

January 4, 1965

Dr. Douglas Grahn,
Associate Director
Division of Biological & Medical Research
Argonne National Laboratory
9700 South Cass Avenue
Argonne, Illinois 60440

Dear Dr. Grahn:

Inferences regarding the effects of radiation upon human male reproduction emanate from three general sources: (1) nuclear explosions and accidents (where dosage can only be estimated, observations generally are random and antecedent control data is unobtainable); (2) extrapolation from animal experiments (with all its built-in hazards); and (3) direct exposure of the testes of normal men, in whom each pertinent parameter has been studied in advance, to known graded doses of radiation.

The former two categories are discussed in the literature. The latter has been made feasible by two circumstances: (1) the cooperation of inmates who volunteer at the Oregon State Penitentiary; and (2) the recent unravelling of the process of spermatogenesis in man by defining, for the first time, all the cell types, the recognition and definition of the stages of the germinal epithelium, the timing of each cycle of spermatogenesis, and the determination of the total duration of spermatogenesis. (Y. Clermont, Am. J. Anat. 112, 35 (1963), C. G. Heller and Y. Clermont, Science, 140: 3563, 184 (1963), and C. G. Heller and Y. Clermont, Recent Progress in Hormone Research, Vol 20, pp. 545-575, Academic Press, N.Y. (1964).)

Our results to date include the following: azoospermia is produced by exposure to a single dose of ionizing radiation at 100, 200, 300, 400 and 600 r.

Decrease in sperm count is not detectible before 46 days elapse (the time of development from preleptotene spermatocyte to spermatozoa) at 100, 200 and 300 r. The decrease is detectible earlier at 400 r and 600 r. (A more mature germinal cell is hit.)

100 r appears to be the threshold dose for azoospermia in that a few spermatozoa (in 7 subjects) continue to be detectible.

50 r results in marked oligospermia.

20 r results in moderate oligospermia.

15 r results in moderate oligospermia.

Necrosis and distortion of cellular elements, as revealed by testicular biopsy specimens, are apparent in 4 to 6 hours. The cells involved at 300 r and below are Type A pale, A dark and B spermatogonia and preleptotene spermatocytes. Many of these cells have disappeared by 12 hours.

Denuding of the entire germinal epithelium occurs at all doses--some complete, 200 r and above, and some incomplete, 100 r and below.

Recovery experiments are in progress. In general, the lower the dose the more rapid the recovery. Recovery has occurred at doses up to 300 r.

Urinary gonadotropins are significantly and unequivocally elevated in any instance of denuding of the germinal epithelium.

Libido and potentia are unaffected up to and including 600 r. More sophisticated measures of Leydig-cell function are being undertaken, such as estrogen partitions and testosterone excretion. Total estrogens and total 17-ketosteroids are unchanged. Leydig-cell morphology (inspection only) is unchanged. Quantitative Leydig-cell studies regarding total numbers and mass are contemplated.

Quantitation (scoring) of the effects upon the germinal epithelium is underway. Our experiments imitate those of Oakberg on the mouse. This tedious but rewarding task is at the point of evaluating the control biopsies only, up to this point. (Each subject serves as his own control in all parameters.)

Chromosomal aberrations have been noted on histological section (translocations, disjunction, sticky chromosomes, etc.).

Squash preparations are being made on all subjects. These have revealed a fine collection of pachytene chromosomes, spermatogonia in mitosis and pachytene in diakinesis. To date only the pachytene chromosomes have been mapped (as yet incomplete) in control subjects, preparatory to mapping of pachytene in subjects exposed to radiation. Note: All inmates are vasectomized before release in order to avoid potential contamination of the general population.

Morphology of the spermatozoa in the ejaculated specimens is being followed by Dr. John MacLeod at Cornell. Below 300 r exposure, azoospermia is achieved without encountering morphological alterations. Recovery ensues without morphological alterations.

Have you or your panel any suggestions regarding other information you should like to have, or other parameters that might be worth studying? This opportunity afforded to us, which may or may not be repeated or continued, should be made to yield the greatest possible pertinent information.

Happy New Year.

Sincerely,

Carl G. Heller, M.D., Ph.D.
Head, Division of
Reproductive Physiology

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