

All the easy experiments

A Berkeley professor, dirty bombs, and the birth of informed consent

by Will Grover



Sixty years ago Berkeley was a campus at war. Plutonium, which had been discovered by Cal chemist Glenn Seaborg and his colleagues in 1940, had been identified by Manhattan Project scientists as a potential bomb-making material; by 1945 it was the subject of intense research at Berkeley, Los Alamos, and the University of Chicago. The frantic pace of wartime research led to numerous accidents: Los Alamos chemist Don Mastick swallowed much of the world's plutonium when a test tube he was holding exploded in his face. Mishaps like this made Manhattan Project leaders anxious to better understand the health effects of plutonium. For answers, they turned to Joseph Hamilton, a young Berkeley professor who was already an expert on the toxicology of radioactive materials.

In the late 1930s, Hamilton made a name for himself by measuring the uptake of various radioisotopes into plants and animals (including himself). His status as a professor at both UC Berkeley and the University of California School of Medicine (now UCSF) provided him with radioactive materials from Berkeley's cyclotron and clinical patients from the hospital. In 1944, Hamilton and his colleagues received eleven milligrams of plutonium earmarked for toxicology studies in rats. His initial rat results were disturbing: plutonium concentrated itself in the bones and seemed to stay there for a long time. Manhattan Project leaders like J. Robert Oppenheimer wanted more detailed information about the effects of plutonium on the human body.

On April 10, 1945 in Oak Ridge, Tennessee, a construction worker named Ebb Cade became the first human to be intentionally dosed with plutonium. Through a solution containing the radioactive element injected into his arm, Cade received almost five times the minimum amount of plutonium believed at the time to cause adverse effects. He was in the hospital following a car wreck but had no life-threatening ailments and was characterized by a doctor at Oak Ridge as "a well developed, well nourished colored male." Sixteen days later, at the University of Chicago's Billings Hospital, a cancer patient named Arthur Hubbard received what was described to his daughter as "some new treatment"—the second plutonium injection. At about the same time, Joseph Hamilton and his colleagues were walking the halls at the UC Hospital in San Francisco looking for their own test subject.

Man and the Rat

Albert Stevens arrived at the UC Hospital in May of 1945 complaining of stomach pains. The 58-year-old house painter was diagnosed with inoperable stomach cancer and given six months to live. Shortly after hearing this diagnosis, Stevens received Hamilton's first plutonium injection. "CAL-I," as Hamilton's team designated Stevens, became the subject of intense analysis. His urine and feces were collected and sent to Hamilton's lab at Berkeley for analysis. A few days after the injection, doctors removed parts of his stomach, liver, spleen, lymph nodes, pancreas, and ribs, and sent these to Berkeley as well.

A UC Hospital pathologist who studied CAL-I's stomach samples concluded that Stevens actually did not have cancer after all—the terminal diagnosis was a mistake, and an otherwise-healthy man had received what was later characterized as a “so-called lethal textbook dose of plutonium.” Hamilton and his colleagues wrote a paper about CAL-I entitled “A Comparison of the Metabolism of Plutonium in Man and the Rat.” The report noted that, like rats, humans collect plutonium in their bones, particularly in the sensitive bone marrow responsible for making blood cells. But humans, Hamilton and his coauthors found, rid themselves of plutonium even more slowly than rats, and plutonium poisoning was “a matter of serious concern for those who must come in contact with this material.” Hamilton's superiors in the Atomic Energy Commission (the successor to the Manhattan Project)

claimed that the Man and the Rat paper “might adversely affect the national interest” and refused to allow its publication.

Less than three months after Albert Stevens became CAL-I, atomic bombs were dropped on Hiroshima and Nagasaki and World War II was over. Although the wartime race to understand the toxicology of plutonium had also ended, Joseph Hamilton's plutonium injections continued. Simeon Shaw, also known as CAL-2, was a four-year-old Australian boy suffering from bone cancer. An injection containing a variety of radioisotopes from the Berkeley cyclotron was administered to Shaw on April 26, 1946, nearly eight months after the end of WWII. Within a year of the injection, the recipient of Hamilton's second injection succumbed to bone cancer.

Hamilton's other war

When he wasn't studying the effects of radioactive materials on CAL-I and CAL-2, Joseph Hamilton was advocating their use as weapons. Radiological warfare—the use of radioactive material not as a bomb but as a radiological poison for military use—had been tossed around in the days before the Manhattan Project (and was apparently an objective of the Nazi bomb project) but was largely forgotten after the Manhattan Project was initiated.

By 1946, Hamilton was one of the few remaining supporters of radiological warfare. Years before, he had written the first of what became a series of letters to his superiors advocating the consideration of radioisotopes from Berkeley's cyclotron as possible radiological weapons. In a letter to Manhattan Project Health Division head and former Berkeley colleague Robert Stone, Hamilton wrote that radioisotopes sprayed from aircraft “offer the possibility of infecting to dangerous levels, large areas such as cities... The poisoning of water supplies such as reservoirs, wells, etc. and food must be kept in mind.” Whether this early letter inspired any reaction from the Manhattan Project leadership is unclear, but Hamilton's enthusiasm about radiological warfare seemed to heighten during his plutonium injection studies. Following the CAL-I and CAL-2 injections, Hamilton outlined the utility of radioactive materials as military poisons in a 1946 letter to his Manhattan Project boss, Colonel Kenneth Nichols. Hamilton detailed strategies for poisoning municipal water supplies with radioisotopes and described the terrorizing psychological aspects of radiological warfare



Syringe shield used for radioisotope injections during the late 1940s and early 1950s at the Oak Ridge Institute for Nuclear Studies.

“It can be well imagined the degree of consternation, as well as fear and apprehension, that such an agent would produce upon a large urban population after its initial use”). He described “radioactive smoke” that could be designed to maximize the absorption of radioactive material in the lungs and the subsequent deposition of the material in the bones. Such a preparation, said Hamilton, would be “well adapted for producing fission product aerosols to subject urban populations to fission product poisoning.” The effects of radiological poisons on the human body are described in detail:

Following absorption into the body the majority of longer-lived fission products whose half-lives extend from the order of two weeks to many years, are accumulated and tenaciously retained in the skeleton. There, *they produce internal irradiation of the very sensitive bone marrow and even rather trivial amounts can produce lethal effects.* [emphasis added]

Hamilton’s assessment of the accumulation and “lethal effects” of fission products in bone marrow echoes the conclusions of his “Plutonium in Man and the Rat” paper, written earlier that year and supported with data from the analysis of CAL-I’s urine, feces, and internal organs.

Informed consent

In December of 1946, a trial began in Nuremburg, Germany for twenty-three Nazi doctors accused of performing medical “experiments” on concentration camp prisoners without their informed consent. That same month, Joseph Hamilton sent a letter to Colonel Nichols outlining Hamilton’s plans for continued human injections. Nichols replied by shutting down Hamilton’s research:

...this report indicates that certain radioactive substances are being prepared for intravenous administration to human subjects... It is felt that such work does not come under the scope of the Manhattan District Program 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.

You will take immediate action to stop this work under this contract, and report to this office upon compliance.

In January of 1947, Nichols and Hamilton’s other Manhattan Project superiors stepped down and the Atomic Energy Commission (AEC) took charge of Hamilton’s research. Undoubtedly conscious of ongoing events in Nuremburg, AEC leaders immediately issued strict rules limiting the use of human subjects. A patient had to be informed about the nature of a proposed experiment and grant their consent before the experiment was initiated, and researchers had to believe that the experiment would benefit the patient. But at the same time, the AEC continued to censor papers about the plutonium injections. In refusing to release a paper describing the results of the injections, an AEC official observed:

Unless, of course, the legal aspects were covered by the necessary documents [informed consent], the experimenters and the employing agencies, including the US, have been laid open to a devastating lawsuit which would, through its attendant publicity, have far reaching results.

Hamilton and his colleagues clearly had not obtained the “necessary documents” from CAL-I or CAL-2. Fearing legal reprisals, the AEC hid evidence that its own scientists, like those on trial in Nuremburg, had performed medical experiments on patients without their informed consent.



Modern Medicine, fresco by Bernard Zakheim, 1935. Joseph Hamilton is the rightmost figure in the upper-left group.



Joseph Hamilton drinking radioactive sodium, 1939.

Two months after the AEC human subjects rules were issued, and with the Nuremberg trial still under way in Germany, sixteen-year-old bone cancer patient Hanford Jang became CAL-A following an injection administered by Hamilton's scientists. The injection was probably administered without Jang's understanding or consent (he couldn't speak English) and Hamilton and his scientists offered no possible therapeutic justification for the injection; Jang was dead within a year. Bay Area resident Elmer Allen, also a bone cancer victim, became CAL-3 after receiving Hamilton's fourth radioisotope injection a month after CAL-A. No documents indicating that CAL-A or CAL-3 granted their informed consent have been found. By November of 1947, the AEC rules on human subjects had grown even stronger:

We believe that no substances known to be, or suspected of being, poisonous or harmful should be given to human beings unless all of the following conditions are fully met: (a) that a reasonable hope exists that the administration of such a substance will improve the condition of the patient, (b) that the patient gives his complete and informed consent in writing, and (c) that the responsible nearest of kin give in writing a similarly complete and informed consent, revocable at any time during the course of such treatment. [emphasis added]

The revised AEC rules marked the first known use of the now-ubiquitous phrase "informed consent." No further plutonium injections were planned at Berkeley, perhaps because another interest was consuming more and more of Joseph Hamilton's time.

From Berkeley to Dugway

While the AEC was anxiously hiding Joseph Hamilton's human experiments on the toxicity of plutonium, the US Army was building a weapons program around the results of his research. In May of 1948, Hamilton's advocacy of radiological warfare convinced Army brass to form a committee of scientists to study the feasibility of radiological weapons, with Hamilton as a member. The committee recommended that biological research into the deleterious health effects of radioisotopes be conducted by the Army Chemical Corps at the University of Chicago, that production of possible radiological weapons be conducted by the AEC, and that military testing of possible radiological weapons be performed by the Army Chemical Corps at a suitable location. That location was the Dugway Proving Grounds in Utah, and the tests, which involved releasing material akin to Hamilton's "radioactive smoke" over the Utah salt flats and monitoring its distribution, began in October of 1949 and continued until 1953.

So why was Joseph Hamilton—a man charged with protecting the health of Manhattan Project workers exposed to plutonium—so enthusiastic about radiological warfare? Some have suggested that he perceived radiological weapons as more humanitarian and less destructive than conventional nuclear explosives. A long-lived but less-potent radioisotope could be used to contaminate factories and farms, rendering them useless without inflicting direct casualties. Others have noted that the opposite could also be true: a short-lived but potent radioisotope could be used to incapacitate or kill the inhabitants of a city while leaving valuable infrastructure intact. Regardless, Hamilton was clearly motivated by the fear that a hostile power could use radiological weapons against the United States:

I strongly feel that the best protection that this nation can secure against the possibilities of radioactive agents being employed as a military tool by some foreign power is a thorough evaluation and understanding of the full potentiality of such an agent.

The purpose of the plutonium injections was, in Hamilton's own words, "to evaluate the possible hazards... to humans who might be exposed to [plutonium], either in the course of the operation of the pile [nuclear reactor], or in the event of possible enemy action against the military and civilian population." Hamilton wrote this four months before Albert Stevens became CAL-1. Clearly, he recognized the material

he was injecting into his patients was a potential weapon—maybe a weapon that could be used against the US, but a weapon nonetheless. And although much of Hamilton’s earlier research was in therapeutic uses for radioisotopes (including his pioneering use of radioactive iodine to diagnose and treat thyroid disorders), attempts to justify the plutonium injections as “experimental therapies” fall short. In 1946, after the injections of CAL-1 and CAL-2 but before CAL-A and CAL-3, Hamilton conceded that “to date no fission products, aside from radioactive iodine, have been employed for any therapeutic purposes.” His superiors recognized this, too: AEC officials refused requests for the declassification of Hamilton’s research because, in addition to the legal risks arising from the lack of informed consent, his work involved “experimentation on human subjects where the material [plutonium] was not given for therapeutic purposes.”

Hamilton’s injections may have been one of the first human radiation experiments, but they were by no means the last: nearly 4000 human radiation experiments were conducted under government contracts from 1944 to 1974. To investigate “reports of possibly unethical experiments funded by the government,” President Clinton formed the Advisory Committee on Human Radiation Experiments in 1994. The various experiments described in the Committee’s 620-page report include the injection of radioactive iodine into 60 students at a Massachusetts school for mentally retarded children in 1962, and the irradiation of 130 healthy Washington and Oregon prison inmates’ testicles from 1963 to 1973 as part of a joint AEC/NASA study. Troubling as they are, Hamilton’s experiments in the 1940s were born of the wartime race for the atomic bomb and conducted at a time when the toxicity of materials like plutonium was poorly understood and the importance of informed consent was still being established. The same cannot be said for the scores of human radiation experiments performed decades later.

What is Easy?

Near death with leukemia undoubtedly caused by reckless exposures to radiation throughout his career at Berkeley, Joseph Hamilton lamented to his colleague Patricia Durbin in 1957, “you know, the sad part is that all the easy experiments have been done.” As long as I’ve been a graduate student at Berkeley and, as such, a scientific descendant of Hamilton, I’ve wondered what



Signed staff photograph of Joseph Hamilton from UCSF Archives

he meant by that. Were these really “easy experiments” to him? Maybe Hamilton and his students fell into the trap described by AEC doctor and Hamilton contemporary Leonard Sagan in an interview conducted by the Advisory Committee on Human Radiation Experiments:

Doctors who were doing research wanted to be professors, and in order to be a professor, you have to have lots of publications, so your highest priority is to conduct research and publish it... What can happen is the patient says, “No, I don’t want to do that.” That’s not in your interest. Your interest is to have that patient participate, so do you tell him or her? No. Does anybody care? No. So you don’t tell them. That’s why [the ethical rules] were ignored, because there’s a conflict between informed consent and the ability to conduct research and the physician is interested not in the patient’s welfare, he’s interested in his or her welfare. So he doesn’t inform him.

Performed in an atmosphere of wartime secrecy, Hamilton’s “easy experiments” never fell under the scrutiny of an independent review panel. Disturbing conflicts of interest like Hamilton’s involvement in the Army radiological warfare program went unrecognized. It was easy, as a researcher, to put one’s own interests ahead of a patient’s interests, and Hamilton was one of a number of researchers who did just that.

Things aren’t so easy today. Berkeley researchers wishing to study human subjects must first obtain approval from the Committee for the Protection of Human Subjects—a rigorous process. Additional rules protect vulnerable subjects like CAL-2 (a minor) and CAL-A (a non-English speaker). And all subjects must grant their informed consent—a term coined partially in response to Joseph Hamilton’s “easy experiments.”

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