

Paul Henshaw
Division of Biology and Medicine, HQ.

November 23, 1966

William M. Harris, Radiation Sciences Branch
Research and Development Division, RL

CONTRACT AT(45-1)-1780 - PACIFIC NORTHWEST RESEARCH FOUNDATION

Enclosed are the following technical reports:

"The Depletion of the Human Germinal Epithelium by X-Irradiation;
A Study of the Timing of Spermatogenesis" 20-175-15

"Leydig Cell Number and size following Human Chorionic Gonadotropin
Administration in Five Normal Men" 20-175-16

"Testosterone Excretion: Index of Testicular Secretion" 20-175-17

These reports were submitted by Dr. Carl G. Heller, principal investigator under the subject contract. These reports have received patent clearance through the RL representative of the Chicago Patent Group.

Enclosure:
Technical Reports (4 each)

cc: DTIE, Oak Ridge w/ cys.
and Forms AEC-427

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GSSC HUMAN TEST SUBJECT STUDIES
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1190303

**REQUEST FOR PATENT CLEARANCE
FOR PUBLIC RELEASE OF UNCLASSIFIED DOCUMENT**

TO: CHIEF, CHICAGO PATENT GROUP
U. S. ATOMIC ENERGY COMMISSION
9800 S. CASS AVENUE
ARGONNE, ILLINOIS

FROM: Acting Chief, Radiation Sciences Branch
Research and Development Division
U.S. Atomic Energy Commission - P.O. Box 550 - Richland, Wash. 99352

1. DOCUMENT IDENTIFICATION:
"The Depletion of the Human Germinal Epithelium by X-Irradiation; a Study of the Timing of Spermatogenesis" (RLO-1700-15) by Mavis J. Rowley and Carl G. Heller
2. RELEASE IDENTIFICATION:
Publication in Clinical Research journal

CONFIDENTIAL (49-3) 1792

3. RETURN OF DOCUMENT IS NECESSARY.
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Nell W. Fraser
Nell W. Fraser

(DATE)

July 8, 1966

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Mr. [unclear]

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25/9/66

THE DEPLETION OF THE HUMAN GERMINAL EPITHELIUM
BY X-IRRADIATION: A STUDY OF THE TIMING OF SPERMATOGENESIS

Mavis J. Rowley* and Carl G. Heller
Pacific Northwest Research Foundation
1102 Columbia Street
Seattle, Washington 98104

The testes of normal male volunteers were exposed to single doses of ionizing radiation. 100r to 300r was sufficient radiation to cause degeneration of spermatogonia without causing damage to spermatocytes and spermatids. Thus spermatocytes and spermatids were permitted to proceed normally with maturation, reduction division and sperm formation.

Biopsies were taken at intervals during cell depletion and compared with the H³-thymidine labeled biopsies of Heller and Clermont (Recent Progress in Hormone Research, vol. 20, 1964). In the thymidine experiment the most advanced labeled cell, the pre-leptotene spermatocyte, was followed. After radiation the least advanced remaining cell to complete development to spermatozoa was followed to maturation. It was also a pre-leptotene spermatocyte. Maturation from a pre-leptotene spermatocyte to spermatozoa required 46 days in each instance.

Thus we find from these data that following radiation the germinal epithelium denudes at the same rate as the normal germinal epithelium matures. These radiation depletion data confirm the timing of human spermatogenesis with tritiated thymidine.

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FROM: Acting Chief, Radiation Sciences Branch
Research & Development Division
U.S. Atomic Energy Commission - P.O. Box 550 - Richland, Wash. 99352
1. DOCUMENT IDENTIFICATION:
"Leydig Cell Number & Size Following Human Chorionic Gonadotropin Administration
in Five Normal Men" (RLO-1730-16) by Joyce E. Pearson, Michael F. Lalli and
2. RELEASE IDENTIFICATION: Carl G. Heller

Publication in Clinical Research journal

*Contract
AT 45-231750*

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(SIGNED) *Nell W. Fraser* (DATE) *Nov. 8, 1966*
Nell W. Fraser

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(SIGNED) *B. J. ...* (DATE) *11/9/66*

LEYDIG CELL NUMBER AND SIZE FOLLOWING HUMAN CHORIONIC
GONADOTROPIN ADMINISTRATION IN 5 NORMAL MEN

Joyce E. Pearson*, Michael F. Lalli* and Carl G. Heller**
Pacific Northwest Research Foundation
1102 Columbia Street
Seattle, Washington 98104

Human chorionic gonadotropin (HCG) stimulates the Leydig cells of the testis to produce increased amounts of testosterone. This study was undertaken to determine if such stimulation results in an increase in the size and/or number of Leydig cells.

Five subjects received injections of HCG, 4 men for 6 weeks (4000 I.U./t.i.w.) and one man for 16 weeks (4000 I.U./q.o.d.). Biopsies taken at intervals during treatment were compared with control biopsies using a new method for quantitating Leydig cells. The number of Leydig cells counted in photographed areas was compared with the number of Sertoli cells in the same areas and results expressed as a ratio (Leydig cell/Sertoli cell). The cytoplasm, nucleus and nucleolus were measured with a Filar ocular micrometer at 1000x.

The Leydig cells did not increase in number or size even though urinary testosterone levels increased at least threefold. The Leydig cell/Sertoli cell ratios among individuals before treatment varied widely (0.19 - 0.67). This variation is generally reflected by the control urinary testosterone values.

These data indicate that although the Leydig cells are stimulated by HCG their increased activity is not reflected by an increase in their size or number.

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ARGONNE, ILLINOIS

Acting Chief, Radiation Sciences Branch

FROM: Research and Development Division - U.S. Atomic Energy Commission,
P.O. Box 550 - Richland, Washington 99352

1. DOCUMENT IDENTIFICATION:

"Testosterone Excretion: Index of Testicular Secretion" by Janice M. Kastella,
Donald R. Brusca and Carl G. Heller (RLO-1790-17)

2. RELEASE IDENTIFICATION:

Publication in Clinical Research journal *Control*

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(DATE)

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(SIGNED)

J. R. Smith

(DATE)

3/7/64

TESTOSTERONE EXCRETION: INDEX OF TESTICULAR SECRETION

Janice M. Kastella*, Donald R. Brusca* and Carl G. Heller**
Pacific Northwest Research Foundation
1102 Columbia Street
Seattle, Washington 98104

A gas chromatographic method of quantitating the combined epimers in urinary testosterone has proved useful in establishing an index of testicular Leydig cell function. The mean daily output from 46 normal males was 89 μ g (range 40 to 176), from 4 normal females, 7 μ g (range 3 to 10), and from a single orchiectomized subject, 17 μ g/day.

Stimulation of testicular steroid production with human chorionic gonadotropin (HCG) in 5 subjects for periods of 6 to 18 weeks caused increases in urinary testosterone of three- to sixfold over the control levels of each individual. Highest testosterone excretion occurred during the first 2 weeks of HCG administration and elevated excretion was not consistently maintained. Clomiphene citrate administered to 3 subjects for 6 to 12 months augmented urinary testosterone threefold but also did not maintain the increased levels. Similar treatment of the castrate male produced no rise in testosterone excretion.

Administration of a progestational agent (SC-9022) to 2 male subjects caused repression of testosterone levels from 98 μ g/day to 25 μ g/day. Testicular x-irradiation of 16 subjects with 15r to 600r generally depressed testosterone excretion from control levels.

These data indicate that urinary testosterone values are a valid and useful index of testicular production of this hormone.