



U.S. Government-Sponsored Radiation Research on Humans 1945-1975

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In early December 1993, a dark chapter of the United States' cold war experience was reopened when Energy Secretary Hazel O'Leary responded to news media reports about government-sponsored radiation research involving hundreds of human subjects, often without their informed consent. At a December 7 press conference on her initiative to declassify some of the U.S. Department of Energy's (DOE) nuclear research records, O'Leary commented on a series of articles about plutonium injection experiments involving 18 subjects published a month earlier in the Albuquerque Tribune [1]. O'Leary acknowledged that these and other experiments beginning in the 1940s involved 600 to 800 subjects and that her department would soon begin to declassify and release documents concerning these and other experiments, which were sponsored by the DOE's predecessors, the Manhattan Project, Atomic Energy Commission (AEC), and the Energy Research and Development Administration (ERDA) [2].

In the following weeks, new details

uncovered in media reports about radiation experimentation and the Energy Secretary's (Fig 1) call for "full disclosure" and her candid statement that "For people who were wronged ...it would seem that some compensation is appropriate," led to a crescendo of public interest and an escalation of the federal government's response [3]. The Energy Department opened a toll-free telephone number to collect information from people who believe they were subjects in improperly conducted radiation experiments. Thousands of people have been unable to get through to the hot line, which has been receiving as many as 700 calls an hour [4]. At the time this article was written, five Congressional committees had also begun inquiries into the disclosures [5,6].

The focus of the interagency investigations, Congressional interest, and news media coverage currently centers on a set of government-sponsored radiation experiments involving at least 695 human subjects from the mid-1940s into the 1970s, most of which were originally documented in a 1986 Congressional staff report issued by Representative Edward Markey (D-MA) [7]. These experiments include: 1) approximately 800 pregnant women administered radioactive iron at Vanderbilt University, Nashville, Tennessee, in the late 1940s [8]; 2) nearly 200 cancer patients exposed to high levels, up to 200 rads, of whole-body gamma radiation at Oak Ridge National Laboratory, Oak Ridge, Tennessee [9]; 3) 18 persons injected with plutonium at Oak Ridge, the University of Chicago, and the University of California at

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Table. Some Examples of Radiation Experimentation on Humans*

Date	Description	Institution
<i>Experiments to develop instrumentation for spying on the Soviet Nuclear Weapons Complex:</i>		
1949	intentional release of iodine-131 to environment	AEC, Air Force ¹
1950	intentional release of radioactive material to the environment	Los Alamos Lab., Air Force ¹
<i>Experiments to develop radiation weapons:</i>		
1948	intentional release of lanthanum-140 to environment	AEC ¹
1949-52	intentional release of tantalum-182 and possibly other radioactive material to the environment	Army, AEC, Air Force ¹
<i>Experiments to determine the effects of radiation on ability of military personnel to function on the nuclear battlefield and/or effects of radiation on astronauts:</i>		
1943-44	whole-body irradiation by X-rays	Univ. of Chicago ²
1953	exposure of hands to radioactive material	Foster D. Snell(consulting firm), Monsanto ² , Air Force ²
1956	exposure of pilots to mushroom clouds from nuclear tests	Univ. of Cincinnati ³
1960-71	whole-body irradiation by X-rays	Oak Ridge Inst. of Nuclear Studies (TN) ⁴
1960-1974	whole-body gamma irradiation	Lawrence Berkeley Laboratory ²
early 1970s	neutron and ion beam irradiation	
<i>Occupational exposure to external radiation:</i>		
1945	exposure of skin to beta rays	Clinton Lab (Oak Ridge, TN) ²
1955	exposure of skin to radium-224	New York Univ. ²
1963-1971	irradiation of the testicles of prisoners by X-rays	Pacific Northwest Research Found., Univ. of Wash. ²
<i>Experiments to determine the effects on metabolism of radioactive materials⁵</i>		
1943-47	polonium injections	Univ. of Rochester ²
1945-47	plutonium injections	Manhattan District Hospital (Oak Ridge), UCSF, Univ. of Rochester, Univ. of Chicago ²
1946-47	injections of uranium-234 and uranium-235 nitrate to induce renal injury	Univ. of Rochester ²
late 40s	administration of radioactive iron to pregnant women	Vanderbilt Univ. ⁵
1946-56	ingestion of radioactive iron and calcium	MIT, Harvard ⁵
1950, 1952	exposure of skin to tritium;also some by ingestion and inhalation	Los Alamos Scientific Lab. ²
1953-57	uranium injections	Mass. General Hospital (Boston), ORNL ²
? (results published '59)	calcium-45 and strontium-85 injections	Columbia Univ., Montefiore Hosp.(Bronx, N.Y.) ²
1960s	uranium-235 and manganese-54 ingestion	Los Alamos Sci. Lab. ²
1961-63	ingestion of real and simulated fallout from nuclear tests	Univ. of Chicago, Argonne National Laboratory ²
1961-1965	radium and thorium injections/ingestion	MIT ²
? (results published '62)	ingestion of lanthanum-140	Oak Ridge Inst. of Nuclear Studies ²
1963	phosphorus-32 injections	Battelle Memorial Institute (Richland, Washington) ²
1962-65	intentional release of iodine-131 to environment/ingestion	ORNL, Nat'l Reactor Testing Station (ID) ²
1965	technetium-95 (metastable) and technetium-96 injections/ingestion	Pacific Northwest Lab. ²
1965-73	inhalation of argon-41/ingestion of various radioactive isotopes	AEC ²
1967	promethium-143 injections/ingestions	Hanford Env. Health Found., Battelle Memorial
? (results published '68)	lead-212 ingestions/injections	Univ. of Rochester ²

*Categories are those considered appropriate from publicly available evidence. The purpose is not always explicitly stated, and in this case, represents the judgments made by IEER staff.

AEC = US Atomic Energy Commission; UCSF = University California, San Francisco; MIT = Massachusetts Institute of Technology; ORNL = Oak Ridge National Laboratory.

⁵Some of these experiments may fit into other categories, and some may have had military applications.

Sources: ¹US Government Accounting Office. Examples of post-World War II Radiation Releases at US Nuclear Sites. GAO/RCED-94-51FS, November 1993; ²US House of Representatives. American Nuclear Guinea Pigs: Three Decades of Radiation Experiments on US Citizens, November 1986; ³Congressional Record - Senate, S 16371, October 15, 1971; ⁴Rosenberg H. Informed consent. Mocher Jones, September/October 1981;31-37,44. ⁵Smolowe J. The widening fallout. Time, January 17, 1994:30-31

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San Francisco [7]; 4) 57 inmates at the Oregon State Prison whose testicles were irradiated between 1963 and 1971 [7]; 5) 64 inmates at the Washington State Prison involved in a similar study to determine the radiation dose necessary to produce temporary sterility [7]; 6) 11 terminally ill cancer patients injected with radioactive calcium and strontium at Columbia University and Montefiore Hospital, New York City, in the late 1950s to determine the rate at which radioactive substances are taken up by human tissues [7]; and 7) 19 mentally retarded teenage boys at a state school in Massachusetts who, without consent, were exposed to radioactive iron and calcium in nutritional studies [8].

Investigators are also interested in intentional releases into the environment of radiation from government nuclear weapons plants, which threatened the health of plant employees and nearby populations. Information about one such experiment, known as the Green Run, began to emerge in the mid-1980s. Details about the Green Run and 12 other releases of radioactivity at three sites in three other states (Utah, New Mexico, and Tennessee) were documented in a Government Accounting Office (GAO) report released on December 16, 1993, by Senator John Glenn (D-OH) [10]. With the exception of the Green Run, these tests were unknown to the public before the release of this report. For a more comprehensive summary of human and environmental experiments, see Table.

The willingness of the Department of Energy and the Clinton White House to disclose the records of human radiation research is new, but families, journalists, and investigators have known of some of the experiments for many years. Many of these experiments have been reported in the open medical research literature. Public interest groups, journalists, and science writers have described many of these experiments on the basis of interviews with subjects and families [11-15]. In proceedings well covered in the press, the work of Eugene Saenger, a Cincinnati radiologist, was brought before the American College of Radiology in the late 1960s. Eugene Saenger was cleared of unethical conduct in irradiating cancer patients without informed consent for military and space science, not medical, objectives [9].

However, the government agencies, universities, hospitals, and the scientists involved have long resisted release of any information concerning these studies. In February 1987, in response to Representative Markey's committee report, "American Nuclear Guinea Pigs," the Energy Department rejected the report's conclusions and strongly rejected recommendations for

follow-up studies and compensation, stating:

There is no scientific reason to expect that any of the subjects who are not already being monitored will incur any harmful effects. Therefore, there is neither any reason for attempting any further follow-up studies on these subjects, nor to propose new legislation to compensate them [16].

Many DOE critics, including Representative Markey, contend that the report fell upon "deaf ears" partly because it might have threatened the Reagan administration's nuclear arms buildup of that period [16].

Barton Hacker, a historian working for the Department of Energy, began his official agency history with his volume, *Dragon's Tail: Radiation Safety in the Manhattan Project 1942-1946*, published in 1987, that hinted at but did not describe human experimentation. The book does make clear that early radiation scientists had a much clearer idea of radiation health effects, including cancer, than present apologists allow [17]. Barton Hacker's second volume, *Elements of Controversy: A History of Radiation Safety in the Nuclear Test Program*, was to have been published by the University of California Press in 1989 [18]. This book, which will be very useful in understanding the human experimentation programs, has been denied approval by the Department of Energy and is still unpublished, according to author Catherine Caufield and Argonne laboratory scientists [19].

Because there is no single repository for human radiation research, the files are held by government agencies, universities, hospitals, and private contractors. Many tens, if not hundreds, of additional government sponsored experiments involving radiation exposure may have been conducted. The full extent of radiation research on humans will not be known for months, possibly years. The DOE and other agencies argue that release of many relevant documents will require their declassification. There is an active debate within government about whether and how long research materials ought to remain classified. Given the harm that was evidently done, the likelihood of litigation, and public concern about environmental radiation contamination, it is likely that this story will unfold in Congress and the courts over a period of years.

Concerns Raised By the Disclosures

Several issues ought be kept in mind as we seek to understand what happened and why it happened. Full disclosure is the first

and most important task. What was done, when, and to whom? It seems clear that in many of these studies the subjects were not fully informed, if at all, about the nature of the research and risks that it might entail. All the research subjects who are still alive clearly deserve to be informed. Subsequent medical care for these subjects may be altered on the basis of knowledge of their prior radiation exposure. The provision of adequate medical follow-up will be an important criterion in the evaluation of these experiments. If evidence can be developed that subjects were harmed or wrongly experimented upon, compensation will be appropriate. National security can no longer be used as an official reason for not releasing complete information concerning these investigations.

Second, were the experiments ethical by today's or prior standards? What judgments and rationales did the research scientists use? Most importantly, do we have adequate protections and procedures in place for subjects in human experimentation in the future?

Third, can scientists in military or other "mission" agencies conduct human experimentation at all, or are conflicts of interest inevitable and unresolvable? What are the right policies for conduct of human research by the military?

A final task will be to reassure the public that radiation and nuclear medicine, with appropriate safeguards, currently have a unique role in medical diagnosis and treatment. Public fear of radiation and mistrust of the government and even of physicians will be heightened by these disclosures. Physicians must reaffirm the benefits and relative safety of current medical uses of radiation and nuclear medicine while acknowledging the inappropriateness and harm of some of the experimentation now being disclosed.

Scope of the Problem: Who Was Affected?

At the outset of an investigation into radiation research experimentation it will be necessary to establish what specific types of research are to be included. These definitions will not be easy. In addition to the radiation research subjects, other groups of Americans have been exposed to radiation in government-sponsored programs since the testing of the first atomic bomb in 1945: the atomic veterans, the downwinders, Marshall Islanders, uranium miners, and nuclear weapons production workers. Many agencies have sponsored radiation research in addition to the Department of Energy (and its precursor agencies: the AEC and the Energy Research and Development Agency [ERDA])

including the Department of Defense (DOD), the National Aeronautics and Space Administration (NASA), the Veterans Administration, the Department of Health and Human Services (DHHS) (formerly the Department of Health, Education and Welfare), and the Central Intelligence Agency (CIA).

In January, President Clinton established a Human Radiation Interagency Working Group to coordinate a government-wide effort to discover the "nature and extent" of government-sponsored experiments involving exposure to ionizing radiation. The Group includes the Secretaries of Energy, Defense, Health and Human Services, and Veterans Affairs, the Attorney General, the Administrator of NASA, and the Directors of the CIA and the Office of Management and Budget (OMB). The group will be supported by the Advisory Committee on Human Radiation Experiments. The advisory committee will be led by Ruth Faden of Johns Hopkins University School of Hygiene and Public Health. The review is intended to be limited to intentional exposures of individuals or environmental releases of ionizing radiation [20].

Other government research programs involving human experimentation might logically be included in a comprehensive review, such as studies done in the development of chemical and biological weapons and countermeasures to their use. Little is known publicly about these highly classified programs. According to a National Academy of Sciences report in 1993 [21], more than 4,000 military recruits were used to test mustard gas and other agents in tests during and after World War II. Some propose that the subject to be reviewed is all government-sponsored testing programs involving human subjects, including the testing programs of the Food and Drug Administration. However, the present investigation is likely to be limited by the Clinton administration to the human radiation experimentation issue.

Relationship To Environmental and Occupational Radiation Exposures

The sudden attention cast upon the cases of human radiation experimentation has renewed concern about other U.S. nuclear weapons activities that exposed large populations to radioactive and toxic materials [8,22]. Now that Energy Department and administration officials have begun to acknowledge the errors of past human radiation experimentation, explore compensation schemes, and declassify long-hidden records, many persons are seeking a renewed inquiry

and better response to the concerns and claims of people subjected to radiation exposure through other government nuclear weapons activities. These exposures include:

* Population exposure, either through atmospheric weapons tests or air, water, and soil contamination at nuclear weapons production plants. "Downwinders" refers to all those individuals who were exposed to radioactive fallout during the atmospheric testing program of nuclear weapons in the United States from 1945 to 1963, a program halted by the signing of the Limited Nuclear Weapons Test Ban Treaty. Hundreds of thousands of people, principally in Nevada, Utah, and Arizona, were exposed to fallout from atmospheric weapons tests (Fig 2). At least seven major epidemiologic studies on these downwinders have found a significant association between the radioactive fallout from atmospheric bomb tests in Nevada and an increased incidence of leukemia [23,24]. Off-site radioactive and toxic contamination has been discovered at nine of the major nuclear weapons complex facilities [25], and federal and state health agencies have only recently begun studies that are designed to reconstruct exposure levels at five facilities and attempt to ascertain whether the exposures have led to adverse health outcomes [26].

* The Marshall Islanders, who were exposed to fallout from atmospheric tests of nuclear weapons conducted by the United States in the South Pacific in the 1950s. The House Committee on Natural Resources holds information suggesting that the fallout from the testing was more widespread than previously believed [21]. Research since 1990 suggests that thyroid nodularity and cancer is present in excessive rates among the exposed islanders [27].

* Nuclear weapons plant workers, including approximately 600,000 persons who have worked since 1945 in the DOE's nuclear weapons plants. Worker exposures have been underreported and poorly monitored, and medical data relating to these exposures have been kept secret from independent investigators. DOE-led researchers have failed to follow up findings that suggest positive associa-

tions between worker exposure and cancer morbidity and mortality [28].

* The atomic veterans, those military personnel who were marched into test areas immediately following nuclear weapon detonations in the South Pacific (Fig 3) and at the nuclear weapons test site in Nevada in the 1940s and 1950s. As many as 250,000 U.S. troops were exposed to nuclear test radiation during the 17 years of atmospheric nuclear weapons testing [29]. The specific purposes of these military exercises varied, but all were linked to improving the U.S. military's capacity to conduct military actions in a nuclear war environment [14]. In 1980 the Centers for Disease Control (CDC) released the first health study of the nuclear veterans in which the leukemia rates were twice the expected rate [30].

These population-centered experiments, like most of the human experiments and intentional environmental exposures, were conducted without the informed consent of exposed populations and often with the knowledge that the exposures put human health at risk. In the case of military exercises, even if soldiers were informed of known risks, they may not have been in a position to disobey orders of their superiors. The population-centered exposures, particularly those affecting workers and off-site populations, were rarely followed by adequate medical monitoring of at-risk groups [28]. There would seem to be little moral distinction between the cases of intentional human and environmental radiation experimentation and other, population-centered radiation exposures that resulted from nuclear weapons design, production, and testing activities. Consequently, as Congress, the Energy Department, administration officials, and others seek to address the human radiation experiments, these agencies should at the same time place a high priority on conducting follow-up studies and providing medical information for all populations subject to radiation exposure.

The Need to Evaluate Individual Studies

The human radiation research studies appear to cover a broad ethical spectrum. Some will warrant comparison to experiments on concentration camp inmates, whereas others were scientifically justified and ethically sound. To establish a basis for compensation, each study will require an

individual assessment. It will be important to identify and consider the purposes of the experiment, the quality of the research design (if any), the intended use of the information gained, the character and competence of the subjects, the use and quality of informed consent, and whether there was appropriate medical follow-up.

The aims of the research varied. A number of the studies were clearly performed for military purposes. In the aftermath of Hiroshima, during the period of atmospheric testing, the military and the nuclear weapons production industry sought information about the biological activity of plutonium and the radioisotopes of atmospheric fallout. The toxicity of plutonium was of particular concern because the metal was extracted from reactor rods and milled and machined for bomb components. Some former AEC scientists claim that plutonium administration to human subjects was used to gather information for setting safety standards for weapons production workers and scientists. Plutonium has no medical uses [31]. Information on radioiodine, strontium, cesium, and other fallout isotopes was sought to justify the unfounded claims of the safety of atmospheric nuclear testing.

In the 1950s, military scientists sought information about sublethal and lethal radiation doses of direct gamma (X-ray) radiation for the design of radiation weapons, the neutron bomb, and battlefield nuclear weapons, as well as to support technology for fighting in areas of high radioactive fallout [32-34]. Studies in which soldiers marched into areas under atmospheric nuclear weapons detonations clearly served only military purposes. As biological science, the research objectives clearly could have been accomplished by animal studies or simulations. No clear scientific or military justification for these human exposures has been offered [12-14]. Finally, the manned space program and President Kennedy's challenge to place a man on the moon created the requirement to investigate the effects of large bursts of gamma radiation that unprotected astronauts might receive from solar flares. Testicular function was of particular concern because the astronauts were all young men in the prime of their reproductive years [35].

Human studies for military or space flight requirements can easily be distinguished from studies for the purposes of improving medical diagnosis and treatment. Occasionally, medical treatment was used by government scientists or sponsors as a justification for research whose purpose was military. For example, at Oak Ridge, a facility was constructed in the 1960s for the adminis-

tration of whole-body gamma radiation to human beings. Cancer patients were given sublethal (100 to 300 rad) whole-body doses in various exposures and their responses studied. Although the patients did in fact have terminal cancer, the research protocols were not designed as tests of advanced cancer therapy. The results of these investigations were published in military medical journals and conferences and are not in the cancer therapy literature [33,34,36].

It should be noted that several of the studies reviewed in the Markey subcommittee report were done in leading medical research facilities by highly regarded medical experts. Informed consent consistent with pre-1976 standards was obtained and only trace amounts of radioactive material were used. The information sought was clearly for improvement of medical therapy, as, for example, in the diagnosis and treatment of thyroid disease where radioiodine is today a standard agent.

The Scientists' Motives

Scientific motivation and behavior must also be criteria in review of these cases. The claim has been reported in the press that the ethical standards for the conduct of medical research were different 40 years ago and, further, that cold war military threats justified human experimentation [37]. But the ethical principles of scientific research were not invented recently. The Nuremberg Principles arising from the trial of Nazi war criminals for crimes including cruel and lethal human experimentation were well known to all American scientists as soon as they were published in 1949 [38,39]. American scientists doing hazardous human experimentation in Air Force and NASA laboratories referred to these principles and published standards for the conduct of research in which humans were subject to dangerous aerospace environments [40]. In a 1950 memorandum to Dr. Shields Warren, the chief medical officer of the AEC, Dr. Joseph Hamilton, a San Francisco neurologist and scientist in the plutonium injection studies, suggested that the experiments might have "a little of the Buchenwald touch," reflecting clear understanding of medical experiments by Nazi prison camp doctors [41].

However, in 1945, there were no clear standards of informed consent or mechanisms for monitoring the process of obtaining and documenting such consent. Scientists were considered to be responsible and, when full disclosure was not made, rationalizations about patient's peace of mind or minimal risk were common. In some cases, national security was blanket permission for secrecy and

even deception in research practices. Foregoing the Nuremberg principles was done with a larger good in mind. For these reasons, when the individual studies are examined, particularly those with clear military sponsorship and purpose, it may be difficult to establish their compliance with Nuremberg principles.

The Comparison to Nazi Crimes

As these research studies have come to public attention, some commentators have likened them to the experiments conducted by Nazi physicians in concentration camps during World War II. This kind of comparison deserves thoughtful scrutiny.

Although many of the U.S. radiation experiments were clearly or questionably unethical, none of the experiments under discussion here is truly comparable to the Nazi experiments. The Nazi concentration camps were part of an explicit program of genocide, or what today might be called "ethnic cleansing." The overall goal was to destroy categories of "undesirable" persons, predominately Jews, but also Gypsies and other minorities. The so-called experiments, most

of which had little or no scientific basis, and which produced little useful scientific knowledge, were inflicted on inmates who were condemned to die and conducted in sadistic ways in which pain and suffering were not in any way prevented.

The moral outrageousness of the Nazi experiments is so great that it deserves to be set aside as a special and horrible reminder of human evil in our own time. Many of the radiation experiments that have come to light in the U.S. are unethical. We understand that the researchers' judgment was distorted by the conflict of interest created by the cold war mentality and the scientific imperative. However, these incidents are nowhere near the magnitude of the Nazi atrocities. We risk trivializing our memory of the Nazi history to compare these radiation experiments to the Nazi tests with humans. It serves as a somber reminder, however, of the susceptibility of physicians and scientists to the temptation to overlook the rights and welfare of human subjects in the presence of conflicting incentives and social and peer pressure. How far this temptation can go is documented in studies of Nazi physicians [42].

One important parallel between some of the U.S. radiation experiments and the experiments of Nazi doctors is the allegiance of the physician to the state, or the government, which obscures their responsibility to the well-being of patients or subjects. (Of course, in the Nazi examples, there is no way the victims can be considered "patients.") This sus-

ceptibility to conflict of interest is the reason for the absolute need for external review of the ethics of research with human beings, and for especially careful review in experiments funded by agencies like DOE or DOD where the primary mission is not related to human health.

Secrecy

Secrecy is perhaps the central problem in this episode. If these experiments had received open discussion in the scientific community, including the importance of the information sought, alternative sources of information, experimental design, potential risk to subjects -- all those issues that concern current day institutional review boards (IRBs) -- might well have resulted in the studies never having been done or being done very differently, with greater concern for fully informed consent and protection of subjects. The argument has been made by Physicians for Social Responsibility and others that scientific oversight responsibility for radiation effects research ought to be housed in a health agency and be subject to open, independent, nongovernmental scientific review, as federal statute requires for all other human experimentation [28,43]. This proposal needs to be strongly reconsidered today.

It is ironic that while these studies have been secret, in that the government would not release information about their existence or the names of subjects or any other details, the results of many of these studies have been published in the open scientific literature and have always been available to knowledgeable scientists. Some radiation scientists involved in the studies now claim that because some results of these studies were published they never were secret, a somewhat disingenuous position after decades of official obstruction of public efforts to gain the information that the Department of Energy is now releasing. Several AEC memos confirm that it was agency policy to make no statement concerning radiation experiments.

Background: The Ethics of Human Experimentation

Three generalizations can be made about the ethics of the radiation research experiments. First, many of these studies must be viewed in the historical context in which different standards of informed consent were prevalent, but some of them must be considered unethical even when viewed within the appropriate historical context. It is vitally important to consider each such incident separately. Second, the major historical reality that led to the unethical conduct of research in those instances where it occurred

was the culture of secrecy and deception within DOE and military research units. Third, the most important goal in the open examination of these events should be the creation of guidelines that would prevent abuses from occurring in the future.

Informed Consent

The primary ethical principle of research with humans is informed consent. This has been a fundamental standard in medical care for almost a century, articulated by the courts as well as by professional societies. Thus, even when a medical treatment is indicated to treat a disease from which the patient is suffering, and no research is involved, it is still required that the patient be fully informed about risks, benefits, and alternatives and that he be permitted to refuse potentially beneficial treatment. Before World War I, the American jurist Benjamin Cardozo articulated the doctrine as follows: "Every human being of adult years and sound mind has a right to determine what shall be done with his own body" [44].

The doctrine of informed consent grew within case law after World War II as part of the growth of malpractice litigation. It was established that physicians were required to inform patients of potential risks of medical treatments. Since it is virtually never possible for a layperson to be as well informed as the physician about complex medical issues, the standard of informed consent that developed was the "community standard," i.e., the physician was required to disclose only as much as was the standard of practice by other physicians in his community. In medical treatment the best interests of the patients themselves are the motivation for whatever risks are involved; in most research the benefit is to other, future, and unknown persons and, therefore, the subject's participation requires even more rigorous ethical standards, especially that of informed consent, to ensure respect for the person.

Hans Jonas has eloquently argued that medical research is an optional human goal of relative rather than absolute value, because it risks objectifying and using another human being for purposes that are not his or her own [45]. Every major ethicist writing about human research argues that it is dangerous to the moral fabric of society to consider potential social goals as higher values than respect for the individual, especially in the framework of research potentially affecting the physical or psychological integrity of the person. Individuals are called on to relinquish autonomy in society for goods that they recognize as social, such as civic government, education, and public health standards.

Becoming the subject of someone else's experiment, however, is such a dramatic infringement of personal civil rights that it may be done ethically only in the context of fully informed consent and voluntary altruism.

The centrality of informed consent to the ethical use of human subjects in research was established as an internationally accepted principle by the Nuremberg Military Tribunal in 1949, reiterated by the Helsinki Code of the World Medical Association in 1963, and updated in 1975 [38,46]. In addition to requiring the informed consent of the subject, these codes require that the experiment be of worthy enough scientific value to justify any -- even minimal -- risk to the subjects, that the investigators guard the subjects against all possible foreseeable pain, suffering, or disability, and that the subjects be able to withdraw from the study at any time. It is likely that most medical investigators in the 1950s knew the Nuremberg Code; but until the 1960s, there was no law in the United States that specifically protected the rights of the subjects of medical research [47].

Government Oversight

Federal oversight of research with human subjects began in the United States with the 1962 amendments to the Federal Food, Drug, and Cosmetic Act, which required that the investigator obtain the consent of the subject to receive an experimental drug "...except where they deem it not feasible or, in their professional judgment, contrary to the best interests of such human beings..." (FFDCA, Section 5 5 [i]) The regulations promulgated in 1966 allowed for no exceptions to the informed consent rule in "nontherapeutic" research, i.e., that which offered no possibility of treating a disorder that the subject suffered from.

In 1966, the National Institutes of Health (NIH) adopted requirements that each institution receiving federal funds provide assurance of the existence of a system of peer review that ensured that studies protect the rights and welfare of the subjects, obtain informed consent, and have a reasonable assessment of risk and potential benefits of the research. These three stipulations are at the core of both the Nuremberg Code and the Helsinki Declaration.

In the late 1960s and early 1970s, numerous unethical human research practices by respected, and often federally funded, researchers were disclosed. A classic article by Henry K. Beecher in 1966 in the *New England Journal of Medicine* catalogued numerous such research projects [39]. The Tuskegee study came to light, in which effective treatment of syphilis had been withheld

from a cohort of black men for more than 25 years after the discovery of penicillin in the name of medical research. Jay Katz, Professor of Law and Psychiatry at Yale, was a member of the commission appointed to study the Tuskegee project, which led to the NIH recommendations for stronger national regulation of human research [48]. Katz subsequently published his compendious book *Experimentation with Human Beings* [49].

The National Commission for the Protection of Human Subjects of Behavioral and Biomedical Research

In 1974 the U.S. Department of Health, Education, and Welfare appointed a National Commission for the Protection of Human Subjects of Behavioral and Biomedical Research. The commission delivered its final report in 1978, recommending, among other things, that every institution receiving any federal funds review all research projects prospectively to ensure ethical treatment of human subjects [50]. Each proposed project had to document the content of this review, as opposed to the earlier general institutional assurances of process. The committees that do this are referred to now as Institutional Review Boards or IRBs.

The National Commission also recommended the creation of a standing body that would review federally funded research at a national level. Thus, the Ethics Advisory Board was established by NIH to review new or particularly complex kinds of research such as in vitro fertilization and fetal tissue research. Although it was intended to be an ongoing body, it was disbanded in 1980 by DHHS. A new charter for the Ethics Advisory Board was approved in 1988, but was never signed by the president. A recent Office of Technology Assessment (OTA) study has strongly recommended the creation of a permanent, ongoing national research review board to consider the ethical implications of certain protocols or classes of federally funded biomedical and behavioral research [51]. Requiring any research linked with military or national security operations to undergo review by such a body would be a logical step toward prevention of future unethical research obscured from public view by policies of secrecy and nondisclosure.

In light of this history, any research done before 1976 was not likely to have been reviewed by an impartial body concerned about the protection of human subjects [37]. Without the IRB mechanism, conflict of interest is a serious problem, and even well meaning investigators may have overlooked ethical issues. Especially if it was expected that no harm would come to the subjects, as in many

of the studies that used radioactive isotopes as metabolic tracers, investigators probably took a paternalistic stance, assuming that there was no need for the subjects to know that radioactivity was being used. IRBs today, however, would insist that subjects be given this information, even if the investigators were sure the material was harmless. (In the 1950s when many of these studies were done, less was known about radiation effects, particularly long-term effects, so it is incorrect, without analysis of the individual studies, to describe the investigators as knowing whether or not radiation doses were harmless.)

Standards Applied to Radiation Research

Informed Consent

Valid informed consent requires: 1) that the subject be given full information about the study to be performed, and, if it is a therapeutic study, about the alternative treatments available; 2) that the subject be competent to understand the information rendered and able to make a decision for himself; and 3) that the decision be free and uncoerced.

Thus, any study in which people were not given full information violates this standard. Studies involving mentally ill or cognitively impaired subjects usually violate the second standard. Many ethicists believe that research on prisoners violates the standard of noncoercion because of the inherent vulnerability of institutionalized persons, especially those incarcerated involuntarily, who might believe that they would be punished for not participating or that their treatment might be better if they do. The Washington and Oregon studies of testicular radiation are examples of this problem, i.e., would an average "man on the street" have agreed to take part in these experiments?

Risk-Benefit

The National Commission in its 1976 report charged the IRBs with assessing two ethical standards in addition to informed consent: risk-benefit analysis and justice in the selection of subjects. Risk-benefit analysis requires evaluation of the scientific merit of the study and weighing whether the risks to the subjects are justified by the potential findings of the study. Thus, subjects should not be allowed to consent to a study that is so poorly designed that little useful information is likely to result or to one where the risks to the subjects are so great that even a study producing valuable information is not warranted.

The environmental release experiments such as the Green Run at Hanford [10] are examples of the former type of ethical prob-

lems. Here the studies were not intended to study effects on human beings, but potentially thousands of people were unknowingly exposed to radiation for the sake of experiments related to understanding spread of fallout or interpretations of aerial intelligence over the Soviet Union. The humans exposed were not studied for any potential medical effects, violating another tenet of the Nuremberg code and requiring the expensive and difficult dose reconstruction studies currently conducted by the CDC.

Vulnerable Persons

Justice requires that persons who are intrinsically vulnerable to exploitation, unable to speak for themselves, or representative of disadvantaged groups not be used as subjects of research unless the research addresses a problem specific to that group that cannot be as easily done in a more general population. The Oak Ridge whole-body radiation experiments, which used enormous doses, are probably examples of studies so potentially dangerous that information to be gained would not have warranted approval of these studies, even if informed consent had been obtained, which it had not [52,53]. That the subjects were said to be terminally ill is not a justification. In fact, by criteria drawn from the Nuremberg and Helsinki Codes and further articulated by the National Commission, these subjects would be considered especially vulnerable to exploitation and, therefore, the ethical standards for research are even stricter.

By these standards, nursing home residents or retarded people in institutions should not be subjects of research unless the studies apply directly to their own well-being and could not be done using other subjects. In particular, institutionalized populations are not to be used only because it is more convenient for the investigator. The study of nutritional physiology done in retarded children in Massachusetts apparently violates this principle, but reflects widespread practice among legitimate investigators of the time who commonly used institutionalized populations for their research simply because it was more convenient [7].

Recommendations

Government Policy

The U.S. government must review and correct its policies regarding: secrecy and declassification of research reports, ethics of the conduct of human experimentation, compensation for unethical research, guidelines for human experimentation in mission laboratories, mistrust of government, and the use

of unethically obtained data.

The government's policy with regard to these disclosures should respond to the pervasive public fear of radiation. Policy should focus on improving radiation protection programs and on efforts to restore public confidence in the agencies responsible for radiation health and safety. Only then can trust in the government's assertions of safety be restored. This restoration will require acknowledgment of the previous policy of secrecy and, in some cases, frank deception, as well as clear statements from the government about how such abuses will be prevented in the future.

Up till now, it has been U.S. government policy, with regard to health and radiation from nuclear weapons production and radiation exposures in general to give blanket reassurance that the health of workers and of the general public has been fully protected and that there has been no risk of disease or injury from radiation in the United States. It has been the policy of the DOE in recent administrations to avoid examination of available health effects data and not to allow independent research scientists to explore claims of harm. Secrecy in the name of national security, data ownership, and subject confidentiality has limited independent scientific review of government information on radiation health effects [28].

National Review Panel

Perhaps the most important recommendation to be made at this time is to establish a national, impartial, and credible scientific and ethical review process for the evaluation of each of the individual cases. Such a panel, like the previous National Institute of Health Ethics Advisory Board, should be national in scope and have authority to review all research in which governmental agencies are involved in any way. There should not be a special body just to review radiation-related research because there are many other issues of potential ethical concern that are hard to predict or categorize at this point. The members should include appropriate scientists, ethicists, public officials, and legal scholars. It should be charged to review prospectively selected proposed studies as well as develop broad policy regarding generally difficult or controversial areas of research.

The panel ought to review all present and past government experimentation with human subjects to inform our future policies regarding medical follow up and compensation. The panel would also analyze published and unpublished research reports to establish the purpose, experimental design, consent, and other scientific ethical and appropriate-

ness issues. It would not be a wise use of the National Institutes of Health Ethics Advisory Board to do the extensive retrospective review of the research studies being investigated because the NIH may have approved studies now being rereviewed. The panel should have the authority to subpoena documents and witnesses, and should include in its membership representatives of an affected class of radiation subjects.

Content and Scope of Research

Responsibility for the conduct of new research, specifically prospective studies of health outcomes of subjects of previous government-sponsored human experimentation, must be transferred from the sponsoring agencies [28]. The barrier of secrecy and the claim of national security must be removed from documents pertaining to any and all human experimentation conducted by any agency of the federal government including the CIA. All radiation workers and potentially exposed public populations should be enrolled in a registry and prospective studies of radiation health effects be undertaken, even in those whose exposures may have occurred many years ago. Finally, the scope of human experimentation to be reviewed should not be limited to radiation research but include studies of chemical and biological warfare.

National Data Archives

A single agency, such as the National Archives and Records Administration, ought to be required to collect and organize the data, which now are spread among many different government bodies, and to create a single data repository for this project. Awaiting the creation of such a resource ought not be a barrier to some studies that could and should proceed with existing databases. The creation of a usable data source, open to the public as well as to investigators, is a complex enterprise requiring expertise in epidemiology, information systems, and strategies to protect the confidentiality of individuals. All these issues have been considered in some depth in the early stages of the development of the Comprehensive Epidemiologic Data Resource (CEDR) [54] recommended by the Secretary's Panel for the Evaluation of Epidemiological Research Activities (SPEERA). In 1989 SPEERA was created and charged with evaluating the DOE's record in occupational safety and protection of its workers from health hazards [55]. CEDR was the proposed database on the some 600,000 nuclear weapons production workers since the inception of the nuclear weapons programs [54]. Unfortunately, the CEDR project

has not been completed.

Identification of Unethical Studies

Much of the knowledge produced by the radiation studies at the center of this current controversy has been put into use in treatment of cancer, in designing studies to evaluate long-term effects of radiation exposure, in designing manned space travel, and in setting occupational safety standards. It would be neither possible nor desirable to pretend this knowledge does not exist. It is, however, important that scientists referring to such studies identify them as unethical studies. This way the authors do not stand to gain in prestige or reputation by the exploitation of subjects and, in addition, future investigators are reminded of the ethical necessity to protect human subjects in their own work. ♣

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