

Chapter 17

THE COLD WAR AND BEYOND: COVERT AND DECEPTIVE AMERICAN MEDICAL EXPERIMENTATION

SUSAN E. LEDERER, PhD*

INTRODUCTION

THE DISCLOSURE OF BIOMEDICAL RESEARCH PROGRAMS

HUMAN EXPERIMENTATION IN THE UNITED STATES BEFORE 1940

Research Conducted by the Military
Government-Sponsored Research

RESEARCH TO SUPPORT THE AMERICAN WAR EFFORT

Research on Chemical Warfare Agents
Research on the Prevention and Cure of Infectious Diseases
The Increasing Concern About Research Risk and Liability

THE POSTWAR WORLD AND “CRIMES AGAINST HUMANITY”

The Judgment at Nuremberg
The Impact of the Nuremberg Tribunal on the American Medical Research Community
Expansion of Rules to Protect Research Subjects
Public Health Service Exemption From Research Controls: The Tuskegee Study

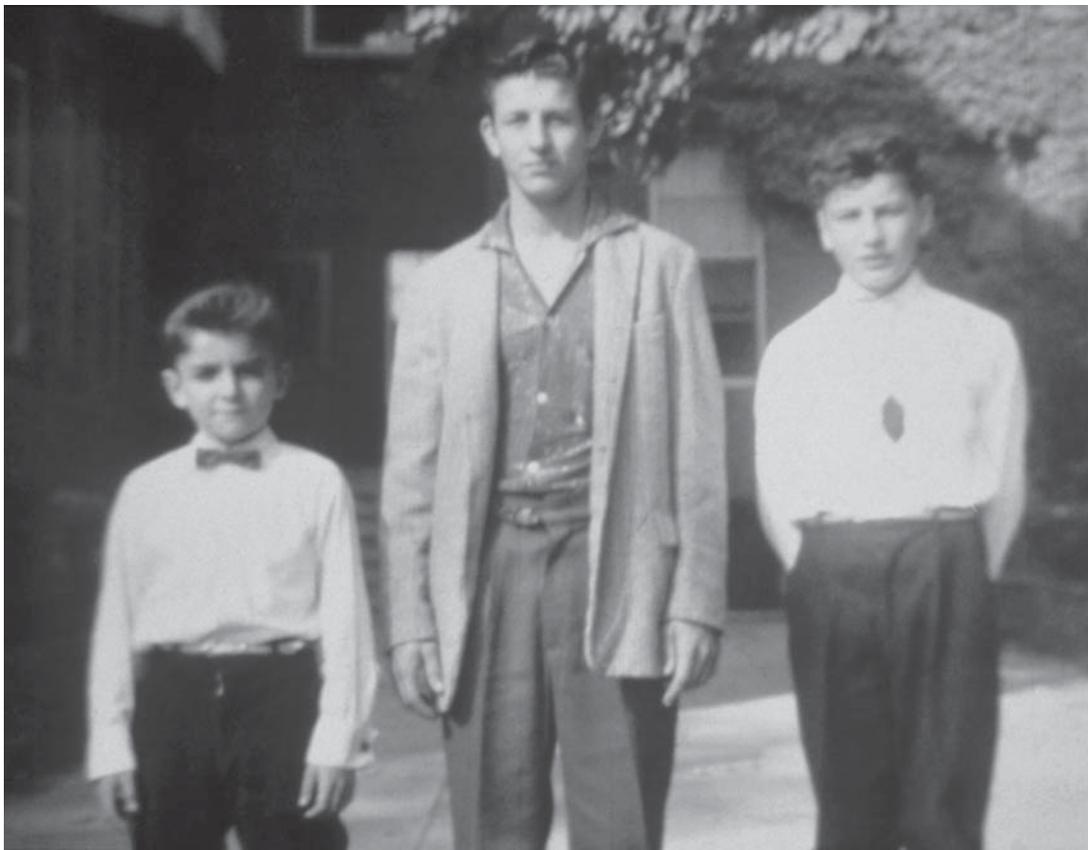
HUMAN EXPERIMENTATION DURING THE COLD WAR ERA

The Nuremberg Code and the United States Government
The Human Radiation Experiments
The Central Intelligence Agency and “Mind-Altering” Substances
The US Army and Biological Warfare Tests in America

SECRECY AND SCIENCE

CONCLUSION

*Formerly, Member (1994 to 1995), President’s Advisory Committee on Human Radiation Experiments; currently, Assistant Professor, Section of the History of Medicine, Yale University School of Medicine, Yale University, 333 Cedar Street, New Haven, Connecticut 06520-8015



More than 70 boys, including these three, at the Fernald State School in Waltham, Massachusetts, participated in tests with cereals containing radioisotopes of iron and calcium. These studies, sponsored by Quaker Oats and the Atomic Energy Commission, were conducted by investigators at the Massachusetts Institute of Technology during the Cold War.

Photograph reproduced with permission from Brooks Kraft/Sygma Corbis.

INTRODUCTION

The three previous chapters in this volume have examined medical experimentation during the 1930s and 1940s in Germany and Japan. It is likely that most readers already knew something of the German biomedical experiments (although perhaps less so of the physicians' leadership in these experiments). It is also possible that many readers knew some of the details of the Japanese biomedical programs (although perhaps less so of the US utilization of the data from these programs). Some readers may wonder why a chapter on covert and deceptive American medical experimentation would immediately follow the graphic descriptions of German and Japanese medical atrocities. Is it my intent to suggest that American transgressions were of similar magnitude or horror? Would such a suggestion not only unfairly characterize the American efforts, but also diminish the horror of the German and Japanese atrocities? It is not my intent to do either, but rather to put these events in perspective.

If, as a country, there is a desire to portray the German and Japanese biomedical experimenters as "evil," and American medical experimenters as "patriotic," or, given the context of the times, their motives as "understandable," then it is important to explore the American medical research community in the 20th century, particularly as it evolved after the end of World War II. If there is indeed a

continuum, or a "slippery slope," of medical excesses toward medical atrocities, then it is imperative that the past activities of the American medical research community be examined.

How is it that the average American could know so much about the German programs and, until recently, so little about the American programs? How is it that the German research programs have been viewed by many as the very embodiment of "evil medicine," while disclosures of unethical American research do not seem to engender the same visceral reaction among the American public as a whole? Is it because American programs were somehow more ethical or is it because in America there was a different standard or a different perception of America's values and its role in the world? These are troubling issues to consider. The first step in such a consideration is to understand the programs themselves.

I will explore covert and deceptive medical experimentation programs as they occurred in the United States before, during, and after World War II. The decisions to conduct these programs were made in the context of the world as it was then. The task now is what can be learned from those decisions to conduct deceptive research, and the human consequences of those actions, to prevent the recurrence of such programs.

THE DISCLOSURE OF BIOMEDICAL RESEARCH PROGRAMS

The experimentation programs in Germany were divulged in stark detail during the Nuremberg Trials that followed Germany's surrender. Among American physicians, the barbarities of the Nazi medical program were also viewed as an aberration. Simply put, this was something that had happened in another place, another culture, a different form of government. It had happened there, but it couldn't happen anywhere other than there, at that time, and in those circumstances. That was now in the past, although it certainly had to be remembered. But as long as it was remembered, it couldn't happen again. And it certainly couldn't happen in any country that had moral and decent citizens and a democratic government, which was how most Americans saw themselves and their country in those years immediately after the end of the war when America had "saved the world from fascism."

Most of the American public at war's end had little, if any, knowledge of the Japanese biomedical research programs that were conducted during this

same time. There was no American or Allied trial of Japanese doctors comparable to the Nuremberg Tribunal, other than a brief trial in the former Soviet Union. There were the tribunals that convicted members of the Japanese military for their involvement in the war, but none targeting the medical establishment. And, just as importantly, there was a tremendous amount of work to be done to rebuild devastated countries. Transportation systems, manufacturing bases, housing, food, and medical needs all had to be addressed. It was easy to assume that the only physicians who had conducted these heinous experiments had been in Germany, and most had been held accountable by the tribunals.

There were other reasons, as well, that the public did not know about the biomedical research programs conducted by the Japanese. Foremost, as detailed in Chapter 16, it was believed to be in America's best interests to utilize the results of the Japanese programs in America's ongoing preparation for confrontation with the former Soviet Union.

Although it had been an ally during World War II, there were no misconceptions about the threat it posed once the war had ended. And although Allied forces had captured Japanese biomedical experimenters at the end of World War II, Soviet forces had taken control of their remaining research facilities and reports. The American government was actively seeking to prevent Soviet knowledge of the Japanese germ warfare tests. A tribunal would have seriously undermined this attempt at secrecy.

The US government had a need to maintain weapons' superiority, and if not superiority, then at least "parity" with the Soviets in any future conflict. These weapons systems included nuclear, biological, and chemical weapons. The US government also saw little need to let the Soviets know what information the Americans had garnered from the Japanese, or to let the American public know that its government was willing to negotiate with the Japanese doctors to gain their information, rather than arresting, trying, and punishing them for their deeds. It was easier and more prudent to simply keep quiet about the Japanese biomedical research.

Thus at war's end, Americans observed the Nuremberg Trials, saw that there were verdicts and punishments meted out, and continued with the task of reestablishing lives that had been disrupted for 4 years during the war. Few if any Americans had any real sense of what their own government had done during those war years, or in the years that followed as the Cold War drug on.

In 1972, as the war in Vietnam wound down and America struggled with the divisiveness that the war had fostered, the public learned of the Tuskegee Syphilis Study. After public disclosure and the report of the Ad Hoc Tuskegee Syphilis Study Panel, the Secretary of the Department of Health, Education, and Welfare terminated the study in 1973. Many Americans were dismayed at the revelation of the study, which had documented the course of untreated syphilis in black men. There was a prevailing sense of outrage that a program that had begun in the 1930s, and clearly seemed racist by standards in the 1970s, could have continued for so long without being halted. There was, however, another prevailing sense: that this was a relatively isolated event, that it could be explained away as something sinister and racially motivated from a previous generation, and that although shameful, it was not indicative of a broader problem within the American medical research community.

It was not until 1994 that most Americans had any real understanding of the magnitude of covert and deceptive medical research that had been on-

going in this country throughout most of the Cold War. In 1994, President William J. Clinton announced that based on information provided to him by Hazel O'Leary, his Secretary of Energy, he was appointing an Advisory Committee on Human Radiation Experiments. The Committee was tasked to explore and document research activities that had begun in the late months of World War II and continued for the next 30 years. I was an appointed member of that committee.

The committee held 16 public meetings and 4 field hearings in 18 months.¹ During that time, the committee researched archival records; the radiation experiments (an estimated 4,000 different studies in all) were examined in detail. We presented our final report, 900 pages in length, summarizing the scope and mass of the research efforts during the Cold War to the president in 1995. After receiving the report, President Clinton apologized to the men, women, and children who had participated in human radiation experiments sponsored by the United States government in the years between 1944 and 1974. Acting on the recommendations of the committee, Clinton acknowledged the Cold War legacy of mistrust and suspicion fostered by government-sponsored radiation experiments, and announced the establishment of the National Bioethics Advisory Commission to insure the future protection of human subjects in biomedical research.² In 1997 President Clinton formally apologized on behalf of the American people to another group of Americans: the participants in the Tuskegee Syphilis Study and their families.

Both the Tuskegee Syphilis Study and much of the radiation research involving human subjects were not covert projects in the strict sense. Results from the Public Health Service (PHS) syphilis study, for example, were published in the medical press (some 13 articles appeared in all from 1936 to 1973). In the popular press in the 1950s and 1960s, reporters described human radiation experiments as "burn" studies (conducted on both African-American college students and white medical students³) and blood studies (involving radioisotopic iron performed on inmates at a state prison⁴). The apparent openness of these and other studies, however, has been contested by many of the participants or their families who insist that they had little understanding of their role in this research, and little knowledge of the risks involved in their participation.

In light of the often imprecise dividing line between covert and openly conducted studies, this chapter includes both those performed clandestinely under federal auspices, as well as studies like

many of the human radiation experiments that were carried out without a security “blanket.” There are two compelling reasons for this inclusion. First, the fact that studies like the syphilis study were not secret should not obscure the deceptions researchers engaged in to secure the cooperation of their subjects when they were alive and the inducements to procure familial cooperation once the subjects were dead. Second, many of the reforms and protections subsequently undertaken to insure the ethical conduct of research involving human subjects have occurred as a result of disclosures about experiments such as the human radiation experiments that were not fully understood by participants in the projects or the general public.

This chapter examines the American experience with human experiments performed in the decades between the 1940s and the 1990s. It begins with the research climate as it prevailed on the eve of Ameri-

can entry into World War II and moves on to a review of the rules for research during wartime. In addition, the chapter considers the creation of the landmark rules for ethical human experimentation in the immediate postwar period, the Nuremberg Code, produced amid the prosecution of 23 medical defendants at the Doctors’ Trial in Nuremberg in 1947. Finally, the chapter considers the conduct of human experimentation in the shadow of Nuremberg, including human radiation experiments—covert and noncovert—sponsored by the United States government, LSD (lysergic acid diethylamide) studies sponsored by Central Intelligence Agency, and biological warfare tests performed on American soil. Only by examining this subject can the medical community, including the military medical community, prevail in preventing the recurrence of such covert and deceptive medical experimentation.

HUMAN EXPERIMENTATION IN THE UNITED STATES BEFORE 1940

On the eve of American entry into World War II, human experimentation remained a small-scale enterprise, involving only limited numbers of medical researchers and human subjects. Much of the research effort in the first four decades of the 20th century was directed at the infectious diseases that continued to threaten American lives and interests, and most of the experiments devised by physicians and researchers were conducted on small numbers of human subjects. Much of the research conducted in this period involved self-experimentation or the use of colleagues and students as research subjects. In other cases, researchers turned to their own family members. In the search for an effective polio vaccine, for example, pathologist John A. Kolmer tested his polio vaccine on himself, his two children, and 23 other children “all immunized at the request or with the written consent of their parents,”^{5(pp107-108)} before proceeding to a larger trial involving some 300 children.

Research Conducted by the Military

Among the most ambitious and successful human experiments conducted in the early 20th century were those sponsored by the US Army. In 1900, Major Walter Reed and his colleagues in the Yellow Fever Board in Havana used American soldiers and Spanish volunteers to document the mode of transmission of yellow fever, which remained a significant detriment to American interests in the Caribbean. Reed developed a novel approach to exposing vol-

unteers to the risk of yellow fever; he drew up a written contract available in Spanish and English that identified the risks and benefits in the yellow fever studies (see Figure 17-1). Although this novel departure would not meet the current federal standards of informed consent for participation in research, Reed’s contract illustrates that rules for research, especially research undertaken without therapeutic benefit to the individual, existed among members of the research community at the turn of the century.

Government-Sponsored Research

Not all research in American-occupied territories turned out as satisfactorily as Reed’s expedition. In the American-occupied Philippines, American researcher Richard P. Strong exploited the availability of inmates in a Manila prison to test a newly available cholera vaccine. In 1906 Strong inoculated 24 men with an experimental cholera vaccine; all the men fell ill and 13 died. The vaccine was later shown to be contaminated with live plague organisms. Apparently the first American to use prisoners for medical research, Strong was subjected to a lengthy investigation and eventually exonerated, although members of the investigating committee believed he had overstepped the bounds of his authority by subjecting the prisoners to an experimental vaccine. In subsequent studies, including a 1912 study of beriberi also involving inmates from Manila’s Bilibid Prison, Strong proceeded with

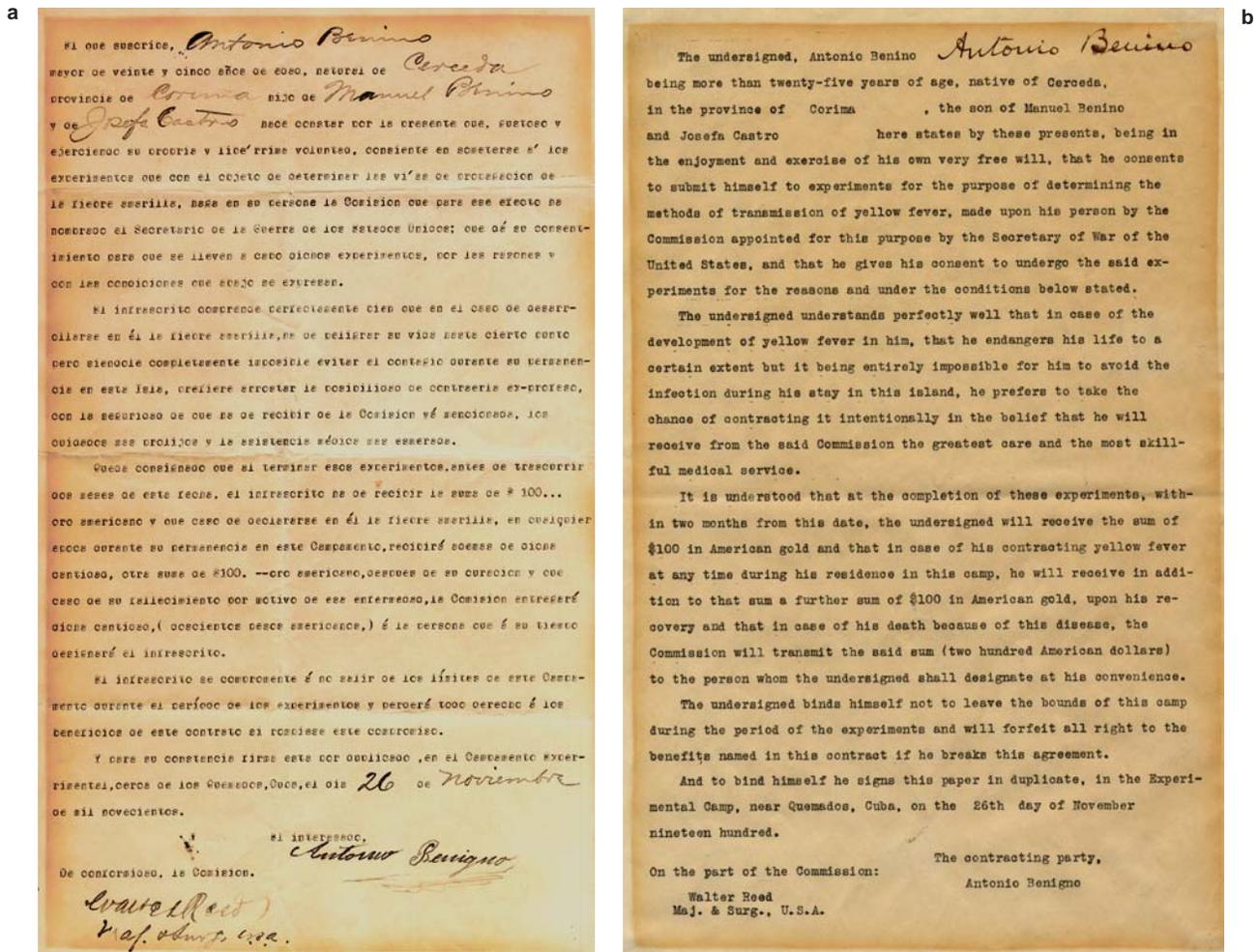


Fig. 17-1. Consent form, completed in Spanish, dated, and signed by both the subject and the experimenter (a). Consent form, translated into English, dated, but not signed (b). Courtesy of Historical Collections and Services, The Claude Moore Health Sciences Library, University of Virginia, Charlottesville.

greater caution, obtaining from each of the prisoners a written statement affirming the voluntary nature of his participation and his willingness to complete the studies.⁶

Government-sponsored research also occurred within the continental United States. In 1932, the Public Health Service (PHS) began the longest running nontherapeutic research study in American history, the Tuskegee Syphilis Study. Initially intended to shed light on racial differences in the natural history of syphilis, the study entailed periodic clinical observations of more than 400 African-American men diagnosed with secondary syphilis who were not receiving treatment for their disease. In order to insure the “success” of the no-treatment study, scientists in the Venereal Disease Division at the Public Health Service actively misled their male

subjects about the nature of their participation in the project. The men, for example, were informed they had “bad blood” rather than syphilis, and they were asked to undergo lumbar puncture, a “special treatment” for their condition. Lumbar puncture is not a treatment but a purely diagnostic procedure involving removal of spinal fluid for testing. When penicillin became available in the 1940s, government scientists took steps to ensure that the men in the study did not receive this new and effective drug. The ethical violations of the Tuskegee study are addressed in detail in the chapter subsection titled “PHS Exemption From Research Controls: The Tuskegee Study.” It is important to note that the legacy of the Tuskegee study still resonates strongly within the African-American community. The study has become a powerful symbol of the exploitation

of unsuspecting and vulnerable African-Americans at the hands of the white medical establishment.^{7,8}

During the 1930s, prisoners in both state and federal prisons in the United States also participated in research on infectious disease. In 1933, researchers at the National Jewish Hospital in Denver tested a newly developed vaccine for tuberculosis on inmates of the Colorado State Prison. In order to gain access to this population, the researchers negotiated with the governor's office and agreed to recruit their subjects using a written consent form drafted by the state attorney general. The document indicated each prisoner understood the potential risks of his participation, and agreed to do so voluntarily and without coercion. From the researcher's point of view, convicted criminals offered considerable advantages as research subjects. They could be readily monitored in conditions controlled by researchers.

In the 1930s, some researchers viewed prisoners in federal penitentiaries as similarly attractive subjects for infectious disease research. In 1933, when St. Louis experienced an epidemic of the encephalitis that would come to be known as St. Louis encephalitis, researchers from the Public Health Service were dispatched to the city to discover how the disease was transmitted. After submitting their own bodies to mosquitoes fed on the blood of those infected with the disease, investigators sought additional subjects. Surgeon General Hugh Cumming approached Sanford Bates, Director of the Federal Bureau of Prisons, for

permission to obtain volunteers at federal prisoners. Bates, however, would not authorize such studies on the grounds that prisoners were not in a position to consent freely and without duress to such research. Ironically, research on federal prisoners was sanctioned at two large facilities built for federal prisoners suffering from drug addiction. In cooperation with the Federal Bureau of Prisons, the Public Health Service built hospitals in Lexington, Kentucky and Fort Worth, Texas where prisoners participated in research for information about the nature of drug addiction and its treatment. Unlike the encephalitis studies, the studies on narcotic addiction offered the possibility of some therapeutic benefit for the prisoners.

In summary, before 1940, most human experiments involved relatively small numbers of research subjects and participants. At no time were investigators completely free to do whatever they pleased with their research subjects. In research involving risk without therapeutic benefit, researchers were expected to have the knowledgeable permission of their research subjects. To be sure, not all investigators adopted the practice instituted by Walter Reed of using written consent documents to ensure that participants recognized the risks and benefits of their role as subjects, but clearly many investigators (though not all, as evidenced by the Tuskegee Syphilis Study) recognized a responsibility for the welfare of their subjects and hesitated to place subjects at risk in experiments.

RESEARCH TO SUPPORT THE AMERICAN WAR EFFORT

Even before the bombing of Pearl Harbor and the subsequent declaration of war, American authorities began to prepare for war in Europe and the Pacific. Part of the humanitarian effort to aid the Allied forces and civilians was a massive collection of plasma for British soldiers and civilians, known as the "Blood for Britain Program."⁹ On other fronts, the American entry into the war signaled an unprecedented coordination of scientific research under federal auspices. In 1941 President Franklin D. Roosevelt established the Office for Scientific Research and Development (OSRD). Led by Vannevar Bush, former dean of engineering at the Massachusetts Institute of Technology, the OSRD's mission was the coordination, funding, and oversight of scientific research for the American war effort. Within the OSRD, the Committee on Medical Research (CMR) was dedicated to wartime medical investigations. Chaired by University of Pennsylvania pharmacologist Alfred Newton Richards, the CMR distributed over \$24 million to 137 institutions

in the United States, the District of Columbia, and the Panama Canal Zone. Among the funding priorities of the CMR was research on chemical warfare agents and the prevention or cure of infectious diseases, especially those likely to be encountered by the armed forces.

Research on Chemical Warfare Agents

Amid vivid memories of mustard gas deployment by the Germans during World War I, the American government readied itself for chemical warfare, conducting extensive research into gas warfare agents. The tests were aimed at prevention, amelioration, and effect of the agents. The tests involved putting agents on human subjects, either with or without test ointments, as well as tests in which human subjects wore suits impregnated with chemicals designed to retard vapor penetration. By the time the war had ended in 1945, more than 60,000 American service personnel had been ex-

posed to mustard gas (sulfur and nitrogen mustard) and Lewisite (an arsenic-containing agent) as part of a large-scale research effort. More than 4,000 servicemen had participated in trials using high concentrations of mustard gas or Lewisite, or in exercises conducted in contaminated areas. The men, whose exposures to these toxic gases ranged from mild to severe, were instructed not to disclose their participation in these trials. For more than 40 years, they continued to keep the nature of their exposure secret. In 1991 an expert committee of the Institute of Medicine (IOM), National Academy of Science, reported there was evidence of a causal relationship between exposure to these chemical agents (mustard gas and Lewisite) and the development of respiratory cancers (including lung, laryngeal, and nasopharyngeal), skin cancer, leukemia, chronic respiratory disease (including asthma and emphysema), and a variety of eye diseases.¹⁰

As the IOM committee's extensive report amply revealed, the men recruited into these studies did so with only limited information about the possible physical and mental effects of their exposure.

Although the human subjects were called "volunteers," it was clear from the official reports that recruitment of the World War II human subjects, as well as many of those in the later experiments, was accomplished through lies and half-truths.^{10(pvii)}

At the Naval Research Laboratory (NRL), for example, soldiers were induced to take part in the gas chamber tests by offers of extra leave and the promise of a "change in scenery." Recruiters were explicitly instructed not to give too much information at the beginning of the experiments, so as not to deter the subjects from participation. Records from the gas chamber work at the NRL indicate that some men experienced severe injuries as a result of their exposure. Perhaps it is not surprising, therefore, that morale became a problem for experimenters. Official reports from the facility provided instructions for managing uncooperative individuals, including administering a "short, explanatory talk and if necessary, a slight verbal 'dressing down.'"^{10(p67)} Despite the knowledge that exposure to these agents produced long-term, debilitating physical effects, the Department of Defense conducted no follow-up, either short-term or long-term, of the effects, and instead swore the men to secrecy. The extensive nature of the World War II research program into chemical warfare became public knowledge only when several veterans approached the Veterans Administration seeking compensation for health injuries resulting from their exposure to the gases.

Research on the Prevention and Cure of Infectious Diseases

In addition to chemical warfare agent research, the CMR funded research projects investigating such infectious diseases as malaria, influenza, dysentery, and sexually transmitted diseases. Many of the human subjects for research into new vaccines for these diseases were not military personnel but civilians, especially children housed in custodial institutions. Cincinnati physicians Merlin Cooper and B.K. Rachford, for example, used children in the Ohio Soldiers and Sailors Home in trials of an immunizing agent effective against dysentery. Utilizing different suspensions applied in different ways (intravenous, intramuscular, and subcutaneous), the researchers caused severe reactions in the children tested, effectively eliminating the vaccine for use among soldiers. Dysentery projects funded by the CMR were also performed at the Dixon Institution for the Retarded, in Illinois, and the New Jersey State Colony for the Feeble-Minded. Indeed, having access to a custodial population where such diseases could be studied enhanced the status of a grant application to the Committee. In some of the trials funded by the CMR, vaccine tests were accompanied by deliberate challenge with the infectious agent. When Werner Henle conducted trials of a vaccine against influenza A he administered the vaccine to children housed in a state facility for the retarded and a correctional institution for youthful offenders. Some of the subjects developed painful nodules at the site of injection.¹¹ Three to six months after the vaccine was administered, residents were fitted with a aviation oxygen mask and exposed to a preparation of the virus for 4 minutes. Some of the subjects developed influenza.¹¹

The Increasing Concern About Research Risk and Liability

In 1942 the National Research Council's Subcommittee on Venereal Disease approached A.N. Richards soliciting the CMR's stance on human experimentation. Such experimentation, Richards informed syphilologist Joseph Earle Moore, was not only desirable, but necessary in light of wartime demands. But Richards also noted that only volunteers should be used as subjects when the experiment posed any risks, and

only after the risks have been fully explained and after signed statements have been obtained which shall prove that the volunteer offered his services with full knowledge and that claims for damages will be waived.^{12(p73)}

Richards also noted the necessity of maintaining a complete record of the “terms in which the risks involved were described.”^{12(p73)}

Richard’s explication of the CMR’s attitude toward human experimentation makes clear the continuing commitment of American researchers to informing volunteers about risks resulting from participation in nontherapeutic research. But it also illustrates a new concern—the issue of liability to a volunteer in case of an adverse outcome—that many researchers began to experience in this period of increasing medical research involving human subjects. Richards had already confronted the problem in the context of wartime experiments involving the search for a blood substitute.

Despite the massive blood collection efforts, the search for an effective blood substitute continued apace during World War II. At the behest of the National Research Council, Harvard protein chemist Edwin Cohn and his team developed a blood substitute, based on bovine albumin, that had considerable promise. After some initial testing of the blood substitute on Harvard medical students and hospital patients in Boston and Minneapolis, the researchers employed Massachusetts prisoners as research subjects. At Cohn’s behest, lawyers for the OSRD met with agents from Lloyd’s of London concerning insurance coverage to indemnify Harvard University against possible financial losses resulting from the research effort. When Lloyd’s agreed to write such a policy for a premium of \$2,000, Harvard officials concluded the cost for the insurance was too high, and conducted the research without insurance coverage. As historian Jon Harkness has shown, the decision haunted university researchers and administrators when one of the prisoner-subjects died on 30 September 1942 as a result of his participation. In a strange turn of events, prisoner Arthur St. Germaine received a posthumous pardon in light of his participation as a research subject, and his burial expenses were charged to Edwin Cohn’s CMR grant.

The unfortunate death of a research subject did not stop human experimentation under CMR auspices, but it inspired some caution on the part of administrators like Richards and Vannevar Bush. When two investigators proposed to infect prisoners with gonorrhea to study the results of chemical prophylaxis of a disease that cost the armed services thousands of man-hours, the CMR conducted an intensive discussion about the political and ethical ramifications of such experimentation with human subjects. The gonorrhea studies would not be the only ones in which the political consequences

of such experimentation received the same consideration as the ethical. In the case of wartime and postwar human radiation experiments, for example, the issue of public relations, rather than national security or the ethics of human experimentation, influenced the decision to keep some experiments hidden from public scrutiny. After protracted discussion about the legality, expediency, and ethical dimensions of the study, the gonorrhea experiments, including the experimental infection of male volunteer inmates, began in 1943. For their willingness to undergo intra-urethral inoculations of gonococci, the prisoners received the sum of \$100, a certificate of merit, and a letter of commendation was forwarded to their parole board.

In summary, hundreds, if not thousands, of Americans—soldiers, prisoners, conscientious objectors, orphans, and the institutionalized mentally ill and mentally handicapped—participated in medical research during World War II. But such research did not take place in an ethical vacuum nor did it occur without consideration of the rights of research subjects and the responsibilities of individual researchers. Some of the research subjects did experience adverse outcomes without adequate understanding of the risks they incurred as a result of the investigations (this was especially true of the work performed using children and mentally incapacitated adults), but this failure should not obscure the fact that the American research community recognized ethical limits in the use of human subjects. Nonetheless, the line between acceptable and unacceptable experiments remained ambiguous. As should be apparent from this discussion, during this period there was inadequate professional guidance to influence these behaviors. What, then, had been the role of the organized medical profession in these research studies?

In 1916 leaders of the American Medical Association (AMA) had briefly considered amending the organization’s code of ethics to include a provision on human experimentation calling for the knowledgeable permission of the subject. The AMA leadership decided not to adopt such a stance believing it both unnecessary in light of the good moral character of American medical researchers and undesirable insofar as such a requirement would impede the progress of medical research.⁵ Despite the decision to forego codifying a position on human experimentation, there existed through World War II an informal, if unwritten, consensus that required consent from healthy subjects when their lives or well-being were potentially threatened by participation in research and responsibility for the welfare of patients who took part in therapeutic studies.

THE POSTWAR WORLD AND “CRIMES AGAINST HUMANITY”

In December 1946, as part of the preparation for the prosecution of 23 Nazi medical defendants at Nuremberg and acting on the advice of its Judicial Council, the American Medical Association (AMA) House of Delegates adopted a formal position on human experimentation. Three conditions had to be satisfied to conform to the ethics of the AMA: (1) the voluntary consent of the individual participating in an experiment had to be secured; (2) previously conducted animal experimentation to ascertain the risks for human subjects had to be reviewed; and (3) the requirement that the research be conducted under proper medical supervision had to be met. The AMA's decision to take this step reflected the behind-the-scenes work of University of Illinois pharmacologist Andrew C. Ivy, who served as one of the principal American advisors to the team of lawyers prosecuting the Nazi physicians. In his capacity as medical adviser to the American prosecutors, Ivy himself underwent tense cross-examination by the German attorneys defending the Nazi doctors, and was called on to explain the reliance of American investigators on prisoners and conscientious objectors as research subjects.¹³ One of the prosecution witnesses, Werner Leibrand, was also questioned on this issue of voluntary participation, as detailed in Exhibit 17-1.

The Judgment at Nuremberg

Part of the final judgment at the Nuremberg Doctors Trial was a set of 10 principles that have come to be known as the Nuremberg Code¹⁴ (Exhibit 17-2). The Nuremberg doctors' trial was essentially an American activity; the judges were all American jurists who relied on their American experts—Ivy and Alexander—to come up with the standard by which to judge the Nazi crimes. The 10 principles in the code set the parameters for ethical human experimentation. The first principle (and the most frequently cited) states that the voluntary consent of the human subject is absolutely essential. Moreover, the human subject in question must be in a position to exercise autonomous decision making, possess the legal capacity to consent to experimentation, and should be presented sufficient information and knowledge to make an informed choice. In addition to the insistence on the knowledgeable participation of an autonomous decision maker, the other principles required investigators to conduct animal experimentation to establish in advance the

risks and utility of experiments on humans, to proceed only when the risk of the procedure is balanced by “the humanitarian importance” of the problem to be solved by experiment, and to be prepared to terminate the experiment at any stage if the experiment seems likely to result in death or injury to the research subject.

The Impact of the Nuremberg Tribunal on the American Medical Research Community

Bioethicists George Annas and Michael Grodin have called the trials of the Nazi physicians “the most important historical forum [ever] for questioning the permissible limits of human experimentation.”^{15(p3)} The Nuremberg Code has become an important milestone in the history of research ethics, but what did it mean to American investigators far removed from the Nazi death camps and the Nuremberg courtroom?

The Nuremberg Medical Trial, like the trials of other Nazi officials, was reported in the American popular press. Moreover, magazines and newspapers published “human interest” stories about the victims of the Nazi experimenters, including the “Ravensbrueck lapins,” the 74 young Polish women used by Nazi medical researchers in experiments on bone and muscle transplantation and wound infection.¹⁶

Such coverage, however, was hardly exhaustive. When the Advisory Committee on Human Radiation Experiments interviewed a number of medical investigators in 1995 about the import of the Nuremberg Code in their working lives in the late 1940s, few had vivid recollections of the trial and its implications for their own work. One exception was Dr. Herbert Abrams, a radiologist who was completing his residency at Montefiore Hospital in the Bronx during the trial. Dr. Abrams, recalling the extensive reportage of the trial, emphasized that the Doctors' Trial was something “we were aware of and that affected the thinking of everyone who was involved in clinical investigation.”¹⁷

It is perhaps not surprising that the atmosphere of Montefiore Hospital would be influenced by the trial. As a traditionally Jewish hospital, it had become home to a number of refugee Jewish physicians who fled Germany in the early years of the Nazi regime. For most American investigators, however, the trial seemingly exerted little impact; it involved doctors and human subjects in a differ-

EXHIBIT 17-1

THE ISSUE OF “VOLUNTARY PRISONER PARTICIPATION” RAISED BY THE DEFENSE AT THE NUREMBERG TRIBUNAL

One of the issues raised during the testimony of Andrew C. Ivy was American reliance on prisoners as subjects of medical experiments. The issue of prisoner experimentation arose during the questioning of Werner Leibbrand, a German psychiatrist and medical historian. American prosecutors hoped that Leibbrand, who had been persecuted by the Nazis, would establish the deleterious effects of Nazi dictatorship on the German medical profession. In his cross-examination of the German physician, Robert Servatius, the German attorney defending Karl Brandt (Hitler’s personal physician) questioned Leibbrand at length about the voluntary participation of prisoners in research.^{1(pp67-69)}

- Servatius: Witness, are you of the opinion that a prisoner who had over ten years’ sentence to serve will give his approval to an experiment if he receives no advantage there from? Do you consider such approval voluntary?
- Leibbrand: No. According to medical ethics, this is not the case. The patient or inmate [is] basically brought into a forcible situation by being arrested ...
- Servatius: Are you of the opinion that eight hundred prisoners under arrest at various places who give their approval for an experiment at the same time do so voluntarily?
- Leibbrand: No.
- Servatius: You do not distinguish as to whether the experiments involve permanent damage ... or whether it is temporary?
- Leibbrand: No.
- Servatius: If such prisoners are infected with malaria because they declared themselves willing do you consider that admissible?
- Leibbrand: No, because I do not consider such a declaration of willingness right from the point of view of medical ethics. As prisoners they were already in a forced situation.

Servatius’s question about infection with malaria became clear when he confronted the German witness and the American jurists with the 4 June 1945 issue of the American periodical *Life* magazine. This issue featured several photographs of the inmates of prisons in Georgia, New Jersey, and Illinois, participants in a federally sponsored malaria research program. After his discussion of the prison malaria experiments and citations to other American experiments involving prisoners, Servatius pointedly asked Leibbrand about the acceptability of such experiments on a captive population:

- Servatius: Now will you please express your opinion on the admissibility of these experiments?
- Leibbrand: On principle I cannot deviate from my view mentioned before on a medical, ethical basis. I am of the opinion that such experiments are excesses and outgrowths of biological thinking.

By this line of questioning, Servatius sought to establish the similarities of the concentration camp experiments with the research conducted in American prisons, thereby mitigating the degree of Nazi culpability. Despite this effective cross-examination, the American judges at Nuremberg found Karl Brandt and 15 of his colleagues guilty of war crimes and medical crimes.

To reach their conclusions about the guilt and innocence of the medical defendants, the judges articulated a set of ten principles of “Permissible Human Experiments.” These principles, which were formulated in the pre-trial preparation and during the trial itself, have come to be known as the Nuremberg Code. In developing the principles, the American judges at Nuremberg relied heavily on two American physicians, the physiologist Andrew C. Ivy and psychiatrist Leo Alexander.²

Sources: (1) Moreno JD. *Undue Risk: Secret State Experiments on Humans*. New York: Routledge; 2001. (2) Weindling P. The origins of informed consent: The International Scientific Commission on Medical War Crimes, and the Nuremberg Code. *Bull Hist Med*. 2001;75:37-71.

EXHIBIT 17-2

THE NUREMBERG CODE

In their book, *the Nazi Doctors and the Nuremberg Code*, Annas and Grodin discussed the American influence on the formation of the Code.^{1(p135)}

At the Nuremberg Doctors' Trial, the American prosecutors relied on two expert American witnesses, the Chicago physiologist Andrew C. Ivy and Boston neurologist and psychiatrist Leo Alexander. For the benefit of the American lawyers, Alexander wrote a 6-point memorandum entitled "Ethical and Non-Ethical Experimentation on Human Beings." The similarity between Alexander's memorandum and the rules for permissible human experimentation (what would come to be known as the Nuremberg Code, [shown below]), especially his first principle that the "legally valid voluntary consent of the experimental subject is essential" have prompted some authors to credit Alexander with the primary authorship of the Nuremberg Code. However, in his summation, chief prosecutor James McHaney relied on both Andrew's memorandum and the testimony supplied by Andrew Ivy during the trial to argue the guilt of the Nazi physicians.

Directives for Human Experimentation

NUREMBERG CODE²

1. The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonable to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment.
The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.
2. The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.
3. The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.
4. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.
5. No experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects.
6. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.
7. Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.
8. The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.
9. During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.

(Exhibit 17-2 continues)

Exhibit 17-2 *continued*

10. During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of the good faith, superior skill and careful judgment required of him that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.

Sources: (1) Annas GJ, Grodin MA. *The Nazi Doctors and the Nuremberg Code: Human Rights in Human Experimentation*. New York: Oxford University Press; 1992. (2) Reprinted from *Trials of War Criminals Before the Nuremberg Military Tribunals Under Control Council Law No. 10*. Vol. 2. Washington, DC: US Government Printing Office; 1949: 181–182.

ent country in a different time, and had little relevance to the search for new drugs and procedures to cure human ills.

The disparity between events in wartime Germany and efforts in postwar America was furthered by the American popular press, which helped sustain an image of human experimentation as a noble, if potentially risky, enterprise as practiced in American hospitals and medical schools. In the years between 1948 and 1960, popular magazines like *The Saturday Evening Post*, *Readers Digest*, and *American Mercury* featured stories about “human guinea pigs” and self-sacrificing scientists who willingly exposed their own bodies to risk for the benefit of science.¹⁷

In 1952, for example, the *New York Times* reported the death of an 18-year-old college honor student at the University of Washington, one of 40 volunteers in “an experiment connected with war research on blood preservation.” What is remarkable about the short article is the matter-of-fact reporting of the boy’s death, the willingness of the physicians—Robert H. Williams and Clement Finch—to “gladly participate in the same experiment tomorrow,” and the father’s insistence that he held no one at fault for his son’s death. Rather than blame the investigators or the institution, Stanley Leedom told reporters “I just don’t want this tragedy [the death of his son] to deter in any way from the blood donor program or these experiments.”^{18(p18)}

Expansion of Rules to Protect Research Subjects

As the pace of clinical research accelerated rapidly in the years after the end of World War II, issues relating to human experimentation did not disappear. The scientific literature and the papers in the archives of medical institutions suggest the strains and tensions that using human subjects created for some experimenters. At the University of California at San Francisco (UCSF), for example, researchers at the Laboratory of Experimental On-

cology (LEO) confronted these issues in the search for treatments for patients with terminal cancer. In the early 1950s cancer researcher Michael Shimkin and his colleagues were criticized for performing “drastic, deleterious procedures on patients” and for using a release form for admission to the research ward that was “psychologically harmful,” including as it did provision for autopsy should the patient die. On a visit to the National Institutes of Health (NIH), which funded the LEO, Shimkin met with NIH director James Shannon to discuss the accusations that his group was performing “vivisection on man.” Following this meeting, Shimkin introduced several “remedial steps,” including review by the cancer board of the medical school of “all new departures in clinical research.”^{19(p127)}

Shimkin organized a public symposium on the issues relating to human experimentation with a physician colleague, Otto Guttentag, in October 1951. Although it may have been difficult for researchers to confront the differences between therapeutic and nontherapeutic studies on human subjects, Guttentag, a homeopath by training, directly explored the tensions in clinical investigation. Distinguishing the “physician-friend” from the “physician-experimenter,” Guttentag worried that the experimenter would not be able to resist taking advantage of a patient’s distress in the interests of advancing knowledge. In his view,

research and care would not be pursued by the same doctor for the same person, but would be kept distinct. The physician-friend and the physician-experimenter would be two different persons as far as a single patient is concerned...^{20(p210)}

The publication of the symposium presentations by Guttentag, Shimkin, Berkeley law professor Alexander Kidd, and W.H. Johnson of the Judge Advocate General Corps of the United States Army was delayed, according to Shimkin, by negotiations over clinical research policies at the soon-to-be-opened Clinical

Research facility at NIH, but the symposium papers eventually appeared in *Science* in 1953.^{20–23}

In the 1960s, NIH director James Shannon confronted disturbing public revelations about two research projects funded by the Public Health Service and NIH. The first involved efforts to transplant chimpanzee kidneys into human patients at Tulane University. In 1963, Tulane surgeon Keith Reemtsma performed 13 transplants using kidneys taken from chimpanzees.²⁴ Although most of his patients died after 9 to 60 days, one patient lived an astonishing 9 months with the xenotransplant. This success spurred transplanters in other medical centers to undertake similar animal–human transplants, surgeries that received considerable public attention^{25–27} and raised moral questions.

The second concerned research into cancer cells conducted at the Jewish Chronic Disease Hospital in Brooklyn, New York. The principal investigator, Chester Southam, a researcher at the Sloan-Kettering Cancer Research Institute, had injected live cancer cells into indigent elderly patients without their consent. In addition to the absence of peer review, Southam proceeded with the project over the objections of three physician consultants who insisted that the patients were not able to consent to the research. Both Southam and the hospital's medical director Ernest Mandel received censure by the New York Board of Regents. Although their medical licenses were suspended, the order was stayed and the doctors placed on probation for 1 year. But the case generated considerable publicity.^{28,29(pp161–162)}

The growing interest in the rights of research subjects prompted Shannon in late 1963 to convene a committee charged with studying the problem of protection for the human subjects of research. This committee, chaired by NIH administrator Robert Livingston, recommended no changes in NIH policies and warned that a code or standards for acceptable research would impede or delay medical research. Shannon, however, continued to believe that the current recommendations were inadequate. Working with Luther Terry, the Surgeon General of the US Public Health Service, Shannon proposed to the National Advisory Health Council, a committee created to advise the surgeon general, that NIH should accept responsibility for formal controls on individual investigators. When William Stewart succeeded Terry as surgeon general in 1966, he ordered all PHS grantee institutions to take steps to review all proposed research involving human subjects, in order to protect the rights and welfare of the individual subjects, to consider the methods used to secure informed consent to the experiment, and to assess the risks and benefits of the investigation.^{30(pp99–100)}

Public Health Service Exemption From Research Controls: The Tuskegee Study

In 1966, at the same time that Public Health Service (PHS) policy required compliance with this directive to protect human subjects, the Venereal Disease Division of the PHS was continuing the Tuskegee Syphilis Study, its long-running study of the effects of untreated syphilis in black men in rural Alabama. None of the guidelines for peer review and the protection of human subjects applied to the PHS's own research projects. When Peter Buxton, a PHS field investigator in San Francisco, continued to question the morality of the syphilis nontreatment study, he was invited to attend a Centers for Disease Control (CDC) meeting on syphilis research where he heard PHS officers defend the research project.³¹

Despite efforts to persuade Buxton that the study would benefit physicians who treated African Americans who had syphilis, he left the meeting feeling that nothing had been resolved. Buxton resigned from the PHS in 1967 and entered law school the following year. In 1968, he wrote a second letter to the CDC about the “political dynamite” that a study restricted to black participants represented. When Dr. David Sencer, director of the CDC, read the letter, he agreed that the study could become a public relations problem for the government agency.

In 1969, the CDC created a blue-ribbon panel to determine whether the Tuskegee Syphilis Study should be terminated. The only member of the panel previously unfamiliar with the study, Eugene Stollerman, chair of the Department of Medicine at the University of Tennessee, was the only one to insist that the Public Health Service had an obligation to treat the men for their disease. Over Stollerman's objections, the committee recommended continuation of the no-treatment study. In light of the “impossibility” of securing informed consent from the poorly educated and impoverished Tuskegee subjects, the committee recommended a form of “surrogate informed consent,” namely approval of the Macon County Medical Society, which by 1969 consisted primarily of black physicians. Rather than criticize the CDC doctors, members of the medical society agreed to help investigators by promising that

if they had a list of individuals [in the study] that they would not knowingly give them antibiotics...but would refer them locally to the health department and to Nurse Rivers [the black nurse who maintained patient contact for the PHS investigators].^{7(pp198–199)}

Only 3 years later, in 1972, did the public revelation that government doctors had withheld penicillin from black men infected with syphilis supply the catalyst for the US Congress to take action on the issue of human subject protections. For nearly a decade, Senators Jacob Javits (Republican, New York), Ted Kennedy (Democrat, Massachusetts), and Walter Mondale (Democrat, Minnesota) had sponsored legislation calling for oversight of NIH research and experimentation conducted under the auspices of the Department of Defense. The public hearings in February through July 1973, chaired by Senator Kennedy, included testimony from several surviving Tuskegee participants who related an extensive list of government evasions, misrepresentations, and deceptions. The heated controversy over human experimentation, fetal research, and psychosurgery created momentum for the passage in 1974 of the National Research Act. Signed into law by President Richard Nixon, the legislation included a provision for the creation of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The National Research Act also required that all research involving human subjects undergo review and that investigators document the written informed consent of their research subjects.

Since 1974, the system of localized institutional review boards (IRBs) set into place by the National Research Act has been criticized as ineffective in protecting the rights of human subjects. In March 1998 the Office of the Inspector General of the Department of Health and Human Services issued a report—*Institutional Review Boards: A System in Jeopardy*—sharply critical of the institutional review board system, and containing recommendations for recasting the federal IRB requirements to strengthen protections for human subjects participating in research and insulate IRBs from conflicts that potentially compromise their responsibility to protect human subjects.³² In June 2000, Donna Shalala, Secretary of Health and Human Services, established a new office to replace the former Office for Protection From Research Risks. At the recommendation of Dr. Harold Varmus, then director of the National Institutes of Health, Shalala created the Office for Human Research Protection, locating it in the Office of the Secretary to give the office greater independence and stature and to provide a platform to influence human subjects protection. To strengthen human subjects protection, new certification programs for individual IRB members and institutions have been developed. According to Dr. Greg Koski, the Director of the OHRP, “we are witnessing the move to a professional model for human research.”^{33(p132)}

HUMAN EXPERIMENTATION DURING THE COLD WAR ERA

The Nuremberg Code and the United States Government

In consideration of preparations necessary to meet the threat of nuclear, chemical, and biological weapons being developed in communist countries, American military interest in human experimentation increased. In 1953 Colonel George Underwood, director of the Office of the Secretary of Defense, noted the need for an agency-wide policy to guide the conduct of human experimentation by military researchers. High-ranking committees within the armed services had debated policies for human experimentation for several years.

On the recommendation of DoD attorney Stephen Jackson, the Armed Forces Medical Policy Council (AFMPC) advised the secretary of defense in 1952 that “the ten rules promulgated at the Nuremberg trials be adopted as the guiding principles to be followed.” Jackson’s recommendation did not sit well with other DoD committees, who preferred to forego a policy statement that might retard research progress. “To commit to writing a policy on human experimentation would focus unnecessary attention on the legal aspects of the subject,”^{34(p57)} noted the

secretary of the Committee on Medical Sciences in November 1952.

Despite this opposition, Charles Wilson, President Eisenhower’s new secretary of defense, signed off on the AFMPC recommendation in February 1953. Issued as a Top Secret Memorandum (Exhibit 17-3) to the secretaries of the Army, Navy, and Air Force, the Wilson memorandum affirmed the Nuremberg principles, required the written consent of research subjects, and prohibited experimentation using prisoners of war. Although the reasons for classifying the rules for research are less than clear, it seems likely that making the document classified information limited its circulation among military researchers.^{35(p308)}

The Army quickly acted to put the Wilson memorandum into effect. Although initially classified, the Wilson order was declassified in 1954. The Army’s memorandum on the Wilson order included a legal analysis identifying the source of the Army’s authority to conduct human experimentation, as well as the limits of that authority in the selection of human subjects. As the Advisory Committee on Human Radiation Experiments noted in its report in 1995, even during the height of the Korean War,

EXHIBIT 17-3

THE WILSON MEMORANDUM: FORMALIZING THE USE OF HUMAN VOLUNTEERS IN DEPARTMENT OF DEFENSE EXPERIMENTAL RESEARCH

26 Feb 1953

Memorandum for the Secretary of the Army

Secretary of the Navy

Secretary of the Air Force

SUBJECT: Use of Human Volunteers in Experimental Research

1. Based upon a recommendation of the Armed Forces Medical Policy Council, that human subjects be employed, under recognized safeguards, as the only feasible means for realistic evaluation and/or development of effective preventive measures of defense against atomic, biological or chemical agents, the policy set forth below will govern the use of human volunteers by the Department of Defense in experimental research in the fields of atomic, biological and/or chemical warfare.
2. By reason of the basic medical responsibility in connection with the development of defense of all types against atomic, biological and/or chemical warfare agents, Armed Services personnel and/or civilians on duty at installations engaged in such research shall be permitted to actively participate in all phases of the program, such participation shall be subject to the following conditions:
 - a. The voluntary consent of the human subject is absolutely essential.
 - (1) This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, overreaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him 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 health or person which may possibly come from his participation in the experiment.
 - (2) The concept [*sic*: consent] of the human subject shall be in writing, his signature shall be affixed to a written instrument setting forth substantially the aforementioned requirements and shall be signed in the presence of at least one witness who shall attest to such signature in writing.
 - (a) In experiments where personnel from more than one Service are involved the Secretary of the Service which is exercising primary responsibility for conducting the experiment is designated to prepare such an instrument and coordinate it for use by all the Services having human volunteers involved in the experiment.
 - (3) The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.
 - b. The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.
 - c. The number of volunteers used shall be kept at a minimum consistent with item b., above.
 - d. The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.
 - e. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.
 - f. No experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur.
 - g. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.

(Exhibit 17-3 continues)

Exhibit 17-3 *continued*

- h. Proper preparation should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.
 - i. The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.
 - j. During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.
 - k. During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of the good faith, superior skill and careful judgment required of him that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.
 - l. The established policy, which prohibits the use of prisoners of war in human experimentation, is continued and they will not be used under any circumstances.
3. The Secretaries of the Army, Navy and Air Force are authorized to conduct experiments in connection with the development of defenses of all types against atomic, biological and/or chemical warfare agents involving the use of human subjects within the limits prescribed above.
4. In each instance in which an experiment is proposed pursuant to this memorandum, the nature and purpose of the proposed experiment and the name of the person who will be in charge of such experiment shall be submitted for approval to the Secretary of the military department in which the proposed experiment is to be conducted. No such experiment shall be undertaken until such Secretary has approved in writing the experiment proposed, the person who will be in charge of conducting it, as well as informing the Secretary of Defense.
5. The addresses [*sic*] will be responsible for insuring compliance with the provisions of this memorandum within their respective Services.

/signed/

C. E. WILSON

Copies furnished:

Joint Chiefs of Staff

Research and Development Board

TOP SECRET

Downgraded to UNCLASSIFIED

22 Aug 75

the Army did not view it as self-evident that the Department of Defense could engage in human experimentation or choose any subjects it wished.^{34(p61)} Limits to the practice of subjecting human subjects to scientific experimentation were recognized in theory, if not always in practice, as the human radiation experiments attest.

The Human Radiation Experiments

In December 1993 Eileen Welsome, a reporter for the *Albuquerque Tribune*, and Hazel O'Leary, US Secretary of Energy, reopened a dark chapter in American Cold War history—the use of human subjects in research involving ionizing radiation. The Cold

War was over and the Department of Energy had embarked on an “openness initiative.”^{36(p424)} Welsome and O'Leary were on separate tracks that eventually collided—Welsome began her inquiries into the plutonium injection cases in 1987; O'Leary was confirmed as Secretary of Energy in 1993. Secretary O'Leary embarked on a campaign to reverse the “culture of secrecy” that had permeated the Atomic Energy Commission/Department of Energy (AEC/DOE). Among other things she changed the name of the Office of Classification to the Office of De-Classification. Her 7 December 1993 press conference was the first in a series to “clear the air.” In the press conference, O'Leary conceded that the government had conducted radiation experiments on American

citizens. This concession was prompted by the 45-page series on the plutonium injections, written by Welsome, that appeared in the *Albuquerque Tribune*.³⁶ Although it is true that the human radiation experiments had never been completely secret, it is also true that the full nature and extent of human radiation experimentation in the years between 1944 and 1974 had not been known to the American public. The report, *American Nuclear Guinea Pigs*,³⁷ commissioned in 1986 by Congressman Edward J. Markey (Democrat, Massachusetts, 7th District) had included information on the 18 patients who had received plutonium injections, as well as many others. Welsome provided additional information on the plutonium injections, including patient names and family photographs of the patients who participated in the studies. In 1994 President Clinton appointed the Advisory Committee on Human Radiation Experiments, chaired by Johns Hopkins bioethicist Ruth Faden, to explore and document the extent of the human radiation studies. The committee produced the most extensive compilation to date of the American use of human subjects at the dawn of the atomic age, the extent of injury to research subjects, and the continuing challenges for human subjects research.

The Plutonium Studies

The experiments that brought renewed national attention to the issue of government-sponsored research involved plutonium, a radioactive metallic element first noted in 1941. As the United States pressed forward with the construction of nuclear weapons, scientists in the Manhattan Project grew concerned about the health effects of the substance for the hundreds of workers involved in the race to build a bomb. In order to answer the question about the biological effects of plutonium, 18 hospital patients were injected with the substance between 1945 and 1947. One received the plutonium injection at Oak Ridge Hospital in Tennessee, three at the University of Chicago, 11 at the University of Rochester, and three at the University of California. Although much remained unknown about plutonium, physicians involved in the research believed that injections posed little, if any, short-term risk to the subjects. Because long-term risk was possible, the doctors selected patients likely to die in the near future. Although several of the patients did die soon after their injections, a number survived for decades, despite the doctors' prognoses about their illnesses.³⁸

The plutonium injections raised (and continue to

raise) difficult moral and policy considerations, including who should serve as subjects for experiments designed to protect workers in wartime. At the beginning of the experiments, even the word plutonium was classified information. One might ask how, under these circumstances, could informed consent be obtained from the participants, and what, if anything, were subjects or their families told about the injections? Did the patients know, for example, that they were taking part in a study that was not intended to benefit them? In all likelihood these individual subjects had no clear understanding of what was being done to them.

The first patient selected for injection was a 53-year-old "colored male," Ebb Cade, hospitalized for serious, but not life-threatening, fractures of his arm and leg.^{38(p144)} Dr. Joseph Howland, an Army physician stationed at Oak Ridge, told AEC investigators in 1974 that he administered the injection of plutonium. There was, he recalled, no consent from the patient. He acted, he testified, only after his objections were met with a written order to proceed from his superior, Dr. Hymer Friedell. (The ACHRE was told by Friedell that another doctor, not Howland, had given the injection to Cade and that he had not ordered the injection.^{38(p144)} ACHRE was not able to resolve this contradiction.) It remains unclear why Cade was selected for the experiment, and why no more injections were performed at Oak Ridge.

The next three plutonium injections took place at the University of Chicago, where all three patients were seriously ill and not expected to survive. (The first two died within 2 years of the injection; the date of death of the third remains unknown.) Like the Oak Ridge injection, the Chicago injections occurred without the consent of the individuals.

At the University of Rochester, the 11 patients who received plutonium injections were part of a larger project designed to set standards for radiation safety for workers in nuclear facilities. In addition to tests of plutonium, researchers under the direction of Dr. Samuel Bassett administered polonium to five patients and uranium to six people who were also selected from "a large group of hospital patients."^{38(p148)} Doctors wanted patients with kidney function that was adequate enough to test the excretion pattern of the element. The patients selected to receive polonium were all suffering from terminal forms of cancer (such as leukemia) and therefore unlikely to live long. The uranium patients included those with rheumatoid arthritis, tuberculosis, cirrhosis, and alcoholism. The patients selected for plutonium and uranium injections did not include those with malignant disease. Although the

ostensible criteria for administering these radioactive substances was short life expectancy due to serious illness or injury, most of the patients injected at Rochester were not, in fact, terminally ill (at least three of the Rochester subjects were known to be living in 1974, and one of the subjects, Eda Schultz Charlton, 49 years old, participated in the experiments as the result of a mistaken diagnosis^{38(pp146-149)}). The evidence assembled by the Advisory Committee supports the claims of family members that patients knew little, if anything, about the research projects and their status as research subjects.^{38(pp146-149)}

At the University of California at San Francisco (UCSF), Doctors Joseph Hamilton and Robert Stone undertook metabolic studies to evaluate the potential risks for workers exposed to plutonium. After experimenting with rats, Hamilton and Stone injected three human subjects with plutonium; they also performed one injection of americium and one injection of zirconium in two different patients in 1947 and 1948. The first plutonium injectee was Albert Stevens, selected in the belief he was suffering from advanced stomach cancer. After the injection, researchers learned that rather than cancer, he had an ulcer. The researchers collected excreta from Stevens for more than a year testing for plutonium content. When Stevens wanted to leave the Berkeley area, the researchers offered him money to continue the collections for the study, but without disclosing to him the nature of his participation. Indeed, documents located by the Committee indicate that researchers considered two different options to retain Stevens, paying for his care in a hospital or a nursing home or placing the man on Dr. Hamilton's payroll in some minor capacity. The researchers were explicitly advised that he not "be paid as an experimental subject only."^{38(p150)} In addition to Stevens, the UC researchers injected a 4-year-old cancer patient and a 36-year-old African-American railroad porter named Elmer Allen with plutonium. In Allen's case, two physicians signed his medical chart indicating that the experimental nature of the injection had been explained to him, that he agreed to be injected, and that he was of sound mind. Part of the reason for this chart notation was the ruling by Atomic Energy Commission (AEC) administrator Carroll Wilson in April 1947 calling for written documentation of consent from the patient-subject of a radiation experiment. Wilson's directive, however, also indicated that radiation experiments could be conducted only in the expectation of therapeutic benefit for the patient. Elmer Allen's physicians had no expectation that the plutonium would benefit him. Allen lived until 1991. Allen's daugh-

ter, Elmerine Whitfield-Bell, continues to dispute the documentation that her father agreed to the plutonium injections. In 1998 the federal government and the families of the patients who received plutonium injections agreed to a financial settlement.

The Other Ionizing Radiation Studies

The plutonium, polonium, and uranium studies were prominent in the public press, and thus there was more information gathered about these studies. However, they represent only a few of an estimated 4,000 human radiation experiments conducted under government auspices during the Cold War. Most of the 4,000 studies involved radioactive isotopes to tag molecules for the study of iron metabolism, thyroid metabolism, calcium uptake, blood volume, and so on. In addition to plutonium injections, notorious studies involving human subjects and ionizing radiation in this period included the studies conducted on "retarded" children at the Fernald School in Massachusetts, fed oatmeal containing radioisotopic iron and calcium as members of the "Science Club" (whose activities included getting a quart of milk daily, going to a baseball game and the beach, and having outside dinners); the Vanderbilt University studies in which pregnant women received a "vitamin cocktail" containing radioactive iron to examine nutritional requirements during pregnancy; experiments at Walla Walla State Prison in Washington state where prisoners were recruited to a study of the effect of radiation on testicles (prisoners agreed to undergo vasectomy after exposure to radiation); and studies in whole-body radiation conducted on a largely African-American patient population at the University of Cincinnati. As in the plutonium case, financial settlements between the subjects and their families and the research sponsors were reached in the late 1990s.

The Central Intelligence Agency and "Mind-Altering" Substances

In April 1953, Allen Dulles, director of the Central Intelligence Agency (CIA), authorized the investigation of biological and chemical materials with the potential to alter mental states. In response to allegations of mind-control techniques performed by Chinese, North Korean, and Russian scientists on American prisoners of war during the Korean War, the MKULTRA program was established. (Little is known about the specifics of the program, or even, for that matter, the precise expansion of the acronym. The "MK" diagraph identifies it as a

project of the Technical Services Staff of the Central Intelligence Agency. The "ULTRA" part may be related to the ULTRA program of World War II,^{39(p61)} the program associated with cracking the German military codes.) Under the direction of scientist Sidney Gottlieb, the program encompassed examination of such drugs as nicotine, cocaine, and, perhaps most sensationally, the effects of the hallucinogenic drug lysergic acid diethylamine (LSD). Although most of the records relating to MKULTRA were intentionally destroyed by the agency in 1973, some details of the more than 150 individual government-funded research projects, especially the testing of LSD on unsuspecting participants, have become available since then.

The CIA-sponsored research was conducted at approximately 80 academic institutions across the nation. In November 1953, Gottlieb, without obtaining explicit permission, secretly extended his LSD studies to men on the staff of the Special Operations Division (SOD) at Fort Detrick. During a staff retreat, Gottlieb added LSD to a bottle of Cointreau, which was consumed by several men. One of those affected was Frank Olson, a scientist on the SOD staff and an expert on the airborne delivery of biological weapons. Following this episode, Olson apparently experienced severe mental distress, for which Gottlieb arranged special sessions with a New York physician with a top secret security clearance. On the eve of Olson's return to Maryland, where he was scheduled to enter a psychiatric facility, he fell through a 10th-floor window of the New York hotel where he was staying with CIA personnel. For more than two decades, the mysterious circumstances of Olson's death were unknown to his family. In 1975, following congressional hearings about CIA secret activities, Olson's surviving family received an apology from President Gerald Ford. In 1976, Congress enacted legislation authorizing a payment of \$750,000 to the family as compensation for their loss.^{40(pp191-192)}

More than a quarter of a century later, questions about Olson's death remain troubling to his family. In January 2000, a New York district attorney reopened the case for a grand jury deliberation in light of forensic evidence that Olson received a blow to the head prior to his fall. Eric Olson, Frank Olson's son, believes his father was deliberately killed because he was deemed a security risk. According to the younger Olson, the CIA's declassified assassination manual from 1953 indicated that a preferred method for eliminating someone was to fake a suicidal jump.^{40(pp316-319),41}

In the 1950s, the Army Chemical Corps secretly contracted with researchers at the New York State

Psychiatric Institute in New York City to test the effects of hallucinogens on their patient population. Under this contract, the Chemical Corps supplied the researchers with mescaline for testing in human subjects. In December 1952, when a 42-year-old tennis player, Harold Blauer, entered the Psychiatric Institute for depression, he was selected to receive five injections of three different experimental mescaline derivatives. Although Blauer experienced severe distress and violent tremors after the fourth injection, his physicians proceeded as planned with the fifth injection, a dose 16 times larger than he had previously received. Blauer died in little more than 2 hours following the fifth injection. The Army and the staff of the Psychiatric Institute and the state of New York actively concealed the embarrassing and distressing information that Blauer's death occurred in trials of a chemical warfare agent. Fearing for the doctors' professional reputations and the financial liability, the New York State attorney general's office offered the family of Harold Blauer \$18,000. The Army Intelligence Division clandestinely provided half of this amount to New York State.⁴²

These details, like some of the details surrounding Frank Olson's death, came to light in 1975 as part of a Congressional probe into research on chemical and biological warfare agents.⁴² In 1978, the family of Harold Blauer, which had pursued the case in the courts since 1953, was awarded \$702,000 in damages by the United States District Court for the Southern District of New York.^{40(p198)}

Reports in the press in the early 1970s of clandestine testing by the CIA and the Department of Defense prompted investigations by Church Committee (named after Senator Frank Church, Democrat, Idaho) in the United States Senate and the Rockefeller Commission, appointed by President Gerald Ford and chaired by Vice President Nelson Rockefeller. Acting on the recommendations of the Church Committee, President Ford in 1976 ordered the first Executive Order on Intelligence Activities,⁴³ which included a provision forbidding "experimentation with drugs on human subjects, except with the informed consent, in writing and witnessed by a disinterested party, of each such human subject." Under the direction of Presidents Carter⁴⁴ and Reagan,⁴⁵ the order was expanded to encompass any kind of human experimentation.^{30(p107)}

The US Army and Biological Warfare Tests in America

Reports of biological weapons development by the Germans and the Japanese prompted the United States to institute a biological weapons research

initiative in 1941. With the support of Secretary of War Henry L. Stimson, the War Research Service, headed by George Merck, president of Merck Pharmaceuticals Company, opened a facility in 1942 at Camp Detrick (renamed Fort Detrick in 1956), Maryland for research on biological weapons. In January 1946 the Army publicly announced the nature of the facility, where research continued for the next 30 years. There were also reports in the public press about planning for the possibility of bacteriological warfare.⁴⁶ At Detrick, government scientists investigated anthrax, botulin and other toxins, and other infectious organisms for their potential as biological warfare agents. During the Cold War, American development of biological weapons encompassed large-scale animal experimentation (Detrick was the world's largest purchaser of guinea pigs), human volunteers, and surreptitious testing in 239 American cities between 1950 and 1969.⁴⁷

In the years between 1954 and 1973, Army authorities recruited 2,200 American soldiers to participate in defensive biological weapons testing. Following a series of meetings between representatives of the Seventh-Day Adventist Church and the Army Surgeon General's Office, researchers were able to employ Seventh-Day Adventists serving in the military as noncombatants in light of the religious objections against bearing arms. In "Project Whitecoat," as the program came to be known, Adventists participated in studies of Q fever, tularemia, Venezuelan equine encephalomyelitis, Rocky Mountain spotted fever, sand fly fever, yellow fever, typhoid fever, and Rift Valley fever.⁴⁸

According to Abram Beneson, director of experimental medicine at Fort Detrick in 1954 and 1955, researchers there were "very conscious" of the Nuremberg Code and insisted that volunteers be uncoerced and comprehending of the risks and benefits they would encounter in an experiment.⁴⁹ Participants in these studies signed written consent forms, which included a clause with a warning that death and injury were possible outcomes. Beneson recalled that Army lawyers informed him that such a consent form would not hold up if legally challenged, but Beneson persisted in order to insure that the men understood what their involvement in the project could mean. There were many more individuals who volunteered than could be accepted for participation in the project.

In addition to tests on human volunteers, Army researchers conducted deliberate releases of bacteria and aerosols in major cities to evaluate the vulnerability of Americans to biological attacks. Although many details about the testing programs remain secret, it is known that the Army conducted

tests over more than 200 cities between 1950 and 1969. Army researchers sprayed zinc cadmium sulfide, an aerosolized fluorescent powder believed to approximate bacterial agents as they were dispersed in the environment, in Minneapolis and St. Louis. In 1966 US Army researchers studied the vulnerability of the New York City subway system to bacterial attack by exposing more than a million people to a bacterium, *Bacillus subtilis variant niger*. Conducted by scientists and technicians, the test involved dropping light bulbs filled with bacteria into the subway system.

Perhaps the most serious known outcome of the bacterial testing program involved the release of the bacteria *Serratia marcescens* and *Bacillus globigii*. During World War II, the Germans had reportedly released *Serratia* bacteria in the subways of London and Paris. Fearing that the Pentagon was vulnerable to a germ attack, scientists from the Special Operations Division (SOD) at Fort Detrick in August 1949 sprayed *Serratia* bacteria into the vents of the Pentagon's air-conditioning system, revealing the vulnerability of the building to a germ attack. In 1950 the SOD demonstrated civilian susceptibility to such attacks by releasing *Serratia* microbes from the decks of two United States naval vessels anchored in the Atlantic. In September 1950 the tests were successfully repeated in the Pacific, where "nearly every one of the 800,000 people in San Francisco exposed to the cloud at normal breathing rate inhaled 5,000 or more fluorescent particles."^{50(p118)}

Although these bacteria were believed to pose little threat to the population, physicians at Stanford University writing in October 1951 reported a startling outbreak of infections at the Stanford University Hospital in San Francisco. The outbreak was extraordinary because *Serratia* infections had never before been reported in hospitals. Moreover, in spite of extensive searching by the physicians, no cause of the outbreak could be traced. During the outbreak 11 patients developed the infection; one, Edward Niven, a pipefitter, died. In 1979 the Niven family sued the federal government for \$11 million for his wrongful death. The family lost the case, and failed to win an appeal from the United State Court of Appeals, but the discovery process in the trial brought much to light about the nature and extent of the government's biological testing program in the Cold War.⁵¹

The releases of these bacterial agents and aerosols were uniformly conducted without the knowledge or permission of the local population. People riding the subway system or simply breathing the air remained unaware of their exposure to either bacteria or aerosolized agents such as zinc cadmium

sulfide. The United States Army Center for Health Promotion and Preventive Medicine (the successor of the Army Environmental Health Agency) conducted three risk assessments for cities where the fluorescent particles were dispersed. In each of the three assessments, risk from exposures were less

than the standards set by the 1994 Occupational Safety and Health Administration. At the Army's request, the Centers for Disease Control (CDC) performed an independent risk assessment, concluding that zinc cadmium sulfide posed only negligible risk for the residents in the affected areas.⁵²

SECURITY AND SCIENCE

One of the principal rationales for covert and deceptive experimentation during the Cold War was the issue of national security. Engaged in an emerging global struggle with the communist bloc, the United States government strove to meet the threat. However, national security was not the only rationale for secrecy. Since the early 1940s, officials of the federal government had also followed regulations that allowed secrets to be maintained not only because their disclosure would endanger national security, but because such disclosure "would be prejudicial to the interests or prestige of the Nation."^{53(p392)}

When it began operation in 1947, the Atomic Energy Commission expanded the practice of maintaining secrecy to encompass public relations, especially the threat of "embarrassment" and legal liability. For example, in 1946 Dr. Hymer Friedell, once the deputy medical director of the Manhattan Engineering District (created by the federal government in 1942 to meet the goal of producing an atomic weapon; the "Manhattan Project" was the central mission of the Manhattan Engineering District), recommended the declassification of one of the early reports describing plutonium injections into human subjects. Two months later, in February 1947, his recommendation was overridden on the advice of AEC officials, who noted that the "coldly scientific manner in which the results are tabulated and discussed would have a very poor effect on the public." Moreover, unless necessary legal documents had been executed, the report left the experimenters and the US government vulnerable to a "devastating lawsuit" with potentially far-reaching results.^{38(p153)} Fears about legal liability and "administrative embarrassment" continued to play a role in AEC decisions to keep secret or reclassify experiments involving what UCSF researcher Robert Stone called "unwitting subjects."

In addition to maintaining the secrecy of human radiation experiments, the AEC adopted policies to forestall access to information relating to health risks that radiation posed to workers and to the public. The Insurance Branch of the AEC, for example, routinely reviewed declassification decisions with

the liability issue in mind. In so doing, they continued a practice adopted by Manhattan Project officials like Robert Oppenheimer, who in 1946 asked that all reports on health problems be separately classified and issued at his request, the purpose being to "safeguard the project [from] being sued by people claiming to have been damaged."^{54(p332)}

Decisions to classify research as secret resulted not only from policy making at federal agencies but also ensued at the request of individual investigators. In the early 1950s, Everett I. Evans, a surgical researcher at the Medical College of Virginia, successfully petitioned the Army to classify his experiments on burns associated with radiation, but not because he feared criticism over human experimentation. Evans grew concerned about the potential adverse public relations of his experiments in which dogs obtained from local municipal shelters received fatal doses of radiation. In January 1951, Evans, alarmed by reporters investigating the dog studies, explained in a letter to Army authorities that "there is much about the [canine studies] that I do not like but we are doing it in a manner as humane as possible. The issue here is one of national security."^{53(p419)} Fearing that local humane societies would prevent access to animals and thereby jeopardize the research program, Evans asked that his radiation studies be classified. The Army in response declared that all work under the Medical College of Virginia contract be identified as restricted. Thus, the desire to insure the continuity of the canine research also blanketed Evans' human radiation experiments on prisoners and hospital patients.

When the reports of the plutonium injections and other Cold War radiation experiments once again became "news" in 1993, many Americans were startled to learn about the extent of secret research programs conducted by the federal government. Many were puzzled by the realization that some things were secret and others were not. How could the radiation experiments be secret when many of them had been published openly in the medical literature and even reported in the public press when they occurred?

What is clear is that public tolerance for the Cold War culture of secrecy and science had changed dramatically. In the public testimony before the Advisory Committee on Human Radiation Experiments, many citizens came forward to express their distrust of government officials and governmental policies as they related to the issue of radiation exposure and research. Although many of the citizens who spoke recognized the need in the past for secrecy (in light of pressing national security concerns), they also expressed skepticism that such secrecy remained necessary in light of the profound changes around the world.

From the dawn of the atomic era, there has been ongoing tension between the openness required for

scientific inquiry and the defense establishment. A case can be made, Senator Daniel P. Moynihan has written, "that secrecy is for losers."^{55(p227)} Secrecy in science corrodes the process of increasing our knowledge of the natural world, and secrecy in governmental science corrodes citizen trust of the government and its leaders. "Openness," noted Moynihan, "is now a singular, and singularly, American, advantage. We put it in peril by poking along in the mode of an age now past."^{55(p227)} Although there are legitimate reasons for secrecy in developing weapons systems and other defense technologies, secrecy should not be permitted in experiments involving human subjects or, at the very least, outside review of the subjects' consent and safeguards to protect them must be ensured.

CONCLUSION

During the last decade Americans have increasingly confronted the tragic record of clandestine and deceptive human experimentation in the 20th century. Expert commissions have issued reports, the injured have sought and received financial compensation, and the government has apologized to citizen-subjects of the Tuskegee Syphilis Study and the human radiation experiments. Lawsuits brought by veterans of biological, chemical, and atomic war-

fare studies continue to wend their way through the courts. These lawsuits permit a financial accounting of loss of life, liberty, and mental distress. They do not take into account the corrosion of trust in American researchers and the American government. Even more disturbing is the fear that these things could happen again unless adequate safeguards remain in effect and the lessons of the past are learned.

REFERENCES

1. Faden RR. Chair's perspective on the work of the Advisory Committee on Human Radiation Experiments. *Kennedy Inst Ethics J*. 1996;6:215-221.
2. *Building Public Trust: Actions to Respond to the Report of the Advisory Committee on Human Radiation Experiments*. United States Government Human Radiation Interagency Working Group. March 1997; Publication 061-000-00880-20.
3. Warren KL. 66 volunteers given 'flash burns' in test. *Richmond News-Leader*. 8 December 1954.
4. 10 San Quentin felons used for atom tests. *San Francisco Examiner*. 12 April 1949.
5. Lederer SE. *Subjected to Science: Human Experimentation in America Before the Second World War*. Baltimore, Md: Johns Hopkins University Press; 1995.
6. Chernin E. Richard Pearson Strong and the iatrogenic plague disaster in Bilibid Prison, Manila, 1906. *Rev Infect Dis*. 1989;11:996-1004.
7. Jones JH. *Bad Blood*. New York: Free Press; 1993.
8. Gamble VN. Under the shadow of Tuskegee: African Americans and health care. *Am J Public Health*. 1997;87:1773-1778.
9. Kendrick DB. *Blood Program in World War II*. Washington, DC: Office of the Surgeon General; 1964.
10. Pechura CM, Rall DP, eds. *Veterans at Risk: The Health Effects of Mustard Gas and Lewisite*. Washington, DC: National Academy Press; 1993.

11. Rothman DJ. *Strangers at the Bedside: A History of How Law and Bioethics Transformed Medical Decision Making*. New York: Basic Books; 1991.
12. Harkness JM. *Research Behind Bars: A History of Medical Experimentation on American Prisoners* [dissertation]. University of Wisconsin; 1996.
13. Harkness JM. Nuremberg and the issue of wartime experiments on US prisoners. *JAMA*. 1996;276:1672–1675.
14. Katz J. The Nuremberg Code and the Nuremberg Trial: A reappraisal. *JAMA*. 1996;276:1662–1666.
15. Annas GJ, Grodin MA, eds. *The Nazi Doctors and the Nuremberg Code: Human Rights in Human Experimentation*. Oxford: Oxford University Press; 1992.
16. Cousins N. Dialogue in Warsaw: Report on the Ravensbrueck Lapins. *Saturday Review*. 1958;41:9–11, 32–36.
17. Faden RR, Lederer SE, Moreno J. US medical researchers, the Nuremberg doctors trial, and the Nuremberg Code. *JAMA*. 1996;276:1667–1671.
18. Contaminated blood injection kills youth in Seattle preservation research project. *New York Times*. 25 March 1952:18.
19. Shimkin M. *As Memory Serves: Six Essays on a Personal Involvement With the National Cancer Institute, 1938–1978*. Bethesda, Md: US Department of Health and Human Services, PHS, NIH; 1983.
20. Guttentag OE. The physician's point of view. *Science*. 1953;117:207–210.
21. Shimkin M. The problem of experimentation on human beings. *Science*. 1953;117:205–207.
22. Kidd AM. Limits of the right of a person to consent to experimentation on himself. *Science*. 1953;117:211–212.
23. Johnson WH. Civil rights of military personnel regarding medical care and experimental procedures. *Science*. 1953;117:212–215.
24. Reemtsma K. Renal heterotransplantation from nonhuman primates to man. *Ann N Y Acad Sci*. 1969;162(1):412–418.
25. Spare parts from chimp to man. *Time*. 27 December 1963:41.
26. 2 monkey kidneys transplanted into woman in pioneer operation. *New York Times*. 12 October 1963.
27. Schmeck HM Jr. Patient is alive after six weeks with two kidneys from a chimpanzee. *New York Times*. 18 December 1963.
28. Katz J. *Experimentation With Human Beings*. New York: Russell Sage Foundation; 1972.
29. Faden R, Beauchamp TL. *A History and Theory of Informed Consent*. New York: Oxford University Press; 1986.
30. Advisory Committee on Human Radiation Experiments. Government standards for human experiments: The 1960s and 1970s. In: *Final Report of the Advisory Committee on Human Radiation Experiments*. New York: Oxford University Press; 1996: 97–112.
31. Testimony by Peter Buxton from the United States Senate Hearings on Human Experimentation, 1973. In: SM Reverby, ed. *Tuskegee's Truths: Rethinking the Tuskegee Syphilis Study*. Chapel Hill: University of North Carolina Press; 2001: 150–156.
32. *Institutional Review Boards: A System in Jeopardy*. Washington, DC: Office of Inspector General, Department of Health and Human Services, Report OEI-01-97-00193; March 1998.
33. The JIM interview with Greg Koski, MD, PhD. *J Investigative Medicine*. 2001;49:131–133.

34. Advisory Committee on Human Radiation Experiments. Government standards for human experiments: The 1940s and 1950s. In: *Final Report of the Advisory Committee on Human Radiation Experiments*. New York: Oxford University Press; 1996: 45–73.
35. Annas GJ, Glantz LH, Katz BF. *Informed Consent to Human Experimentation: The Subject's Dilemma*. Cambridge, Mass: Ballinger Publishing; 1977.
36. Welsome E. *The Plutonium Files: America's Secret Medical Experiments in the Cold War*. New York: Dial Press; 1999.
37. *American Nuclear Guinea Pigs: Three Decades of Radiation Experiments on US Citizens*. Report prepared by the Subcommittee on Energy Conservation and Power of the Committee on Energy and Commerce, US House of Representatives, November 1986. Washington, DC: US Government Printing Office; 1986.
38. Advisory Committee on Human Radiation Experiments. Experiments with plutonium, uranium, and polonium. In: *Final Report of the Advisory Committee on Human Radiation Experiments*. New York: Oxford University Press; 1996: 139–171.
39. Marks J. *The Search for the Manchurian Candidate: The CIA and Mind Control*. New York: Norton; 1979.
40. Moreno JD. *Undue Risk: Secret State Experiments on Humans*. New York: Routledge; 2001.
41. Frank Olson Legacy Website. Available at: <http://www.frankolsonproject.org/index.html>. Accessed 26 November 2001.
42. US Army Inspector General. *Use of Volunteers in Chemical Agent Research*. Washington, DC: US GPO; 1975.
43. Executive Order 11905 (19 February 1976).
44. Executive Order 12036, Section 2-301 (26 January 1978).
45. Executive order 12333, Section 2-10 (4 December 1981).
46. Parr L. The professor talks about bacterial warfare. *Hygeia*. 1942;20:344–345, 364, 368–369.
47. Mobley JA. Biological warfare in the twentieth century: Lessons from the past, challenges to the future. *Mil Med*. 1995;160:547–552.
48. Smith KT. Adventists and biological warfare. *Spectrum*. 1996;25:35–50.
49. LoLordo A. Project Whitecoat: Human testing done with care. *Baltimore Sun*. 3 April 1994;1E.
50. Regis E. *The Biology of Doom: The History of America's Secret Germ Warfare Project*. New York: Henry Holt; 1999.
51. Cole L. *Clouds of Secrecy: The Army's Germ Warfare Tests Over Populated Areas*. Savage, Md: Rowman & Littlefield; 1990.
52. Committee on Government Operations, Subcommittee on Legislation and National Security, US House of Representatives, 28 September 1994, Oversight Hearing On Cold War Era Human Subject Experimentation, Statement of Michael A. Parker.
53. Advisory Committee on Human Radiation Experiments. Secrecy, human radiation experiments, and intentional releases. In: *Final Report of the Advisory Committee on Human Radiation Experiments*. New York: Oxford University Press; 1996: 390–420.
54. Intentional releases: Lifting the veil of secrecy. In: *The Report of the Advisory Committee on Human Radiation Experiments*. New York: Oxford University Press; 1996: 317–353.
55. Moynihan DP. *Secrecy*. New Haven, Conn: Yale University Press; 1998.

