

UNITED STATES GOVERNMENT

Memorandum

Boffarney
Dr. Bourne
Dr. Bruner
Dr. Storey
Boffarney
DATE: January 23, 1968

TO : John R. Totter, Director
Division of Biology and Medicine

FROM : *Boffarney*
Elmer B. Harvey
Medical Research Branch
Division of Biology and Medicine

SUBJECT: ANALYSIS OF SITE REVIEW OF DRS. HELLER'S AND PAULSEN'S PROJECTS,
DECEMBER 14-15, 1967, SEATTLE, WASHINGTON, AND RECOMMENDATIONS FOR
FUTURE ACTION

703866

Dr. Heller's studies of the effects of irradiation on volunteer human testicular function was initiated in 1963 and those of Dr. Paulsen's were initiated in 1964. It was anticipated at the inception of these studies that the work could be completed in five to seven years.

During the tenure of both of these contracts, new studies have been initiated and justified on the basis that alterations in sperm count, motility and abnormalities as well as changes in hormone levels as measured were not precise enough indicators of irradiation damage to the testes. Attempts to refine measurements, to determine new parameters that may be better indicators of damage, the discovery by Heller's group that distribution of spermatogenesis in testicular tubules has a different pattern in man than other species and the potential that irradiation may be a useful tool in determining the relationship between hypothalamic-pituitary-gonadal axis and spermatogenesis in man has tended to result in both laboratories expending an increasing effort in these ancillary studies.

It should be noted at this point that studies on the effects of neutron irradiation on testicular function by Dr. Paulsen should be underway before the summer of 1968. Applicable analytic methods developed and refined in the x-irradiation studies will be utilized for this investigation.

Drs. Heller's and Paulsen's projects were site visited in March 1967 at which time it was strongly urged that both laboratories add a biometrician to their staffs. This was accomplished in June 1967 by the addition of Dr. O'Keefe who spends half time on each project. A review of the projects by a panel of biometricians was also recommended and this was carried out in September 1967 under the direction of

(Their comments are appended.)

✓
✓
✓



Buy U.S. Savings Bonds Regularly on the Payroll Savings Plan

1001814

REPOSITORY DOE-FORESTAL

COLLECTION HARVEY FILES

BOX No. 2 OF 6

FOLDER PAULSEN & HELLER (GENERAL FILES)

In brief the biometrics panel were of the opinion that the studies as presented to them were of good quality and that the biometric problems could be solved within the limits of the experimental conditions. They also agreed that the addition of Dr. O'Keefe to the projects would bring an important new capability to both studies. Nevertheless, ~~Dr. [redacted]~~ lists six problems that should be worked on in the studies. Dr. O'Keefe is aware of these and is presently working on them. The panel recommended that both laboratories publish not only experimental results but also publish in detail on methodology and biometrics.

Outside reviewers at both the March 1967 and December 1967 reviews were of the opinion that the studies as conducted by Dr. Paulsen's and Dr. Heller's laboratories were being done in a satisfactory manner and that the research personnel were competent and conducting their studies in a professional manner. The March reviewers all were concerned by the lack of publications by Dr. Heller. Dr. Heller has been informed of this concern. It should be noted that his support from the National Institutes of Health was curtailed and finally terminated in part because of this deficiency.

Both the March and December review teams were not satisfied with the electron microscopic studies conducted by Dr. Vilar on biopsy specimens for Dr. Paulsen. Dr. Heller was given an electron scope to carry out preliminary studies of biopsy material. It is considered important that the ultrastructural changes of cells of human testicular tissues should be described if these tissues are available. However, determination of ultrastructural changes in human testicular tissues either following biopsy, irradiation, or both, cannot be justified as an independent study in the human at this time.

A serious deficiency in both studies and alluded to by the outside reviewers was the lack of quantitative data on the volume of ejaculate on which sperm counts were conducted. This concern has been transmitted to both Drs. Heller and Paulsen.

Most of the reviewers were of the opinion that use of human material for basic studies of endocrine function was ancillary to the direct studies and that perhaps these studies might more profitably be done on experimental animals. Dr. ~~[redacted]~~, however, expressed satisfaction with the progress in these areas and suggested that they should continue. He also pointed out that results from these studies would be important to structuring new research in animals.

The reviewers were not complimentary to the studies on abnormalities produced in chromosomes and chromatids as carried out by Dr. Paulsen.

1001815

RECOMMENDATION:

In view of the outside review comments this year and in previous years the following recommendations with respect to the research of Drs. Heller and Paulsen on effects of radiation on human testicular function is presented for early discussion:

1. The x-irradiation studies should be concluded at the earliest date that reliable and valid data can be attained on:
 - a. Testicular function following five dose levels of irradiation, low (7.5-8), 25r, 50r, 100r, and 400r. (Adequate data may already be available on the 100r level.)
2. The minimum information should consist of:
 - a. Sperm count, motility, ^{viability} abnormalities and ejaculate volume.
 - b. Completion of studies on histologic description at the light microscopic level by Dr. Heller's group.
 - c. Description of the ultrastructure of control and irradiated testes.
 - d. Measurement of the LH-FSH and testosterone levels by the best techniques presently available.
 - e. Suspension of chromosomal and chromatid studies.
 - f. Suspension of isoantibody studies.
3. Neutron irradiation studies should be completed in two years utilizing techniques already established in the x-ray studies.
4. RBE studies as presently conceived by Dr. Paulsen should be discouraged.
5. No new studies should be initiated under the present contracts. However, proposals to carry out new studies should be encouraged and given every consideration.

Attachments:

Correspondence on Dr. Heller's
and Paulsen's research projects

1001816