was made, more in keeping with the conventions in nontherapeutic research with healthy subjects than in research with patients (see chapter 2). We cannot reconcile the account of the polonium experiment with the historical record on the other injections.

The Advisory Committee is persuaded that these experiments were motivated by a concern for national security and worker safety and that, particularly in the case of the plutonium injections, they produced results that continue to benefit workers in the nuclear industry today.[180] However, with the possible exception of the polonium experiments, we believe that these experiments were unethical. In the conduct of these experiments, two basic moral principles were violated—that one ought not to use people as a mere means to the ends of others and that one ought not to deceive others—in the absence of any morally acceptable justification for such conduct. National security considerations may have required keeping secret the names of classified substances, but they would not have required using people as subjects in experiments without their knowledge or giving people the false impression that they or their family members had been given treatment when instead they had been given a substance that was not intended to be of benefit.

The egregiousness of the disrespectful way in which the subjects of the injection experiments and their families were treated is heightened by the fact that the subjects were hospitalized patients. Their being ill and institutionalized left them vulnerable to exploitation. As patients, it would have been reasonable for them to assume that their physicians were acting in their best interests, even if they were being given "experimental" interventions. Instead, the physicians violated their fiduciary responsibilities by giving the patients substances from which there was no expectation they would benefit and whose effects were uncertain. This is clearest at Rochester where at least the uranium subjects, and perhaps the plutonium subjects, were apparently the personal patients of the principal investigator.

Concern for minimizing risk of harm to subjects is evident in several of the planning documents relating to the experiments, an obligation that many of those involved apparently took seriously. At Chicago, for example, where the highest doses of plutonium were used, care was taken to ensure that all the subjects had terminal illnesses. In those cases where this concern for risk was less evident and subjects were exposed to more troubling risks, the moral wrong done in the experiments was greater. Where it was not reasonable to assume that subjects would be dead before a cancer risk had a chance to materialize, or in the case of the uranium injections at Rochester where acute effects were sought, the experiments are more morally offensive.

Consideration for the basic moral principle that people not be put at risk of harm is apparently what animated the decision to give higher doses to only "terminal" patients who could not survive long enough for harms to materialize. A person who is dying may have fewer interests in the future than a person who is not. This does not mean, however, that a dying person is owed less respect and may be used, like an object, as a mere means to the ends of others. There are many moral questions about research on patients who are dying; the desperation of their circumstances leaves them vulnerable to exploitation. At a minimum, nontherapeutic research on a dying patient without the patient's consent or the authorization of an appropriate family member is clearly unethical.

Uranium was also injected in eleven patients with terminal conditions at Massachusetts General Hospital in an experiment conducted jointly by the hospital and Oak Ridge National Laboratory from 1953 to 1957. ORNL's purpose was to obtain data for setting nuclear worker safety standards. A second purpose was to identify a radioisotope that would localize in brain tumors and destroy them when activated by a neutron beam. Although all but one of the patient-subjects had brain cancer, the limited purpose of the experiment—to establish whether uranium would localize sufficiently—meant that there was no expectation that patient-subjects might benefit medically from the uranium injections.

The uranium doses in the Boston experiment were comparable to or higher than the one that caused measurable physical harm in the Rochester subject. Boston subjects were apparently subjected to brain biopsies, presumably solely for scientific purposes. At least three Boston subjects showed kidney damage at the time of death. In one of these cases, a trauma victim who was found unconscious, the autopsy report recorded clinical evidence of some amount of kidney failure and pathological evidence of kidney damage due to the chemical toxicity of uranium.

The only evidence available about what the Boston subjects were told comes from 1995 testimony of one of the investigators, Dr. William Sweet, who said it was his practice to "give a patient all the information we had ourselves." Presumably this would have included that the injections had no prospect of benefiting the patient. The Boston Project was an instance in which high doses were given to dying patients. Some of these patients were comatose or otherwise suffering from severe, irreversible central nervous system disease. Unless these patients, or the families of comatose or incompetent patients, understood that the injections were not for their benefit and still agreed to the injections, this experiment also was unethical. There was no justification for using dying patients as mere means to the ends of the investigators and the AEC. In at least one case, this disrespectful treatment clearly occurred. The trauma victim who arrived at the hospital unconscious was used as a subject despite the fact that his identity was never known. Presumably he was not accompanied by any family or friends who might have authorized such a use of his body.

Only extraordinary circumstances can justify deception and the use of people as mere means by government officials and physicians in the conduct of research involving human subjects. In the case of the injection experiments, we see no reason that the laudable goals of the research could not have been pursued in a morally acceptable fashion. There is no reason to think that people would not have been willing to serve as subjects of radiation research for altruistic reasons, and indeed there is evidence of people writing to the AEC to volunteer themselves for just such efforts (see chapter 13).

That people are not likely to live long enough to be harmed does not justify failing to respect them as people. Concerns about adverse public relations and legal liability do not justify deceiving subjects, their families, and the public. Insofar as basic moral principles were violated in the conduct of the injection experiments, the Manhattan Engineer District, the AEC, the responsible officials of these agencies, and the medical professionals responsible for the injections are accountable for the moral wrongs that were done.

NOTES

1. Don Mastick, telephone interview with Steve Klaidman (ACHRE), 23 July 1995 (ACHRE No. IND-072395–F), 1.
2. L. H. Hempelmann, Los Alamos Laboratory Health Division Leader, to J. R. Oppenheimer, Director, Los Alamos Laboratory, 16 August 1944 ("Health Hazards Related to Plutonium") (ACHRE No. DOE-051094–A-17), 1.
3. J. R. Oppenheimer, Director, Los Alamos Laboratory, to L. H. Hempelmann, Los Alamos Laboratory Health Division Leader, 16 August 1944 ("Your memorandum of August 16, 1944") (ACHRE No. DOE-051094–A-17), 1.
4. L. H. Hempelmann, Los Alamos Laboratory Health Division Leader, to J. R. Oppenheimer, Director of the Los Alamos Laboratory, 29 August 1944 ("Medical Research Program") (ACHRE No. DOE-051094–A-17), 1.
5. Interview with Mastick, 23 July 1995, 1.
6. Glenn Seaborg, head of Chemistry Section C-1 of the Metallurgical Laboratory, to Robert Stone, Health Director of the Metallurgical Laboratory, 5 January 1944 ("Physiological Hazards of Working

with Plutonium") (ACHRE No. DOE-070194–A-3), 1.

7. Ibid.

8. Robert Stone, Health Director of the Metallurgical Laboratory, to Glenn Seaborg, Head of the Chemistry Section C-1 of the Metallurgical Laboratory, 8 January 1944 ("Hazards of Working with Plutonium") (ACHRE No. DOE-070194–A-4), 1.

9. Seaborg suggested that several milligrams of the first shipment of plutonium from Oak Ridge be sent on to Dr. Hamilton at Berkeley. A minute amount of plutonium was sent to Hamilton, who began his studies on rats in February 1944. Next came more animal work at Chicago, focusing on the toxic effects of plutonium, as well as its distribution in various tissues. These studies showed that plutonium, like radium, was a "bone-seeking" element, the potential deadly consequences of which radium had already demonstrated. Furthermore, these studies demonstrated that in rats, plutonium distributed itself in bone in a potentially more hazardous way than radium. J. Newell Stannard, *Radioactivity and Health: A History* (Oak Ridge, Tenn.: Office of Scientific and Technical Information, 1988), 1424.

10. Richard Rhodes, *The Making of the Atomic Bomb* (New York: Simon and Schuster, 1986), 547–548.

11. Ibid., 560.

12. The most likely route of worker exposure to plutonium would be inhalation. Hempelmann and others wrote to Oppenheimer in March 1945 that "the very important and difficult problem of detection of alpha active material in the lungs has been studied only at this project and here only on a very limited scale. This problem should be given much higher priority here and at other projects." L. H. Hempelmann, Los Alamos Laboratory Health Division Leader et al., to J. R. Oppenheimer, Director of the Los Alamos Laboratory, 15 March 1945 ("Medical Research of Manhattan District concerned with Plutonium") (ACHRE No. DOE-051094–A-17), 1. Inhalation experiments with rodents were undertaken, starting in 1944, at the University of California's Radiation Laboratory and the University of Chicago's Metallurgical Laboratory, although these studies did not result in extensive analysis of data until the latter half of the 1940s. W. H. Langham and J. W. Healy, "Maximum Permissible Body Burdens and Concentrations of Plutonium: Biological Basis and History of Development," in *Uranium–Plutonium–Transplutonic Elements*, eds. H. C. Hodge et al. (New York: Springer-Verlag, 1973), 576. Wright Langham wrote in 1945 that "if a limited amount of human tracer data are to form the basis of a method of diagnosing internal body contamination," it would be necessary "to assume that [plutonium] is metabolized in the same way regardless of the route of absorption or administration." Wright Langham, Los Alamos Laboratory Health Division, 28 July 1945 ("Report of Conference on Plutonium—May 14th and 15th") (ACHRE No. DOE-051094–A-427), 29. Since the time of the experiments, it has become clearer that the deposition of plutonium in the body can differ in cases of chronic inhalation exposure versus other types of exposures.

13. Langham and Healy, "Maximum Permissible Body Burdens and Concentrations of Plutonium," 576.

14. L. H. Hempelmann, Los Alamos Laboratory Health Division Leader, to J. R. Oppenheimer, Director of the Los Alamos National Laboratory, 26 March 1945 ("Meeting of Chemistry Division and Medical Group") (ACHRE No. DOE-051094–A-17), 1.

15. J. R. Oppenheimer, Director, Los Alamos Laboratory, to Colonel S. L. Warren, 29 March 1945 ("We are enclosing a record of discussions . . .") (ACHRE No. DOE-051094–A-17), 1.

16. Samuel Bassett [attr.], undated ("Excretion of Plutonium Administered Intravenously to Man. Rate of Excretion in Urine and Feces with Two Observations of Distribution in Tissues") (ACHRE No. DOE-121294–D-10), 29.

17. Division of Biomedical and Environmental Research and Division of Inspection, AEC, 13 August 1974 ("Disclosure to Patients Injected with Plutonium") (ACHRE No. DOE-051094–A-586), 11.

18. Ibid.

19. Ibid., 10.

20. Wright Langham, Los Alamos Laboratory Health Division, to Hymer Friedell, Executive Officer of the Manhattan District's Medical Section, 6 April 1945 ("Although we sent you directions for the 49 experiment along with the material . . .") (ACHRE No. DOE-120894–E-1), 1.

21. Wilson O. Edmonds, AEC Resident Investigator, to Jon D. Anderson, Director, Division of Inspection, 15 July 1974 ("Division of Biomedical and Environmental Research, Headquarters—Request to Locate Mr. Ebb Cade") (ACHRE No. DOE-051094–A-611), 2.

22. Undated document ("Experiment I on P. 49+4") (ACHRE No. DOE-113094–B-5), 1.

23. The Committee uses names of subjects in this chapter only where the names were already a matter of public record.

24. "Experiment I on P. 49+4," 1.

25. Ibid.

26. Hannah E. Silberstein, University of Rochester, to Wright Langham, Los Alamos Laboratory Health Division, 25 October 1945 ("This letter is to report the injection on the second human *product* subject, HP-2 . . .") (ACHRE No. DOE-121294–D-19), 1.

27. W. H. Weyzen, 25 April 1974 ("Visit with Dr. Joe Howland, Chapel Hill Holiday Inn, April 24, 1974") (ACHRE No. DOE-121294–D-18), 1.

28. Hymer Friedell, interviewed by Steve Klaidman and Ron Neumann (ACHRE), transcript of audio recording, 23 August 1994 (ACHRE Re-

search Project Series, Interview Program File, Targeted Interview Project), 49–50.

29. "Experiment I on P. 49+4," 3.

30. Ibid.

31. Ibid., 2.

32. Captain David Goldring, Medical Corps, to Wright Langham, Los Alamos Laboratory Health Division, 19 September 1945 ("Enclosed is a brief resume of E. C.'s medical history . . .") (ACHRE No. NARA-082294–A-47), 1.

33. Karl Morgan, interviewed by Gil Whittemore and Miriam Bowling (ACHRE), transcript of audio recording, 6 January 1995 (ACHRE Research Project Series, Interview Program File, Targeted Interview Project), 147.

34. Edmonds to Anderson, 15 July 1974, 3.

35. "Experiment I on p. 49+4," 3.

36. On 7 May 1945 Germany had surrendered to the Allied forces. The Manhattan Engineer District continued on with the building and testing of the first atomic bomb (the first test was scheduled for July of that year).

37. Robert Stone, Health Director of the Metallurgical Laboratory, to Stafford Warren, Hymer Friedell et al., undated ("On Monday, May 14th, we plan to have an all day meeting dealing with plutonium . . .") (ACHRE No. NARA-082294–A-51), 1.

38. Wright Langham, Los Alamos Laboratory Health Division, 28 July 1945 ("Report of Conference on Plutonium—May 14th and 15th") (ACHRE No. DOE-051094–A-427), 29.

39. Colonel Hymer Friedell, Executive Officer of the Manhattan District's Medical Section, to L. H. Hempelmann, 11 April 1945 ("Enclosed is a protocol of the clinical experiment as we intend to carry it out . . .") (ACHRE No. DOE-121294–D-1), 1.

40. Ibid.

41. J. J. Nickson to R. S. Stone, 23 January 1946 ("Abstract of Monthly Report for January, 1946") (ACHRE No. DOE-051094–A), 1.

42. E. R. Russell and J. J. Nickson, 2 October 1946 ("The Distribution and Excretion of Plutonium in Two Human Subjects") (ACHRE No. DOE-051094–A-370), 1.

43. Ibid.

44. Ibid.

45. Ibid., 2.

46. Ibid.

47. Nickson to Stone, 23 January 1946, 1.

48. Sidney Marks, 3 May 1974 ("Interview with Dr. Leon Jacobson . . . by Marks and Miazga at about 1:30 p.m. on 4/16/74") (ACHRE No. DOE-121294–D-15), 2.

49. W. H. Weyzen, 25 April 1974 ("Visit with Edwin R. Russell, Savannah River Plant, April 23, 1974") (ACHRE No. 121294–D-17), 1.

50. Andrew H. Dowdy, Director of AEC Rochester Project ("Proposed Research Program and Budget: July 1, 1947—July 1, 1948") (ACHRE No. DOE-061794–B-16).

51. William F. Bale, Head of Special Problems Division, undated ("Contributions of the Division of Special Problems to the Manhattan Project") (ACHRE No. DOE-113094–B), 1.

52. L. H. Hempelmann and Wright H. Langham, undated ("Detailed Plan of 'Product' Part of Rochester Experiment") (ACHRE No. 121294–D-2), 5.

53. W. H. Langham, undated ("Revised Plan of 'Product' Part of Rochester Experiment") (ACHRE No. DOE-121294–D-3), 2.

54. The choice not to use subjects suffering from malignant conditions is discussed retrospectively in a partial draft version of the 1950 report (probably written by Dr. Bassett). This discussion was not included in the final version of the report:

> The individuals chosen as subjects for the experiment were a miscellaneous group of male and female hospital patients for the most part with well established diagnoses. Preference was given to those who might reasonably gain from continued residence in the hospital for a month or more. . . . Patients with malignant disease were also omitted from the group on the grounds that their metabolism might be affected in an unknown manner.

Bassett, "Excretion of Plutonium Administered Intravenously to Man," 2.

55. Ibid.

56. Wright Langham et al., 20 September 1950 ("Distribution and Excretion of Plutonium Administered Intravenously to Man") (ACHRE No. DOE-070194–A-18), 10.

57. Wright Langham, 27 September 1957 ("Proceedings of the Second Annual Meeting on Bio-Assay and Analytical Chemistry: October 11 and 12, 1956—Panel Discussion of Plutonium") (ACHRE No. DOE-120894–C-1), 80.

58. W. H. Langham et al., "The Los Alamos Scientific Laboratory's Experience with Plutonium in Man," *Health Physics* 8 (1962): 755.

59. Addison's disease is an endocrine disease produced by adrenal gland failure. Today this disease is treated with steroid therapy that was developed in the 1940s and that was extremely expensive at the time of the experiments. HP-6, diagnosed with Addison's, was given steroid treatment as part of his care at the University of Rochester; he lived until 1984.

Scleroderma is a collagen-vascular disease that can produce extreme pain, especially in the hands; can affect eating and swallowing if the esophagus is involved; and eventually leads to organ failure and death. Steroids are the treatment of choice today, but if this disease is not well controlled it can still be fatal. HP-8, who was diagnosed with scleroderma, lived until 1975.

60. Bassett, "Excretion of Plutonium Administered Intravenously to Man," 2. Her provisional diagnosis according to this report was mild hepatitis and malnutrition. Ibid, 18. Her medical records indicate, however, that she had symptoms related to nutritional

deficiencies, which appear to have been alleviated with proper diet and rest. Strong Memorial Hospital, 20 December 1945 ("Discharge Summary Form") (ACHRE No. DOE-051094–A-612), 1.

61. Wright Langham, Los Alamos Laboratory Health Division, to Samuel Bassett, Head of Metabolism Ward of Strong Memorial Hospital, 13 March 1946 ("Your letter of February 27 regarding Hp 11 was startling, to say the least . . .") (ACHRE No. DOE-121294–D-4), 1.

62. Document dated 17 April 1974 ("Comments on Meeting with Dr. Hempelmann on April 17, 1974") (ACHRE No. DOE-121294–D-16), 1.

A 1955 letter from Dr. Hempelmann to the AEC's Division of Biology and Medicine (discussed in more detail in chapter 13) indicates Hempelmann's belief that, in general, patients could be easily deceived about the true research purpose of a medical intervention. In this letter, Hempelmann (who was by then professor of experimental radiology at Rochester) is proposing that researchers present themselves as life insurance agents to AEC workers as a ruse, in order to conceal the true purpose of follow-up medical examinations. He observes that it would be more difficult to deceive workers than it would be to mislead patients in a hospital:

> If you feel that the physical examinations are vital to the survey, then, perhaps, you could offer to pay the people to compensate them for the time and effort that they will spend on the part of your alleged survey for the insurance company. They would think they were getting something for nothing and might not feel that you were worried or they were seriously ill. I don't know if these ideas are helpful at all. It is more difficult to find an excuse for these individual workers than it is in the case of patients who were treated for something or other at a hospital.

Louis Hempelmann, University of Rochester, to Charles Dunham, Director, AEC Division of Biology and Medicine, 2 June 1955 ("I did not have an opportunity . . .") (ACHRE No. DOE-092694–A), 1.

63. Patricia Durbin, 9 December 1971 ("Report on Visit to Rochester") (ACHRE No. DOE-121294–D-12), 1.

64. Patricia Durbin, 10 December 1971 ("Dr. Wright Langham, of the Los Alamos Scientific Laboratory, was the biochemist who performed the Pu analyses . . .") (ACHRE No. DOE-121294–D-13), 1.

65. "Comments on Meeting with Dr. Hempelmann on April 17, 1974," 1.

66. Langham further instructed Rochester to look for the following longer-term "symptoms" in the examination of the patients: "Judging from the recent observations that Robley Evans has made, a generalized osteitis with rarefaction of the bones of the feet, the jaw and the heads of the long bones with coarsening of the trabeculae are the most likely symptoms." Wright Langham, Los Alamos Health Division, to Dr. Joe Howland, Chief of University of Rochester's Division of Medical Services, 2 October 1950 ("I am very glad to hear that you will manage to get follow-ups on the two subjects . . .") (ACHRE No. DOE-121294–D-11), 1.

67. Wright Langham, Los Alamos Laboratory Health Division, to Samuel Bassett, Head of Metabolism Ward of Strong Memorial Hospital, 25 October 1946 ("I just received a shipment of samples which I am sure are the ones you collected on HP-3 . . .") (ACHRE No. DOE-121294–D-5), 1.

68. Samuel Bassett et al., 19 July 1948 ("The Excretion of Hexavalent Uranium Following Intravenous Administration II. Studies on Human Subjects") (ACHRE No. CON-030795–A-1), 8.

69. Andrew H. Dowdy, Director, Manhattan Department, University of Rochester, to the Area Engineer, Rochester Area, 22 October 1946 ("Clearance of Material for Seminar") (ACHRE No. DOE-120994–A-4), 1.

70. Madison Square Area Engineer, 24 October 1946 ("Uranium Studies in Humans") (ACHRE No. DOE 120994–A-4), 1.

71. Robert M. Fink ("Biological Studies with Polonium, Radium, and Plutonium") (ACHRE No. CON-030795–A-2), 122.

72. K. Z. Morgan, Oak Ridge National Laboratory Health Physics Division, to R. S. Stone, Health Director of the Metallurgical Laboratory, 5 May 1945 ("Tolerance Values for Polonium Used at Clinton Laboratories") (ACHRE No. DOE-113094–B-6), 2.

73. Fink, "Biological Studies with Polonium, Radium, and Plutonium," 122.

74. A supplemental volume contains a chapter on the development of human subject research at the University of California at Berkeley and San Francisco.

75. Hamilton's work with plutonium had begun in 1942 with support from the Office of Scientific Research and Development; it was later supported by the Manhattan Engineer District.

76. Joseph Hamilton, Radiation Laboratory of University of California at Berkeley, to Colonel E. B. Kelly, 28 August 1946 ("Summary of Research Program for Contract #W-7405–eng-48–A") (ACHRE No. DOE-113094–B-8), 2.

77. Joseph Hamilton, 11 January 1945 ("Proposed Biochemical Program at University of California") (ACHRE No. IND-071395–A-14), 2.

78. Ibid.

79. At least eleven patients were injected with columbium (later renamed niobium) or zirconium between 1948 and 1950. These experiments appear to have been outside the federal effort.

80. Joseph Hamilton, 10 May 1945 ("Progress Report for Month of May 1945") (ACHRE No. DOE-072694–B-65), 4.

81. Joseph Hamilton, 14 June 1945 ("Progress Report for Month of June 1945") (ACHRE No. DOE-072694–B-66), 4.

82. Ibid.

83. Joseph G. Hamilton, Radiation Laboratory, University of California, Berkeley, to Captain Joe W. Howland, 23 April 1946 ("The problems of the research program . . .") (ACHRE No. DOE-120894–E-40), 2.

84. Joseph G. Hamilton, Radiation Laboratory, University of California, Berkeley, to Robert Stone, Metallurgical Laboratory, 7 July 1945 ("I am writing concerning our experimental subject . . .") (ACHRE No. IND-071395–A), 1.

85. Joe W. Howland, First Lieutenant, Medical Corps, to the Area Engineer, California Area, 12 July 1945 ("Status of Experimental Subject") (ACHRE No. IND-071395–A), 1.

86. Kenneth Scott, interviewed by Sally Hughes (University of California Oral History Project), transcript of audio recording, 17 December 1979, 49–50.

87. Ibid.

88. Hamilton, "Progress Report for Month of June 1945," 4.

89. Joseph Hamilton, 14 September 1945 ("Progress Report for Month of September 1945") (ACHRE No. DOE-072694–B-67), 5.

90. "Mercy Flight Brings Aussie Boy Here: Suffering From Rare Bone Ailment, He Seeks U.S. Treatment," *San Francisco Examiner*, 16 April 1946, 1.

91. In addition to this injection, which was not performed for his benefit, the child also received superficial external radiation (five doses of 250 rad over five days) for palliation of his pain. A 1995 report written by an ad hoc committee at the University of California at San Francisco (UCSF) described the child's prognosis as having been "grave with palliation the only option." With that in mind, superficial irradiation was performed to reduce the patient's pain, not to destroy the sarcoma of the right leg. University of California at San Francisco, February 1995 ("Report of the USCF Ad Hoc Fact Finding Committee on World War II Human Radiation Experiments, February 1995, Appendix 19: Summary of the medical record of CAL-2") (ACHRE No. UCSF-022495–A-6), 3.

92. UCSF, "Report of the USCF Ad Hoc Fact Finding Committee," 27.

93. Loren J. Larson, Assistant in Orthopedic Surgery, University of California Hospital, 11 June 1946 ("To Whom It May Concern . . .") (ACHRE No. DOE-051094–A-605), 2.

94. Joseph Hamilton, Radiation Laboratory of the University of California at Berkeley, to Samuel K. Allison, 11 September 1945 ("Plans for Future Biological Research") (ACHRE No. IND-071395–A-2), 3.

95. UCSF, "Report of the USCF Ad Hoc Fact Finding Committee," 27.

96. Joseph Hamilton, Radiation Laboratory of the University of California at Berkeley, to John Fulton, Historical Library, Yale University Medical Center, 19 July 1946 ("Inasmuch as both the Lawrence brothers are away at the moment, I thought it best that I answer your letter of July 16, 1946, to John . . .") (ACHRE No. DOE-122294–A-3), 1.

97. T. S. Chapman, Chief of Operations Branch, Research Division, to Area Engineer, Berkeley Area, 30 December 1946 ("Human Experiments") (ACHRE No. DOE-112194–D-3), 1.

98. Form dated 2 May 1946 ("Consent for Operation and/or Administration of Anaesthetic") (ACHRE No. DOE-051094–A-604), 1.

99. Colonel K. D. Nichols, Corps of Engineers, to the Area Engineer, California Area, 24 December 1946 ("Administration of Radioactive Substances to Human Subjects") (ACHRE No. DOE-113094–B-2), 1. This order followed a renewed request to the Army by Hamilton for additional plutonium, "to be used for certain human studies," and a further progress report on the injection of Albert Stevens.

100. John L. Burling, AEC Legal Division, to Edwin E. Huddleson, AEC Deputy General Counsel, 7 March 1947 ("Clinical Testing.") (ACHRE No. DOE-051094–A-468), 1.

101. Undated document ("CH-3607 . . . Excerpts from statements of reviewers") (ACHRE No. 113094–B-9), 1.

102. Ibid.

103. Ibid. For discussion of classification levels, see chapter 13.

104. "Off Project" probably refers to work not sponsored by the AEC.

105. Major B. M. Brundage, Chief, Medical Division, to Declassification Section, 19 March 1947 ("Clearance of Technical Documents") (ACHRE No. DOE-113094–B-4), 1.

106. Hoylande D. Young, Argonne National Laboratory, to Charles A. Keller, 25 July 1947 ("Declassification has been refused for the following reports . . .") (ACHRE No. NARA-050995–A-6), 1.

107. Carroll Wilson, AEC General Manager, to Robert Stone, University of California Medical Center, 12 August 1947 ("Declassification of Biological and Medical Papers") (ACHRE No. DOE-061394–A-111), 1.

108. Wright Langham, Los Alamos Laboratory Health Division, to Stafford Warren, University of California, 1 July 1950 ("Dr. Bassett has been here and helped me finish the semi-final draft of the Plutonium Report . . .") (ACHRE No. DOE-082294–B-72), 1.

109. Wright Langham, Los Alamos Laboratory Health Division, to Joe W. Howland, Chief, Division of Medical Services, University of Rochester School of Medicine and Dentistry, 15 April 1950 ("I am curious to hear your reaction to the names that I sent you . . .") (ACHRE No. DOE-082294–B-73), 1.

110. Andrew H. Dowdy, Director of the Manhattan Department, University of Rochester, to Norris E. Bradbarry [*sic*], Director of the Los Alamos Labo-

ratory, 18 February 1947 ("Dr. Wright Langham and Dr. Samuel Bassett were discussing with me today the technical details relative to writing the report . . .") (ACHRE No. DOE-121294–D-6), 1.

111. Langham to Warren, 1 July 1950, 1.

112. Walter D. Claus, Acting Chief, Biophysics Branch, AEC Division of Biology and Medicine, to Wright Langham, Los Alamos Laboratory Health Division, 30 August 1950 ("You will be pleased to learn that Dr. Shields Warren has approved your report for CONFIDENTIAL classification . . .") (ACHRE No. DOE-082294–B-2), 1.

113. It is not clear when CH-3607, the report Dr. Friedell recommended for declassification in December 1946, was declassified. The copy retrieved by the Committee bears a 31 December 1946 declassification date and no indication of subsequent reclassification. Russell and Nickson, "The Distribution and Excretion of Plutonium in Two Human Subjects," 1. In 1956 Dr. Langham made a brief reference to fifteen experimental subjects at an unclassified technical conference. Langham, "Proceedings of the Second Annual Meeting on Bio-Assay and Analytical Chemistry," 80. In 1951, a report, based on Metallurgical Laboratory Memorandum MUC-ERR-209 ("Distribution and Excretion of Plutonium") appeared in a volume of the public Manhattan District research history.

114. While the Wilson letters do not expressly reference the plutonium experiments, the context seems to leave little question that the policies stated in the letters were arrived at with the plutonium experiments in mind. In 1974, when asked what steps had been taken when the plutonium injections had been brought to the attention of the AEC, Shields Warren, who became director of the AEC's Division of Biology and Medicine in late 1947, said that it had been decided "that the rules [should be] properly drawn up by the . . . Human Applications Isotope Committee . . . so that use without full safeguards could not occur, and that . . . nothing of the sort could happen in the future." Shields Warren, interviewed by L. A. Miazga, Sidney Marks, and Walter Weyzen (AEC), transcript of audio recording, 9 April 1974 (ACHRE No. DOE-121294–D-14), 10.

115. Carroll Wilson, AEC General Manager, to Stafford Warren, University of California, 30 April 1947 ("This is to inform you that the Commission is going ahead with its plans to extend the medical research contracts . . .") (ACHRE No. DOE-051094–A-439), 2.

116. Carroll Wilson, AEC General Manager, to Robert Stone, University of California Medical School, 5 November 1947 ("Your letter of September 18 regarding the declassification of biological and medical papers was read . . .") (ACHRE No. DOE-061395–A-112), 1.

117. Dowdy, "Proposed Research Program and Budget: July 1, 1947–July 1, 1948," 25.

118. A December 1947 memorandum from Dr. Bassett recorded:

> In the autumn of 1945 the Section on Human Metabolism was activated under your direction at the request of the Manhattan Engineer District to carry out certain tracer studies with long-lived isotopes. As you know, this program was discontinued in the spring of 1947 under a directive from the Atomic Energy Commission although we were instructed to keep the personnel of the section intact. When this directive was received, it was anticipated that follow-up studies on the several subjects of the original investigation would provide occupation for the employees of the section.

Samuel H. Bassett, Section on Human Metabolism, University of Rochester, to William F. Bale, Head of Special Problems Division, University of Rochester, 2 December 1947 ("Proposal of Work for Metabolism Section") (ACHRE No. DOE-121294–D-7), 1.

Dr. Bassett proposed an interim activity for the employees of the section—a study of certain aspects of radiation injury. This was approved by Bale until "the project research program of the Metabolism Section . . . with regard to tracer studies with heavy elements is clarified." William F. Bale, Head of Special Problems Division, University of Rochester, to Andrew H. Dowdy, Director of AEC's Rochester Project, 3 December 1947 ("Program of Work for Metabolism Section") (ACHRE No. DOE-121294–D-8), 1.

119. Gilbert Whittemore, 3 March 1995 ("Shields Warren Papers: A Cumulative Update of Excerpts") (ACHRE No. BU-030395–A-1), 3.

120. Ibid.

121. Interview with Warren, 9 April 1974, 11.

122. Ibid.

123. Ibid. According to Dr. Durbin, it is likely that the "other substances" referred to were probably phophorus 32 and strontium 89, which were used at the University of California between 1941 and 1944 as experimental tracers or for palliation of pain. Dr. Patricia Durbin, telephone interview with Miriam Bowling (ACHRE), 2 August 1995 (ACHRE No. ACHRE-081095–A), 1.

124. Undated note in medical record of CAL-A from "K.G.S." (Ken G. Scott [attr.]) ("The day after solution is injected . . .") (ACHRE No. UCLA-111094–A-1), 1.

125. Telephone interview with Durbin, 2 August 1995, 1.

126. Lori Hefner; telephone interview by John Kruger (ACHRE), 6 July 1995 (ACHRE No. IND-070695–A), 1.

127. Note in medical record of CAL-3 dated 18 July 1947 ("Elmer Allen Chart") (ACHRE No. DOE-051094–A-615), 2.

128. Wilson to Warren, 30 April 1947, 2.

129. UCSF, "Report of the USCF Ad Hoc Fact Finding Committee, Appendix 20: Summaries of the medical record of CAL-3," 3–4.

130. Ibid., 4. If the diagnosis was correct, surgi-

cal amputation would have been appropriate treatment at the time to completely excise the tumor.

131. B. V. Low Beer et al., Radiation Laboratory, University of California, Berkeley, 15 March 1948 ("Comparative Deposition of Zr-95 in a Reticulo-Endothelial Tumor to Normal Tissues in a Human Patient") (ACHRE No. DOE-101194–B-4), 4.

132. Ibid. The test dose was administered to the patient just twenty-four hours prior to the midthigh amputation of her leg for cancer.

133. Shields Warren, Director of AEC's Division of Biology and Medicine, to Albert H. Holland, Jr., AEC Medical Adviser, 19 August 1948 ("Review of Document") (ACHRE No. DOE-101494–B), 1.

134. Albert H. Holland, Jr., AEC Medical Adviser, to Shields Warren, Director of AEC's Division of Biology and Medicine, 9 August 1948 ("Review of Document") (ACHRE No. DOE051094–A), 1.

135. Langham to Howland, 2 October 1950, 1.

136. Wright Langham, Los Alamos Laboratory Health Division, to Albert H. Holland, AEC Director of Research and Medicine, 20 March 1950 ("It seems that I really fouled up regarding my promise to you at the Washington meeting . . .") (ACHRE No. NARA-082294–A-155), 1.

137. L. H. Hempelmann, University of Rochester, to Charles Dunham, AEC Division of Biology and Medicine, 23 May 1953 ("There are several things on my mind that I would like to bring to your attention . . .") (ACHRE No. DOE-041495–A-1), 1.

138. Walter D. Claus, Acting Chief of the Biophysics Branch, AEC Division of Biology and Medicine, to Charles L. Dunham, Chief, Medical Branch, 31 August 1950 ("Physical Examinations at Rochester") (ACHRE No. DOE-051094–A-471), 1.

139. Interview with Warren, 9 April 1974, 8.

140. Patricia W. Durbin, University of California, to William E. Lotz, AEC Division of Biology and Medicine, 13 September 1968 ("You will never guess what I found today . . .") (ACHRE No. DOE-051094–A-606), 1.

141. Ibid.

142. Ibid.

143. Patricia Durbin, 1972 ("Plutonium in Man: A New Look at the Old Data") (ACHRE No. DOE-051094–A-160), 469.

144. R. E. Rowland, Argonne National Laboratory's Center for Human Radiobiology, 8 November 1973 ("Plutonium Studies at the Center for Human Radiobiology [CHR]") (ACHRE No. DOE-051094–A-608), 4.

145. I. E. Kirch, Radiological and Environmental Research Division, Argonne National Laboratory, 13 June 1973 ("Center for Human Radiobiology: Radiologist's Report") (ACHRE No. DOE-051094–A-616), 1. The report records: "In the proximal portions of both humeri as well as in the adjacent acromions, there are some changes in the trabeculae which are consistent with findings in early radium deposition, but not yet completely specific. The mandible shows abnormal trabeculae, suggestive of damage due to radiation."

Subclinical bone changes were also observed in a deceased subject who was exhumed for the Argonne study. The same radiologist summarized that an "abnormality is present, namely, that there are very many very small very dense deposits on the surfaces of a number of the bones, and other such deposits in the soft tissues very close to the bone surfaces. This abnormality is attributed to the plutonium which has been administered during the subject's life. The radiographic pattern is unique." I. E. Kirch, Radiological and Environmental Research Division, Argonne National Laboratory, 15 November 1974 ("Center for Human Radiobiology: Radiologist's Report") (ACHRE No. DOE-051094–A-618), 1.

146. AEC Division of Biomedical and Environmental Research and Division of Inspection, 13 August 1974 ("Disclosure to Patients Injected With Plutonium") (ACHRE No. DOE-051094–A-586), 10.

147. Ibid.

148. Ibid.

149. Ibid.

150. Ibid.

151. Robert E. Rowland, Argonne National Laboratory, to H. A. Schultz, 21 December 1972 ("Plutonium Cases") (ACHRE No. DOE-080795–A), 1.

152. Robert E. Rowland to Miriam Bowling (ACHRE Staff), 7 August 1995 ("Attached is the memo of December 21, 1972 . . .") (ACHRE No. DOE-080795–A), 1.

153. Ibid.

154. James L. Liverman to Miriam Bowling (ACHRE Staff), 20 August 1995 ("With your fax of August 9 was included . . .") (ACHRE No. IND-082095–A), 1.

155. James L. Liverman, 29 April 1974 ("Briefing on Plutonium Project by Dr. James L. Liverman on April 29, 1974") (ACHRE No. DOE-051094–A-196), 8. The 1971 protocol referred to in this briefing had covered a follow-up project involving the radium dial painters. Although the procedures for the two follow-up studies were similar, the original conditions of exposure were quite different. The radium dial painters, unlike the plutonium-injection subjects, had not been chosen as subjects in a carefully planned medical experiment organized by the government. They had been exposed either occupationally as dial painters or therapeutically as patients receiving one of a variety of prewar radium treatments.

156. Signed form dated 28 August 1974 ("Acknowledgement of Disclosure") (ACHRE No. DOE-051094–A-619), 1.

157. Document dated 24 May 1974 ("Patients Injected with Plutonium [Draft Report of 5–24–74]") (ACHRE No. DOE-051094–A-607), 1.

158. There is some evidence suggesting that at least one subject had a serious emotional reaction to the news, many years after the fact, that she had been injected with plutonium. This suggests that physicians

involved in the follow-up had cause to be concerned about how at least some patients might respond to knowledge of the injections.

159. K. F. Eckerman to Barry A. Berven, 7 January 1994 ("The Boston-Oak Ridge Uranium Study") (ACHRE No. DOE-051094–A-425), 1.

160. John C. Gallimore, Associate Health Physicist, to Dr. W. H. Sweet, Massachusetts General Hospital, 22 March 1954 ("First Results of Uranium Distribution and Excretion Study") (ACHRE No. NARA-082294–A-35), 1.

161. S. R. Bernard, "Maximum Permissible Amounts of Natural Uranium in the Body, Air and Drinking Water Based on Human Experimental Data," *Health Physics* 1 (1958): 288–305.

162. According to the 1957 interim report on the study, it was Harold Hodge of the University of Rochester's Atomic Energy Project, who had been involved with the MED metabolism work at Rochester, who ultimately coordinated the beginning of the joint research. S. R. Bernard and E. G. Struxness, 4 June 1957 ("A Study of the Distribution and Excretion of Uranium in Man: An Interim Report") (ACHRE No. DOE-051094–A-369), 3.

163. Bernard, "Maximum Permissible Amounts of Natural Uranium in the Body, Air and Drinking Water Based on Human Experimental Data," 296–298; *Standards for Protection Against Radiation*, 9 C.F.R. 20 (1958–1994).

164. Robert Bernard, interviewed by J. Newell Stannard, transcript of audio recording, 17 April 1979 (ACHRE No. DOE-061794–A), 8.

165. A continuation of the study *at lower doses* was proposed by the ORNL in 1958; it is unclear whether this project went forward. Karl Morgan, Director of ORNL's Health Physics Division, to William Sweet, Massachusetts General Hospital, 16 July 1958 ("Your help in our cooperative study on the distribution and excretion of uranium in man has been of great value to us . . .") (ACHRE No. DOE-021695–A-1), 1. A study similar to the one proposed by the ORNL in 1958 may have taken place during the mid-1960s at Argonne Cancer Research Hospital. K. Z. Morgan to W. H. Jordan, 3 September 1963 ("Proposed Study of Distribution and Excretion of Enriched Uranium Administered to Man") (ACHRE No. DOE-051094–A-620), 1.

166. Interview with Morgan, 6 January 1995, 118–119.

167. Form dated 3 November 1953 ("Application for Approval of Radioactive Isotopes: Massachusetts General Hospital") (ACHRE No. MGH-030395–A-1), 4.

168. Leonard Atkins, M.D., 26 June 1954 ("Necropsy No. ___: June 26, 1954 at 12:30 p.m.") (ACHRE No. DOE-050895–D-1), 6.

169. Ibid., 1.

170. Ibid. The "Anatomic Diagnoses" include "Uranium nephrosis, acute."

171. Ibid., 5.

172. Bernard and Struxness, "A Study of the Distribution and Excretion of Uranium in Man: An Interim Report," 6.

173. Undated document ("#1 Cloudy swelling of the epithelium of proximal and distal convoluted tubules . . .") (ACHRE No. DOE-050895–D-2), 1. The document records a diagnosis for the two additional patients as "acute nephrosis," and for subject VI, as "severe subacute nephrosis."

174. Bernard and Struxness, "A Study of the Distribution and Excretion of Uranium in Man: An Interim Report," 4.

175. William Sweet, interviewed by Gil Whittemore (ACHRE), transcript of audio recording, 8 April 1995 (ACHRE Research Project Series, Interview Program File, Targeted Interview Project), 46.

176. By the end of the Committee's deliberations, MGH had not yet completed its search for the patient records of the Boston Project subjects.

177. Chapman to Area Engineer, Berkeley Area, 30 December 1946, 1.

178. Weyzen, "Visit with Edwin R. Russell, Savannah River Plant, April 23, 1974," 1.

179. Interview with Warren, 9 April 1974, 11.

180. The relatively small population that has been exposed to substantial levels of plutonium precludes definitive conclusions about risks to humans, but the available evidence clearly suggests that an epidemic of cancer of the magnitude that afflicted the radium dial painters from an earlier era has not occurred in plutonium workers. In the case of the radium dial painters, the unprotected handling of only a few pounds of radium led to hundreds of deaths; in contrast, studies of plutonium workers suggest that to date there is no definite excess mortality in this population. A forty-two-year follow-up of twenty-six Manhattan Project workers who worked with plutonium found a total of seven deaths, including three cancers (two lung and one osteogenic sarcoma), a substantially lower mortality rate than expected based on the U.S. population. The authors concluded that "the diseases and physical changes noted in these persons are characteristic of a male population in their 60s." G. L. Voelz and J. N. Lawrence, "A 42–year Medical Follow-up of Manhattan Project Plutonium Workers," *Health Physics* 61 (1991): 181–190. A larger study of 15,727 LANL workers followed through 1990, some of whom had plutonium exposures, found no cause of death significantly elevated among the plutonium-exposed workers compared with unexposed workers, although there was a nonsignificant 78 percent elevation in lung cancer (a site that is directly exposed) and a single osteogenic sarcoma, a rare cancer that has been associated with plutonium exposure in animal studies. L. D. Wiggs, E. R. Johnson, C. A. Cox-DeVore and G. L. Voelz, "Mortality Through 1990 Among White Male Workers at the Los Alamos National Laboratory: Considering Exposures to Plutonium and Ionizing Radiation," *Health Physics* 67 (1994): 577–588. Another study

of 5,413 workers at the Rocky Flats Nuclear Weapons Plant found elevated risks for various cancers comparing workers with body burdens of 2 nanocuries (nCi) or greater, but with wide uncertainties; no excesses were seen for bone or liver cancers. The authors concluded that "these findings suggest that increased risks for several types of cancers cannot be ruled out at this time for individuals with plutonium body burdens of ≥ 2 nCi. Plutonium-burdened individuals should continue to be studied in future years." G. S. Wilkinson et al., "Mortality Among Plutonium and Other Radiation Workers at a Plutonium Weapons Facility," *American Journal of Epidemiology* 125 (1987): 231–250.