

Dr. Heller

Appendix A

HELLPROT 6/18/90

Draft Medical Protocol

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Draft Protocol for the Medical Followup of Oregon
Prisoners Exposed to Ionizing Radiation and Drugs
In the Experiments of Dr. Carl G. Heller

In January, 1988, the Oregon Department of Human Resources and the Oregon Department of Corrections asked the Center for Environmental Health and Injury Control, Centers for Disease Control (CDC) to help develop a plan for the medical followup of prisoners who were exposed to ionizing radiation in experiments conducted at the Oregon State Penitentiary (OSP). These prisoners were subjects in experiments on the effects of ionizing radiation on the testes, which were conducted by the late Dr. Carl G. Heller. At the time of the experiments, Dr. Heller was a researcher at the Pacific Northwest Research Institute in Seattle, Washington. This request was pursuant to House Bill 2914 of the 64th Oregon Legislative Assembly, mandating the Department of Corrections to offer annual evaluations of the consequences of the radiation experiments and provide care or treatment for any condition directly related to such experiments.

In the process of reviewing documents on the radiation experiments at OSP, the CDC became aware of another research program directed by Dr. Heller. This program included a number of experiments on the effects of hormones and other drugs on male reproduction. A review of the data on drugs that were

administered to inmates in this study indicated that many of the drugs could have elevated the risks for chronic diseases in the former subjects. Because of this possibility, the Oregon Department of Corrections directed CDC to evaluate the drug exposures and recommend an appropriate diagnostic program for those who participated in these experiments.

The following protocol outlines recommended procedures for establishing this medical followup.

Background

In 1957, Dr. Carl G. Heller, an endocrinologist at the University of Oregon Medical School, Portland, Oregon, began a series of endocrinologic experiments on various aspects of male reproductive function. Subjects in these experiments included male and female prison inmates from the OSP who were given hormones and other drugs and who provided samples of blood, semen and tissue for biochemical and microscopic analysis.

In 1963, Dr. Heller (by this time affiliated with the Pacific Northwest Research Foundation, Seattle, Washington) began a study of the effects of X-rays on the human testes. Between 1963 and 1973, 67 male inmates received acute testicular irradiation from X-ray beams in doses ranging between 8 and 600 rads (1). Periodic semen samples and testicular biopsies were performed to assess the effects on somatic and germinal cells. The hormone and radiation experiments continued until 1973, when the director of the Department of Corrections stopped all medical experimentation in Oregon prisons.

In 1963, Dr. C. Alvin Paulsen of the University of Washington School of Medicine also began a research program on the effects of hormones and radiation at the Washington State Penitentiary in Walla Walla, Washington. Dr. Paulsen completed his residency under Dr. Heller and worked on the hormone studies at OSP. His radiation research in the Walla Walla prison was also supported by the Atomic Energy Commission, and apparently involved about sixty subjects. Dr. Paulsen reported that subjects received testicular irradiation at doses been between 12.5 and 400 rads. He also conducted experiments with hormones and other fertility or anti-fertility drugs, but information on the specific drugs, doses, and number of subjects in the experiments were not made available to the CDC.

After reviewing published descriptions of the hormone and drug experiments, the CDC and the Oregon Department of Corrections concluded that the possible long-term health effects of these experiments should also be evaluated. It was also concluded that if these experiments subjected inmates to an increased risk for disease, then they should be offered a program of medical followup similar to that those in the radiation experiments.

Assessment of Toxic Effects From Experiments with Hormones and Other Drugs

Staff at CDC reviewed the records of Dr. Heller's experiments on file at the OSP, those stored at the Department of Energy offices in Richland Washington (the radiation experiments were funded by the Atomic Energy Commission, the predecessor of

the Department of Energy), and his scientific papers that were published. Former collaborators in Dr. Heller's experiments were also contacted by the CDC in order to request records and documents, clarify details of the experiments, and to identify other research which was not described in available records.

As a result of these efforts, records of the doses of hormones and other drugs administered to many of the individual subjects have been located and copied for storage with the Oregon Department of Human Resources. The CDC has not been able to locate records of the experiments conducted by Dr. Heller while he was on the faculty of the University of Oregon.

The CDC has reviewed the prison medical records of those inmates who have been identified as participants or possible participants in either the drug or radiation experiments. This review provided little information on the drugs or dosages of drugs administered to inmates. However, the review did help identify other inmates involved in these experiments, as memos authorizing passes to the prison medical clinic included the names of all the research subjects who visited the clinic on any given day. The medical records of individual inmates also included orders for testicular biopsies and some notes made about the experiments by prison staff.

Comparing Dr. Heller's personal records of drugs administered to subjects with prison medical records revealed that subjects with documented drug administration almost never had these or any other data recorded in the prison records.

Appendix A lists descriptions of the drugs and doses of these drugs that were administered by Dr. Heller in experiments at OSP. These data were obtained from Dr. Heller's personal records, records in the files of the warden at OSP, and from the scientific publications of Dr. Heller and his associates.

All data for individual drug exposures were abstracted from the forementioned sources and recorded on a computerized database designed for this project. If specific doses to individuals were recorded, they were summarized and recorded on the database.

Consultants to CDC reviewed the data on drug exposures and concluded that some of the drugs, particularly androgens administered over long time periods, raised the risk for neoplasia in the testicles and prostate. [INDICATE EVIDENCE FOR OTHER RISKS SUCH AS LIVER CANCER AND CATARACTS?] The consultants recommended annual medical examinations for persons exposed to the androgens.

The CDC has determined that records for the subjects who participated in the drug experiments are incomplete, and that it is not possible to accurately determine the drugs or drug dosages received by persons identified as having participated in the experiments. Therefore, the CDC recommended that medical examinations be offered to all subjects who have been identified as possible participants in the drug experiments.

Assessment of Toxicity of Exposures To Ionizing Radiation

Because the Oregon State Legislature mandated a medical followup for all radiation subjects, there is no need to justify this effort from a scientific standpoint. A review of the X-ray apparatus and exposure procedure by CDC and its consultants suggests that radiation exposure to organs or tissues other than the testicles is negligible. There is currently debate about the health risks associated with testicular irradiation. Based on theoretical considerations, any exposure to ionizing radiation increases the risk for testicular cancer. It is not clear to what extent doses of 600 rads or less would increase the risk for cancer.

High doses of ionizing radiation can permanently destroy hormone-producing tissue in the testicles. Persons with such damage may require periodic administration of testosterone. It is not clear whether doses of 600 rads or less are high enough to produce this effect.

Because of the theoretical risk and the uncertainty of the magnitude of this risk, most clinicians and scientists who were consulted agreed that offering annual medical exams is appropriate.

The CDC has obtained all records of X-irradiation that were stored with the DOE. These records include the original records of the radiation dose administered for most subjects. A review of all available data indicates that all former subjects in the radiation experiments can be identified by name. All dosimetry data have been recorded for the subjects on a computerized

database designed for this project.

Definition of Eligibility for Medical Evaluations

Because of the inability to accurately determine drug exposures for former research subjects, the CDC recommends that medical evaluations be offered to all inmates who have been identified as possibly having participated in the research projects. Of the persons identified on the list of all possible participants, only those for which there is evidence of non-participation will not be eligible for periodic medical evaluation and treatment. The CDC also recommends offering the same examinations to the former subjects in the radiation experiments and to those identified as possibly having participated in the drug experiments.

This definition of eligibility probably includes persons who were not actually in the drug experiments. It is also possible that there are other former subjects who cannot be identified through existing records. Because records of the experiments are incomplete, there is no way to identify additional subjects.

The CDC will prepare a final list of eligible subjects and provide this list to the OSP and the Oregon Health Division. The CDC will also provide the Oregon Health Division with a computerized database containing all the data abstracted for each eligible person.

Recommended Routine Medical Examinations And Laboratory Testing for All Eligible Subjects

The CDC consulted with a number of specialists in the fields of endocrinology, urology, and toxicology to determine the medical examinations and tests that would be appropriate for the former research subjects. Originally, consultants were asked to make separate recommendations for the subjects in drug experiments and radiation experiments. The final recommendations for both groups were quite similar. Because CDC determined that it is not possible to know whether or not the subjects in the radiation experiments also received experimental drugs, a single set of diagnostic procedures was specified for all former research subjects.

The CDC recommends that these procedures be offered on an annual basis. The Oregon Health Division, in consultation with the CDC, will prepare a more detailed description of the examination protocol to be provided to clinicians who will conduct these exams. The Oregon Health Division will also prepare a data collection form for clinicians to use for reporting the examination and test results.

Medical Examination and Laboratory Tests

A. Medical History and Physical Examination (Performed by a licensed physician)

1. A medical history and review of systems should be taken in order to identify all current and past significant medical problems that may be related to participation in hormone or radiation experiments. Loss or changes in distribution of hair should be described, as well as

changes in body habitus and wide fluctuations in weight. Past surgery and therapy should also be noted.

2. A routine physical examination will be performed and will include a fundoscopic examination of both eyes, an examination of the neck for masses and thyroid enlargement or nodularity, an examination of the breasts, and an abdominal exam with an assessment of liver size.

B. Genital Examination (To be performed by a board-certified urologist)

1. A survey of sexual function should be made. Changes in libido and erectile function should be described. Subjects should be asked specifically about the administration of any hormonal therapy or the performance of hormone assays, and records of these should be retrieved, if possible. The history of exposure to heat, chemicals (particularly petroleum distillates and pesticides), and lower urinary tract infection, particularly orchitis or epididymitis should be noted.
2. Body habitus should be described and height and weight recorded.
3. Hair distribution should be described and Tanner staging of pubic hair performed.

4. Testicles should be examined for consistency (firm, soft, or normal) and testicular volume measured with an orchidometer.
5. Digital examination of the prostate should be done and consistency, enlargement, asymmetry and nodularity assessed.
6. Testicular ultrasonography should be performed to document testicular volume for assessing fertility potential and to screen for occult testicular tumors.
7. On the initial examination, two semen samples should be obtained and analyzed for any subject who has not been vasectomized. The results of these analyses should be used to determine appropriate followup exams.
8. Testicular biopsy, from at least one testis, may be offered to those vasectomized patients who desire further documentation of fertility status.

C. Clinical Laboratory Tests

1. Serum FSH, LH (performed on pooled sera from three samples collected over 60 minutes), testosterone, prolactin, and estradiol should be performed annually.

Identification, Location, and Notification of Exposed Inmates

In order to offer former subjects in the Heller experiments an opportunity to receive annual medical evaluations, each will have to be located. The most efficient strategy for locating them is to have the Federal Bureau of Investigation (FBI) search computerized files for recent arrest records and jail sentences or probation terms for each former subject. This search involves forwarding fingerprints and other personally identifying information to the FBI, and awaiting the results of these searches. Since OSP has maintained these records on all inmates, this search can be performed with minimal cost and effort.

Persons who have not been arrested recently will have to be found through traditional techniques including motor vehicle licensure records and credit information services. The Oregon Health Division will prepare a written plan for locating former research subjects, utilizing resources they deem appropriate.

Once former subjects have been located, they will be notified of the availability of the medical followup. This notification will be done in a manner that assures that the former subjects understand completely the reasons for which they have been located and that they are made fully aware of the diagnostic and treatment services that are offered. The Oregon Health Division, in consultation with the CDC, will prepare a written plan for notifying eligible persons.

Eligible persons who are incarcerated in an Oregon prison at the time of a scheduled medical examination will be offered the option of having the examination performed at the prison, or the

option of being transported to a community medical facility for examination. Similar arrangements will be made for former subjects incarcerated outside the state of Oregon.

The Oregon Health Division will work with each eligible person to select local physicians who are appropriate for administering the specified examinations and tests. The Oregon Health Division will also make arrangements for transporting eligible persons to the medical facilities selected for the examinations and tests.

Providing Care and Treatment for Conditions Resulting from Participation in Experiments

House Bill 2914 directs the Corrections Division of the Oregon Department of Human Resources to provide "...care or treatment for any condition directly related to such experiments." The CDC has also interpreted this bill to include additional diagnostic tests deemed necessary by clinicians conducting the annual examinations. In addition, the Oregon Corrections Division has extended the coverage of House Bill 2914 to include those subjects who were involved in the drug experiments at OSP.

The determination of whether a diagnosed medical condition has resulted from past participation in the experiments will be made by the Advisory and Oversight Committee. This committee will establish a procedure for reviewing the medical diagnoses for each subject who is examined. They will consider medical evidence and exposure records, as well as evidence in the scientific literature before making a decision. The criteria for

establishing causality will be based on whether there is a reasonable chance that the condition in question is related to participation in the experiments.

The Committee may consult with experts of its choosing to receive assistance in making these determinations, and the Division of Corrections will pay for these services.

Former participants in the experiments can appeal any decision of the Advisory and Oversight Committee, provided the appeal is in writing and made no later than sixty (60) days after the original decision.

Advisory and Oversight Committee

The successful maintenance of the long-term followup depends upon full cooperation of former subjects and upon the routine adherence to all procedures described in the protocol. The diagnostic procedures should be acceptable to the former subjects, who should also be able to have input on the design of all aspects of the followup. The OSP should also have assurance that the followup is being conducted according to accepted standards.

For these reasons, an oversight committee will be established to periodically evaluate the long-term followup, to recommend changes that are appropriate in light of new diagnostic and therapeutic techniques, and to respond to any suggestions or complaints of subjects in the followup. This committee should include one former research subject, a medical epidemiologist, a urologist with experience in evaluating sexual function, an

endocrinologist with experience in assessing the toxicity of hormones and fertility/anti-fertility drugs, a psychologist with experience in counseling prison inmates, an attorney, and an expert on medical ethics. The committee should meet periodically and have a mechanism for providing timely responses to suggestions or complaints from subjects and professional staff.

Appointment to the committee will be for a period of two (2) years. The original appointments will be made by CDC, and subsequent appointments will be made by the committee itself. If either the Oregon Division of Health or the Oregon Corrections Division is unhappy with the performance of the committee, they may make a formal request to the Director of CDC to review the complaint and to make changes in the committee membership or its duties.