SHARON R. KAUFMAN

THE WORLD WAR II PLUTONIUM EXPERIMENTS: CONTESTED STORIES AND THEIR LESSONS FOR MEDICAL RESEARCH AND INFORMED CONSENT

ABSTRACT. During the Second World War medical researchers around the USA injected 18 hospital patients with radioactive plutonium in order to learn its effects on the body. Two documents, a newspaper account and a university committee report, tell divergent stories of the scientists and patients involved in that experiment. This article uses those documents – plutonium narratives – as a catalyst for exploring the problematic representation of past human experimentation, assumptions of moral progress in medical research, and the nature of informed consent today. Informed consent is shown to be an evolving process and discursive practice that cannot be understood apart from its historical and cultural embeddedness.

"The past is not dead; it's not even past."
William Faulkner

BACKGROUND: REPRESENTING THE WAR YEARS

The recently celebrated 50th anniversary of two of the Second World War's most profound events – the liberation of the Auschwitz death camp (January 1945) and the dropping of the atomic bomb on Hiroshima (August 1945) – was fraught with public emotion and controversy about how those events should be memorialized and how those stories should be told. Jews felt that the official Polish commemoration of the liberation obscured and devalued their losses while exaggerating Polish martyrdom. A long-planned exhibit at the Smithsonian Air and Space Museum about the Enola Gay was cancelled amidst heated debate over the museum's portrayal of the USA as aggressor against Japan.[1] Those two anniversaries and the conflicts they generated received widespread media coverage and are perhaps the most recent and obvious examples of contested memory and controversial historical representation of the Second World War.

In 1994 I became involved in representing the war years through my appointment to a university committee whose charge was to investigate

Culture, Medicine and Psychiatry **21:** 161–197, 1997.

a series of problematic medical experiments performed on patients at the hospital of the University of California San Francisco (UCSF) between 1945 and 1947. The committee was assembled by the Chancellor of UCSF[2] in the wake of US Department of Energy (DOE) Secretary Hazel O'Leary's call for 'openness' about the role the federal government played in secret research on humans during the Second World War and Cold War eras. O'Leary ordered the DOE to declassify and release to the public thousands of documents about the nuclear weapons industry, including information about experiments that exposed civilians to radiation.

The release of previously classified government materials provoked a far-reaching response including: a two-year period of public outrage (1994–1996), press accounts of government mistreatment of prisoners, children, and people in mental institutions, congressional hearings, university and hospital committee investigations, lawsuits, and demands for truth and financial compensation from 'victims' of experiments and their families.[3] A great deal of attention was paid by at least several medical institutions as well as federal agencies to comprehensive fact-finding, the morality of federal policy and practice, and the problem of interpreting events that had occurred 50 years before.

The stimulus both for O'Leary's end to government secrecy and the formation of the UCSF committee was a report, published in 1993 in the *Albuquerque Tribune*[4] by prize-winning investigative journalist Eileen Welsome, about 18 patients at three university hospitals in the USA – including three patients at UCSF – who were injected with radioactive plutonium during the war years. Welsome claimed the 18 patients were part of secret research sponsored by the Manhattan Project, the government agency formed during the Second World War that was responsible for the production of atomic weapons. The purpose of the experiments was to determine the excretion rate of plutonium in human beings so that the government could set safety standards for workers who would be exposed to that substance in atomic bomb development and production. Welsome's report came to the attention of Energy Secretary O'Leary in January 1994.

The three UCSF patients cited in Welsome's report were injected with plutonium at the hospital of the University of California between May 1945 and July 1947. Although studies resulting from those injections were reported in a textbook published in 1951 and the experiment was the subject of Congressional hearings in the 1980s and was reported in newspapers in the 1970s and the 1980s, it was Welsome's 1993 report – in which the identities of five of the 18 experimental subjects are revealed – that generated enormous public concern about the role of government in secret medical research and public deception.

The university committee was appointed to respond to Welsome's allegations, as well as allegations from other media sources, about deception, harm, and immoral medical science. Three of the most commonly articulated statements issued in the public media were: (1) the patients at UCSF hospital received 'lethal' doses of plutonium from researchers; (2) patients were not informed about the experiments, did not consent to participate, and were unaware of their participation in a secret government-sponsored experiment; and (3) the experiment was comparable to the research performed by Nazis during the same era. The task of the committee was to examine both the scientific and ethical nature of the experiments that were conducted on UCSF patients – the three Welsome cited as well as others – during the 1940s. We met weekly for 15 months in 1994 and 1995, sifted through hundreds of documents[5] and argued, often without resolution, about their interpretation and significance. We issued a report with extensive appendices and, several months later when we had read more documents, an addendum to the report. Those materials were shared with the university community and the public, reported and discussed in the media, and sent to the National Advisory Committee on Human Radiation Experiments (established by President Clinton in 1994) for use in its report on the full range of radiation experiments conducted in the USA. since the Second World War period.[6]

PLUTONIUM NARRATIVES

This paper considers the *Albuquerque Tribune* account (published in 1993) and the UCSF committee report[7] (completed in 1995) as two competing narratives about the 'facts' and interpretation of the plutonium experiments. Taken together, those narratives speak to a number of thorny issues surrounding human experimentation today and they provide the catalyst for examining contemporary concerns. The paper describes these plutonium experiments in an effort to explore the conduct of medical research on humans and the construction of harm, blame, and an ethics of experimentation during the 1940s. Because assumptions about the contemporary conduct of human experimentation, especially the ideology and practice of 'informed consent', are embedded in the two narratives, the paper goes on to consider ways in which the narratives are useful for thinking about informed consent as a site of ambiguity and tension in relationships among biomedical science, the state, doctors, patients, and therapy.

The term, narrative, is used here in reference to the *different* stories told by an investigative journalist and a 16-member university committee about the *same* events: historical and institutional context, the organiza-

tions, and the players involved in a series of experiments with radioactive plutonium as well as some of the outcomes of those experiments. Unlike the now widely reported narrative representations produced by individuals, communities, or cultural groups about illness, healing, vulnerability, and medical choice-making (Balshem 1993; Frank 1995; Kleinman 1988; Mattingly and Garro 1994; Sandelowski and Jones 1996), the plutonium narratives are not person-centered accounts of individual or shared experience. Rather, they make use of previously classified documents, interviews, and a variety of secondary sources to create consciously motivated tales of 'what happened' 50 years ago. Their production was intended for public display. They do share with personal narratives, however, the fact that they are situated in particular social and political fields which influence their creation (Gordon 1994; Saris 1995).

The juxtaposition of the two plutonium stories points to ways in which multiple yet only partial truths are produced. The narratives are grounded in local worlds of political agendas and professional life in which particular goals and knowledge claims guide both the discovery of what counts as historical fact and the production of a 'what happened' story-line. Thus each narrative defines the scope of its concern differently.

The journalist's goal was three-fold: to show that the government kept secrets which undermined the health and welfare of the civilian population; to make visible government disregard for personal autonomy and the right to information; and to disclose malevolent treatment of sick patients in an effort to further certain morally reprehensible aspects of the war effort. To those ends, the *Albuquerque Tribune* account emphasizes the long-term cover-up of the experiment, the "ghoulish" nature of an extremely dangerous project with a toxic substance, and the use of sick people as "guinea pigs" who were betrayed, victimized, and denied the truth for years by their government. It focuses most of its attention on the five of the 18 research subjects who were identified by Welsome through her research (and includes two of the three UCSF patients), and it documents how those ordinary lives were devalued, disregarded, and probably harmed by the injections. The report is replete with photos of the subjects, in some cases with family members, and quotations from family and friends attesting to the immorality of the research and the suffering of its victims. As a cultural document, the *Albuquerque Tribune* report speaks to the misuse and vulnerability of average American citizens and the power of government to harm and deceive. It reflects the suspicion of big government common in this historical moment.

The university committee had two goals: to discover whether the 'science' – that is, the actual design, methodology, and implementation of the

experiment – conformed to practices of the era, and to learn whether or not the experiment was 'ethical', that is, whether the subjects participating in the project were morally wronged or physically harmed. The UCSF report de-emphasizes (althought it does not disregard) the secrecy issue as a moral problem. It concentrates on untangling the research context of the plutonium injections. It dwells also on the biological effects of plutonium in the body, standards and practices of patient consent during the 1940s as the Nuremberg Code was being formulated and drafted, and the problem of making ethical pronouncements about past experiments when guidelines and practices differed from today and when evidence by which to judge past behavior of physicians and scientists is incomplete or unavailable.

The UCSF report is constituted by the contemporary rationality of the biomedical research world and it is organized according to the categories of meaning in that world. For example, it investigates the background of the University of California investigators who participated in the experiments, the extent and nature of their animal research prior to human experimentation, the immediate and long-term risks posed to patient-subjects, and whether or not subjects were informed, harmed, or wronged. It ponders the moral context of research during the 1940s and the Second World War. It considers the changing federal standards for oversight of biomedical research on humans since the war years and the emergence of the contemporary ethical stance.

Both the journalist and the committee of (mostly) academic scientists were conducting their investigations and writing their reports 'truthfully', that is, within the contexts of their moral-political worlds of practice and responsibility. Their embeddedness in those worlds and their respective lines of inquiry framed the 'facts' they discovered and the production of their revelations. Though constructed to have very different effects on the public, both narratives express a great deal of concern about the history of radioactive substance use in medical research and the role of government in that research. Taken together, the narratives may be viewed as examples of publicly constructed memory. They represent part of the battle over the interpretation of government involvement with human experimentation.

I reconstitute, summarize, and juxtapose the narratives below with three broad aims in mind. First, as illustrations of publicly constructed memory, the juxtaposed narratives raise questions about the evaluation of past human experimentation. Authority, accuracy, and authenticity become problematic when the narrative texts are taken together. Each interprets differently the practices of (now dead) actors, the contexts in which they worked, the focus of their concern, their motivations, and the fate of experimental

patients. Each views separate issues as particularly important, problematic, and central for the understanding of events.

Second, the plutonium narratives speak to an assumption of moral progress: in today's relatively more enlightened scientific environment, they imply, research on humans cannot, does not, take place without informed, signed consent from uncoerced volunteers. 'Informed consent' is presented through the narratives as a particular set of activities which can be known *a priori*, which have evolved over the years and have arrived now at a morally correct position, and which everyone – physician-investigators, patient-subjects, university and hospital administrators, etc. – understands both conceptually and pragmatically. The lack of problematization of this concept is one guide to the interpretation of past events. The gloss over informed consent in both these historical reconstructions invites us to ponder a larger and more nuanced story about how the human subject considerations of clinical experimentation during the 1940s compares with the use of human subjects, and the ethical evaluation of that use, today.

Third, the term informed consent – the use of knowledge about risks, benefits, and alternatives to make an unencumbered choice about research participation – is scrutinized in this paper as a dynamic site or "social space" (Kleinman 1995: 49) of medico-cultural tension and deliberation. As a site of ever-changing and contested knowledge, practice, and ideology, 'informed consent' specifies the relationship of the state to human experimentation, articulates as well as muddles the goals of clinical investigation, and speaks to the power of a reified notion of 'science' – an abstraction about 'objective' methods used to discover 'truth' – to determine what counts as an appropriate use of humans in experimental medical work.

THE PROBLEM OF REPRESENTATION

The act of ethnographic reconstruction is problematic for all textual analyses and has been widely discussed in the anthropological literature (Clifford and Marcus 1986; Geertz 1988; Marcus and Fischer 1986; Young 1987). I faced that problem directly in deciding how to represent the quite lengthy narratives in order to foster a discussion about both thinking with narrative and contemporary issues in medical research. The texts below are my reconstitutions of the narratives. They include what I consider to be the main topical points of each story. Yet I selected certain features from the narratives and omitted others in order to set the stage for the exploration of the three aims described above. The texts which follow are not 'real.' That is, they are not portraits of actual events. Rather they are represen-

tations of representations and they are reflexively designed and offered.[8] I present them here with an analytic and specifically motivated purpose: to expose one problematic area of medical experimentation – informed consent. I have reconstituted them to argue that by paying attention to contradictory stories and contested interpretations of historical documents and contemporary evidence, a complex world of human experimentation and ethical comportment – both 50 years ago and presently – is revealed. Moral dilemmas in the field of human experimentation are more nuanced than either narrative expresses. Implied in their comparison is a larger story of profound confusion and troubled decision-making about relationships between moral positions and actual research activities.

The following discussion is divided into three major sections in keeping with my three aims. First, I present the two texts (titled The *Albuquerque Tribune* Story and The UCSF Committee Report) which reconstitute the *voices*, the interpretations, of the journalist and the university committee, respectively. Because the texts are quite lengthy, the reader is asked to remember throughout that they represent those voices and not my own. In the second section, my own voice re-emerges to provide context for the texts by looking at the world of experimentation during the 1940s. That discussion highlights the historical embeddedness of the idea and practice of consent. The third section moves from the 1940s to the present era to show how informed consent in medical experimentation has evolved over time, making evaluation of the World War II plutonium experiments problematic. That section explores the nature of informed consent today – as dynamic process, discursive practice, and elusive ideal.

TEXT 1
THE *ALBUQUERQUE TRIBUNE* STORY
SECRECY AND LONG-TERM COVER-UP

Americans recoiled when the Nazis conducted brutal experiments on humans. But as the world was learning of those horrors, US scientists injected plutonium into 18 people without their informed consent to see how the element that fuels atomic bombs reacts in the body. The identities of these human guinea pigs were hidden for almost 50 years. Until now.

Opening sentences, Welsome report

The *Albuquerque Tribune* twice made requests to the Department of Energy under the Freedom of Information Act for information and documents related to the experiments. Though the DOE eventually released selected information to the *Tribune*, it stalled for months and withheld most documents, including medical files that would identify the subjects.

The DOE's reluctance to make information about the research public is merely the most recent phase of a 50-year cover-up.

Plutonium and the experiment

In the flurry to complete the atomic bomb in 1944, a small amount of plutonium exploded in the face of a chemist working in the Los Alamos National Laboratory. Medical officials associated with the Manhattan Project realized they had no way of calculating how much plutonium was in the worker's body, nor how serious the accident was. Everyone involved in the building of the bomb seemed to agree that research was needed to understand the effects of plutonium on the human body so that safety standards for exposed workers could be set. It is unclear exactly who authorized the experiments but Stafford Warren, chief of the Manhattan Project's medical section, and J. Robert Oppenheimer, the director of the Project, could have authorized them. Various memos of the period reveal that a biological research program was put into place over a period of months in 1944 by scientists and physicians associated with the Project. Scientists at Los Alamos and atomic researchers at Chicago, Berkeley, Rochester, and Oak Ridge, Tennessee, were anxious to begin a research program. Animal studies were conducted; then tracer experiments on humans began in order to determine the excretion rates of plutonium. Those rates were to be applied to accidentally exposed workers.

From today's perspective, the scientific usefulness of the experiments is equivocal. Some claim that data produced by these studies, because they are the only data, are relied on by scientists in many locations to set exposure limits for nuclear workers. Others state that the sample size was too small to arrive at a reliable conclusion about the metabolism of plutonium or excretion rates. To those latter critics, the risks of plutonium injection far outweighed any scientific benefit of the endeavor.

Plutonium – variously described by scientists interviewed for this report as "lethal," "the most poisonous chemical known," "one of the most toxic substances on Earth," and "one of the most potent cancer producing chemicals" – was injected into 18 people between 1945 and 1947. The contents of the injections were to be kept secret; even the word plutonium was classified and was referred to simply as "the product." The research subjects included one patient at a military hospital in Oak Ridge, Tennessee, the first person to be injected; 3 patients at UCSF Hospital, 3 patients at Billings Hospital, University of Chicago; and 11 patients at Strong Memorial Hospital, University of Rochester. Five of the research subjects were identified by piecing together information gathered from many sources. Two of those were at UCSF and three were at Rochester. Some information was found

about the other 13 subjects. Of the 18, 3 were African American; 15 were white. Five, including the two identified UCSF patients, lived for more than 20 years after the injections.

The two identified UCSF patients[9]

Albert Stevens, a white, 58-year-old house painter, came to UCSF Hospital in 1945 from a small town in Northern California for treatment of stomach pain. At the hospital he was diagnosed as having stomach cancer, singled out by scientists working on the secret project, and injected with 'a massive dose' of plutonium, 446 times the radiation the average person receives in a lifetime. After his injection and major surgery to remove a portion of his stomach and other organs, he was rediagnosed as having an ulcer, not cancer. For almost a year after the injection and the surgery, Stevens collected his urine and feces in a shed behind his house. Government scientists came weekly to collect those specimens, never telling the subject or his family why. He was designated CAL-1 by the scientists and he became one of the most important subjects of the research. His collected excreta was analyzed and the information gained about plutonium excretion rates went into a secret report, classifed for years, titled "A Comparison of the Metabolism of Plutonium in Man and the Rat."

Stevens was never informed about the contents or purpose of the injection, nor were his wife or children informed about the injection or the fact that he was misdiagnosed. They lived for decades with a belief that their family had a history of cancer. The "Man and Rat" report concluded that humans excrete plutonium more slowly than rats and that chronic plutonium poisoning is thus a matter of serious concern. Requests to declassify that secret report in 1947 were refused because the Atomic Energy Commission (AEC), which replaced the Manhattan Project on January 1 of that year, thought it contained information that would adversely affect the national interest.

Ten years after the injection, Stevens went back to UCSF hospital for a check-up. His medical records show that he had degeneration in the lumbar region of the spine and several degenerated disks. Those problems may have been caused by radiation from the plutonium. Stevens lived 21 years after the injection. He died in 1966 at the age of 79 from cardio-respiratory failure caused by heart disease.

In 1975 Stevens's son was called by a scientist asking for permission to examine his father's ashes – to "carry out a series of studies" – with the promise that the ashes would be returned. The remains were shipped to Argonne National Laboratory near Chicago, the laboratory that coordinated the follow-up studies on the four subjects who had survived to the

early 1970s. Staff there were specifically prohibited from using the word plutonium, in connection with the follow-up work. Indeed, the word plutonium was never mentioned to Stevens's son or in the written release and authorization forms used by the Argonne Laboratory to acquire Stevens's ashes. Although scientists at Argonne claimed the remains were shipped back to the funeral home in California, that institution claimed it never received them. The whereabouts of Stevens's ashes are unknown to this day.

The second identified UCSF patient, Elmer Allen, was designated CAL-3 by the scientists. The saga of the black railroad porter begins with his fall on a train in 1946 at the age of 36; his left knee was injured when the train lurched. A year later, unable to work because of pain and swelling, he was referred to UCSF hospital where he was diagnosed with a fracture, infection, and some time later, with bone cancer. *Tribune* interviews with various physicians and scientists indicate there is contemporary ambivalence over the cancer diagnosis since most people with that form of cancer do not survive longer than five years. Amputation, the treatment still used today for rare bone cancers, was considered the only method that would potentially save his life. Three days before the amputation, Allen was injected with plutonium in his left calf.

Allen, the last of the 18 subjects to be included in the experiments, was the only patient asked for his consent to receive an injection. However it is not known, and the consent document does not say, what he was told about the injection. His medical records state that the experimental nature of the injection was explained and that the patient, "fully oriented and in sane mind," agreed to the procedure. He may have been told that he would receive a radioactive substance. Three doctors and a nurse witnessed Allen's agreement to the procedure, assisted with the injection, and signed their names in his medical chart. Allen's daughter told the *Tribune* that her father had an 8th grade education and would not have understood the medical explanation given to him.

Unable to find steady work after the amputation, Allen and his wife and two children returned to his wife's small hometown in Texas. Over the years, he suffered from epileptic seizures, alcoholism, and eventually was diagnosed as a paranoid schizophrenic, which his family doctor and daughter claimed was partly due to his feelings about how he had been used in the experiment.

In 1973, Allen's family doctor received a letter from scientists at Argonne trying to locate Allen, asking that he come to Chicago, all expenses paid, for follow-up studies because he had survived a rare bone cancer for so many years. The studies were to be observational and non-

invasive. Mr. and Mrs. Allen went on a 19-day trip – complete with flowers and nice hotel rooms – first to Chicago, then to Rochester, where Mr. Allen was tested for traces of plutonium. Yet plutonium was never mentioned to Allen or his wife. Allen died at age 80 of respiratory failure caused by pneumonia, 44 years after the injection.

The long-term cover up

The 1974 AEC investigation of the 1973 follow-up studies revealed 'a web of deceit' dating back to the original war-time experiments. The investigation showed there was no written consent from any of the 18 subjects, although witnesses stated that some patients were told they were going to be injected with a radioactive substance. Plutonium, a classified word, was never mentioned in the original experiment or in the follow-up studies. Indeed, memos from the follow-up period state that subjects were to be told only that they were of interest because they had received a radioactive substance in the 1940s. The subjects studied in 1973, including Elmer Allen, were not told why they were being studied, nor did they give written consent to the follow-up work. In addition, scientists who contacted relatives of patients such as Albert Stevens in order to exhume their bodies for more tests also used deception. They never mentioned the real reason for wanting the bodies. In 1974 the AEC ordered that remaining survivors be told the truth about the injections.

TEXT 2
THE UCSF COMMITTEE REPORT UNTANGLING THE PURPOSE AND EFFECTS OF THE EXPERIMENT

The record is clear that no one received a lethal dose of plutonium. Further, even though plutonium is toxic and radioactive, the amount given to the subjects was on the order of 1000-fold less than the acute lethal concentration as determined in animal studies. The amount of plutonium given to these subjects was so small that it posed an insignificant risk to their health. None of the subjects suffered from acute radiation effects nor did they have long-term complications that are typically associated with excessive radiation exposure.

The most troubling ethical issue was patient consent. The ethical standards during the World War II era and the ethical standards of today call for explaining the nature of the research and risks and obtaining consent from volunteer subjects . . . if these patients were not told about the experiment and were not given a free choice about whether to participate, they were wronged.

Press statements by UCSF Committee members on completion of report

The committee first assumed, following the *Albuquerque Tribune* story, other media accusations, and the initial documents circulated to members,

that the three UCSF patients injected with radioactive plutonium between 1945 and 1947 were participants in the Manhattan Engineer District (MED) sponsored plutonium project. That assumption was seriously doubted as the investigation proceeded. But the initial task was to discover the facts about the University's relationship to the MED research project, the role the three patients played in that research, and whether or not the patients were harmed.

The investigation hinged on attempting to answer the following questions fundamental to the contemporary scientific review of any biomedical research project and to the protection of human subjects in research: Was there adequate scientific rationale for the research? What are the biological effects of plutonium on human beings? How were study subjects chosen? What was the quality of the subjects' medical care? Were the patients harmed physically? What were patients told? Did they volunteer to participate in the experiments? Was there third-party review and approval of the experiments? What was the balance of benefits and risks to human subjects? Was experimentation with radioactive substances appropriate and justifiable, both in the context of 1940s research on humans, and from the viewpoint of contemporary standards?

Background to the experiments

Plutonium was first produced in 1941 in the cyclotron of the University of California at Berkeley (UCB). Recognizing its potential use in atomic weapons, the MED began large-scale production of plutonium in 1943. Medical scientists became concerned about the occupational exposure to plutonium among workers in atomic weapons plants, worried about acute and chronic toxicity, but did not understand the biological consequences of human exposure. In 1945, J. Robert Oppenheimer, Scientific Director of the MED, requested that medical scientists investigate the hazards of human plutonium exposure.

Beginning in the 1930s, Joseph Hamilton, M.D., a physician who held joint appointments at the Department of Physics, UCB, and the Radiology Department, UCSF, along with physician and scientist colleagues, had pioneered in the use of radioisotopes, specifically Iodine 131 (from the mid-1930s) and Strontium 89 (from 1941), for cancer therapy. Hamilton and his colleagues were among a very small group of early researchers in nuclear medicine who were searching for a 'magic bullet', a selectively localizing radioisotope, for use in the treatment of a variety of cancers. Their experiments with radioactive strontium began well before US involvement in the Second World War and before the existence of the

MED. They proceeded without government oversight or secrecy. In the 1940s, their work seems to have focused on bone cancers.[10]

Hamilton's experience with radioisotopes became evident to the MED and, through secret MED contracts with the University of California, he and his colleagues became involved in a multi-institutional effort to determine permissible exposure levels of plutonium in atomic plant workers. There were two specific objectives of the MED-sponsored research: to determine the excretion rate of plutonium in humans and its correlation with exposure, and to determine how plutonium was deposited in human and animal tissue.

In February 1944 Hamilton received 11 mg of plutonium and he and investigators at other sites began animal experiments. There was significant variation among animal species regarding excretion rate and tissue deposition which made extrapolation from animals to humans impossible. Nevertheless, animal studies established that plutonium deposited in bone, so human studies were designed to establish the deposition of plutonium in bone as well as its excretion rate. This could be done by injecting a known amount of plutonium into experimental subjects, then monitoring its excretion rate and calculating the extent to which it was deposited in bone. Sufficient bone samples could only be obtained from amputations or certain surgical procedures requiring rib resections. Therefore, research subjects who were scheduled for amputations or rib resections had to be found. Both the animal and human studies were carried out in war-time secrecy. The word 'plutonium' was classified. It was never mentioned to patients and was probably not mentioned to health professionals who cared for them. The director of the project at Los Alamos had decided not to fully inform subjects of the nature of the injections. The committee does not know if, or how much, the UCSF doctors responsible for patient care knew about the plutonium experiments.

The three UCSF patient-subjects

There were two general inclusion criteria for experimental subjects found in the MED and AEC documents. Patients chosen for plutonium injections had to be age 45 or older and had to have a diagnosed condition likely to result in the patient's death within 10 years. The committee did not discover a specific rationale for the selection of each of the three patient-subjects. Indeed, two of them did not fit the inclusion criteria. CAL-1, a 58-year old white male, initially diagnosed with advanced stomach cancer, was apparently chosen as a research subject because surgery for his suspected disease would, and did, remove a piece of rib. It was assumed that he would not live beyond 10 years. He was injected with plutonium in May 1945. Shortly after the injection, he was found to have a benign gastric ulcer, not

cancer. He lived for 21 years and died of heart disease in 1966. CAL-2, a 4-year old boy from Australia who had bone cancer and was flown to UC Hospital by a US army transport plane, was injected with a combination of plutonium, cerium, and yttrium[11] in 1946. He was scheduled to have his leg amputated several days after the injection but had a biopsy of bone tumor instead. He returned to Australia two months later as UCSF doctors could do nothing more for him. He died of his disease a few months later. CAL-3, a 36-year old black male suffering from bone cancer, was injected in 1947. He was not expected to die within 10 years if treated by the surgical methods available at the time. Indeed, his left leg was amputated shortly after the injection, curing him of the disease, and he lived for 44 years, dying of respiratory failure in 1991.

CAL-1, until he was properly diagnosed, fit both MED inclusion criteria. CAL-2, a child, did not fit the age criterion. The committee puzzled over his inclusion in the MED project both because use of a child in experiments raises the ethical question of voluntary participation, and because the excretion of plutonium from a child would differ from that of adult atomic bomb workers. CAL-3 did not fit either inclusion criterion.

The medical care received by the three subjects was not altered or compromised because of their participation in the plutonium experiments. Other than the injection, the only deviation from standard care was the collection from them of urine and fecal specimens. The injections were noted in the medical records of CAL-2 and CAL-3 but identified as plutonium only in the case of CAL-3. The details of the plutonium injections and analyses were not kept in the medical charts.

Explaining the choice of patients: Dual purpose research

Some historical documents reviewed suggested that all three patients were part of the MED-sponsored project. The AEC arrived at that conclusion in 1974 after follow-up studies were conducted on individuals still alive, including CAL-3, who had known amounts of internalized plutonium. Other documents reviewed suggested that CAL-2 and CAL-3 were not part of the MED-sponsored experiment. The committee pondered what could explain this discrepancy.

In probing further, the committee discovered that during the period 1941–1947, 12 patients at UCSF hospital, all of whom had cancer, received injections of bone-seeking radioisotopes: 8 strontium, 3 plutonium, and 1 americium. Of these 12 cancer patients, 9 had primary bone cancer, rarely found in the population. CAL-2 and CAL-3 were the only patients with primary bone cancer who received plutonium. No documents indicated that CAL-2 and CAL-3 were participants in a specific clinical investigation

to discover a treatment for bone cancer. But the committee infers that CAL-2 and CAL-3 were part of a selected group of rare cancer patients, chosen to determine the potential therapeutic effects of plutonium on their tumors. When plutonium became available to Hamilton and his colleagues because of their government contract in 1943, they presumably thought of it as another potential therapeutic agent, like radium and strontium. After americium was discovered at the UC Berkeley cyclotron in 1944, it also became an experimental substance.[12]

The injection of CAL-2 followed the strategy employed by the investigators in previous years for patients injected with strontium. In fact, the laboratory data gathered on CAL-2 following his injection resemble data gathered on the strontium patients far more than it resembles data collected on CAL-1 to determine plutonium excretion. The amputation specimen of CAL-3 was analyzed in a similar fashion to the biopsy specimen from CAL-2. The scientists were analyzing plutonium in sarcomas. While data gathered from these three patients on plutonium kinetics may have been, and later were found to be, useful to the MED/AEC, the UCSF scientists were primarily interested in clinical research for bone cancer therapies.

The committee ultimately suspected that Hamilton and his colleagues were conducting dual-purpose experiments, piggybacking two experimental designs, in an effort to satisfy the MED contract, its objectives, and its restrictions *while at the same time* continuing their own clinical research begun in the 1930s, that is, the search for new treatments for bone cancer. Hamilton and the MED ultimately had different interests in plutonium: the MED was concerned with deleterious effects on exposed workers; Hamilton and colleagues were searching for promising therapies.[13] The dual-purpose experiments were an entirely unexpected finding from the committee investigation of the science and ethics of the plutonium injections.

Regardless of whether the plutonium experiments were conducted specifically for the government as part of secret war-related research to determine excretion rates, to show promise as therapeutic agents, or both, the injections of the three CAL patients were not intended to be of therapeutic or medical benefit to them. The injections did not physically harm them, but neither did the injections benefit them in any way. The plutonium injections of the 1940s can be interpreted as similar to contemporary 'phase 1' clinical trials in which the goal is to determine the toxicity level of particular substances.[14]

The problem of consent

Voluntary consent from experimental subjects was necessary regardless of the nature of the experiments. There was no explicit consent to the injections for CAL-1 or CAL-2, as part of either a secret research project or a clinical investigation. There was no documentation of discussion of risks with any of the three research subjects. None of them gave signed consent to participate in the plutonium experiments *per se*.[15] Because standards of consent existed, were commonly understood, and were sometimes practiced during the 1945-1947 period, the University of California research was unethical if the injections were performed on the patients without their free participation, consent, or knowledge about risks. Furthermore, the injection of CAL-2, a child, was unethical if done without the consent of a parent.[16] Although the committee cannot know what was said to the three subjects or the extent of their understanding of the injections or their potential risks, it inferred that subjects were only told that they were to receive a radioactive substance. Probably no discussions about risks were held. The subjects, therefore, were wronged, though they did not suffer any medical complications from the injections.

Committee conclusions

The MED sponsored plutonium experiments on the UCSF patients and on the patients at two other hospitals in the US produced data that helped establish permissible exposure levels for plutonium workers, data on the deposition of plutonium in human tissues, and information about animal models useful for future research. Information gained from the experiments was published in scientific reports, books, and journals. The experiments addressed a legitimate problem, were scientifically valid, and resemble in principle product testing by pharmaceutical companies today. Nevertheless the urgency and secrecy of war-time human experimentation did not justify a departure from prevailing standards either about the use of human beings in medical research or about the voluntary consent of subjects. Regardless of whether the three CAL patients participated in the MED sponsored project on plutonium deposition, a university-based clinical investigation of treatments for bone cancer, or both, practices of obtaining consent did not meet the standards of the time or the standards of today.[17]

THE WORLD OF EXPERIMENTATION: 1940S

Taken together as contested stories, these texts and the narratives from which they derive raise questions about what is at stake – for patients, med-

ical researchers, and society – in the evaluation of past medical research *and* in contemporary understandings of the practice and politics of informed consent as it has evolved in recent US history. I turn first to a discussion of the world of medical experimentation during the 1940s in order to provide some historical context for these texts. Next, I briefly consider ways in which the problems of informed consent have been construed in recent history. I then look at ambiguities in the contemporary scene.

War-related notions of purpose and common good, especially those in which average citizen involvement was a moral imperative, provided one context for the activities described above. Another context for the plutonium experiments was the medico-cultural world of clinical investigation, a world characterized by medicine's emerging identity as a scientific enterprise. By the mid-1940s science had gained popular prestige and scientists were heroes. The idea that scientific discoveries could accomplish almost anything was widely held (Susman 1984). At the same time two other developments occurred. Medicine totally embraced science when thousands of scientists, doctors, and technicians confronted the medical problems created by the War. Penicillin, which became available for military use in 1942 and civilian use in 1945, transformed medicine by its ability to routinely cure infectious diseases (Dowling 1977; Kaufman 1993). As a result, there was a strong societal belief that medical research could eventually eradicate all disease and promote social progress. Beginning with the war years, the federal government began its multimillion dollar support of scientific medicine, pouring money into laboratory and clinical research. The National Institutes of Health were established immediately following the war. By the late 1940s medicine, for the first time, was considered a scientific profession (Starr 1982: 338–351). The world of clinical research during that period was perceived to be one of limitless ability and discovery. It included the following four features relevant for the discussion of the use of human subjects.

First, physician-scientists did not consider their research subjects to be completely free-choosing beings for the following reasons. Patients generally were very ill, and many hopelessly so. In an era before routine cure of many diseases, doctors assumed patients to be thankful for any medical attention, whether its intent was therapeutic or not. Subjects were mostly drawn from charity hospitals (this was before the existence of Medicare and Medicaid), where their nonpaying status somehow made them grateful in physicians' eyes for personal contact and justified their use as subjects. In addition, doctors did not identify with many of their study subjects because they were different from them ethnically and socioeconomically. Thus the race, class, and illness status of patients inhibited their power in

the doctor-patient relationship to make unencumbered choices (Kaufman 1993).

Second, experimentation was not fraught with perceived ethical dilemmas. Interests surrounding human experimentation that we now take for granted as potentially conflicting – clinical, scientific, ethical, and legal – usually were not distinguished during the war years by doctors, patients, or others. Thus those interests were not subject to evaluation nor conceived as problematic by a public forum. What today are considered potential physical or psychological risks of participating in a study were not conceived as such, nor were they weighed against the benefits of research participation. Considerations of risk, benefit,and alternatives were not even publicly formulated, let alone examined. Moreover, patient choice, autonomy, and education did not exist as widely-shared values. Legal ramifications were rare or minimal (Fox, Swazey and Watkins 1992; Kaufman 1993; Romano 1974).

Third, clinical research programs in the 1940s were infused with a moral certainty that transcended potential ethical problems about the use of human subjects. Investigators did not question the value of their own research endeavors, nor did their peers or superiors. Risks of participation – even those risks which had potential to be life-threatening – were in service to the knowledge gained by the research findings. Moral certainty legitimized human experimentation and helped keep any moral conflicts from surfacing.

Fourth, bedside doctors and clinical investigators were the same person (Fox 1959; Fox, Swazey and Watkins 1992). Although this feature of medical research sometimes raises profound conflict-of-interest questions today, in the 1940s it was merely the way things were (Taylor 1992). Patients who served as research subjects in most university-based studies did give their consent, in the form of *verbal permission*, to let *their doctors* perform some treatment or procedure on them. But it is important to note that the purpose or details of treatment were not necessarily explained to patients. Research, as an activity distinguishable from medical practice, was usually not understood by patients nor articulated by doctors to them. Moreover, patients did not necessarily 'volunteer' – as we currently understand that term – to participate in research. That is, they were not always told as are potential subjects today: (1) that a study was in progress; (2) that they were free to decide whether or not to participate; and (3) that they could withdraw from the study any time they chose. Nevertheless, 'consent' was almost always given after doctors talked with patients, however briefly and superficially, about what they were going to do to them.

An eminent investigator of that era described his own research practice during the 1940s in his recollection of what now is now considered to be path-breaking clinical research in cardiac catheterization – the insertion of a catheter into the femoral artery in order to collect blood samples from the heart, and later the liver:

> Some of the ethical problems about that sort of investigation that trouble us now never dawned on us then. There wasn't much clinical investigation as such in the early 1940s. There were very few people engaged in full-time clinical research anywhere. We never asked the permission of those patients to go through this procedure. We certainly never explained it. We never told them, 'This isn't going to help you a bit, but it may give us a better understanding.' No patient ever refused to participate. It wouldn't have occurred to them. We would go by the night before and say, 'We are going to do a special study on you in the X-ray department tomorrow,' and they would say, 'All right.' They never challenged what a doctor was going to do.[18]

In another context he reported:

> . . . my recollection is that little thought was given to the propriety of carrying out this work. We explained to the patients that we proposed to make a special kind of examination in an x-ray laboratory, and their agreement was easily obtained. Nothing resembling current guidelines for informed consent was available for them or their families. In retrospect, I can only hope that some or all of them, being gravely ill and not receiving any other form of aggressive treatment, got some comfort from the brief period of intense attention given them by the doctors and nurses who were members of the 'shock laboratory' team. (Beeson 1985)

It is important to emphasize that patients agreed to participate in research on the basis of *trust*, not on the basis of informed consent. Patients trusted their physicians not to harm them, to do something positive for them (even if they could not cure them – and cure was not routinely expected in the 1940s), and to act in their best interests (Cassell 1986; Fox 1959; Kaufman 1993).

Ethical standards for consent during the war years

At the same time that the medico-cultural world of clinical investigation was framing the practices of experimentation and consent, both formal standards for the conduct of ethical research, which have a long history (Beauchamp and Faden 1995; Faden and Beauchamp 1986), and informal practices, which were influenced by the moral-political context of the war, continued to evolve. The idea that patient-subjects should volunteer to participate in medical research was accepted well before the Second World War years, as was the idea that they should be informed about the nature of the study. At the time the plutonium experiments were being conceived, the term 'informed consent' was not yet widely used, but the principle had been established in court cases during the 1930s, and some researchers

did follow it (Faden and Beauchamp 1986; Mann 1994). Published ethical principles of the 1940s state that a research subject should be told about "the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his/her health which may possibly come from participation in the experiment" (Katz, Capron and Glass 1972). Historical studies of the war years indicate that those principles were not invoked consistently or even generally throughout the research community. Indeed, many government-sponsored experiments were conducted during the war years in which participants, both civilians and soldiers, did not volunteer or did not give consent (Rothman 1991: 33).

World War II changed the scope of medical research. What had been sparse efforts by a relatively few individual researchers became extensive projects, involving teams of researchers, funded by the federal government. Human research lost its intimate character as an endeavor among doctors and *their* patients and was instead devoted to seeking solutions to combat and war-related problems. Consent, however informal in character before the war, frequently took a back seat to the sense of urgency and necessity for human experimentation brought on by the war (Fox, Swazey and Watkins 1992; Rothman 1991). In the logic of the period, "Researchers were no more obliged to obtain the permission of their subjects than the Selective Service was to obtain the permission of civilians to become soldiers" (Rothman 1991: 49). The public response to the use of prisoners in research, for example, was

> not to ask whether prisoners were able to give voluntary consent, but to congratulate 'these one-time enemies to society' for demonstrating 'to the fullest extent just how completely this is everybody's war'.[19]

Subjects were only informed about details of a war-related research project and asked to sign consent forms, historian David Rothman notes, if investigators felt "negative fallout was likely" (1991: 48), as, for example, in a study in which prisoners were deliberately infected with gonorrhea in order to investigate the prevention and cure of that disease (1987; 1991: 43–50). Thus, the ethics of American research during the war years was entirely utilitarian (Rothman 1987).

Published discussion of guidelines for human experimentation was sporadic before 1946. Awareness of the Nazi atrocities influenced the public discussion of ethical guidelines and ultimately the development of the Nuremberg Code. In a December 1946 editorial titled, "The Brutalities of Nazi Physicians," the American Medical Association outlined basic ethical standards for medical research that were based on a report of war

crimes conducted by Andrew C. Ivy, MD. Those standards included the following:

> 1) Consent of the subject must be obtained. All subjects have been volunteers in the absence of coercion in any form. Before volunteering, the subjects have been informed of the hazards, if any.
> 2) The experiment to be performed must be so designed and based on the results of animal experimentation and the knowledge of the natural history of the disease . . . and must not be random and unnecessary in nature.
> 3) The experiment must be conducted only by scientifically qualified persons. . . . Such rules are required to insure the human rights of the individual, to avoid the debasement of a method for doing good, and the loss of the faith of the public in the profession. (Ivy 1946)

These points were first published in the *Journal of the American Medical Association* after the plutonium experiments had been underway for well over a year. They anticipated the ten articles of the Nuremberg Code[20] which were published in *JAMA*, 29 November 1947. But by then the plutonium experiments were over.

It is well known among medical historians and researchers who worked through that era that few investigators seriously or deliberately followed the 1947 AMA guidelines, and then the Nuremberg Code, in their actual research practices, especially the directives that subjects must knowingly volunteer and be informed about the nature of a study and its risks (Rothman 1991: 31). That fact does not necessarily imply that individual investigators were 'immoral' or 'unethical' in their research practices. It does mean, however, that investigators generally did not use the 1947 guidelines or the articles of the Nuremberg Code as frameworks for designing their research studies or considering the use of human subjects – from recruitment to withdrawal – in those studies. It must be emphasized that well into the 1960s, when Henry Beecher published his exposé of abuses in human experimentation (Beecher 1966), the American medical research community considered the Nuremberg findings and the Nuremberg Code irrelevant to its own work (Rothman 1987; 1991: 31). And prior to 1960, there was 'little law' in the USA that specifically concerned protecting the rights of the subjects of medical research (Curran 1969).

THE 'PROBLEM' OF CONSENT

Although the articles of the Nuremberg Code focused broad attention, for the first time in the USA, on the necessity of voluntary and informed consent, decisions about the ethics of enrolling certain subject populations in research (prisoners, children, the mentally-retarded), the type and amount of information to disclose to individual subjects, and the choice of drugs or

procedures to use in experiments were left solely to individual investigators. There were no federal guidelines or mandatory peer review systems in place to oversee actual practices of physician-investigators or to protect human subjects from potential injury, death, or exploitation (Rothman 1995). Consent emerged as a problematic enterprise in 1966, when Henry Beecher, a professor of Anesthesia at Harvard Medical School, published his whistle-blowing article, "Ethics and Clinical Research," in the *New England Journal of Medicine*. There he cited twenty-two examples of medical research at American universities, medical centers, and hospitals in which investigators had not informed research subjects about the nature of their participation, had not obtained their permission to participate, and had risked their health and, in some cases, their lives (Beecher 1966). His exposé initiated widespread scrutiny of experimentation on humans subjects both within and outside of medicine. Most importantly, it brought academic theologians, philosophers, lawyers, and biological and social scientists into public debate with physicians about the ethics of experimentation, the process of medical decision-making in general, and the importance of informed consent in all clinical work.[21]

For the first time, non-physicians began to frame both the problems and the solutions for the conduct of research on humans. Two national commissions,[22] comprising more academic philosophers and lawyers than physicians, were created in 1973 and 1978 to outline the problematic areas of informed consent and to propose guidelines for investigators. Commission members, whose perspectives were firmly grounded in philosophy and law and who looked to the principles of the Nuremberg Code itself for guidance, formulated a range of concerns in the implementation of consent. Their constructions of the consent 'problem' and its potential solutions continued to be articulated in reports written into the 1980s and those constructions remain salient today. Following publication of the commission reports, growing numbers of interested persons from many disciplines began to scrutinize various features of the consent process, and they continue to do so, in ongoing attempts to refine both ethical standards and practical mechanisms for achieving informed consent in research.

Recent summaries of the tenacious problems in the ethics of consent (some of which were identified well before the Nuremberg Code) include the following questions: (1) How can consent be truly informed when most patients cannot comprehend complex medical information nor can they recall that information to make decisions? (2) How can consent procedures be implemented, or how can a process of dialogue be started, when many patients do not want to be involved in decision-making? (3) How much disclosure of information is beneficial and how much is harmful

to patients' well-being? (4) How can an investigator know how a patient interprets information about an experiment? (5) Is the consent form the appropriate instrument through which researchers may fulfill their obligation not to treat research subjects merely as means to an end? (6) Are subjects 'free to choose' to participate if they are prisoners? children? offered financial compensation? terminally or critically ill? (7) How can competence to consent be assessed? (8) Can research conducted on demented or cognitively-impaired persons with proxy consent be considered ethical? (Arnold and Lidz 1995; Levine 1995).

Institutional Review Boards (IRBs), now established at all medical institutions, started to engage at least some of these questions when they were mandated by federal policy, in 1974, to protect the rights of human subjects by overseeing federally-funded human research. These questions have remained central to the conduct of human research and they continue to underlie IRB scrutiny and refinement of the consent documents which patient-subjects must read and sign in order to participate in experiments. In fact, careful consideration of consent documents constitutes the major part of day-to-day IRB work.[23]

Since the national commissions were established, these questions have been debated in medical, academic, and legal circles, in the larger community of concerned citizens, and in the media. Although the nature of particular experiments has changed over the past two and half decades (for example, new chemotherapies, the transplantation of multiple organs, gene therapies, and most recently xenotransplantation), and the environment of research has grown to encompass law and bioethics, these questions have remained troubling and continue to fuel academic and public debate.[24]

WHAT'S AT STAKE: THE PROBLEM OF SITUATING EXPERIMENTATION AND CONSENT

The two plutonium stories, each in its own way, confront a deeply troubling episode in the history of American medical research with reasoned yet entirely different responses. The stories, while appropriate to the professional worlds in which they were created, make two assumptions which underlie their 'plot' and motivation and which ignore the cultural and historical complexities of informed consent in medical research. First, the narratives assume the present- day existence of an explicit, singular, and unified moral position about the roles and responsibilities of investigators in the conduct of human experimentation. They assume secondly that today's research practices can be located at a more ethical site along an Enlightenment-derived continuum of moral progress than the secret exper-

iments of the 1940s, a site where rules for appropriate conduct are more precisely defined and where actual behavior is closer to (or even has arrived at) some ethical ideal. It is true that the experiments Beecher described in 1966 could not occur today, both because of federal oversight and because of heightened social awareness about the rights of patients and study subjects. The existence of federal policy and of Institutional Review Boards at all universities, medical centers, and hospitals where human experiments are conducted does provide evidence of greater explicit ethical comportment in medical research than was possible during the World War II era. Yet a brief overview of the features of contemporary human experimentation reveals the flaws in these two assumptions.

Clinical investigation today is a huge and highly varied enterprise that includes such activities as the following: randomized double-blind, placebo controlled trials to test treatment efficacy or assess treatment safety; the comparison of experimental surgical devices, procedures, and techniques with those considered standard; transplantation of normal cells, tissues, and organs into diseased tissue or to replace diseased organs; and the use of recombined or altered genetic materials in the attempt to cure diseases caused by genetic abnormalities. A study may include thousands of persons at multiple medical centers, hospitals, and clinics (as in some drug trials) or, at the opposite extreme, only one person (as in gene therapy). Risks to individual subjects vary enormously as does the health status of persons who participate in research projects.

Various kinds of contemporary medical research are considered to be ethically problematic by some observers because scientific methods and patient care are at odds. Critics focus largely on whether or not the interests of the patient can be served given the inherent features of scientific biomedical research (see for example, Appelbaum et al. 1987; Fox and Swazey 1992; High 1992; Kodish, Lantos and Siegler 1990; McNeill 1993; Taylor et al. 1984). Problems these observers and others highlight include (but are not limited to) the following: (1) Experimental drugs or procedures may or may not prove to be beneficial to individual patients, and may prove to be toxic. (2) Randomization to either a course of treatment or non-treatment compromises patient care. In placebo controlled trials for instance, those subjects randomly assigned to the placebo group do not receive treatment for their disease (for example schizophrenia, depression, ulcer, or cardiac disease) during some or all of the study. (3) In double-blind studies physicians do not know what kind of medication or procedure their patients receive until the study is over or until there is a problem. (4) Chemotherapy trials for certain kinds and stages of cancer frequently worsen patients' quality of life without extending life itself.[25] (5) Some experiments include

a 'wash out' period in which subjects are taken off medications for weeks – placing them at risk for relapse or symptom exacerbation – before they are allowed to receive the experimental drug(s). (6) Some subject populations such as children, the mentally retarded, the demented elderly, and patients in emergency departments do not freely volunteer and cannot give (relatively) informed consent. (7) The early stages of some 'therapeutic innovations', such as organ transplantation, involve high death rates and low quality of life for survivors. (8) Studies which experiment on stored tissue are frequently conducted without asking persons for consent, raising the question of ownership and the right to information about use of body parts.

These features of contemporary human experimentation lead us to consider at least three unanswered questions that plague the evaluation of present *and* past research involving human subjects, including the attribution of moral wrong-doing. First, how much information about a drug, substance, or procedure must be or should be disclosed to human subjects for research to be considered 'ethical' and for subjects to be 'truly' or 'fully' 'informed' (Gotay 1991; Schain 1994)? And how much information is considered overwhelming for the patient? Second, what constitutes permissible or excessive risk to subjects and how is that decided? How much or how well does something have to 'work' to be considered successful, so that the benefits are thought to outweigh the risks (Cho 1994; Kolata 1995)? Third, given the *practical and moral* problem of distinguishing between 'experiment' and 'therapy' in many instances both historically and in current research practice (Applebaum et al. 1987; Fox and Swazey 1974; 1992; Jonas 1969; King 1995; Taylor 1992), how is the consent process understood by patient-subjects and how can physician-investigators know if their patients understand enough about the research and its procedures or treatments to evaluate the risks of participation?[26]

It is important to remember that clinical research practices, including regulatory procedures and standards, are embedded today in a cultural, political, and economic context that is enormously different from the research context of the 1940s. Today's world of practice includes the following dimensions: consumer rights to information and patient rights to autonomy as guiding frameworks for both federal and local policy debates about ethical comportment in experiments; tension produced by medicine's orientation to prolong lives with the best technology available in conflict with consumer demands for dignity and control; the (especially) Anglo-American value placed on open communication between physician and patient combined with the difficulty of realizing that value in work with multicultural patient populations and persons who are cognitively

impaired; societal demand for clinical research and an unprecedented financial investment in it; the creation of presidential commissions, institutional review boards, and bioethics as an oversight institution; and cultural confusion about the role of the research physician as healer, patient advocate, competitive clinical investigator, or some combination of the three.

The contemporary construct of informed consent emerges from these dimensions of clinical care and research. It is *a discursive practice*, defined through the myriad ways in which it is produced in local situations. It is not a stable and known fact. Rather, it is an elusive ideal, brought into existence by law and philosophy (Beauchamp and Faden 1995; Arnold and Lidz 1995) and mandated by evolving federal policy. The research establishment must strive to achieve its tenets. 'Informed consent' did not exist, *as we invoke it today*, during the era of the plutonium experiments. Attempts to apply our current understandings of such a fluid concept to a previous era in order to assess 'ethical behavior' are misguided and miss a very important point – consent today is a highly problematic construct.

Consent as elusive project

Today, consent – in theory – is the process through which patients (and their families) learn something about the goals of a study, some details of a drug, treatment, or procedure, associated side-effects, and the short and long-term risks to their bodies, minds, and overall health in order to 'freely' decide whether or not to become research subjects.[27] In most circumstances, consent is not understood by patients from the research and regulatory perspective that investigators take for granted. Consent is simply not part of the background knowledge or cultural world (Gordon 1994) of most medical patients or potential research subjects. In many if not most cases, patients 'consent' to what they interpret to be hopeful *therapy*, that is, treatment intended to ameliorate their condition, lessen the severity of their symptoms, and foster their well-being. They assume that those therapies are prescribed with their best interests in mind (Applebaum et al. 1987). They give consent from a position of vulnerability and in some cases, relative desperation. Doctors and other health professionals are thought to have the tools – which patients do not claim to understand – to heal and to reduce suffering.

Since federal guidelines for informed consent were instituted beginning in 1966 (Rothman 1995), it is both easy and comforting to assume that a body of federal regulations assures societal understanding of the term and ensures compliance, in all cases, with a list of rules or guidelines.[28] For more than two decades, various observers have noted the difficulty with maintaining that assumption. Beginning in 1969, Blumgart noted that the

quality of informed consent depends on the quality of the information communicated by the physician or investigator to potential subjects. Informed consent involves subjective judgments on the part of the investigator since patients or their representatives usually do not understand the scientific basis of the study nor the criteria used to evaluate inclusion or risk. Under these circumstances "informed consent is a goal we strive to attain, but one that is impossible to achieve in any complete sense" (Blumgart 1969: 256). This particular problem has not disappeared. In a recent review of cancer studies Schain (1994) focuses on the patient-subject side of the informed consent negotiation and notes that there is a great deal of variation regarding what prospective subjects want to know about a study in order to consider themselves informed. Some people demand to know everything in minute detail; others prefer minimal information. She notes that informed consent documents do not distinguish between the various styles in which prospective study subjects gather information.

In addition, a major deficiency in standardized informed consent procedures is not knowing what a potential subject intuits or perceives from a discussion of risks and benefits. Patients do not usually formulate questions about risk versus benefit. Rather, they tacitly assume that a prescribed treatment would never harm them and should be of benefit to them. One recent study has shown that some persons 'consent' to a particular therapy because they are following a doctor's advice; they do not understand that they are participating in medical research with associated risks (Harth and Thong 1995). Other studies suggest first, that subjects misinterpret the risk/benefit ratio of participation because they do not understand the methods of study (Appelbaum, Roth and Lidz 1982) and second, that subjects assume treatment decisions are made in their best interests even when the use of placebos and non-treatment control groups are explained to them (Appelbaum et al. 1987).[29]

While informed consent is both a discursive enterprise and elusive goal, it must be noted that it is practiced as discrete, knowable activities which include (but are not limited to): the formulation of study inclusion criteria for subject selection; decisions about how much and what kind of information about procedures and risks to discuss with patients face-to-face and to include in consent forms; and consideration of what populations are 'vulnerable' and what that might mean for consent procedures. Only in infrequently problematic instances, such as the unexpected death or near-death of a research subject or in an investigation or lawsuit brought by a patient or family, do the broader questions about the *nature* of consent and *degree* of risk and the inherent tension between investigation and patient care emerge as foundational issues and the focus of conscious deliberation.

Experiment and therapy: Confounding consent

The vocabulary available in the culture of medicine to describe the complex and varied practices that constitute experimental work is quite impoverished[30] and is, in fact, limited to two terms, 'experiment' and 'therapy'. It is unfortunate that neither the medical nor lay communities has addressed this problem directly. The lack of a precise, well-developed vocabulary misleads potential research subjects and their families, fosters the conceptualization of a straightforward dichotomy among physician-investigators, and perpetuates the use of simplistic and unrealistic federal policies. Each of these points is discussed below.

It is a rare patient who can frame communication with his or her doctor about potential research participation through separately conceived categories of 'experiment' and 'therapy'. As in the 1940s, patients, perhaps especially very sick people participating in medical research, *trust* their doctors always to provide personally tailored care with the most appropriate and efficacious treatment available. This is true despite the well-known and negatively viewed changes that have occurred in the past several decades in the structure of health care delivery and the values of medical practice. Trust appears to be an enduring theme in medicine (Cassell 1991; Jonas 1969). Sick people need and want to trust their doctors. It is somewhat ironic that this dimension of the doctor-patient relationship remains strong at the same time that it exists in an environment of litigiousness, defensive medical practice, consumer choice, and the demise of paternalism. It is virtually impossible, in practical terms, to tease apart trust from informed consent in patients' (and families') actual decisions to participate in experiments.

It was noted a generation ago by both physicians and social scientists that the line between experiment and therapy is never clearly drawn in clinical practice (Moore 1969) and that therapeutic innovation should be regarded as a process that moves along a continuum between 'research' and 'therapy' (Fox and Swazey 1974). In their study of organ transplantation, Fox and Swazey note that "whatever its stage of development, clinical investigation entails an interplay between research and therapy, and the balance shifts as the new treatment evolves" (1974: 64). They suggest that the evolution from experiment to therapy is not necessarily in one direction, that physicians have a great deal of difficulty verbalizing "what is experimental" and "what is therapeutic" (p. 65), and that physicians maintain an attitude of "structural ambivalence" (p. 61) regarding their dual role as investigator-clinicians. In their detailed investigation of kidney transplantation in particular they note that even after renal transplants had been performed for nearly 20 years, there was no obvious agreement in that

medical field as to the experimental-therapeutic status of the procedure: debate still raged over *how* experimental or *how* therapeutic the procedure was.

While 'experiment' and 'therapy' have been shown for at least two decades to be ambiguous yet inextricably linked notions, impossible to tease apart in physician-investigator explanations of their work or in actual research practice (Appelbaum et al. 1987; Cho 1994; Fox and Swazey 1974, 1992; King 1995; Taylor 1992) federal policy and local institutional review boards construct them as clearly dichotomous through the strict monitoring now required for research conducted on humans. Since the 1970s, investigators must classify certain practices as *experimental*, that is, designed to reveal what works and does not work in medicine through scientific means, usually by the administration of 'treatment' offered to subjects for its learning value to the investigator and for the potential benefit of future patients. Yet experimental treatment may or may not have therapeutic value for the patient-subject to whom it is administered (Katz 1995).

Patients presume, and their investigator-physicians may think, hope, and desire, that a particular 'experimental' or 'innovative' treatment or procedure is in fact a new therapy with known, positive attributes which will unquestionably help them. Physicians, aware of a theoretical distinction between the experiment and therapy concepts, may pragmatically recruit subjects by stressing the therapeutic potential of participation and de-emphasizing the experimental nature of a project and the importance of informed consent (Katz 1995). Then consent sometimes can seem superfluous or irrelevant to the physician-scientist (Appelbaum et al. 1987). Thus incommensurable understandings between sick people and the doctors with whom they communicate, as well as confusion on the part of research physicians about whether a particular practice constitutes 'experiment', 'treatment', or some other ambiguous category such as 'experimental therapy' or 'innovative treatment' confound the consent process.

CONCLUSION: INTERPRETING THE PLUTONIUM NARRATIVES

Consent cannot be reduced to a monolithic fact or static entity; it is not a discrete set of behaviors amenable to legislation from afar. Rather, consent is produced in local worlds of research, institutional evaluation, and investigator-health care team-patient interactions. It is an evolving concept and practice. The actual form consent takes vis-à-vis any particular study is shaped by those contexts as well as by the attitude of the physician-investigator toward the consent process, his or her communication skills

with potential subjects, subjects' perceptions of the study and their role in it, and the local politics of approving, and then conducting, an experimental trial. Contemporary understandings of consent and practices of acquiring consent are variable and malleable, and they contain a great deal of ambiguity. Because consent is so protean and because distinctions between experiment and therapy vary from project to project and place to place and are frequently obscure, it is misleading for observers to claim that ethical oversight now exists, unequivocally, in the world of human experimentation. Awareness of the ambiguities and discursive practices of the contemporary situation should guide our approach to the past. Evaluation of consent, risk, and experiment as they were lived during the war years is indeed complicated.

The two plutonium narratives reconstituted in the texts above can remain only partial truths, shaped by their own historical and political embeddedness which includes the idea of moral progress. Each story assumes that evaluation of the past takes place from a position of relatively greater rationality, oversight, and moral clarity than was practiced during the war years. Each story implies that the world of human experimentation has changed for the better, evolved to a less ambivalent, more virtuous position about ethical dimensions of research on human beings. Yet a brief exploration of the historical context and informed consent today illustrates that although 'times have changed' and the contemporary context of clinical research differs from that of fifty years ago, the world of medical research has not moved along a continuum of ethical comportment to a less ambivalent site. What has changed are the various ways in which doctors and patients, investigators and research subjects understand their choices, constraints, responsibilities, and evaluative positions.

As representations of a particular historical moment, the plutonium narratives illustrate how memory is publicly constructed through a newspaper account and a committee report. Juxtaposing the narrative texts points to the value of each for understanding the problem of 'knowing', and then evaluating, the past. Each narrative fails to acknowledge both the medico-cultural context of clinical investigation during the 1940s and the ways in which and extent to which informed consent was a lived practice during that era. As evocations of a moral stance, the narratives challenge us to compare the past with the present and to reconsider the idea of moral progress in human experimentation. They promote scrutiny of contemporary ethical discourses about trust, risk, and the nature of the physician/investigator-patient/subject relationship. The importance of the plutonium narratives is that they show first, how the history of human experimentation is produced; second, that assumptions of moral progress

are embedded in historical reconstructions; third, that informed consent is an ongoing process, an elusive goal, and a cultural site of tension and ever-changing knowledge; and fourth, that the politics and science of medical research today mask the many troubling features of consent and experimentation which underlie the biomedical research enterprise.

ACKNOWLEDGMENTS

This paper results both from my 15-month service on the UCSF Ad Hoc Fact Finding Committee on World War II Human Radiation Experiments (1994–1995) and my membership on the UCSF Committee on Human Research (1993–1994). I am indebted to the following people who made valuable comments on earlier drafts: Charles Bosk, Sharon Friend, Hugh Gusterson, Charles Hackman, Susan Kelly, Pamela Sankar, Carolyn Wiener and an anonymous reviewer. In addition, I wish to thank Renée Fox for her insights about the history and sociology of medical research and human experimentation and for specific suggestions which I have incorporated here. Portions of this paper were presented at the American Anthropological Association meetings in 1995 and 1996.

NOTES

1. *New York Times*, 29 January 1995. Ideas and Trends: "Whose Memory Lives When the Last Survivor Dies?" by Gustav Niebuhr.
2. The committee comprised 15 university employees and one community member. I was the only social scientist in a group that included physicians, clinical investigators, research scientists, and the director of the office of Public Affairs.
3. This outburst of public concern over the ethics of medical research is only the most recent manifestation in the USA of widespread scrutiny of medical practices. Technological advances in medical care, such as mechanical life support, that came into use in the late 1960s and 1970s also caused an outburst of public concern and led to the development of bioethics as a social movement and discipline of oversight and attention (Fox 1991). The most recent outburst of concern about the secret medical experiments is a response to political rather than medico-technical developments. It reflects a contemporary suspicion of the role of government in individual lives.
4. Eileen Welsome, "The Plutonium Experiment": A Three-Part Report. *Albuquerque Tribune*, 15–17 November 1993.
5. The documents included patient medical records, laboratory notes, government directives and memos, and letters, notes, and memos written by the investigators of the experiments, their colleagues, and administrators of the Manhattan Engineer District. The committee also reviewed scientific texts of the war era as well as contemporary secondary sources.

6. The National Advisory Committee on Human Radiation Experiments released its final report to the public in 1995 (Advisory Committee on Human Radiation Experiments 1995).
7. UCSF Ad Hoc Fact Finding Committee, "Report on World War II Human Radiation Experiments," UCSF, February 1995.
8. Thus they may be viewed as anthropological inventions or "fictions" (Clifford 1986: 6). Some may consider the fact that I was part of the production of one of the texts problematic: I know more about the construction of the Committee report than I do about the journalistic account. There can be no doubt that my situated knowledge of the biomedical research perspective contributed to my overall interpretation.
9. The *Albuquerque Tribune* report detailed the lives of the five patients Welsome was able to identify, including two of the three UCSF patients. For brevity, and to provide comparison with the UCSF report, only the stories of the two identified UCSF patients are reconstituted in this text.
10. Their early research can be viewed as the advent of modern cancer therapy.
11. These are radioactive substances also.
12. All of these substances are bone-seeking radioisotopes and, during the 1930s and 1940s, were considered potential therapeutic agents for bone cancer. All of them were used in medical experiments. The laboratory data gathered for CAL-2 was similar to the laboratory data gathered on the strontium patients. Only the plutonium injections were carried out in war-time secrecy.
13. Other documents read by the committee support the idea that the investigators were carrying on their own long-term series of clinical experiments. First, reports written by them in the few years following the government project mention only CAL-1. CAL-2 and CAL-3 were 'discovered' in Hamilton's files in 1971. Second, the ages and exact prognoses of CAL-2 and CAL-3 become irrelevant when seen in the context of the bone cancer research. For example, 6 of 12 patients in Hamilton's research were children, who compose a significant proportion of patients diagnosed with bone cancer. Third, the two-year time period between the injection of CAL-1 and CAL-3 is consistent with the suggestion that Hamilton was waiting for the admission of relatively rare primary bone cancer patients to UCSF hospital.
14. In 'phase 1' trials, patient participants are 'guinea pigs' in the sense that the experimental substance is not usually of benefit to individual test subjects. In this phase, investigators are seeking to determine toxic and toleration levels only. These clinical trials are performed on relatively few persons, and only after animal studies have been conducted.
15. Only in the case of CAL-3 is there written evidence, the signature of 3 physicians and 1 nurse in his medical chart, attesting to his consent to the injection. It is most unlikely that CAL-3 knew at the time what was in the injection, or that its purpose was for a secret government-sponsored study. It is noteworthy that the date of CAL-3's injection followed an AEC memo that required investigators to show in writing that research subjects understood the nature and possible risks of the experiment and to have witnesses sign the written document. Subjects were not required to sign anything themselves. The notation and signatures in the chart of CAL-3 indicate that Hamilton and his colleagues were fulfilling that particular requirement of the AEC memo.
16. Today studies on children are not done until studies on adults have been completed, and Phase 1 experiments on children are considered unethical.
17. This conclusion reflects the majority opinion of the 16 University Committee members but not a consensus. All agreed that CAL-1, CAL-2, and CAL-3 were not physically

harmed by the trace amounts of plutonium they received either in the short or long term. Committee members did not reach full agreement about whether or not the investigators were conducting a clinical investigation of potential bone cancer treatments at the same time they were participating in the MED sponsored experiment. There was speculation, but no consensus, about the motivations of the investigators. In addition, there was no consensus about whether or not the investigators acted ethically with regard to informing patient-subjects about their research participation.

18. Dr. Paul B. Beeson, quoted in Kaufman 1993, p. 170.
19. Rothman (1987) citing the *New York Times*, 5 March 1945: 1, 30.
20. Especially articles 1,2,3,4,5 and 8.
21. The first published, multi-disciplinary consideration of the range of ethical problems in human research was the Spring 1969 issue of *Daedalus*, titled "Ethical Aspects of Experimentation with Human Subjects" (issued as Volume 98, Number 2, Proceedings of the American Academy of Arts and Sciences). In that issue, philosophers, physicians, lawyers, and social scientists reflected on questions surrounding the doctor-patient relationship that had been troubling American medical research since the World War II era.
22. 1973: National Commission on the Protection of Human Subjects; 1978: President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research.
23. In addition to scrutinizing and revising consent forms, IRBs also concern themselves with whether or not subjects freely volunteer to participate in research, the extent to which a study protects the anonymity and confidentiality of the subject, and consideration of physical, psychological, and social risks versus benefits of participation.
24. It is interesting to note that very recently, AIDS and breast cancer activists are reworking practices of consent by insisting on their right to receive treatments, however unproven, instead of placebos, regardless of what that insistence does to both the 'science' of experimentation and the protection of human subjects. While the goals of Institutional Review Boards and federal guidelines for two decades have been to protect the human subject from potential harm by investigators, now research participation is viewed as positive when the traditional rules can be changed when necessary, and in some cases, as the only means to receive the best therapy. Certain patient populations are demanding access to experimental drugs and procedures and feel confident weighing risks and benefits of participation regardless of federal oversight. Consumer activism in experimentation is altering public perception of the ethics of informed consent (Edgar and Rothman 1990; Levine 1994; Hugh Gusterson, personal communication; Susan Kelly, personal communication).
25. In some studies, the goal is to push doses up to the highest tolerable level.
26. Renée Fox has suggested that uncertainty is irreducible beyond a certain point (1959, 1974; personal communication).
27. In that process they also learn about treatment alternatives should they choose not to participate.
28. It is important to note that federal regulations, themselves, have evolved over the years and continue to do so. While 1966 is widely cited as the year in which guidelines were first established, regulatory procedures were modified over the next decade. In 1971 the Department of Health, Education, and Welfare (DHEW) issued an "Institutional Guide to DHEW Policy on the Protection of Human Subjects." In 1974 the US National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research began a four-year process of review and policy development about informed consent

concerns. Institutional review boards were established in most institutions receiving federal funds beginning in 1974 in order to monitor human subject issues in medical research. By 1978 the Commission issued *The Belmont Report*, a set of fundamental ethical principles and guidelines for human research (Beauchamp and Faden 1995; Levine 1986). Throughout the first half of the 1980s, other federal commissions and agencies issued reports refining and creating guidelines for specific populations such as patients with Alzheimer's Disease or other conditions of impairment (High 1992). Thus guidelines and regulations are themselves dynamic processes.

29. Members of the UCSF IRB have asked how a parent can make an 'informed' choice when a child's life is at stake.
30. Renée Fox and Judith Swazey (1974 and 1992), and Renée Fox (personal communication).

REFERENCES

Advisory Committee on Human Radiation Experiments
1995 Final Report. Washington DC: US Government Printing Office (061-000-00-848-9).

Appelbaum, Paul S., Loren H. Roth, and Charles W. Lidz
1982 The Therapeutic Misconception: Informed Consent in Psychiatric Research. International Journal of Law and Psychiatry 5: 319–329.

Appelbaum, Paul S., Loren H. Roth, Charles W. Lidz, Paul Benson, and Willliam Winslade
1987 False Hopes and Best Data: Consent to Research and the Therapeutic Misconception. Hastings Center Report 17: 20–24.

Arnold, Robert M. and Charles W. Lidz
1995 Clinical Aspects of Consent in Health Care. *In* Ency. of Bioethics, rev. ed., Warren Reich, ed. pp. 1250–1256. New York: Simon and Schuster/Macmillan.

Balshem, Martha
1993 Cancer in the Community. Washington DC: Smithsonian Institute Press.

Beauchamp, Tom L. and Ruth R. Faden
1995 History of Informed Consent. *In* Ency. of Bioethics, rev. ed., Warren Reich, ed. pp. 1232–1238. New York: Simon and Schuster/Macmillan.

Beecher, Henry
1966 Ethics and Clinical Research. NEJM 274: 1354–1360.

Beeson, Paul B.
1985 Retrospective Commentary on the Bacterial Endocarditis Study. Reviews of Infectious Disease 7: 574–576.

Blumgart, Herrman L.
1969 The Medical Framework for Viewing the Problem of Human Experimentation. Daedalus 98: 248–274.

Cassell, Eric J.
1986 The Changing Concept of the Ideal Physician. Daedalus 115: 185–208.
1991 The Nature of Suffering and the Goals of Medicine. New York: Oxford University Press.

Cho, Mildred K.
1994 Are Clinical Trials of Cell Transplantation for Duchenne Muscular Dystrophy Ethical? IRB 16: 12–15.

Clifford, James
1986 Introduction: Partial Truths. *In* Writing Culture, James Clifford and George E. Marcus, eds., pp. 1–26. Berkeley: University of California Press.
Clifford, James and George E. Marcus
1986 Writing Culture. Berkeley: University of California Press.
Curran, W.J.
1969 Governmental Regulation of the Use of Human Subjects in Medical Research. Daedalus 98: 542–594.
Dowling, Harry F.
1977 Fighting Infection: Conquests of the Twentieth Century, chapters 8–10. Cambridge: Harvard University Press.
Edgar, H. and D.S. Rothman
1990 New Rules for New Drugs: The Challenge of AIDs to the Regulatory Process. Millbank Q. 68, Supplement 1: 111–142.
Faden, Ruth and Tom Beauchamp
1986 A History and Theory of Informed Consent. New York: Oxford University Press.
Fox, Renée C.
1959 Experiment Perilous. Philadelphia: University of Pennsylvania Press.
1991 The Evolution of American Bioethics: A Sociological Perspective. *In* Social Science Perspectives on Medical Ethics, George Weisz, ed., pp. 201–217. Philadelphia: University of Pennsylvania Press.
Fox, Renée C. and Judith P. Swazey
1974 The Courage to Fail. Chicago: University of Chicago Press.
1992 Spare Parts. New York: Oxford University Press.
Fox, Renée C., Judith P. Swazey and Judith C. Watkins, Eds.
1992 The Study of the Sick: Proceedings of an Oral History Conference on the Development of Clinical Research, 20–22 May 1991. Philadelphia: The Acadia Institute and the Medical College of Pennsylvania.
Frank, Arthur
1995 The Wounded Storyteller. Chicago: University of Chicago Press.
Geertz, Clifford
1988 Works and Lives: The Anthropologist as Author. Stanford: Stanford University Press.
Gordon, Deborah
1994 The Ethics of Ambiguity and Concealment around Cancer. *In* Interpretive Phenomenology, Patricia Benner, ed., pp. 270–322. Thousand Oaks, CA: Sage.
Gotay, Carolyn Cook
1991 Accrual to Cancer Clinical Trials. Soc Sci Med 33: 569–577.
Harth, S.C. and Y. H. Thong
1995 Parental Perceptions and Attitudes about Informed Consent in Clinical Research involving Children. Soc Sci Med 40: 1573–1577.
High, Dallas
1992 Research with Alzheimer's Disease Subjects: Informed Consent and Proxy Decision Making. J Am Geriatr Soc 40: 950–957.
Ivy, Andrew C.
1946 The Brutalities of Nazi Physicians. JAMA 132: 714–715.
Jonas, Hans
1969 Philosophical Reflections on Experimenting with Human Subjects. Daedalus 98: 219–247.

Katz, Jay
1995 Do We Need Another Advisory Commission on Human Experimentation? Hastings Center Report 25: 29–31.
Katz, Jay, Alexander Capron, and E.S. Glass
1972 Experimentation with Human Beings. New York: Russell Sage Foundation.
Kaufman, Sharon R.
1993 The Healer's Tale: Transforming Medicine and Culture. Madison: University of Wisconsin Press.
King, Nancy M.P.
1995 Experimental Treatment. Hastings Center Report 25: 6–14.
Kleinman, Arthur
1988 The Illness Narratives. New York: Basic Books.
1995 Writing at the Margin. Berkeley: University of California Press.
Kodish, Eric, John D. Lantos and Mark Siegler
1990 Ethical Considerations in Randomized Controlled Clinical Trials. Cancer 65: 2400–2404.
Kolata, Gina
1995 Scientists Claim Gene Therapy's First Success. New York Times, 20 October 1995.
Levine, Robert J.
1986 Ethics and Regulation of Clinical Research, 2nd ed., Baltimore: Urban and Schwarzenberg.
1994 The Impact of HIV Infection on Society's Perception of Clinical Trials. Kennedy Institute of Ethics Journal 4: 93–98.
1995 Consent Issues in Human Research. *In* Ency. of Bioethics, rev. ed., Warren Reich, ed., pp. 1241–1250. New York: Simon and Schuster/Macmillan.
Mann, Charles C.
1994 Radiation: Balancing the Record. Science 263: 470–473.
Marcus, George E. and Michael M.J. Fischer
1986 Anthropology as Cultural Critique. Chicago: University of Chicago Press.
McNeill, P.
1993 The Ethics and Politics of Human Experimentation. Cambridge: Cambridge University Press.
Mattingly, Cheryl and Linda C. Garro
1994 Introduction: Narrative Representation of Illness and Healing. Soc Sci Med 38: 771–774.
Moore, Francis D.
1969 Therapeutic Innovation: Ethical Boundaries in the Initial Clinical Trials of New Drugs and Surgical Procedures. Daedalus 98: 502–521.
Paget, Marianne A.
1988 The Unity of Mistakes: A Phenomenological Interpretation of Medical Work. Philadelphia: Temple University Press.
Romano, John
1974 Reflections on Informed Consent. Archives of General Psychiatry 30: 129–135.
Rothman, David
1987 Ethics and Human Experimentation: Henry Beecher Revisited. NEJM 317: 1195–1199.
1991 Strangers at the Bedside. New York: Basic Books.
1995 Research, Human: Historical Aspects. *In* Ency. of Bioethics, rev. ed., Warren Reich, ed., pp. 2248–2258. New York: Simon and Schuster/Macmillan.

Sandelowski, Margaret and Linda C. Jones
1996 'Healing Fictions': Stories of Choosing in the Aftermath of the Detection of Fetal Anomalies. Soc Sci Med 42: 353–361.
Saris, A. Jamie
1995 Telling Stories: Life Histories, Illness Narratives, and Institutional Landscapes. Culture, Medicine and Psychiatry 19: 39–72.
Schain, Wendy S.
1994 Barriers to Clinical Trials. Cancer 74: 2666–2671.
Starr, Paul
1982 The Social Transformation of American Medicine. New York: Basic Books.
Susman, Warren I.
1984 Culture as History. New York: Pantheon.
Taylor, Kathryn M.
1992 Integrating Conflicting Professional Roles: Physician Participation in Randomized Clinical Trials. Soc Sci Med 35: 217–224.
Taylor, Kathryn M., R.G. Margolese, and C.L. Soskolne
1984 Physicians' Reasons for not entering eligible patients in a randomized clinical trial of surgery for breast cancer. NEJM 310: 1363–1367.
UCSF Ad Hoc Fact Finding Committee
1995 Report on World War II Human Radiation Experiments. UCSF, February.
Welsome, Eileen
1993 The Plutonium Experiment. The Albuquerque Tribune, A Three-Part Report, 15–17 November 1993.
Young, Katharine
1987 Taleworlds and Storyrealms: The Phenomenology of Narrative. Dordrecht: Martinus Nijhoff.

Address for correspondence: Sharon R. Kaufman, Deptartment of Social and Behavioral Science, Medical Anthropology Program, University of California, San Francisco, CA 94143-0612, USA
Phone: (415) 476-3005; Fax: (415) 476-6552; E-mail: kaufman@itsa.usf.edu