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TRIP REPORT
DR. Goldstein + Dr. Richmond

Dr. Paulsen is associated with the University of Washington School of Medicine. The University has a cooperative plan whereby staff members do research at the County Hospital and the USPHS Marine Hospital in Seattle. Dr. Paulsen works at the latter as an endocrinologist and where he was visited on February 18 with the aim of clarifying the experimental design of his study. Dr. Paulsen is attempting to establish a dose response curve for an acute dose x-irradiation to the human testes. A 250 kvP x-ray was used as the radiation source. Six different exposure doses were used with a target to skin distance of 75 cm. Because he used two different dose rates, the comparative values of dose-response could not be determined during the interview. The test population totaled 209 volunteers who are inmates at the State Prison at Walla Walla. Of these, 60 were irradiated at one of the six exposure dose levels, and the remainder were used for control and procedural development.

Three end points selected for study were:

1) sperm count
2) blood and urinary gonadotropins
3) testicular biopsy (histopathology)

Sperm results to date are summarized as follows:

Dose (rad)	No. of Subjects	(days) Time to Oligospermia*	(days) Time to Azospermia	(days) Time to Recover**
400	8	68	101	1065 (none to date)
100	25	100	132	767 (521-1447)
50	8	155	187	720 (586-853)
30	5	180		incomplete
15	8			647 (549-745)
7.5	6			

*Less than 10^6 sperm per cubic centimeter

**Time for sperm count to return to pre-irradiation mean level ($\pm 2\sigma$). Range of values shown in parentheses. Pre-irradiation means were based on a minimum of 20 specimens. Normal range is from 30 to 200 x 10^6 per cm^3.

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In the preceding table the 15 rad exposure was the lowest level where sperm counts 1×10^6 and 5×10^6 per cubic centimeter were found (oligospermia). Analysis of the 30 rad group is incomplete. There was no large reduction in sperm count until 68 days following irradiation, at which time a precipitous drop to essentially a stabilized zero level was observed. This zero level remained until recovery began. A significant overlap of time ranges required for recovery at the various doses is apparent.

The above data on sperm counts are currently being reduced and reanalyzed by Dr. Thorslund of the University of Washington Mathematics Department (who previously served on the ABCC). Dr. Thorslund will reevaluate the experimental design and recommend changes and additional exposures if warranted. Results of this analysis was suggested to be forwarded to DBM when completed.

In the Gonadotropin study, Follicle Stimulating Hormone (FSH) increased in urine as the result of testicular damage but was not correlated with the number of germ cells as determined by histopathology. Blood plasma testosterone levels did not change and suggest a sparing of the Leydig cells at the exposure doses used. Blood plasma FSH studies were begun during the past several weeks because of the recent introduction of radioimmunoassay at Dr. Paulsen's laboratory.

One patient was given testosterone to produce oligospermia prior to 100 rad x-irradiation to the gonads and his course of recovery from azospermia was essentially similar to the 100 rad exposure group not receiving testosterone.

Tissue studies revealed that in all the volunteers receiving exposures of ~~15~~ 100 or greater rads, the germinal epithelium was depleted, as expected, leaving only Sertoli cells in the tubules. Two unexpected findings were that there was an absence of vascular involvement in the interstitial tissue and no fibrosis in the tubular basement membrane was seen.

During the last six months exposures have been discontinued pending another review of the experimental procedures by the University of Washington Human Use Committee which will also include exposures to neutrons. With neutron exposures Dr. Paulsen plans to establish the RBE for 2.4 and/or 14 Mev neutrons. Initially, the end point will be sperm counts but Dr. Paulsen will also consider gonadotropin levels and testicular biopsy data as additional end points, if warranted. At first, Dr. Paulsen plans to compare neutron exposures with the 30 rad x-ray exposure assuming a theoretical RBE of 2 and 10 for neutrons. The pilot exposures at 15 and 3 rad will yield a calculated 30 rem neutron dose respectively. Plans are to expose 4 volunteers as a pilot experiment to observe the biological results of exposures to approximately 30 rem of neutrons using two subjects at each assumed RBE. Subsequently, the experimental design will be formulated by Drs. Paulsen and Thorslund and forwarded to DBM to be included into the existing protocol.

Assistance with dosimetric problems is received from the Battelle-Northwest group. (See BNWL-589-Fast Neutron Medical Research Facility - Dosimetry, Swinth and Brabry, 1967). Neutrons of 2.4 and 14 Mev will be obtained from generators. The estimated dose rate for the 2.4 Mev neutrons is about 1 rad per hour and a two hour exposure will be required to deliver a total dose of 2 rad divided anteriorly and posteriorly. The dose rate for 14 Mev neutrons was not available but should be higher. In either case, the dose rate will not be the same as that used for the x-ray exposures.

Comment: Because of the sensitivity of these studies, and the noted inadequacies of the past experimental design, positive surveillance by DBM is advisable to insure meaningful information as early as possible with the smallest acceptable population of test subjects.

Joseph D. Goldstein, M. D.
Medical Research Branch
Division of Biology and Medicine

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