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Contract No. AT(45-1)-1780 - Pacific Northwest Research Foundation - Seattle, Washington
Investigator: Dr. Carl G. Heller
Title: "Effects of Ionizing Radiation on the Testicular Function of Man"

PURPOSE OF STUDY:

--To determine the minimal dosage of irradiation that causes temporary and permanent reduction and/or cessation of sperm production.

--To determine the time required for recovery from any given dose.

--To determine the influence of radiation-produced testicular alteration upon hormone excretion.

JUSTIFICATION:

Man is different from other mammalian species in the kinetics of spermatogenesis. The cellular associations in the tubules are different, fewer generations of spermatogytes exists between the stem cell and the mature sperm and the duration of ~~the~~ spermatogenetic ~~process~~ is longer in man than other species studied. Recovery time following irradiation is apparently prolonged in man as compared to other mammals. Thus, man is so different from other species studied, extrapolation of information obtained from the study of laboratory animals seems hazardous if not impossible. On the other hand knowing the dosage, the effect and the duration of the effect of irradiation on man might well dispell many of the uncertainties and consequent fears that now exist.

SELECTION OF PARTICIPANTS

Inmates of the Oregon State Prison request an interview with Dr. Heller and members of his staff. A detailed person-to-person explanation in laymen

terminology is given of the experimental procedures and the resultant effects. Each volunteer is further interviewed by a Chaplain, a ~~doctor~~ physician and a clinical psychiatrist to screen for medical history, present health status, ~~religious background~~ religious background, motivation and his mental and emotional stability. The applicant must sign a request for a vasectomy, and if married his wife must sign the request also. About 10% of the initial volunteers are selected for participation in the program. All participants have a vasectomy prior to release from the program.

SAFEGUARDING HUMAN SUBJECTS

Dr. Heller's experimental protocol has been and continues to be reviewed by the Review Committee for Investigations Involving Human Subjects of the Pacific Northwest Research Foundation. This Review Committee is made up of mature, competent individuals in the fields of surgery, internal medicine, ophthalmology and microbiology, the Director of the Swedish Hospital Medical Center, the Head of the Department of Pathology, the Director of the Tumor Institute, and the Chaplain of the Swedish Hospital Medical Center. Also serving as members of the committee are an attorney, a local business man, a Registered Nurse and the President of the Board of Trustees of the Pacific Northwest Research Foundation. The Committee operates under the provisions of the Nurenburg Code.

The last Committee review of this project was conducted on May 21, 1970.

STATUS OF PROJECT

Sufficient data has been collected and analyzed for some parameters so that statistical validity of the experimental data has been established. These areas are primarily the effects on hormone excretion. Additional data are required to establish statistical validity for the dose-response curve for

the cellular elements, the recovery times and certain hormone excretion effects. A total of 72 subjects will have been irradiated by May 1971, at which time the irradiation phase of the project will be completed and terminated. An additional 2 to 5 years will be required to obtain the data on recovery of spermatogenesis. The budget will undergo a sequential reduction beginning with the next contract year and continued until the data on recovery has been collected and the project is terminated.

RESULTS TO DATE:

Preliminary findings to date include:

a) Decrease in sperm counts can be detected at exposures as low as 8 R.

b) Azoospermia (no sperm) occurs at exposure levels of 100 R and above.

c) At 300 R and below only spermatocytes appear to be effected. Above 300 R all the spermatogenic cells are effected.

d) Length of recovery period appears to be dose related.

e) Dose level for permanent sterility has not been determined but the data indicate it would be above 600 R. The investigator will not irradiate above the 600 R level. Some subjects exposed at 600 R are showing early stages of recovery beginning about 3 years post-irradiation.

f) Complete recovery from 100 R and below occurs within 18 months.

g) Ultrastructural damage to the spermatogonia occur within 16 minutes following irradiation. (This is the minimum time a biopsy can be obtained).

h) Plasma ICSH (interstitial cell stimulating hormone) levels rise following irradiation; whereas, the urinary ICSH levels do not change.

i) Both plasma and urinary FSH (follicle stimulating hormone) levels rise following irradiation.

j) Insufficient data have been obtained to draw conclusions on the testosterone level changes following irradiation. However, since the Leydig cells (that produce testosterone) are more radioresistant than the germinal cells it would appear that relatively large doses would be required to effect the testosterone level.

Frank T. Brooks, D.V.M.