

## Prisoners: A Captive Research Population

I N July 1949 a medical advisory panel met in Washington, D.C., to discuss psychological problems posed by radiation to crews of a then-planned nuclear-powered airplane. During the meeting an Air Force colonel noted that crewmen were concerned about anything physically harmful, but especially anything seen as a threat to what he delicately called, using a euphemism of that gentler era, the "family jewels."<sup>1</sup> The nuclear-powered airplane was never built, but concern about radiation hazards to testicular function in space flight, weapons plants, nuclear power plants, and on an atomic battlefield remained.

This concern provides some of the context for a brace of almost identical experiments carried out between 1963 and 1973 in which 131 prisoners in Oregon and Washington submitted to experimental testicular irradiations with national security and other societal goals, but no potential for therapeutic benefit for the subjects. The studies were directed by Carl G. Heller, M.D., a leading endocrinologist of his day, and by Dr. Heller's protégé, C. Alvin Paulsen, M.D. Perhaps because they involved irradiation of the testicles, they have caused great public concern. They were also noted briefly among the thirty-one experiments Representative Edward J. Markey of Massachusetts publicized in his 1986 report on radiation research on

human subjects.<sup>2</sup> Both studies were funded solely by the Atomic Energy Commission. Drs. Heller and Paulsen were interested in the effects of radiation on the male reproductive system, especially the production of sperm cells. The government was interested in the effects of ionizing radiation on workers, astronauts, and other Americans who might be exposed, in a nuclear attack for example.

Both doctors viewed prisoners as ideal subjects. They were healthy, adult males who were not going anywhere soon. In 1963 few if any researchers had moral qualms about using them as subjects, although there seems to have been a consensus in the research community on the rules that should govern such experimentation. By 1973, however, some ethicists, researchers, and others, such as the investigative journalist Jessica Mitford, pointed out that incarcerated people were not well placed to make voluntary decisions. In 1976, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research recommended the banning of almost all research on prisoners. Prison experimentation effectively came to an end in this country a few years after the commission offered its recommendations.

The Heller and Paulsen experiments were groundbreaking scientifically, and they were conceived as having an important government

purpose—protecting Americans engaged in building the nation's high-priority nuclear and space programs. But looking back through the lens of history, there appears to be an inconsistency between the way human subjects were treated in this research and the standards intended to govern their treatment. Although both Dr. Heller and Dr. Paulsen showed sensitivity to some ethical issues, in both cases the researchers themselves and some of those charged with oversight at both the federal and state levels did not completely live up to what appear to have been well-understood standards applicable to their research. In this failure they were no different from many if not most of their contemporaries. Times were changing, however, and in the end, state officials shut down both sets of experiments, bringing practice more into line with the standards already on the books of some government agencies and private research organizations.

Among researchers who used prisoners as subjects, as early as 1958 the Nuremberg Code was recognized as a model set of rules for conducting human subject research.<sup>3</sup> It is equally clear that the work in the Oregon and Washington prisons did not carefully follow all these rules. Moreover, the funding agency, the Atomic Energy Commission, had its own rules for the conduct of research with human volunteers, which were not fully observed in these experiments. As discussed in chapter 1, in 1956 the AEC's Isotope Division program provided that where healthy subjects were used for research, they needed to be volunteers "to whom the intent of the study and the effects of radiation have been outlined." A 1966 memorandum from the AEC's office of general counsel to the director of the Division of Biology and Medicine sheds some light on the agency's standards at that time, and why it had them. The specific experiments referred to in the memo—plutonium and promethium injections or ingestion—appear not to have been carried out, but the "use of human volunteers in experiments" is addressed in general terms. The memo calls for "volunteer[s]" to sign a written, witnessed agreement attesting to their sound mental state and free will, to their understanding of the purposes and risks of the planned experimentation, and

that the experiment was not being done for their benefit. The relevant paragraph concludes: "Assuming complete understanding and no unequal bargaining factors (e.g. pressure on prisoners to submit), such an agreement would protect against liability for unauthorized invasion of the person."<sup>4</sup>

Finally, those attending a 1962 conference on research using prisoners as subjects reached a consensus on a higher standard for subject selection and informed consent than was typically observed in Oregon and Washington. For example, the conferees argued that potential prisoner subjects should have enough information to avoid their being deceived and that inducements to prisoners should not be so high as to invalidate consent.

The surviving researchers disagree somewhat about the genesis of the testicular irradiation experiments, which the available documentary evidence does not completely resolve. What follows is a version based on and consistent with both the Heller and Paulsen accounts.

Early in 1963 the AEC held a conference in Fort Collins, Colorado, for investigators who were using radiation in studies of reproduction in animals. Dr. Heller was invited. In a bedside deposition taken after he suffered a stroke in 1976, he recounted what happened:

The whole conference finally focused on man. A given group at Fort Collins was working on mice and another group was working on bulls, and then they concluded, what would happen to man[?] They extrapolated the data from bulls or mice to man. I commented one day to Dr. [Paul] Henshaw, who was then . . . with the AEC, that if they were so interested in whether it was happening to man, why were they fussing around with mice and beagle dogs and canaries and so on? If they wanted to know about man, why not work on man[?]<sup>5</sup>

According to Dr. Heller, that remark stimulated the AEC to solicit a research proposal from him to study the effects of radiation on the male reproductive system.

Dr. Paulsen, however, recalled a different scenario in a 1994 interview by Committee staff at his office in Seattle.<sup>6</sup> He said he was invited to the AEC's Hanford, Washington, facility in 1962 to act as a consultant after three workers were accidentally exposed to radiation. Like Dr.

Heller, Dr. Paulsen had no previous experience with radiation exposure. He said he was brought in because of a chapter he had written on the testes in an endocrinology text. As a result of that experience, Dr. Paulsen said, he became interested in doing work on the effects of radiation on testicular function, discussed his idea with colleagues, and contacted the AEC to see if the agency would be interested in funding his work.

Whether or not Drs. Heller and Paulsen initiated their projects separately, the practical result was that both received AEC funding and carried out their research projects during the 1960s and early 1970s in the Oregon and Washington state prisons, respectively. Although the two studies were very much alike in their methods and objectives, there were small differences. They used different consent forms, different levels and means of irradiation, and different subject-selection procedures.

This chapter provides accounts of the Washington and Oregon experiments that focus on the failure of these two research projects to live up fully to ethical standards of their time; the Committee's analysis of the risk to subjects in the two experiments; capsule descriptions of a number of other radiation experiments using prisoners as subjects; and a general ethical analysis of radiation experiments using prisoners as subjects.

## THE OREGON AND WASHINGTON EXPERIMENTS

### Oregon

In 1963 Carl Heller was an internationally renowned medical scientist, a winner of the important Ciba Prize. In the field of endocrinology, he was a preeminent researcher, so it is not surprising that when the AEC decided to fund work on how radiation affects male reproductive function, they would turn to him. He designed a study to test the effects of radiation on the somatic and germinal cells of the testes, the doses of radiation that would produce changes or induce damage in spermatogenic cells, the amount of time it would take for cell production to recover, and the effects of radiation on hormone excretion.<sup>7</sup> To accomplish this

he had a machine designed and built that would give a carefully calibrated, uniform dose of radiation from two sides. The subject lay face down with his scrotum in a small plastic box filled with warm water to encourage the testes to descend. On either side of the box were a matched set of x-ray tubes. The alignment of the x-ray beams could be checked through a system of peepholes and mirrors. Subjects were required to agree to be vasectomized because of a perceived small risk of chromosomal damage that could lead to their fathering genetically damaged children. To carry out this work Dr. Heller was to receive grants totaling \$1.12 million over ten years.

Mavis Rowley, Dr. Heller's former laboratory assistant, who was interviewed by Advisory Committee staff in 1994, said that the AEC "was looking for a mechanism to measure the effect of ionizing radiation on the human body. . . ." She said testicular irradiation was promising because the testes have "a cell cycle and physiology which allows you to make objective measurements of dosimetry and effect without having to expose the whole body to radiation."<sup>8</sup>

Although official documentation is fragmentary, it is clear from other evidence such as interviews and contemporary newspaper articles that the concerns cited above—worker exposures, potential exposures of the general population as a result of accidents or bomb blasts, and exposures of astronauts in space—were of interest to the AEC.

In the case of the astronauts, the National Aeronautics and Space Administration has been able to find no evidence of direct involvement in Dr. Heller's project. Yet Ms. Rowley remembers with clarity that NASA representatives, even astronauts themselves, attended meetings with their research team. In her 1994 interview, she said, "NASA was also very interested in this. . . . There was a section of activity which was devoted to what effect would the sun flares and so forth, which give out significant radiation have on the astronauts. And so there were meetings that went on which actually included some of the astronauts attending them. . . ." Rowley explained that the astronauts were concerned that reduced testosterone production might make them lose muscle function, which could

compromise their mission, but, belying the comment of the colonel in the 1949 nuclear-powered airplane meeting who said that crewmen were concerned about anything physically harmful, she said they seemed altogether unconcerned "about their own health."<sup>9</sup> During his 1976 deposition, Dr. Heller remarked: "What we would like to supply the medical community with is what happens when you give continual very small doses such as might be given to an astronaut."<sup>10</sup> Moreover, in 1965, Dr. Heller served as a consultant to a Space Radiation Panel of the National Academy of Sciences-National Research Council. And finally, Harold Bibeau, an Oregon subject, recalls that Dr. Heller told him when he signed up for the program that NASA was interested in the results.<sup>11</sup>

At the time the Oregon experiment got under way, using prisoners as research subjects was an accepted practice in the United States. And in this particular study Oregon law was interpreted by state officials as permitting an inmate to give his consent to a vasectomy, which they appear to have seen as analogous to consenting to becoming an experimental subject. However, important ethical concerns of today such as balancing risks and benefits, the quality of informed consent, and subject-selection criteria appear, on the whole, not to have been carefully addressed or not addressed at all by the investigators or those responsible for oversight.

With respect to the health risks associated with the testicular irradiations, there was very little reliable "human" information at the time about the long-term effects of organ-specific testicular exposure to radiation. Hiroshima and Nagasaki bomb data, however, which of course were not organ specific, suggested that the likelihood of inducing cancers with the amount of radiation Dr. Heller planned to use was small. By way of comparison, today's standard radiotherapy of the pelvis, for prostate cancer for example, often results in doses to the testicles in the ranges encountered in these experiments.

So what did Dr. Heller tell subjects about the chronic risk? The answer appears to have been nothing in the early years and, later on, perhaps a vague reference to the possibility of "tumors" but not cancer. In a deposition taken in 1976 a subject named John Henry Atkinson said he was

never told there was a possibility of getting cancer or any kind of tumors as a result of the testicular irradiation experiments. Other subjects deposited in 1976 also said they had not been warned of cancer risk, and when asked by one subject about the potential for "bad effects," Dr. Heller was reported to have said, "one chance in a million."<sup>12</sup> When asked in his own deposition what the potential risks were, Dr. Heller said, "The possibility of tumors of the testes." In response to the question "Are you talking about cancer?" Dr. Heller responded, "I didn't want to frighten them so I said tumor; I may have on occasion said cancer."<sup>13</sup>

The acute risks of the exposures included skin burns, pain from the biopsies, orchitis (testicular inflammation) induced by repeated biopsies, and bleeding into the scrotum from the biopsies. Using consent forms and depositions as a basis for determining what the subjects were told, it appears that they were adequately informed about the possibility of skin burns; sometimes informed, but perhaps inadequately, about the possibility of pain; informed about the possibility of bleeding only from 1970 on; and never informed of the possibility of orchitis.

As far as the quality of consent is concerned, the evidence suggests that many if not most of the subjects might not have appreciated that some small risk of testicular cancer was involved. It is also not clear that all subjects understood that there could be significant pain associated with the biopsies and possible long-term effects.

In selecting subjects, Dr. Heller appears to have relied on the prison grapevine to get out the word about a project he apparently believed the Atomic Energy Commission did not want publicized. In a 1964 memorandum he was paraphrased as saying "at Oregon State Penitentiary, the existence of the project is practically unknown."<sup>14</sup> In a 1966 letter to the National Institutes of Health describing the review process at the Pacific Northwest Research Foundation, a respected, free-standing research center, Dr. Heller and two colleagues wrote that "the inmates are well informed by fellow inmates regarding the general procedures concerned (i.e., collecting seminal samples, collecting urines for hormone studies, submitting to testicular biopsies, receiving medication orally or by injection,

and having vasectomies . . . ).<sup>15</sup> If the volunteers were healthy and normal they were accepted for a trial period during which they donated semen samples. If all went well, in a matter of weeks they were accepted into the radiation program, as long as the prison's Roman Catholic chaplain certified that they were not Roman Catholics—because of the church's objection to their providing masturbated semen samples—and they could pass what appears to have been a cursory psychological screening designed to ensure they had no underlying objections to the required vasectomy. A copy of a form titled "Psychiatric Examination" provided by Harold Bibeau and signed with the initials of the examining psychiatrist, WHC for William Harold Cloyd, says in full:

11-4-64 Seen for Dr. Heller—Never married, quite vague about future. Feels he doesn't want children—shouldn't have any. I agree. No contraindication to sterilization.

As far as potential health benefits to the subjects are concerned, there were none, and the inmates who volunteered for the research were told so. The benefits were in the form of financial incentives. A review of applications for Dr. Heller's program, and depositions of prisoners who sued Dr. Heller, various other individuals, and the state and federal governments for violation of their rights, clearly indicates that money was in most cases the most important consideration in deciding to volunteer. In prison industry inmates were typically paid 25 cents a day. For participating in the Heller program they received \$25 for each testicular biopsy, of which most inmates had five or more, plus a bonus when they were vasectomized at the end of the program, which appears to have been an additional \$25. Some inmates indicated that they were grateful for an opportunity to perform a service to society. An obvious ethical question is whether the money constituted a coercive offer to prisoners.<sup>16</sup>

During the course of his study between 1963 and 1973 Dr. Heller irradiated sixty-seven inmates of the Oregon State Prison. Nominally, three institutions had some oversight responsibility for Dr. Heller's work—the Oregon Department of Corrections, the Atomic

Energy Commission, and the Pacific Northwest Research Foundation, where Dr. Heller was employed. Practically speaking, however, it appears that Dr. Heller conducted his research independently. As an example of his independence, as recounted by Ms. Rowley, the AEC requested that Dr. Heller begin irradiating subjects at 600 rad and work upward, but he refused and in the end set 600 rad as an upper limit.<sup>17</sup> (It is not clear whether Dr. Heller was concerned about risk to the subjects' health or other research criteria.) Dr. Heller also was a member of the committee at Pacific Northwest Research Foundation that had responsibility for overseeing his research, giving him a voice in the oversight process. This committee was authorized under a foundation regulation titled "Policy and Procedures of the Pacific Northwest Research Foundation With Regard to Investigations Involving Human Subjects." In a section on ethical policy, the document says: "Since 1958 the investigators of this Foundation have conducted all research under the ethical provisions of the Nuremberg [*sic*] Code, modified to permit consent by parents or legal guardians."<sup>18</sup>

In January 1973, in a rapidly changing research ethics environment, the Oregon irradiations were terminated when Amos Reed, administrator of the Corrections Division, ordered all medical experimentation programs shut down essentially because he concluded that prisoners could not consent freely to participate as subjects. It is not known exactly what was behind the timing of Reed's decision, but according to *Oregon Times Magazine*, he had recently read Jessica Mitford's article in the *Atlantic Monthly* titled "Experiments Behind Bars" and an article in *The (Portland) Oregonian* headlined "Medical Research Provides Source of Income for Prisoners."<sup>19</sup>

In 1976, a number of subjects filed lawsuits effectively alleging poorly supervised research and lack of informed consent. In their depositions they alleged among other things that prisoners had sometimes controlled the radiation dose to which they were exposed, that an inmate with a grudge against a subject filled a syringe with water instead of Novocain, resulting in a vasectomy performed without anesthetic, and that the experimental procedures resulted in

considerable pain and discomfort for which they were not prepared.<sup>20</sup> These suits were settled out of court in 1979. Nine plaintiffs shared \$2,215 in damages.<sup>21</sup>

For the last twenty years all efforts to put in place a medical follow-up program for the Oregon subjects have been unsuccessful. Dr. Heller and Ms. Rowley explicitly favored regular medical follow-up. During the period between 1976 and 1979, the pending lawsuits might have been the reason for the state's reluctance to initiate a follow-up program, but it is less clear why during other periods such efforts have also failed. Two possible reasons suggested by state officials are the cost of such a program and the difficulty of finding released convicts. Other possible reasons are that a follow-up program would not provide a significant health benefit to former subjects and that it would not provide significant new scientific knowledge. According to Tom Toombs, administrator of the Corrections Division of the State of Oregon at the time of the lawsuits, the Corrections Division wrote to the AEC's successor (the Energy Research and Development Administration) in early 1976 recommending medical follow-up for the subjects. Mr. Toombs said there was no record of a response to this request.<sup>22</sup> In 1990, James Ruttenber, an epidemiologist at the Centers for Disease Control, designed a follow-up program for Oregon, but it has not been implemented. In an interview with Advisory Committee staff, Dr. Ruttenber said state officials told him that Oregon does not have sufficient funds to carry out his plan.<sup>23</sup>

#### Washington

C. Alvin Paulsen was a student of Carl Heller at the University of Oregon in the late 1940s, and in the early 1950s he was a fellow in Heller's lab. But by 1963 he was ready to direct a substantial research program on his own. His chance came when he was called to Hanford to consult on an accidental radiation exposure of three workers. The upshot of this experience was a \$505,000 grant from the Atomic Energy Commission to study the effects of ionizing radiation on testicular function. Dr. Paulsen remarked in the 1994 interview with Advisory Committee staff that

the main research questions he was trying to answer were what would constitute "a reasonably safe dose" of ionizing radiation to the testes as well as what dose "would cause some change in sperm production and secondly, to determine the scenario of recovery."<sup>24</sup> He recalled a 1962 letter to the Washington State Department of Institutions in which he wrote that he would like to find out "the maximum dose of radiation that would not alter spermatogenesis" and "the maximum dose of radiation that affects spermatogenesis, but only temporarily."<sup>25</sup> Dr. Paulsen said in a 1995 telephone interview, however, that for reasons he can no longer remember, he limited dosage to 400 rad, not enough to test a maximum-dose thesis.<sup>26</sup>

In the 1994 interview, Dr. Paulsen said:

When I recognized a tremendous void of information relative to human exposure, and space travel had started and there was the question of solar explosions and ionizing radiation exposure in space, the nuclear power plants were going in then, a few men throughout the world were exposed . . . I then contacted the Atomic Energy Commission to determine . . . whether they would entertain receiving an application.<sup>27</sup>

Obviously, Dr. Paulsen too was interested in the space applications of his research. In 1972 he and a colleague published their work titled "Effects of X-Ray Irradiation on Human Spermatogenesis" in the proceedings of the National Symposium on Natural and Manmade Radiation, a NASA-sponsored symposium. And Dr. Paulsen said that when he explained his research to potential subjects, one of the things he referred to was concern about exposures in space.<sup>28</sup> An August 1, 1963, article in the *Oregonian* about the Washington experiments said, "Although one of the primary benefits of the research will be in space exploration, the findings are also expected to be of value to an atomic industry where an occupational hazard might exist."<sup>29</sup>

One major difference between the Heller and Paulsen projects was that from the outset Dr. Paulsen planned to eventually move from x rays to neutron irradiation, which, among other things, is more analogous than x rays with the radiation encountered in space.<sup>30</sup> A neutron generator was purchased, calibrated, and shielding

was developed. However, the work took years to complete, and this part of the research was never carried out. Dr. Paulsen has expressed the belief on a number of occasions that one reason his project was terminated by the state of Washington in 1970 was concern about the possibly greater risks of exposing subjects to neutrons. Another difference was that Dr. Paulsen used a standard General Electric x-ray machine, which he says he believed would deliver as precise and well-targeted a dose of radiation as Dr. Heller's specially designed machine.<sup>31</sup>

Still another difference was that at a certain stage of the Washington study, Dr. Paulsen used the prison bulletin board to advertise for volunteers. Under the headline "Subject: Additional Volunteers for Radiation Research Project," a notice said in part:

The project concerns effects of radiation on human testicular function and the results of the project will be utilized in the safety of personnel working around atomic steam plants, etc. . . . It is possible that those men receiving the higher dosages may be temporarily, or even permanently, sterilized. It should be understood that when sterilized in this manner, a man still has the same desires and can still perform as he always has. . . . Submit to surgical biopsy. (This is a simple procedure performed under local anesthesia. It is not a very painful procedure.)<sup>32</sup>

According to a March 9, 1976, report prepared for then-Governor Daniel J. Evans by Harold B. Bradley, director of Washington state's Adult Corrections Division, neither Dr. Paulsen's 1963 outline of his research project nor the November 1964 announcement to inmates mentioned a requirement to undergo a vasectomy at the end of the experiment to ensure that subjects would not father genetically damaged children.<sup>33</sup> Dr. Paulsen said he did not recall precisely when in the recruitment process the vasectomy requirement was conveyed to subjects, but he pointed out that once it was they had the option of dropping out of the project without penalty.<sup>34</sup>

Dr. Paulsen's review process and consent procedures are less well documented than Dr. Heller's, but he says his research application, including provisions for subject selection and consent, was approved by what he described as

a "human experimentation committee" at the University of Washington. He said the process was "very informal," noting that it was done over the phone. Paulsen added that "somewhat later" his work was also reviewed by a "radiation safety committee."<sup>35</sup> His recollection of both processes is vague. The minutes of a December 10, 1969, meeting of a University of Washington Research and Clinical Investigations Committee at the U.S. Public Health Service Hospital in Seattle includes a recommendation that Dr. Paulsen's consent form be modified to indicate that "a risk of carcinoma of the testes exists although it is extremely small."<sup>36</sup> According to Mr. Bradley's report, his department's records show that Dr. Paulsen's project was reviewed and approved on two occasions—March 1963 and June 1966—by the University Hospital Clinical Investigation Committee. The report shows no state Department of Institutions review until mid-1969.<sup>37</sup>

The Bradley report and related correspondence from 1970 show that at that time some state officials had a sharp concern for research ethics. In mid-1969 a review of all experimentation in the prison system was undertaken by Dr. Audrey R. Holliday, chief of research for the Department of Institutions. At this time Dr. Holliday took steps to temporarily halt the irradiation phase of the project. After investigating the origins of Dr. Paulsen's research, Dr. Holliday asked the University of Washington to conduct a new review of the study, emphasizing her concern about the state's responsibility to safeguard human rights. The university stood by its initial findings allowing the research to continue, although at about the same time it turned down Dr. Paulsen's request to move into the neutron-irradiation phase of his project.<sup>38</sup>

Dr. Holliday then debated the issue with Dr. William Conte, director of the Department of Institutions, who was disposed to allow the project to continue. On March 18, 1970, she wrote a letter to Dr. Conte noting,

. . . There is no question but what the Federal Government has made considerable investment in this project. The Federal Government, however, as a reading of any newspaper will show, has supported a number of projects over which there have been many moral-ethical questions (both large and small) raised, e.g., nerve gasses, toxins, etc. I remind you that the

Federal Government is not responsible for the care, safety and safeguarding of human rights of populations under the purview of the Department of Institutions. This is a responsibility we must discharge, regardless of the amount of money that the Federal Government is willing to invest in a project. . . .

There is no doubt but what the prison setting is an ideal setting for this type of research. . . . I suppose concentration camps provided ideal settings for the research conducted in them. . . . If, in fact, non-inmates were to volunteer in the substantial numbers of persons Dr. Paulsen needs, then I would have less qualms about offering up a captive population for this research, i.e., I would have some evidence, assuming the volunteers were, in fact, normal, that non-captive populations might make the same decision as a captive population. . . .

I am not against high risk research. I have engaged in some myself. I am not against federally sponsored research. I have engaged in some myself. However, the risk should be commensurate with the probable benefits to be received by the population or others like it to follow. I don't think we can argue that in this case.

Neither am I opposed to use of a prison population on a volunteer basis for research projects that may not be of direct benefit to the population, but which are of clear benefit to society or mankind. I don't think we can argue that in this case either.<sup>39</sup>

Dr. Holliday also argued that the study should have been done on "lower order primates" and that if the state allowed Dr. Paulsen's study to continue it would forfeit its right to speak out on behalf of human rights relating to future research proposals.<sup>40</sup>

While favoring continuation of Dr. Paulsen's research, Dr. Conte authorized a review by the Department of Institutions's Human Rights Review Committee. The committee recommended that the study be shut down, noting that the Paulsen project "seems clearly inconsistent with the standards laid down by the Nuremberg Code" for the protection of human subjects with respect to freedom of choice and consent. The recommendation went on to say that "within the context of Dr. Paulsen's project, it is largely irrelevant whether or not a volunteer declares his 'desire to undergo vasectomy' since there is no assurance that his real reasons would be ethically-morally acceptable or that his reasons (whatever they may be) will stand the test of reality after

release." It specified that the money paid for participation and the expectation of privileges, "real or imagined," could constitute undue inducements.<sup>41</sup>

This review, according to the report, "recommended that Dr. Paulsen's request for continuation of his study be rejected as it was found to be inconsistent with standards for the protection of the individual as a research subject. The essential issue raised by departmental personnel was that of informed consent." On March 23, 1970, Dr. Holliday wrote to Dr. Paulsen to inform him that his project was over.<sup>42</sup> The Bradley report added that "so far as is known to departmental personnel, no ill effects have been reported by subjects of the experiments."<sup>43</sup> In 1994, however, a former Washington state inmate named Martin Smith told Karen Dorn Steele of the Spokane *Spokesman-Review* that ever since participating in the experiment he has suffered testicular pain.<sup>44</sup> Dr. Paulsen notes, however, that Smith was a control and therefore not actually irradiated, although he did have one testicular biopsy.<sup>45</sup>

There has been less debate than in Oregon on the subject of medical follow-up. This may be in part because Dr. Paulsen has taken the position, based on his conversations with inmates, that the subjects of the Washington experiments want their privacy protected, and he has refused to disclose their names. A December 1975 AEC memorandum from Nell W. Fraser, a government contract administrator, to Oscar J. Bennett, director of the Contracts and Procurement Division, paraphrases Dr. Paulsen as saying that a follow-up program was not medically indicated and "a follow-up program would be harmful because most of the prisoners wish to disassociate themselves with the prison experience."<sup>46</sup> According to the memorandum, Dr. Paulsen also noted that his medical malpractice insurance would apply in the event that litigation resulted from his radiation study.<sup>47</sup> In recent years, however, a handful of former subjects have told reporters such as Karen Dorn Steele that they would like to be followed up.<sup>48</sup> In late 1994 state officials said they would seek federal funds to carry out a follow-up program or ask the Department of Health and Human Services to mount such a program.



The Advisory Committee conducted its own analysis of the risks incurred by the Oregon and Washington testicular irradiation subjects based on a 600-rem dose, which was the maximum testicular exposure of any subject in either state. For purposes of this analysis we assumed that the testicles have average radiation sensitivity; that there is a linear relationship between cancer incidence and dose, and that there is a linear relationship between the risk of cancer and the amount of tissue exposed. Using these assumptions, we calculated that it would take more than double the dose received by any prisoner-subject to yield an effective dose of 1 rem. This means that the predicted increase over the expected cancer rate for the individuals who received the greatest exposure would be less than four-hundredths of 1 percent. For those who received smaller doses of radiation, the risk would, of course, be smaller, too.<sup>49</sup>

#### OTHER RADIATION EXPERIMENTS

There is no comprehensive list of radiation experiments with prisoners as subjects, but in the course of the Advisory Committee's historical research a handful of such experiments other than those in Oregon and Washington has been identified. In many cases there is only fragmentary information available, which the Committee has not always been able to verify. To provide a sense of what else might have been going on at the time (which may or may not have been representative), consider the following:

- A former prison administrator in Utah has confirmed that experiments were conducted on prisoner subjects in the late 1950s or early 1960s in which blood appears to have been removed, irradiated, and returned to the body. Prisoners at the time who were interviewed by the *Deseret News*, a Salt Lake City newspaper, said they believed that about ten prisoner-volunteers were studied in this way. One subject said, "They told us nothing about the tests. They just said it wouldn't bother us."<sup>50</sup> In a 1959 confidential report to the president of the

University of Utah, Lowell A. Woodbury, the radiological safety officer said: "One group of medical experimenters with authorization for human experimentation was administering isotopes to volunteers at the state prison. This was in direct violation of the terms of their license and while not an extremely serious violation was apt to result in a citation [from the Atomic Energy Commission]."<sup>51</sup>

- Experiments were conducted at the Medical College of Virginia in the early 1950s under the sponsorship of the Army and possibly the Public Health Service using radioactive tracers. The goal was to study the life cycle of red blood cells. As discussed in more detail in chapter 13, Dr. Everett I. Evans, in a letter to the superintendent of the state penitentiary, quoted from a letter from Colonel John R. Wood of the Army surgeon general's office, which provided that no information related to research being conducted for the Army surgeon general be released without review by the Public Information Office of the Defense Department. Dr. Evans said the reason for this was that "the problem of the use of prisoner volunteers is not yet clarified."<sup>52</sup>
- During the 1960s "prison volunteers" in the Colorado State Penitentiary were used as subjects in an experiment designed to determine the survival time and characteristics of red blood cells during periods of rapid red cell formation and during periods of severe iron deficiency. Red cells transfused into normal recipients were tagged with either radioactive iron or radioactive phosphorus.<sup>53</sup> In a 1976 report on the study, which used five subjects, the investigators wrote:

The rights of the prisoners were respected in conformance with the Helsinki Declaration of the World Health Organization and the Nuremberg Code. Approval was obtained from the Governor, Attorney General, and Director of Institutions of the State of Colorado, the warden and psychiatrist of the Colorado State Penitentiary, and the nearest of kin of each volunteer.<sup>54</sup>

It is not clear from this publication or other documents available to the Committee precisely what use was made of the principles stated in the Nuremberg Code and the Declaration of Helsinki in obtaining the consent of the prisoner-subjects in this experiment. However, if the investigators did accept Nuremberg and Helsinki as standards for consent in the 1960s it adds weight to other evidence (for example, the citation of Nuremberg by the Human Rights Review Committee of the Department of Institutions in the Washington testicular irradiation experiment) that these standards were considered relevant to research on prisoners in the 1960s.

- Other federally sponsored experiments on prisoner volunteers appear to have been conducted in Pennsylvania (Holmesburg State Prison, the effects of radiation on human skin), Oklahoma (Oklahoma State Penitentiary, routine metabolic studies of experimental drugs using tracer amounts of radionuclides), Illinois (Stateville Prison, measurements of radium burden received from drinking water), and California (San Quentin, tracking movement of iron from plasma to red blood cells using a radioactive marker).<sup>55</sup>

#### HISTORY OF PRISON RESEARCH REGULATION

Dr. Paulsen reported in a recent interview that he had "asked a lot of people" in 1963 about the use of prisoners as research subjects. He went on to say that at that time "no one said no" to the use of such subjects in his research. However, Dr. Paulsen explained in the same interview that he had started to sense a shift in public opinion around 1970. In particular, he pointed to comments critical of prison experimentation that he had heard at a New York Academy of Sciences conference, "New Dimensions in Legal and Ethical Concepts for Human Research," which he attended in the spring of 1969.<sup>56</sup> Of course, we cannot rely solely on Dr. Paulsen's recollections to provide historical context for experiments in which he was so intimately involved—

and which have now become controversial. But ample evidence suggests that Dr. Paulsen was essentially correct in his impression that testicular irradiation experiments in Washington and Oregon bridged a transitional period in the history of human experimentation generally and particularly in the history of experimentation in American prisons.

Isolated incidents of prison-based research before World War II formed the foundation for a practice that would become firmly embedded in the structure of American clinical research during World War II. Perhaps the most significant wartime medical research project in which American scientists employed prisoners as research subjects was centered in Illinois's Stateville Prison. Beginning in 1944, hundreds of Illinois prisoners submitted to experimental cases of malaria as researchers attempted to find more effective means to prevent and cure tropical diseases that ravaged Allied forces in the Pacific Theater.<sup>57</sup> In 1947, a committee was established by the governor of Illinois to examine the ethics of using state prisoners as research subjects. The committee was chaired by Andrew Ivy, a prominent University of Illinois physiologist and the chief expert witness on medical ethics for the prosecutors at the Nuremberg Medical Trial, where prison research was a salient topic (see chapter 2). The committee pronounced the wartime experiments at Stateville Prison "ideal" in their conformity with the newly adopted rules of the American Medical Association concerning human experimentation. The AMA rules, which Ivy had played a key role in developing, included provisions stipulating voluntary consent from subjects, prior animal experimentation, and carefully managed research under the authority of properly qualified clinical researchers.<sup>58</sup> Perhaps most significantly, the findings of Ivy's committee were announced to the American medical community when the group's final report was reproduced in the *Journal of the American Medical Association*.<sup>59</sup> The appearance of this report in the nation's leading medical journal both represented and reinforced the sentiment that prison research was ethically acceptable.

Publicly aired assertions that experimentation on prisoners relied on exploitation or coercion

were extremely rare in the United States before the late 1960s. One criticism of medical research behind bars did, however, emerge with some frequency: prisoners who participated in research were somehow escaping from their just measures of punishment. Inmates were usually offered rewards in exchange for their scientific services, ranging from more comfortable surroundings, to cash, to early release. Perhaps the most powerful statement of the concern that convicts should not receive special treatment because they had participated in an experiment came from the AMA. In 1952, this organization formally approved a resolution stating its "disapproval of the participation in scientific experiments of persons convicted of murder, rape, arson, kidnapping, treason, or other heinous crimes." The AMA was alarmed that some such criminals "have not only received citations, but have in some instances been granted parole much sooner than would otherwise have occurred."<sup>60</sup> (In the Oregon testicular irradiation experiments it appears that this recommendation against using inmates accused of "heinous crimes" was not always observed.)

It should be noted that the use of prisoners as research subjects seems to have been a uniquely American practice in the years following World War II. The large-scale successes of prison experimentation during World War II—and the authoritative pronouncement of the Ivy Committee that prison research *could* be conducted in an ethical fashion—seem to have given the practice a kind of momentum in this country that it did not have elsewhere. In other countries it seems that the first clause of the Nuremberg Code was interpreted to preclude the use of prisoners in experimentation.<sup>61</sup> This clause begins with the assertion that the only acceptable experimental subjects are those who are "so situated as to be able to exercise free power of choice."

It is difficult to overemphasize just how common the practice became in the United States during the postwar years. Researchers employed prisoners as subjects in a multitude of experiments that ranged in purpose from a desire to understand the cause of cancer to a need to test the effects of a new cosmetic. After the Food and Drug Administration's restructuring of drug-

testing regulations in 1962, prisoners became almost the exclusive subjects in nonfederally funded Phase I pharmaceutical trials designed to test the toxicity of new drugs. By 1972, FDA officials estimated that more than 90 percent of all investigational drugs were first tested on prisoners.<sup>62</sup>

It appears that throughout the history of medical experimentation on American prisoners many inmates have valued the opportunity to participate in medical research. One must quickly add that such an observation points to the paucity of opportunities open to most prisoners. The common perception among inmates that participating in a medical experiment was a good opportunity has had an important impact on the racial aspects of prison experimentation. Because of the large numbers of African-Americans in prison (and the overt racial exploitation of the notorious Tuskegee syphilis study, in which black men with syphilis were observed but not treated), it might be assumed that minorities predominated as research subjects in prisons. The opposite has generally been true; white prisoners have usually been overrepresented in the "privileged" role of research subject. In most prison studies before and during World War II, it seems that all of the research subjects were white.<sup>63</sup> In 1975, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research carefully examined the racial composition of the research subjects at a prison with a major drug-testing program. The commission found that African-Americans made up only 31 percent of the subject population, while this racial "minority" formed 68 percent of the general prison population.<sup>64</sup>

The shift in public opinion against the use of prisoners as research subjects, which began in the late 1960s, was no doubt tied to many other social and political changes sweeping the country: the civil rights movement, the women's movement, the patients' rights movement, the prisoners' rights movement, and the general questioning of authority associated with the anti-Vietnam War protests. But, as has been common in the history of human experimentation, scandal galvanized public attention, brought official inquiry, and resulted in significant change. A major scandal in prison experimentation came

when the *New York Times* published a front-page article on July 29, 1969, detailing an ethically and scientifically sloppy drug-testing program that a physician had established in the state prisons of Alabama.<sup>65</sup> Even more sensational was Jessica Mitford's January 1973 *Atlantic Monthly* article. In this article, Mitford portrayed experimentation on prisoners as a practice built on exploitation and coercion of an extremely disadvantaged class.<sup>66</sup> When the article reappeared later in 1973 as a chapter in her widely read book critiquing American prisons, she had come up with an especially provocative and suggestive title for this section of the book: "Cheaper than Chimpanzees."<sup>67</sup> Mitford, and most of the growing number who condemned experimentation on prisoners during the 1970s (and after), offered two arguments against the practice. First, prisoners were identified as incapable of offering voluntary consent because of a belief that most (some argued, *all*) prisons are inherently coercive environments. Another line of argument was based on a principle of justice that stipulated that one class—especially a disadvantaged class such as prisoners—should not be expected to carry an undue burden of service in the realm of medical research.

A few months after the publication of Mitford's article, Senator Edward M. Kennedy of Massachusetts held hearings to investigate human experimentation. Kennedy was primarily fired into action by the revelations of the Tuskegee syphilis study, which made headlines in 1972, but he devoted one full day of his hearings to the issue of prison experimentation.<sup>68</sup> The chief outcome of Kennedy's hearings was the formation of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, which, among other topics, was specifically charged with investigating experimentation on prisoners (see chapter 3).

The eleven commissioners, including Advisory Committee member Patricia King—with the assistance of twenty staff members—gathered a wealth of data on prison medical research, made site visits to prisons, held extensive public hearings, and engaged in long debates among themselves.<sup>69</sup> After their deliberations, the commission concluded that it was "inclined toward

protection as the most appropriate expression of respect for prisoners as persons."<sup>70</sup> But the commission did not call for an absolute ban on the use of prisoners in medical research. A steadfast minority on the commission held to a belief that prisoners should not arbitrarily be denied the opportunity to participate in medical research. An excursion to the State Prison of Southern Michigan, where Upjohn and Parke-Davis pharmaceutical companies had cooperatively built and maintained a large Phase I drug-testing facility, served to reinforce the opinions of this contingent. In candid conversations with the visiting commissioners, randomly selected inmates spoke in convincing terms about their support for the drug-testing program in the Michigan prison.<sup>71</sup>

The commission's final report reflected this hesitancy to call for a complete halt to the use of prisoners in nontherapeutic experimentation. The commission recommended that prisoners could be considered ethically acceptable experimental subjects if three requirements were satisfied: (1) "the reasons for involving prisoners in . . . research [were] compelling," (2) "the involvement of [the] prisoners . . . satisfie[d] conditions of equity," and (3) subjects lived in a prison characterized by a great deal of "openness" in which a prisoner could exercise a "high degree of voluntariness." The final requirement involved a detailed prison accreditation scheme intended to ensure the possibility of voluntary consent.<sup>72</sup>

The National Commission derived its primary power from the fact that the secretary of the Department of Health, Education, and Welfare (DHEW) was legally compelled to respond to the commission's findings and to justify the rejection of any commission recommendations.<sup>73</sup> Joseph Califano, DHEW secretary in the Carter administration, spent nearly a year formulating his response regarding the use of prisoners in medical research. Califano explored the possibility of an accreditation scheme as suggested by the commission. However, in a letter to the commission, Califano reported that the American Correctional Association, "the one currently qualified [prison] accrediting organization," had no interest in "accrediting correctional institutions as performance sites for medi-

cal research." "On the contrary," Califano went on to explain, the ACA had recently decided it "would not fully accredit any institution which permitted research on prisoners."<sup>74</sup> After his interchange with the ACA, Califano ultimately decided to issue regulations that, for almost all intents and purposes, brought an end to federally funded nontherapeutic medical research in American prisons.<sup>75</sup>

In the interest of uniform federal regulations, Secretary Califano also "directed" the FDA to issue similar rules governing the use of prisoners in "research that the FDA accept[ed] to satisfy its regulatory requirements."<sup>76</sup> The FDA published final rules in the spring of 1980 that were intended, on the planned effective date of June 1, 1981, to eliminate prisons as acceptable sites for nontherapeutic pharmaceutical testing.<sup>77</sup> However, in July of 1980, almost a year before the FDA's regulations were scheduled to take effect, a group of prisoners at the State Prison of Southern Michigan filed suit against the federal government. These inmates claimed that the impending FDA regulations threatened to violate their "right" to choose participation in medical research. The case was settled out of court when FDA attorneys decided to reclassify the agency's prison drug-testing regulations as "indefinitely" stayed. The FDA's regulations still exist in this bureaucratic limbo.<sup>78</sup>

But even before the FDA issued its proposed regulations on the use of prisoners in drug testing, pharmaceutical companies had already largely abandoned a practice that had been so widespread only a few years earlier. Most significantly, pharmaceutical researchers, along with other medical scientists, had discovered that sufficient numbers of experimental subjects could be found beyond prison walls. Students and poor people proved to be especially viable alternative populations from which to draw participants for nontherapeutic experiments—if the cash rewards were sufficient. The growing controversy surrounding the use of prisoners as research subjects, combined with the realization that they could find enough alternate subjects for their needs, led drug companies to make decisions that were based not so much on ethics as expediency. The comments of an administrator associated with an Eli Lilly testing operation

at an Indiana prison are revealing and provide a fitting conclusion to this brief historical analysis: "The reason we closed the doggone thing down was that we were getting too much hassle and heat from the press. It just didn't seem worth it."<sup>79</sup>

## ETHICAL CONSIDERATIONS

It is quite clear that all of the radiation experiments that have come to the Advisory Committee's attention in which prisoners were employed as research subjects would have been in violation of federal standards as they exist today. Federal regulation stipulates an extremely limited range of permissible medical research in prison populations. Only four types of investigations can currently receive approval: (1) low-risk studies of "the possible causes, effects, and processes of incarceration, and of criminal behavior"; (2) low-risk studies of "prisons as institutional structures or of prisoners as incarcerated persons"; (3) "research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere . . .)"; and (4) research that has "the intent and reasonable probability of improving the health or well-being of the subject." Almost certainly, none of the various episodes of radiation research on prisoners treated in this chapter would have fallen into any one of these categories.

But as noted above, widespread concern about coercion and exploitation of prisoner-subjects—which brought about these restrictive federal regulations—arose relatively recently in this country. For the period before roughly 1970, it is almost certainly unfair to condemn, in retrospect, a research project as unethical *solely* because researchers employed prisoners as subjects; historical sensitivity demands some appreciation for what seems to have been a genuine lack of widespread professional or public concern for the ethical problems of prison research that came to the fore during the 1970s. Only in the case of the Washington and Oregon testicular irradiation experiments do we know enough to make any legitimate claims about the extent to which researchers conformed with reasonable contem-

porary standards for the ethical conduct of prison experimentation. And, even for these relatively well-known studies, the individual complexities of each series of experiments have grown hazier with time.

One of the first known efforts to examine the ethics of using prisoners as research subjects was organized by the Law-Medicine Research Institute (LMRI) of Boston University. The conference was called "The Participation of Prisoners in Clinical Research," and it opened on February 12, 1962. The conference was part of a larger LMRI project to study and report on "the actual practices, attitudes, and philosophies currently being applied in the legal and ethical aspects of clinical investigation" (see chapter 2). LMRI's conference on prison research was one of several "invitational work conferences" organized to gather information on several important topics in human experimentation (other conferences were devoted to "the concept of consent," pediatric research, and pharmaceutical testing). The participants at each conference received an agenda and briefing book in advance of the meetings, but discussions tended to be free-ranging. Those who attended the conferences understood that their words were being recorded, but they tended to speak in a frank and revealing fashion because LMRI pledged to preserve their anonymity when reporting on the meetings.<sup>80</sup>

A copy of the list of participants at the conference on "The Participation of Prisoners in Clinical Research," which survives at Boston University, confirms the following characterization of those who attended:

[T]he thirty-six invited participants comprised two main categories. The first was composed of clinical research administrators and clinical investigators with a variety of academic, commercial, and governmental affiliations, who have had experience in conducting medical studies with prisoners as subjects. The second category consisted of prison administrators and prison medical officers with various federal, state, and municipal correctional programs. Also participating in the conference were representatives of various related fields such as behavioral science, criminal law, organized medicine, pharmaceutical manufacturing, and the military services.<sup>81</sup>

Unfortunately, a copy of the actual meeting transcript has not survived. However, the

lengthy unpublished "Analytic Summary," which contains many (anonymous) transcript excerpts, seems to be a fair representation of the daylong meeting.<sup>82</sup> It is relatively easy to extract several important points of agreement about the proper conduct of experimentation in prisons from this report. And, given the broad cross section of those involved in prison experimentation who attended this 1962 conference, it seems reasonable to employ the standards enunciated at this conference as evidence of prevailing interpretation of ethical standards for prisoner experiments that began in 1963.

First, the "conferees generally agreed that experimental risks must be balanced against benefits." In the case of research that was not intended to be of potential direct benefit to the subject, which was generally the case in prison experiments, most meeting participants believed that the social or scientific value of new knowledge that might result from an experiment should be weighed as a benefit.<sup>83</sup> However, when "confronted with the direct question of whether or not a relatively high degree of risk can ever constitute a legitimate reason for the use of prisoner subjects, the conferees were almost unanimous in rejecting this position."<sup>84</sup> Interestingly, those at the conference believed that the *general public was less* inclined to worry about subjecting prisoners to high levels of experimental risk. Two brief transcript excerpts are revealing:

When the public hears that inmates are [participating in a seemingly very hazardous study], they rationalize, "Well, I wouldn't do it, but it's all right with prisoners."<sup>85</sup>

[T]he public will allow the investigator to go a lot further, with regard to risks taken with prisoners, than the investigator would go himself.<sup>86</sup>

The conferees spent a large portion of their day together discussing the matter of consent. They reached agreement that meaningful consent should be both voluntary and informed, provided the reach of these terms is carefully circumscribed. The report stated;

[T]he legal prerequisites of consent are, first, not absolute free will, but sufficient free choice to avoid coercion or duress; and, second, not absolutely perfect knowledge, but enough information to avoid fraud or deceit.<sup>87</sup>

The conference participants "unanimously agreed that rewards offered to prisoner volunteers should not be so high as to invalidate their consent to participate as research subjects."<sup>88</sup> There seems to have been considerable disagreement about exactly where to draw the line between ethically acceptable and unacceptable rewards to prisoners for service as experimental subjects, but there was a general desire to "minimize rewards" because it was "consistent with the penological desirability of maximizing prisoners' opportunity for altruism."<sup>89</sup> As for sentence reductions, some thought that small amounts of "good time" credits were appropriate, but all agreed that "maximum rewards of this type, i.e., definite promises of pardon or parole, should not be given."<sup>90</sup> There seems to have been little discussion of the possibility that the authoritarian structure of prison life was in itself coercive and therefore limited a prisoner's ability to make an autonomous decision.

The disclosure component of consent received extensive attention at the conference. The following was offered as a summation of what the conferees perceived as the "essential content and emphasis" of the information that should be conveyed to "prospective prisoner-subjects":

The explanation of a clinical research project . . . should describe completely the procedures entailed and should stress the possible consequences of these procedures. Even though it may be necessary to "stop somewhere short of full revelation when you reach intricacies a layman would never comprehend," there should be no omission of any adverse consequences, detriments, or risks.<sup>91</sup>

To strive toward this level of communication, the conference participants cited procedures that were "usually" followed in most prison experiments: a general announcement of the research project to the inmates (usually by notices posted on bulletin boards or printed in prison newsletters); a general explanation of the project (often in an auditorium) to groups of prisoners who expressed initial interest in an experiment; and, finally, one-on-one meetings between prospective participants and research personnel.<sup>92</sup> Conferees who had administered or conducted prison experiments also reported that prisoner-subjects "usually sign[ed] some type of 'consent

agreement."<sup>93</sup> (Generally speaking the provisions specified above were followed in the Washington and Oregon experiments, but the information provided was often inadequate.)

Even with all of these measures, some meeting participants asserted that the "ideals of comprehension, evaluation, and decision on the part of prisoners were seldom attained in practice." They pointed to two general difficulties in achieving these ideals. First, "the lack of intelligence, education, or 'medical sophistication' among many prisoners." Second, they cited "various 'motives or pressures which so often stand in the way of objective understanding."<sup>94</sup> The participants in the conference also recognized that the consent forms used in prison experiments were often less than perfect. They understood that the "waiver or release" components of many forms were probably inappropriate. They also recognized that reasonably predictable risks of an experiment were not always carefully listed on consent forms, but at the same time they "agreed that 'no serious' risk should ever be disguised or concealed" on these forms.<sup>95</sup>

In sum, the records from this conference suggest that even apart from formal, federal rules for experimentation on prisoners, ethical conditions for the conduct of prison research were articulated in the early 1960s. Now, with these conditions in mind, let us turn to a more detailed analysis of the Washington and Oregon testicular irradiation experiments.

As we have noted, the Committee's ability to assess the quality of consent obtained from a research subject thirty or forty years earlier can be confounded in a thousand ways. To begin with, the records are invariably incomplete; then, the investigators are either no longer alive or their memories have grown hazy or selective with time; the same is true of subjects; and, of course, there are confidentiality considerations, which limit the availability of records, the concern of researchers for their reputations, and so on. All of these considerations, to greater or lesser degrees, apply to the Oregon and Washington experiments.

With respect to these experiments, however, we believe we have a clear-enough picture of the standards and practices of the time to evaluate the conduct of the research against them with-

out reference to the standards and practices of today.

In both Oregon and Washington, some subjects were not warned, warned only after enrolling in the experimental program, or inadequately warned that there was potential risk, albeit small, of testicular cancer. While it might not have been uncommon at the time for physicians to avoid using the word *cancer* with sick or even terminally ill patients for paternalistic reasons, such avoidance is harder to justify, even by the standards of the time, in the case of healthy subjects who are participating in research that offers them no direct benefit.<sup>96</sup>

As far as acute effects are concerned, the pain of testicular biopsy may have been understated in both programs, and the risk of orchitis from repeated biopsies seems to have been ignored. Some former subjects have complained of long-term pain, sexual dysfunction, and skin rashes. It is not clear whether these conditions were caused by the experiments, nor is it certain that long-term medical follow-up can answer this question.

Subjects in both sets of experiments were required to have a vasectomy at the end of the program because of concerns about possible chromosomal damage. In both cases the vasectomy consent forms signed by the subjects, and their wives if they were married, adequately described the procedure, its consequences, and the small possibility it could be reversed. However, appropriate questions have been raised about the reasons inmates might agree to vasectomy in the circumstances of prison research, and the possibility, as actually occurred in a number of cases, that in the end the subject would refuse to undergo the procedure.

Finally, there appears to be little doubt that the financial incentives offered for participation were the main reason most inmates volunteered. Payments totaling more than \$100 could be seen as unduly influencing the judgment of potential volunteers. While money also is a powerful incentive for research participation outside prison walls, we believe that the conditions of confinement *can* magnify the perceived value of the reward. Whether the payments offered to participants in these programs constitute an unfair inducement to participate in research may vary from inmate to inmate.

While the prison experiments were unethical with respect to current requirements for disclosure of risk and noncoercion, the researchers functioned during a period of rapid evolution of the interpretation of ethical principles in the prison context. Their actions, however, were less than fully consistent with the existing AEC requirements, especially concerning the information the prisoner-subjects were provided.

## NOTES

1. Colonel Don Flickinger, NEPA Medical Advisory Panel, Subcommittee IX, Washington, D.C., 22 July 1949 (ACHRE No. DOE-121494-A-2), 17.
2. Subcommittee on Energy Conservation and Power, Committee on Energy and Commerce, House of Representatives, *American Nuclear Guinea Pigs: Three Decades of Radiation Experiments on U.S. Citizens*, 99th Cong., 2d Sess., 3.
3. Pacific Northwest Research Foundation, undated ("Policy and Procedures of the Pacific Northwest Research Foundation with Regard to Investigations Involving Human Subjects") (ACHRE No. IND-011195-A-1).
4. Bertram H. Schur to Dr. Charles L. Dunham, 13 May 1966 ("Use of Human Volunteers in Biomedical Research") (ACHRE No. DOE-051094-A-138).
5. Deposition of Mavis Rowley and Carl G. Heller, 19 July 1976, Poulsbo, Washington (ACHRE No. CORP-013095-A-2), 18.
6. C. Alvin Paulsen, interview by Steve Klaidman (ACHRE), 8 September 1994, Seattle, Washington, transcript of recording (ACHRE Research Project Series, Interview Program File, Targeted Interview Project), 10-11.
7. Pacific Northwest Research Foundation, proposal for Atomic Energy Commission, Division of Biology and Medicine, February 1963 ("Effects of Ionizing Radiation on the Testicular Function of Man") (ACHRE No. DOE-122994-A-2); Carl Heller, Pacific Northwest Research Foundation, 27 April 1967 ("Fifth Yearly Proposal, June 1, 1967-May 31, 1968") (ACHRE No. DOE-122994-A-2); Carl Heller, Pacific Northwest Research Foundation, May 1972 ("Effects of Ionizing Radiation on the Testicular Function of Man: 9 Year Progress Report") (ACHRE No. DOE-122994-A-2); Mavis Rowley, Division of Nuclear Medicine, Tumor Clinic, Swedish Research Hospital, undated ("The Effect of Graded Doses of Ionizing Radiation on the Human Testis: Progress Report, October 1, 1975-September 30, 1976") (ACHRE No. DOE-011895-B-3). The following is a staff-prepared abstract of Dr. Heller's research based on annual reports, the final report, and his research proposal:



## I. OBJECTIVES

To determine the nature of the cytological changes, both somatic (Sertoli cell) and germinal (spermatogonia) induced by acute irradiation.

- To determine the dosage required to produce these changes, as well as the dose to induce permanent damage to spermatogenic cells.
- To determine recovery time.
- To determine radiation-produced alteration of testicular parameters, such as total gonadotropin, interstitial-cell hormone excretion, estrogen excretion, and androgen excretion.

## II. METHODOLOGY

Subjects received varying doses of X-irradiation to both testes from 8- to 600-rad single dose. Testicular effects were determined by histological (light microscopy) examination of pre- and serial postirradiation biopsy specimens. Sperm counts, motility, morphology, and seminal fluid volume were monitored in serial postirradiation ejaculates. Hormonal excretion was to be monitored by serial urine and plasma analyses.

- Radiation exposure was controlled by a specially constructed device that assured uniform (plus or minus 5%) irradiation at a dose rate of 100 r/min, approximately 140 kVp with 5 mA tube current, and 2 mm Al filter.
- Some subjects received 10 mCi <sup>3</sup>H-thymidine injected intratesticularly to assess (via autoradiography) effects of radiation on incorporation into spermatogonial DNA as a measure of chromosome replication.

## III. RATIONALE FOR THE USE OF HUMAN SUBJECTS

- To determine radiosensitivity of germinal elements in man. According to Dr. Heller, man is unique among commonly studied species in being able to submit to serial testicular biopsy without damage and biopsy-induced testicular artifacts. (Mavis Rowley has pointed out that improved techniques have made it more practical to do biopsies on large animals.)
- To determine germinal cell recovery, thereby allowing prognosis in cases of accidental irradiation.

## IV. FINDINGS

- Sperm count reduction and recovery of sperm count are both dose related. At 400-600 rad, sperm count was zero at 156 weeks.
- By autoradiographic studies of <sup>3</sup>H-thymidine up take into spermatocytes in nonirradiated subjects, it was shown that there are approximately four cycles of spermatogenesis of approximately sixteen days each, so that the complete evolution of spermatogonia to mature sperm is approximately sixty-four days. This is approximately the same as other mammalian species.
- Urinary and plasma gonadotropins rose in proportion to testicular dose and fell with germinal-recovery. Plasma FSH and LH also rose. Urinary es-

trogen remained unchanged. Urinary testosterone fell slightly after irradiation.

- Histologically, spermatogonia were the most radio sensitive. Spermatocytes were damaged above 200-300 rads. Spermatids showed no overt damage.
- Germinal cell recovery time increased as radiation dose increased. Complete recovery occurred with in nine to eighteen months for doses of 100 rad and below. Complete recovery required five or more years for doses of 400-600 rad. Germinal tissue appears to be somewhat more radiosensitive in humans than other studied species.

## V. FINANCIAL SUPPORT

Contract AST (45-1) 1780, U.S. Atomic Energy Commission.

8. Mavis Rowley, interview with ACHRE staff, 8 September 1994 (ACHRE No. ACHRE-051795-B) 6.

9. *Ibid.*, 12-13.

10. Deposition of Mavis Rowley and Carl Heller, 19 July 1976, 32.

11. Harold Bibeau, telephone interview with ACHRE staff, 11 August 1994 (ACHRE No. IND-081194-A).

12. Depositions of John Henry Atkinson, 54; Ivan Dale Herland, 22, 68; Donald Eugene Mathena, 94; taken 14 October 1976 in *Donald Mathena et al. v. Amos Reed et al.* Civil nos. 73-326, U.S. District Court, Dist. Oregon (ACHRE No. CORP-013095-A).

13. Deposition of Carl Heller, 19 July 1976.

14. L. C. Wertz to Warden C. T. Gladden, 10 July 1964 ("Dr. Heller stopped in the office . . .") (ACHRE No. IND-061594-A-1).

15. William B. Hutchison, M.D., Joseph E. Primeau, and Carl G. Heller, M.D., Ph.D., to Dr. John C. McDougall, Assistant Director for Operations, National Institute of Child Health and Human Development, National Institutes of Health, 12 May 1966 ("This letter is in response . . .") (ACHRE No. DOE-082294-B-70).

16. C. T. Gladden, Warden, to Mark Hatfield, Governor, 8 May 1963 ("I am glad to provide . . .") (ACHRE No. IND-061594-A), 2; C.T. Gladden, Warden, to Hon. Robert Thornton, Attorney General, 9 September 1963 ("Carl Heller, Medical Research Programs") (ACHRE No. IND-061595-A); undated ("Consent and Release") (ACHRE No. IND-110994-A).

17. Mavis Rowley, interview with ACHRE staff, 8 September 1994, 36.

18. Pacific Northwest Research Foundation, undated ("Policy and Procedures of the Pacific Northwest Research Foundation with Regard to Investigations Involving Human Subjects").

19. William Boly, "The Heller Experiments," *Oregon Times Magazine*, November 1977, 45.

20. *Robert Case v. State of Oregon et al.*, Civil no. 76-500; *Paul Tyrell v. State of Oregon et al.*, Civil no. 76-499.

21. Tom Toombs, Administrator of Corrections Division, undated testimony before Oregon legislature (ACHRE No. IND-101294-D-1), 7.

22. *Ibid.*, 11.

23. James Ruttenber, telephone interview with Steve Klaidman (ACHRE staff), 20 July 1995 (ACHRE No. IND-072095-E).

24. C. Alvin Paulsen, proposal to Atomic Energy Commission, undated ("Study of Irradiation Effects on the Human Testis: Including Histologic, Chromosomal and Hormonal Aspects") (ACHRE No. IND-110994-A-2). The following has been abstracted by staff from Dr. Paulsen's research proposal and annual progress reports:

#### I. OBJECTIVE

- To determine the dose-dependent relationship between external irradiation and cell kill and inhibition of mitosis in spermatogenic cells. The cells in question are spermatogonial stem cells, and the dose response would be expected to differ from other kinds of cells.

#### II. METHODOLOGY

- Subjects with normal ejaculates received 7.5-400 rad to both testes. The details of irradiation are not specified.
- Weekly seminal fluid was examined for the endpoint response of azoospermia. Duration was not specified.
- Subjects and some controls received periodic unilateral testicular biopsies. Number not specified.
- Irradiated subjects agreed to be vasectomized at the completion of the experiment.

#### III. RATIONALE FOR THE USE OF HUMAN SUBJECTS

One cannot directly relate animal data to the human male with security. Among other things, the rate of spermatogenesis in man is different from that in various animal species.

#### IV. FINDINGS

- The average presterile period was 142 days.
- The maximum sterile period was 501 days.
- Spermatogenesis in man is more radiosensitive than in rodents and recovery time is longer. Man is more radiosensitive to complete sterility than rodents.
- Testicular biopsy by itself can reduce seminal fluid sperm concentration.

#### V. FINANCIAL SUPPORT

AEC contracts AT (45-1) 1781 and AT (45-1) 2225.

25. C. Alvin Paulsen, telephone interview with Steve Klaidman (ACHRE), 20 July 1995 (ACHRE No. IND-072095-D).

26. C. Alvin Paulsen, telephone interview with Steve Klaidman (ACHRE), 7 March 1995 (ACHRE

No. ACHRE-030995-A).

27. C. Alvin Paulsen, interview with ACHRE staff, 8 September 1994, 9.

28. T. W. Thorslund and C. Alvin Paulsen, "Effects of X-Ray Irradiation on Human Spermatogenesis," *Proceedings of the National Symposium on Natural and Manmade Radiation in Space*, ed. E. A. Warman (NASA Document TM X-2440, 1972), 229-232.

29. "Prison Inmates Sought in Prison Experiment," *The (Portland) Oregonian*, August 1963.

30. C. Alvin Paulsen, proposal to Atomic Energy Commission, undated ("Study of Irradiation Effects on the Human Testis: Including Histologic, Chromosomal and Hormonal Aspects").

31. C. Alvin Paulsen, interview with ACHRE staff, 8 September 1994, 56-57.

32. C. E. Heffron, M.D., Prison Physician, to All Inmates Interested, 2 November 1964 (ACHRE No. WASH-112294-A-1).

33. Harold Bradley, Director, Adult Corrections Division, to Hon. Daniel J. Evans, Governor, Washington State, 9 March 1976 ("Secretary Morris has asked . . .") (ACHRE No. WASH-112294-A-2).

34. Paulsen, telephone interview with ACHRE staff, 20 July 1995.

35. *Ibid.*

36. University of Washington, Research and Clinical Investigations Committee, proceedings of 10 December 1969 (ACHRE No. WASH-112294-A-3), 4.

37. Bradley to Evans, 2.

38. George Farwell, Vice President for Research, University of Washington, to John Totter, Division of Biology and Medicine, 16 July 1969 ("Thank you very much for your prompt response") (ACHRE No. DOE-082294-B-71).

39. Audrey Holliday, Research Administrator, Department of Institutions, to William Conte, Director, Department of Institutions, 18 March 1970 ("I received the review . . .") (ACHRE No. WASH-112294-A-4), 2.

40. *Ibid.*

41. Research Review Committee, Department of Institutions, to Audrey Holliday, Research Administrator, Department of Institutions, 13 March 1970 ("Disposition of Division Review Committee in Regard to Irradiation Project of Dr. C. Alvin Paulsen at the State Penitentiary") (ACHRE No. WASH-112294-A-5), 2.

42. Audrey Holliday to C. Alvin Paulsen, 23 March 1970 ("The Department of Institutions received copies . . .") (ACHRE No. WASH-112294-A-6).

43. Bradley to Evans, 9 March 1976, 2.

44. Karen Dorn Steele, "Experiments A Life Sentence," *Spokane Spokesman-Review*, 19 June 1994, 1.

45. C. Alvin Paulsen, telephone interview with ACHRE staff, 7 March 1995 (ACHRE No. ACHRE-030795-A).

46. Nell Fraser to Oscar Bennett, 23 December 1975 ("Contracts AT[45-1]-1780-1781, Irradiation

of Prison Volunteers") (ACHRE No. DOE-082294-B).

47. Ibid.

48. Karen Dorn Steele, "State Agrees to Find Victims of Experiments." *Spokane Spokesman-Review*, 16 December 1994, 1.

49. The Advisory Committee calculated the risk from the testicular irradiation study as follows:

The radiation dose to the testicles ranged from 7.5 to 600 rem. The Committee's risk analysis was based on a 600-rem dose and the following three assumptions:

1. The testicles have average radiation sensitivity.
2. The risk of cancer is linearly related to dose.
3. The risk of cancer is linearly related to the amount of tissue exposed.

Based on these assumptions, the Committee calculated the maximum risk expected to any of the prisoner subjects using the following two steps:

1. Calculate effective dose by multiplying a 600-rem testicular dose by the proportion of the body exposed:  $(2 \times 25 \text{ grams} / 70 \text{ kilograms})$ , or  $(50 / 70,000) \times 600 \text{ rem} = 429 \text{ mrem}$ .
2. Calculate the risk (assuming average radiosensitivity) by multiplying this effective dose by the age-specific risk for males age 25:  $(0.429 \times 921 / 1,000,000 \text{ person rem})$ , or a risk of about 0.4 / 1,000 for males age 25.

50. Lee Davidson, "Did Secret Radiation Tests on Inmates Doom Offspring?" *Deseret News*, 10 November 1994, A1.

51. Lowell A. Woodbury, Radiological Safety Officer, to Dr. A. Ray Olpin, President of the University of Utah, 9 July 1959 ("Resume of Activities While Acting as Health Physicist and Radiological Safety Officer to the University of Utah Isotope Committee") (ACHRE No. UTAH-111394-A-2). A 1964 article titled "The Kinetics of Granulopoiesis in Normal Man" appears to describe the experiment. The article compares methods of labeling white blood cells with various radioisotopes and formulates a concept of forming white cells in normal man based on information obtained using a DFP32 (diisopropylfluorophosphate) label. G. E. Cartwright, J. W. Athens, and M. M. Wintrobe, "The Kinetics of Granulopoiesis in Normal Man," *Blood* 24, no. 6 (December 1964).

52. Everett Evans, Professor of Surgery, Medical College of Virginia, to W. F. Smyth, State Penitentiary, 13 December 1951 ("We continue to enjoy and appreciate . . .") (ACHRE No. VCU-012595-A-17).

53. Matthew Block to John Lawrence, 10 April 1969 ("I have met a very serious . . .") (ACHRE No. DOE-121294-B-7).

54. Matthew Block, *Text-Atlas of Hematology* (Philadelphia: Lea & Febiger, 1966), 503.

55. Henry De Bernardo, "University of Pennsylvania and the Holmesburg Connection," *Philadelphia*

*News Observer*, 12 October 1994, 12; Shelby Thompson, Director (Acting), Division of Information Services, AEC, to H. C. Baldwin, Information Officer, Chicago Operations Office, 21 August 1953 ("Information Guidance on Any Experimentation Involving Human Beings") (ACHRE No. DOE-051094-A-473); "10 San Quentin Felons Used for Atom Tests," source unknown, 12 April 1949; Oak Ridge National Laboratory Human Studies Review Taskforce, University of Oklahoma Human Studies Reviews, undated ("Findings for License 35-03176-01") (ACHRE No. NRC-012695-A).

56. C. Alvin Paulsen, M.D., interview with ACHRE staff, 8 September 1994. The meeting Paulsen referred to took place on 19-21 May 1969. The proceedings of the conference are reported in the *Annals of the New York Academy of Sciences* 169 (21 January 1970): 293-593. Paulsen is not listed among those who offered formal presentations.

57. Published accounts of this research include Alf S. Alving et al., "Procedures Used at Stateville Penitentiary for the Testing of Potential Antimalarial Agents," *Journal of Clinical Investigation* 27, no. 3 (part 2) (1948): 2-5; Joseph E. Ragen and Charles Finston, *Inside the World's Toughest Prison* (Springfield, Ill.: Charles C. Thomas, 1962), 391-395; Nathan F. Leopold, Jr., *Life Plus 99 Years* (Garden City, N.Y.: Doubleday, 1958), 305-355. David J. Rothman, in *Strangers at the Bedside: A History of How Law and Bioethics Transformed Medical Decision Making* (New York: Basic Books, 1991), gives some considerable attention to this tropical disease research in Illinois in a chapter entitled "Research at War," 30-50.

58. These rules, as approved by the AMA House of Delegates on 11 December 1946, read as follows:

1. The voluntary consent of the individual on whom the experiment is to be performed must be obtained;
2. The danger of each experiment must be previously investigated by animal experimentation, and
3. The experiment must be performed under proper medical protection and management.

From "Minutes of the Supplemental Session of the House of Delegates of the American Medical Association, Held in Chicago, December 9-11, 1946," *Journal of the American Medical Association* 133 (4 January 1947): 35. For more background on the development of the AMA standards for human experimentation, see chapter 2 of this report.

59. "Ethics Governing the Service of Prisoners as Subjects in Medical Experiments: Report of a Committee Appointed by Governor Dwight H. Green of Illinois," *Journal of the American Medical Association* 136 (14 February 1948): 457-458.

60. "Abstract of the Proceedings of the House of Delegates Meeting, Denver, 2-5 December 1952," *Journal of the American Medical Association* 150 (27 December 1952): 1699. The Illinois delegation to this meeting introduced the resolution. It is likely that the Illinois group was motivated by the possibility that Nathan Leopold, who had participated in a highly

- publicized kidnapping and murder that had been dubbed by the press as "the crime of the century," might be paroled as a result of his participation as a subject in the wartime tropical disease research at Stateville Prison.
61. Martin Jaffe and C. Stewart Snoddy, "An International Survey of Clinical Research in Volunteers," in *Appendix to Report and Recommendations: Research Involving Prisoners*, National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (Washington, D.C.: DHEW, 1976).
62. Aileen Adams and Geoffrey Cowan, "The Human Guinea Pig: How We Test New Drugs," *World* (5 December 1971): 20.
63. Jon M. Harkness, "Vivisection and Vivisectioners: Medical Experiments on American Prisoners before 1950," paper presented at "Regulating Human Experimentation in the United States: The Lessons of History," Columbia College of Physicians and Surgeons, New York, 23 February 1995.
64. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, *Report and Recommendations: Research Involving Prisoners* (Washington, D.C.: DHEW, 1976), 36.
65. Walter Rugaber, "Prison Drug and Plasma Projects Leave Fatal Trail," *New York Times*, 29 July 1969, 1, 20-21.
66. Jessica Mitford, "Experiments Behind Bars: Doctors, Drug Companies, and Prisoners," *Atlantic Monthly* 23, January 1973, 64-73.
67. Jessica Mitford, *Kind and Usual Punishment: The Prison Business* (New York: Alfred A. Knopf, 1973), 138-168.
68. For an analysis of the chain of events leading up to Senator Kennedy's hearings, see Mark S. Frankel, "Public Policymaking for Biomedical Research: The Case of Human Experimentation" (Ph.D. diss., George Washington University, 1976), 190-192. For the transcripts of the actual hearings, see U.S. Congress, Senate, Committee on Labor and Public Welfare, Subcommittee on Health, *Hearings on Quality of Health Care—Human Experimentation*, on S. 974, S. 878, and S. J. Res. 71, 93d Cong., 1st Sess., part 3, 7 March 1973 (Washington, D.C.: GPO, 1973).
69. A record of the National Commission's work can be found in a complete set of the commission's papers in the archives of the National Reference Center for Bioethics Literature, Kennedy Institute of Ethics, Georgetown University. For a useful (and critical) overview of the commission's work with regard to prisoners see Roy Branson, "Prison Research: National Commission Says 'No, Unless . . .,'" *Hastings Center Report*, February 1977, 15-21.
70. The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, *Report and Recommendations: Research Involving Prisoners*, 8.
71. Branson, "Prison Research," 17; National Commission, Staff Paper, "Biomedical and Behavioral Research Involving Prisoners," 5 March 1976, 12-13, Archives, National Reference Center for Bioethics Literature, Kennedy Institute of Ethics, Georgetown University, National Commission Papers, Box 6; form letter sent to randomly selected prisoners for permission to conduct an interview, 3 November 1975, Archives, National Reference Center for Bioethics Literature, Kennedy Institute of Ethics, Georgetown University, National Commission Papers, Box 22.
72. National Commission, *Report and Recommendations: Research Involving Prisoners*, 16-19.
73. Frankel, 402; see also the enabling legislation for the commission, the *National Research Act*, P.L. 93-348.
74. Joseph Califano to Kenneth J. Ryan, Chairman of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 2 May 1978; see also a memorandum from Julius P. Richmond, Assistant Secretary for Health, to Califano, 26 July 1977. Both documents can be found in the Office of the Director (OD) Files, National Institutes of Health, Central Files, "Human Subjects" folders.
75. For the proposed DHEW regulations see the *Federal Register* 43 (5 January 1978), 1050-1053; the final regulations can be found in the *Federal Register* 43 (16 November 1978), 53652-53656. These regulations remain essentially unchanged today and can be found at 45 C.F.R. part 46, subpart C. These regulations have also been adopted by other federal agencies that have any concern with human experimentation as part of the so-called Common Rule, with the exception of the FDA (see below).
76. *Federal Register* 43 (5 January 1978), 1051.
77. *Federal Register* 45 (30 May 1980), 36386-36392.
78. *Henry Fante et al. v. Department of Health and Human Services et al.*, U.S. District Court, Eastern District of Michigan, Southern Division, Civil Action No. 80-72778. The records from this case are now kept at the National Archives, Great Lakes Regional Archives, Chicago, Accession No. 21-88-0016, Location No. 331792-332283, Box No. 269. FDA officials announced the decision to stay indefinitely the regulations in the *Federal Register* 46 (7 July 1981), 35085. The current "stayed" status of the FDA prison research regulations can be found at 21 C.F.R. part 50, subpart C.
79. Charles Miller, as quoted in Stephen Gettinger and Kevin Krajick, "The Demise of Prison Medical Research," *Corrections Magazine* 5 (December 1979): 12.
80. On 1 January 1960, NIH awarded \$97,256.00 to the LMRI of Boston University to carry out this study. Irving Ladimer, who had completed a doctor of law dissertation at George Washington University in 1958 on the legal and ethical aspects of human experimentation, served as the project's principal investigator through June 1962, when he left Boston University. Ladimer was replaced as principal investigator by

his chief assistant, Donald A. Kennedy, an anthropologist by training, who saw the project through to completion. The first characterization of the purpose of the project is taken from page 1 of Kennedy's preface to the final report: "A Study of the Legal, Ethical, and Administrative Aspects of Clinical Research Involving Human Subjects: Final Report of Administrative Practices in Clinical Research, Research Grant No. 7039," Law-Medicine Research Institute, Boston University (1963) (hereafter cited as LMRI final report); both chapter and page numbers will be provided because pages within chapters are numbered separately. The second, and lengthier purpose statement is taken from page 1 of chapter 1 of the LMRI final report, "Focus of the Inquiry." This unpublished report is in the collections of the Mugar Memorial Library, Boston University (ACHRE No. BU-053194-A). This report, which is more than 360 typewritten pages, is a wealth of information that has remained largely untapped by recent scholars interested in the development of research ethics in this country. The few citations of the project that do appear in the published literature almost all refer to the summary that appears in William J. Curran, "Governmental Regulation of the Use of Human Subjects in Medical Research: The Approach of Two Agencies," *Daedalus* 98 (spring 1969): 546-548. In this very brief reference to the project, Curran makes no mention of the "invitational work conferences," which the project staff identified as the investigational technique that "yielded the most valuable information." This characterization appears on page 8 of chapter 2, which is devoted to research method; pages 3-5 of the same chapter provide more details on the specific methodology employed in these conferences.

81. LMRI final report, chapter 8, Roger W. Newman, LL.B. [of the project staff], "The Participation of Prisoners in Clinical Research: Analytic

Summary of a Conference," 1-2. A collection of documents related to the project is located in the files of the Center for Law and Health Sciences, School of Law, Boston University. This entity is the successor to the Law-Medicine Research Institute (ACHRE No. BU-062394-A).

82. Newman's "Analytic Summary" is more than 100 pages of typescript and seems to cover the conference in considerable detail. Also, comparisons between the transcripts of other LMRI "invitational work conferences" that have survived with the related summaries produced for the final report reveal a skillful and fair rendering of the meetings.

83. LMRI final report, chapter 8, 27.

84. *Ibid.*, 18.

85. *Ibid.*, 31.

86. *Ibid.*

87. *Ibid.*, 85.

88. *Ibid.*, 71.

89. *Ibid.*, 72.

90. *Ibid.*, 74.

91. *Ibid.*, 88-89.

92. *Ibid.*, 85-86.

93. *Ibid.*, 93.

94. *Ibid.*, 89-90.

95. *Ibid.*, 96.

96. Deposition of Carl Heller, 19 July 1976, 32. Heller said he avoided the word *cancer* because "I didn't want to frighten them [the prisoners]." Dr. Paulsen said in a telephone interview on 12 September 1995 that he explained to the inmates that data from Hiroshima and Nagasaki "showed no additional incidence of testicular cancer." Undated consent forms from the Washington experiment differ. Some specify an "extremely small" risk of testicular cancer, and others do not specifically mention cancer. C. A. Paulsen, interview with ACHRE staff, 12 September 1995 (ACHRE No. ACHRE-091295-A).