

716207

EFFECTS OF IONIZING RADIATION
ON THE TESTICULAR FUNCTION OF MAN
AEC Contract No. AT(45-1)1780
RENEWAL PROPOSAL
Grant Period: 8-1-70 thru' 7-31-71
Carl G. Heller, M.D., Ph.D.
Pacific Northwest Research Foundation

3000930

PACIFIC NORTHWEST RESEARCH FOUNDATION
Division of Reproductive Physiology
1102 Columbia Street
Seattle, Washington 98104

RENEWAL PROPOSAL FOR AT (45-1) 1780

Division of Biology and Medicine
U.S. Atomic Energy Commission
Washington, D.C. 20025

TITLE

EFFECTS OF IONIZING RADIATION ON THE TESTICULAR FUNCTION OF MAN

Principal Investigator: Carl G. Heller, M.D., Ph.D.

Support Period: August 1, 1970 - July 31, 1971

| | | |
|---------|------------------|-------------------------------|
| Amount: | First year | \$ 99,631 |
| | Second year | 87,000 + 8,113 modification |
| | Third year | 94,023 |
| | Fourth year | 96,000 |
| | Fifth year | 100,000 + 22,000 modification |
| | Sixth year: | |
| | 6-1-68/7-31-68 | 20,000 |
| | 8-1-68/7-31-69 | 120,000 |
| | Seventh year | 120,000 |
| | Succeeding years | To be arranged |

Carl G. Heller

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

William B. Hutchinson

William B. Hutchinson, M.D.
Director, Pacific Northwest
Research Foundation

3000931

I. OBJECTIVES

In the progress report and proposal for the current year's research (1969-70) we stated that our objectives were 1) to determine the exact nature of the cytological defect produced in the development of the germinal epithelium and to relate the extent of the defect to dosage and time; 2) to find the minimal dosage that will affect the germinal epithelium; 3) to determine the time of recovery from any given dosage; 4) to determine the minimal dosage that leads to permanent damage of spermatogenic cells; 5) to determine the simultaneous effects of any dosage upon Leydig cell cytology; 6) to determine the influence of any given radiation-produced testicular alteration upon other parameters such as the excretion of total gonadotropic hormones, follicle-stimulating hormone (FSH), interstitial cell-stimulating hormone (ICSH), estrogens and androgenic hormones; and 7) to determine the influence of any given radiation-produced testicular alteration upon plasma FSH, ICSH and testosterone. Our final objective is a complete statistical examination of all parameters and their interactions.

These objectives will not change for the coming year. We have been working and accumulating data to help fulfill these parameters during this current year although only the determinations involving urinary estrogens, total gonadotropins and pregnanediol and pregnanetriol have been completed.

The following charts, similar to those submitted last year, will demonstrate data collected during the current year (Charts A, B, & C), and data to be collected during the coming year (Charts B & C).

3000932

II. CHARTS

A. BIOPSY TIMES FOLLOWING IRRADIATION

1. - 5.

B. PARAMETERS MEASURED AND RESPONSE RECORDED DURING RECOVERY

C. PARAMETERS MEASURED AND RESPONSE RECORDED DURING DEPLETION

3000933

A I.

| DOSE | SUBJECT | 1 day | 1wk | 2wk | 3wk | 4wk | 6wk | 8wk | 10wk | 15wk | 20wk |
|------|---------|-------|-----|-----|-----|-----|-----|-----|------|------|------|
| 8r | | | | | | | | | | | |
| 8r | | | | | | | | | | | |
| 8r | | | | | | | | | | | 17wk |
| 8r | + | | | | | | | | | | |
| 10r | | | | | | | | | | | |
| 10r | | 24h | | 2wk | | | | | | | |
| 10r | | 24h | | 2wk | | 25d | | 7wk | | | 16wk |
| 15r | | | | | | | | | | | |
| 20r | | 4h | | | | 26d | | 44d | | | 17wk |
| 20r | | 24h | | | 15d | | 29d | | 64d | | 17wk |
| 20r | | | | | | | | | | | |
| 20r | | | | | | | | | | | |
| 20r | | | | | | | | | | | |

+ second irradiation
 * cannot be quantitated
 N.C. no control biopsy

h hour
 d day
 wk week

PRIVACY ACT MATERIAL REMOVED

3010934

A 2.

| DOSE | SUBJECT | 1 day | 1wk | 2wk | 3wk | 4wk | 6wk | 8wk | 10wk | 15wk | 20wk |
|------|---------|-------------|-----|-----|-----|-----|-----|-----|------|------|------|
| 25r | | 6h | | | | 24d | 40d | | | | |
| 25r | + | 24h | | | 15d | | 29d | | 64d | | 18w |
| 50r | (N.C.) | 4½*/ 7*h | | | | 24d | 40d | | | | |
| 50r | | | | | | | | | | | |
| 50r | | | | | | | | | | | |
| 50r | + | | | | | | | | | | 20wk |
| 55r | | | | | | | | | | | 17wk |
| 78r | | | | | | | | | | | |
| 78r | | | | | | | | | | | |
| 78r | | | | | | | | | | | |
| 78r | | | | | | | | | | | |
| 100r | | | | | | | | | | | |
| 100r | | 24h | | 2wk | | 25d | | 7wk | | | 16wk |

+ second irradiation
 * cannot be quantitated
 N.C. no control biopsy

PRIVACY ACT MATERIAL REMOVED

3000936

A 3.

| DOSE | SUBJECT | 1 day | 1wk | 2wk | 3wk | 4wk | 6wk | 8wk | 10wk | 15wk | 20wk |
|------|---------|-------------|-----|-------|-----|-----|------------|-------|-------|------|------|
| 100r | (N.C.) | 16h* | | | | | 33d* | 46½d* | 62½d* | | |
| 100r | (N.C.) | 4*/ 6½*h | | | | | 31d* | | | | |
| 100r | | | | | | | | | | 15wk | |
| 100r | | | | | | | | | | 11wk | |
| 100r | | | | | | | | | | 11wk | |
| 100r | + | 24h | | | 15d | | 29/ 37d | | | 14wk | |
| 100r | | | | | | | | | | | |
| 100r | | 24h | | 2wk | | | 35d | | | | 17wk |
| 200r | (N.C.) | 13h* | | 14½d* | | | | 46½d | | | |
| 200r | | 22½h | | 14½d | | | 29d | | | 12wk | |
| 200r | | | | | | | | | | | |
| 200r | | | | | | | | | | | |
| 200r | | | | | | | | | | | |
| 200r | | | | | | | | | | | 19wk |

+ second irradiation
 * cannot be quantitated
 N.C. no control biopsy

h
d
wk
hour
day

PRIVACY ACT MATERIAL REMOVED

3000038

| 25wk | 30wk | 40wk | 50wk | 60wk | 80wk | 100wk | 120wk | 140wk | 160wk | 180wk | 200wk | 220wk | 240wk |
|------|------|------|------|------|-------------|----------------|---------------|---------------|-------|-------|-------|-------|-------|
| | 29wk | 36wk | | | 70wk | | | | | | | | |
| | | | | | | 87wk | 105wk | 125wk | 153wk | | 183wk | | 232wk |
| | 28wk | | | | | 81/89/ 99wk | 109wk | 129wk | | | | | |
| | | | | | | | | 125/ 135wk | | | | | |
| | | 37wk | | | 61wk | | | | | | | | |
| | | | | 45wk | | | | | | | | | |
| | | 31wk | | | | | | | | | | | |
| | | 35wk | | | | | | | | | | | |
| 21wk | | 33wk | 43wk | 57wk | | 81wk | | | | | | | |
| 22wk | | 37wk | | | | | | | | | | | |
| | | | | | | | | 139wk | | | | 203wk | |
| | 30wk | | | 53wk | 66/ 80wk | | 101/ 119wk | 136wk | | 165wk | | | |

3000939

A 4.
SUBJECT

| DOSE | 1day | 1wk | 2wk | 3wk | 4wk | 6wk | 8wk | 10wk | 15wk | 20wk |
|----------------|-----------|------|-----|-----|-----|-------------|------|------|------|------|
| 200r | | | | | | | | | | |
| 200r | | | | | | | | | | |
| 235r | | | | | | | | | | |
| 300r (N.C.) | 15h* | | | | | 33/ 40½d | 62½d | | | |
| 300r | | | | | | 40½d | | | | |
| 400r | 6/ 4½h | | | | 24d | 40d | | | | |
| 400r | | | | | | | | | 72d | |
| 600r | 4h | | | | 26d | | 44d | | 13wk | |
| 600r | | 22½h | | | | 29d | | | 12wk | |
| 600r | | | | | | | | | | 20wk |
| 600r | | | | | | | | | | |
| 600r | | | | | | | | | | |

+ second irradiation
 * cannot be quantitated
 N.C. no control biopsy

h
d
wk

hour
day
week

A b.

| DOSE | SUBJECT | 1 day | 1wk | 2wk | 3wk | 4wk | 6wk | 8wk | 10wk | 15wk | 20wk |
|------|---------|-------|-----|-----|-----|-----|-----|-----|------|---------------|------|
| 600r | | 18min | | | | 24d | | 8wk | | | |
| 600r | | 16min | | | | 24d | | 8wk | | | |
| 600r | | | 1wk | | | | | 46d | | 13wk | |
| 600r | ++ | | 1wk | | | | 6wk | | | 13wk/ 15wk | |
| 600r | | | | | | | 5wk | | | | |
| 600r | | | | | | | 5wk | | | | |

++ third irradiation
* cannot be quantitated
N.C. no control biopsy

h d wk
hour
day
week

PRIVACY ACT MATERIAL REMOVED

| 25wk | 30wk | 40wk | 50wk | 60wk | 80wk | 100wk | 120wk | 140wk | 160wk | 180wk | 200wk | 220wk | 240wk |
|------|------|------|------|------|------|-------|-------|-------|-------|-------|-------|-------|-------|
| 22wk | | 37wk | 45wk | 58wk | | | | | | | | | |
| 22wk | | 37wk | 45wk | 57wk | 67wk | | | | | | | | |
| | 26wk | | 51wk | 58wk | 66wk | | | | | | | | |
| | | | | | | | | | | | | | |
| | | | | | | | | | | | | | |
| | | | | | | | | | | | | | |
| | | | | | | | | | | | | | |

3000944

B. PARAMETERS MEASURED AND RESPONSE RECORDED

C Y T O L O C

GERMINAL CELL RECOVERY

| Dose (r) | Number of subjects | Start of Histological Recovery | First Sperm OR First Increase of Sperm in Seminal Fluid | Complete Recovery | Germinal Cell Ultrastructure | Sperm Concentration in Seminal Fluid |
|----------|--------------------|--------------------------------|---|-------------------|------------------------------|--------------------------------------|
| | | | | | | |
| 10-25 | 11 | Complete | Complete | Incomplete | Incomplete | Complete |
| 20 | 4 | 4 | 4 | 4 | 4 | 4 |
| 50-100 | 19 | Complete | Complete | Incomplete | Incomplete | Complete |
| 75 | 4 | 4 | 4 | 4 | 4 | 4 |
| 200-300 | 11 | Complete | Complete | Incomplete | Incomplete | Complete |
| 200 | 6 | 6 | 6 | 6 | 6 | 6 |
| 400-600 | 13 | Complete | Complete | Incomplete | Incomplete | Incomplete |
| 600 | 4 | 4 | 4 | 4 | 4 | 4 |

Current status of all samples collected to date

Number of subjects to be irradiated to complete adequate analysis of each parameter

Current status of all samples collected to date

Number of subjects to be irradiated to complete adequate analysis of each parameter

Current status of all samples collected to date

Number of subjects to be irradiated to complete adequate analysis of each parameter

Current status of all samples collected to date

Number of subjects to be irradiated to complete adequate analysis of each parameter

DURING RECOVERY

| I C A L | | H O R M O N A L | | | | | | |
|-----------------|-----------------|-----------------|-----------------|---------------|---------------------------------|---------------|-----------------|-----------------|
| | | URINARY | | | PLASMA | | | |
| Leydig Cells | Sertoli Cells | ICSH | FSH | Estrogen | Testosterone & Epi-testosterone | ICSH | FSH | Testosterone |
| Incomplete 4 | Incomplete 4 | Complete 0 | Complete 0 | Complete 0 | Complete 0 | Complete 4 | Incomplete 4 | Incomplete 4 |
| Incomplete 4 | Incomplete 4 | Complete 0 | Complete 0 | Complete 0 | Complete 0 | Complete 4 | Incomplete 4 | Incomplete 4 |
| Incomplete 6 | Incomplete 6 | Incomplete 3 | Incomplete 3 | Complete 3 | Incomplete 3 | Complete 6 | Incomplete 6 | Incomplete 6 |
| Incomplete 4 | Incomplete 4 | Incomplete 1 | Incomplete 1 | Complete 1 | Incomplete 1 | Complete 4 | Incomplete 4 | Incomplete 4 |

300094b

C. PARAMETERS MEASURED AND RESPONSE RECORDED

C Y T O L O G

| | Dose (r) | Number of subjects | GERMINAL CELL QUANTITATION | | | | Sperm Concentration Seminal Fluid |
|---|----------|--------------------|----------------------------|----------------|-------------|-------------------------------|-----------------------------------|
| | | | Sperma-togonia | Sperma-tocytes | Sperma-tids | Germinal Cell Ultra-structure | |
| | | | Complete | Complete | Complete | Incomplete | |
| Current status of all samples collected to date | 10-25 | 11 | Complete | Complete | Complete | Incomplete | Complete |
| | 20 | 4 | 4 | 4 | 4 | 4 | 4 |
| Number of subjects to be irradiated to complete adequate analysis of each parameter | 50-100 | 19 | Complete | Complete | Complete | Incomplete | Complete |
| | 75 | 4 | 4 | 4 | 4 | 4 | 0 |
| Current status of all samples collected to date | 200-300 | 11 | Complete | Complete | Complete | Incomplete | Complete |
| | 200 | 6 | 0 | 0 | 0 | 6 | 0 |
| Number of subjects to be irradiated to complete adequate analysis of each parameter | 400-600 | 13 | Complete | Complete | Complete | Incomplete | Complete |
| | 600 | 4 | 0 | 0 | 0 | 4 | 0 |

DURING DEPLETION

C A L H O R M O N A L

| | | URINARY | | | | | | PLASMA | | |
|------------------|------------|----------|----------|----------|--|----------|------------|-------------------|------------|--|
| | | ICSH | FSH | Estrogen | Testos- terone & Epi- testos- terone | ICSH | FSH | Testos- terone | | |
| Leydig Cells | Incomplete | Complete | Complete | Complete | Complete | Complete | Incomplete | Incomplete | Incomplete | |
| | 4 | 0 | 0 | 0 | 0 | 4 | 4 | 4 | 4 | |
| Sertoli Cells | Incomplete | Complete | Complete | Complete | Complete | Complete | Incomplete | Incomplete | Incomplete | |
| | 4 | 0 | 0 | 0 | 0 | 4 | 4 | 4 | 4 | |
| Incomplete | Incomplete | Complete | Complete | Complete | Complete | Complete | Incomplete | Incomplete | Incomplete | |
| | 6 | 0 | 0 | 0 | 0 | 6 | 6 | 6 | 6 | |
| Incomplete | Incomplete | Complete | Complete | Complete | Complete | Complete | Incomplete | Incomplete | Incomplete | |
| | 4 | 0 | 0 | 0 | 0 | 4 | 4 | 4 | 4 | |

III. IRRADIATION SCHEDULE

The irradiation schedule approved by the committee last year is as follows:

600r - 6 subjects - November 1969
200r - 6 subjects - May 1970
75r - 4 subjects - November 1970
20r - 4 subjects - May 1971

This schedule has fallen slightly behind for three reasons:

1. We were asked not to irradiate until the Research Committee had made their recommendations. Since these were not received until the middle of November, 1969, it was already too late to complete the first section during that month.

2. When we did prepare to irradiate the six at 600r, we found that the x-ray machine was out of order. The repair took two months and several trips to Salem to discover just where the problem was.

3. After the riot at the penitentiary new programs of work release and parole were instituted. This resulted in unexpected release of some of our subjects who were previously in for long terms. New control data had to be accumulated on new subjects to be irradiated

It would indeed be easier to be back on schedule, as far as numbers of subjects irradiated, if we irradiated at either of the lower doses first (20r or 75r) - recovery on these lower doses occurring reasonably rapidly (1 - 2 years) versus 3 to 6 years for the higher doses. The reason is that we want to be very careful to use only men with long sentences for the high doses in order to follow them through

3000949

to recovery, and it is important to do the high doses first because of the time necessary for recovery.

Recently the volunteers have tended to be youthful (early 20's). We do not, for ethical reasons, want to irradiate anyone who might regret in later years that he had been vasectomized. Therefore, we are selecting only men who will obviously be apart from society most of their lives or those in their 30's and 40's who make their decisions based on more experience. As a result we have refused irradiation and vasectomy to many who have requested access to this program.

Even despite these drawbacks, we expect to be back on schedule by September 1970 and to have all of the irradiations at 600r and 200r completed by that time.

IV. RESULTS

A. HISTOLOGICAL

Results have shown that the secretory activity of Leydig cells is apparently depressed by irradiation since the urinary testosterone levels decrease in most irradiated men. Preliminary results following 600r show a definite increase in Leydig cell number in one subject, a slight increase in another and a possible, but slight, decrease in two subjects. Quantitation of biopsies from two recent subjects who received 600r are underway along with those of two other subjects who have had a series of post-irradiation biopsies. Data from these eight

3000950

subjects should give us statistically conclusive results as to whether an increase or decrease is occurring. If these data show a definite rise or a definite fall we will quantitate biopsy specimens from subjects to whom lower doses of irradiation were administered. If there is a threshold dose for effects of irradiation on Leydig cell numbers, this should be revealed by quantitating the biopsies and analyzing the data.

Quantitation of the germinal epithelium has proceeded by accumulating more data for adequate statistical analysis. No "new" findings can be reported although preliminary results previously reported are being further substantiated.

Ultrastructural examination of testicular cells indicate that major ultrastructural damage is visible within 16 minutes following irradiation of the germinal cells. (This time is the most rapid that a subject can be moved and prepared for biopsy surgery.) Sertoli cell nuclei become swollen and disintegrating cells (mainly spermatogonia) are engulfed by Sertoli cell cytoplasm. The Sertoli cell nucleus always appears to position itself directly above (toward the lumen) the disintegrating cell and the deep infolding commonly seen in the normal Sertoli cell nucleus becomes much shallower. Other ultrastructural changes also occur many of which involve smaller organelles. The significance of these changes has yet to be determined.

3000951

B. HORMONAL

Radioimmunoassay of ICSH has proceeded very well. Although complete statistical analysis will not be done until more samples have been completed at each dose level, preliminary results indicate that plasma ICSH levels rise at all irradiation doses checked except 8r. This is a direct contrast to urinary ICSH levels which did not change following irradiation at any dose level.

The technique for the radioimmunoassay of FSH has been established and is currently being applied routinely. To date only samples taken before and after doses of 600r have been assayed. Preliminary results indicate that plasma FSH levels rise greatly following irradiation and follow the same rate pattern as denuding of the germinal epithelium. The early plasma FSH results appear to confirm the urinary FSH results.

The method of protein-binding in the determination of testosterone (1 - 9) has been described by several investigators . It is reasonable to expect an accuracy of approximately 10% in the assay; however, this laboratory is experiencing problems with a nonreproducible blank. This problem is shared by other laboratories (10, 11) and seems to be independent of particular extraction or chromatography procedure. We are planning to consult with a laboratory which is not having the problem during May or June of 1970. Hopefully this will alleviate our difficulties and allow full exploitation of the collected plasma currently in storage.

3000952

Pertinent References

1. Maeda, R., Okamoto, M., Wegienka, L. C. and Forsham, P. H.: A clinically useful method for plasma testosterone determination, *Steroids*, 13:83, 1969.
2. Mayes, D. and Nugent, C. A.: Determination of plasma testosterone by the use of competitive protein binding, *J. Clin. Endocr. & Metab.*, 28:1169, 1968.
3. Heyns, W., Verhoeven, G., Van Baelen, H. and DeMoore, P.: Measurement of testosterone in plasma by competitive protein binding, *Ann. d'Endocr.*, 30:1(bis), 153, 1969.
4. Pizarro, M. A. and Arrendondo, R.: Measurement of plasma testosterone by competitive protein binding, *Ann. d'Endocr.*, 30:1(bis), 159, 1969.
5. Frick, J. and Kincl, F. A.: The measurement of plasma testosterone by competitive protein binding assay, *Steroids*, 13:495, 1969.
6. Horton, R., Kato, T. and Sherins, R.: A rapid method for the estimation of testosterone in male plasma, *Steroids*, 10:245, 1967.
7. Rosenfeld, R. L., Eberlein, W. R. and Bondiovanni, A. M.: Measurement of plasma testosterone by means of competitive protein binding analysis, *J. Clin. Endocr. & Metab.*, 29:854, 1969.
8. Hallberg, M. C., Zorn, E. M. and Wieland, R. G.: A sensitive testosterone assay by protein binding, *Steroids*, 12:241, 1968.
9. Kato, T. and Horton, R.: A rapid method for the estimation of testosterone in female plasma, *Steroids*, 12:631, 1968.
10. Sherins, R. (Personal communication)
11. Thorneycroft, I. (Personal communication)

3000953

V. CURRICULUM VITAE

Carl G. Heller, M.D., Ph.D.

Born: 1913 - Syracuse, New York

Nationality: U.S. Citizen

Education:

| | |
|------|---|
| 1936 | Ph.B. - Zoology, University of Wisconsin, Madison, Wisconsin |
| 1940 | M.D., University of Wisconsin, Madison, Wisconsin |
| 1940 | Ph.D. - Physiology, University of Wisconsin, Madison, Wisconsin |

Honors:

1947, Travel Award to Oxford for the International Physiological Congress

1948, Ciba Award in Endocrinology

1962, Squibb Award of the Pacific Coast Fertility Society

1965- Consultant to Space Radiation Panel, NAS-NRC

1962- Member, Medical Committee, Oral Advisory Group of the Evaluation Subcommittee, International Planned Parenthood Federation

1966, Elected to membership of Royal College of Medicine

1967-68, President, Pacific Coast Fertility Society

1968, Winner Wyeth Exchange Lectureship, Canadian Fertility Society, June 1969, Toronto, Canada

Guest Lectureships:

1965, 9th Oliver Bird Trust Lecturer at the Royal College of Physicians, London, England.

1966, Guest Lecturer, University of Buenos Aires, Human Spermatogenesis and Gonadotropins.

1966, Guest Lecturer, Third International Pharmacological Congress, Sao Paulo, Brazil, Factors Affecting Testicular Function in Man.

1966, Guest Lecturer, Council for the Advancement of Science Writing, Gatlinburg, Tennessee, Factors Depressing Sperm Production in Men.

1967, Guest Lecturer, Gordon Research Conference on Medicinal Chemistry, Crystal Mountain, Washington, Approaches to the Control of Male Fertility.

1968, Guest discussant, Sixth Annual Meeting of the American Association of Planned Parenthood Physicians, San Antonio, Texas, Human Male Fertility/The Inhibition of Human Spermatogenesis.

1968, Guest Lecturer, III International Congress on Endocrinology, Mexico City, June 30-July 5, Mammalian Spermatogenesis: Human Spermatogenesis.

1969, Guest Lecturer, III Schering Symposium on Mechanisms Involved in Conception, Berlin, Germany, March 12-15.

3000954

PRIVACY ACT MATERIAL REMOVED

1970, Guest Lecturer, Workshop Conference on the Human Testis, Positano, Italy, April 23-25, The Role of FSH, ICSH, and Endogenous Testosterone During Testicular Suppression by Exogenous Testosterone in Normal Men.

1970, Guest participant, Conference on the Regulation of Mammalian Reproduction, The Center for Population Research and the Fogarty International Center, DHEW, NIH, Bethesda, Maryland, June 21-25.

Experience:

1940-41 Internship, Wisconsin General Hospital.
1941-44 Residency Training, City of Detroit Receiving Hospital, Internal Medicine.
1941-42 Fellowship, Wayne State Hospital.
1942-43 American College of Physicians Fellowship.
1942-44 Instructor, Wayne State University, Internal Medicine.
1944-45 Assistant Professor, Wayne State University, Physiology.
1945-48 Associate Professor, University of Oregon Medical School, Physiology and Internal Medicine.
1948-57 Head, Division of Endocrinology and Associate Professor of Medicine, University of Oregon Medical School.
1958-present Head, Division of Reproductive Physiology, Pacific Northwest Research Foundation, Seattle, Washington.

3000955

Personal Publications:

- Lauson, H., Heller, C. G. and Sevringhaus, E. L.: The effect of graded doses of estrin upon the pituitary, adrenal and thymus weights of mature ovariectomized rats, *Endocrinology*, 21:735, November, 1937.
- Heller, C. G., Lauson, H. D. and Sevringhaus, E. L.: The immature rat uterus as an assay end-point for gonadotrophic substances, *Amer. J. Physiol.*, 121:364, 1938.
- Heller, C. G., Lauson, H. D. and Sevringhaus, E. L.: Inadequacies of estradiol substitution in ovariectomized albino rats, *Endocrinology*, 23:479, October, 1938.
- Heller, C. G. and Heller, E. J.: Gonadotrophic hormone: Urine assays of normally cycling, menopausal, castrated, and estrin treated females, *J. Clin. Invest.*, 18:171, March, 1939.
- Heller, C. G. and Heller, E. J.: Gonadotrophic hormone: Clinical application of extraction methods for assay purposes, *Endocrinology*, 24:319, March, 1939.
- Heller, C. G., Lauson, H. D., Golden, J. B. and Sevringhaus, E. L.: The immature rat uterus in the assay of estrogenic substances, and a comparison of estradiol, estrone and estriol, *Endocrinology*, 24:34, January, 1939.
- Heller, C. G.: Metabolism of the estrogens: The effect of liver and uterus upon estrone, estradiol and estriol, *Endocrinology*, 26:619, April, 1940.
- Heller, E. J., Heller, C. G. and Sevringhaus, E. L.: Gonadotropic hormone: Assay of human male urine, *Endocrinology*, 29:1, July, 1941.
- Heller, C. G.: Gonadotropin excretion in women, *J. Clin. Endocrinol.*, October, 1941.
- Heller, C. G., Heller, E. J. and Sevringhaus, E. L.: Does estrogen substitution materially inhibit pituitary gonadotropic potency? *Endocrinology*, 30:309, 1942.
- Heller, C. G., Farney, J. P., Morgan, D. N. and Myers, G. B.: Relation of gonadotropin hormone to oophorectomy, climacteric symptoms and diethylstilbestrol therapy in women, *Endocrinology*, 30:S1031, 1942 (abstract).
- Heller, C. G. and Chandler, R. E.: Gonadotropin hormone: Modification of the alcohol-precipitation assay method, *J. Clin. Endocrinol.*, 2:252, April, 1942.

3000956

- Heller, C. G. and Myers, G. B.: The male climacteric: Its physiology, symptomatology, diagnosis and treatment, *J. Clin. Invest.*, 21:622, 1942.
- Heller, C. G., Segaloff, A. and Nelson, W. O.: Effect of testosterone propionate on the pituitary gonadotropic potency of the castrated male rat, *Endocrinology*, 33:186, September, 1943.
- Heller, C. G. and Heller, E. J.: Metabolism of estrogens: Effect of pregnancy upon metabolism *in vitro* of estrone, estradiol and estriol, *Endocrinology*, 32:64, January, 1943.
- Heller, C. G., Nelson, W. O. and Roth, A. A.: Functional prepuberal castration in males, *J. Clin. Endocrinol.*, 3:573, November, 1943.
- Heller, C. G., Chandler, R. E. and Myers, G. B.: Effect of small and large doses of diethylstilbestrol upon menopausal symptoms, vaginal smear and urinary gonadotrophins in 23 oophorectomized women, *J. Clin. Endocrinol.*, 4:109, March, 1944.
- Heller, C. G., Farney, J. F., Morgan, D. N. and Myers, G. B.: A correlation of the ovarian and endometrial histology, vaginal epithelium, gonadotrophic hormonal excretion and the day of the menstrual cycle in 28 women, *J. Clin. Endocrinol.*, 4:95, March, 1944.
- Heller, C. G., Farney, J. P. and Myers, G. B.: Development and correlation of menopausal symptoms, vaginal smear and urinary gonadotrophin changes following castration in 27 women, *Clin. Endocrinol.*, 4:101, March, 1944.
- Heller, C. G. and Myers, G. B.: The male climacteric, its symptomatology, diagnosis and treatment: Use of urinary gonadotrophins, therapeutic test with testosterone propionate and testicular biopsies in delineating the male climacteric from psychoneurosis and psychogenic impotence, *J.A.M.A.*, 126:472, October, 1944.
- Heller, C. G., Nelson, W. O. and Roth, A. A.: Functional prepuberal castration in males, *J. Clin. Endocrinol.*, 3:573, 1943.
- Hirschfeld, J. W., Williams, H. H., Abbott, W. E., Heller, C. G. and Pilling, M. A.: Significance of the nitrogen loss in the exudate from surface burns, *Surg.*, 15:766, May, 1944.
- Nelson, W. O. and Heller, C. G.: Hyalinization of the seminiferous tubules associated with normal or failing Leydig cell function; microscopic picture of the testis and associated changes in the breast, *J. Clin. Endocrinol.*, 5:13, 1945.
- Heller, C. G. and Nelson, W. O.: Hyalinization of the seminiferous tubules associated with normal or failing Leydig cell function. Discussion of relationship to eunuchoidism, gynecomastia, elevated gonadotrophins, depressed 17-ketosteroids and estrogens, *J. Clin. Endocrinol.*, 5:1, January, 1945.

3000957

- Heller, C. G., Hirschfeld, J. W., Abbott, W. E., Pilling, M., Meyer, F., Williams, H. H., Richard, A. J. and Obi, R.: Metabolic alterations following thermal burns, *Arch. Surg.*, 50:194, April, 1945.
- Heller, C. G. and Nelson, W. O.: Hyalinization of seminiferous tubules and clumping of Leydig cells. Notes on treatment of the clinical syndrome with testosterone propionate, methyl testosterone and testosterone pellets, *J. Clin. Endocrinol.*, 5:27, 1945.
- Maddock, W. O. and Heller, C. G.: Gonadotrophic hormone: Protection against inactivation, *Endocrinology*, 41:177, August, 1947.
- Heller, C. G. and Maddock, W. O.: The clinical uses of testosterone in the male, *Vitamins & Hormones*, 5:393, 1947.
- Nelson, W. O. and Heller, C. G.: Primary and secondary failure of the human testis, *Fed. Proc.*, 6:169, 1947 (abstract).
- Jungck, E. C., Maddock, W. O., Van Bruggen, J. T. and Heller, C. G.: Blood vitamins, A, C, and E and seminal fluid vitamin C in human male sterility, *Fed. Proc.*, 6:139, 1947 (abstract).
- Heller, C. G., Nelson, W. O., Jungck, E. C. and Maddock, W. O.: Correlation of urinary gonadotropin titers with the degree of seminiferous tubule involvement in human male sterility, *Fed. Proc.*, 6:127, 1947 (abstract).
- Heller, C. G. and Jungck, E. C.: Regulation of ovarian growth: Inhibition by estrogen or stimulation by gonadotrophins? *Proc. Soc. Exp. Biol. Med.*, 65:152, 1947.
- Jungck, E. C., Heller, C. G. and Nelson, W. O.: Regulation of pituitary gonadotrophic secretion: Inhibition by estrogen or inactivation by the ovaries? *Proc. Soc. Exp. Biol. Med.*, 65:148, 1947.
- Maddock, W. O. and Heller, C. G.: Dichotomy between hypophyseal content and amount of circulating gonadotrophins during starvation, *Proc. Soc. Exp. Biol. Med.*, 66:595, 1947.
- Jungck, E. C., Maddock, W. O. and Heller, C. G.: Gonadotrophic hormone: Comparison of ultrafiltration and alcohol-precipitation methods of recovery from urine, *J. Clin. Endocrinol.*, 7:1, January, 1947.
- Heller, C. G. and Maddock, W. O.: The use of androgens in men, *Bull. New York Acad. Med.*, 24:179, March, 1948.
- Maddock, W. O., Jungck, E. C. and Heller, C. G.: Antigonadotrophin formation to sheep FSH; effectiveness against endogenous gonadotrophic hormones in men, *Fed. Proc.*, 7:(No.1), 1948.

3000958

- Heller, C. G. and Nelson, W. O.: Classification of male hypogonadism and a discussion of the pathologic physiology, diagnosis and treatment, *J. Clin. Endocrinol.*, 8:345, May, 1948.
- Heller, C. G. and Nelson, W. O.: The testis in human hypogonadism, *Rec. Prog. Hormone Res.*, 3:197, 1948.
- Heller, C. G. and Nelson, W. O.: The testis-pituitary relationship in man, *Rec. Prog. Hormone Res.*, 3:229, 1948.
- Jungck, E. C. and Heller, C. G.: Failure of estradiol inactivation products to inhibit pituitary gonadotrophic content and secretion, *Proc. Soc. Exp. Biol. & Med.*, 69:1948.
- Jungck, E. C., Maddock, W. O., Heller, C. G. and Nelson, W. O.: Anti-hormone formation complicating pituitary gonadotropin therapy in infertile men. II. Effect on number of sperm, morphology of the testis and urinary gonadotrophins, *J. Clin. Endocrinol.*, 9:355, April, 1949.
- Maddock, W. O., Jungck, E. C., Rigas, D. A. and Heller, C. G.: Assay of FSH, ICSH and luteotrophin in the hypophysectomized rat: Clinical applications, *Fed. Proc.*, 8:(No.1), March, 1949.
- Jungck, E. C. and Heller, C. G.: Nutrition in Endocrinology, *Nutrition Reviews*, 7:97, April, 1949.
- Jungck, E. C., Maddock, W. O., Fearl, C. L. and Heller, C. G.: Suppression of urinary chorionic gonadotrophin, symptoms and pulmonary metastases in chorioepithelioma by diethylstilbestrol, *Fed. Proc.*, 8:(No.1), March, 1949.
- Heller, C. G., Maddock, W. O., Jungck, E. C. and Nelson, W. O.: The role of the Sertoli cell in the testis-pituitary axis in men, *Fed. Proc.*, 8:(No.1), March, 1949.
- Heller, C. G.: Uterine weight method (Estrogen assay), *Methods in Medical Research*, 2:1950.
- Heller, C. G., Nelson, W. O., Hill, I. B., Henderson, E., Maddock, W. O., Jungck, E. C., Paulsen, C. A. and Mortimore, G. E.: Improvement in spermatogenesis following depression of the human testis with testosterone, *Fertil. & Steril.*, 1:415, September, 1950.
- Nelson, W. O. and Heller, C. G.: Diseases of the reproductive system, *Ann. Rev. Med.*, 2:179, 1951.
- Rigas, D. A. and Heller, C. G.: The amount and nature of urinary proteins in normal human subjects, *J. Clin. Invest.*, 30:853, August, 1951.

3000959

- Mortimore, G. E., Paulsen, C. A. and Heller, C. G.: The effect of steroids and lactone derivatives on hypophyseal gonadotrophin content, *Endocrinology*, 48:143, February, 1951.
- Paulsen, C. A., Mortimore, G. E. and Heller, C. G.: The pituitary action and estrogenic effect of parahydroxypropiophenone, *J. Clin. Endocrinol.*, 11:892, August, 1951.
- Heller, C. G.: Hypogonadism in the male, Sharp & Dohme Seminar, pp. 6, May, 1951.
- Heller, C. G., Nelson, W. O., Maddock, W. O., Jungck, E. C., Paulsen, C. A. and Mortimore, G. E.: The effect of testosterone upon the human testis, *J. Clin. Invest.*, 30:648, 1951 (abstract).
- Heller, C. G., Paulsen, C. A., Mortimore, G. E., Jungck, E. C. and Nelson, W. O.: Urinary gonadotrophins spermatogenic activity and their classification of testicular morphology -- their bearing on the utilization hypothesis, *Biology of the Testes*, New York Acad. Sciences, 55:685, January, 1952.
- Rigas, D. A., Maupin, T. J. and Heller, C. G.: A mechanical sampling device for use with the standard electrophoresis apparatus, *J. Lab. & Clin. Med.*, 39:492, March, 1952.
- Mortimore, G. E., Paulsen, C. A. and Heller, C. G.: Gonadal defects in the male, *Cyclo. of Med. Surg. & Specialties*, 13:767, 1954.
- Maddock, W. O., Leach, R. B., Tokuyama, I., Paulsen, C. A., Nelson, W. O., Jungck, E. C. and Heller, C. G.: Antihormone formation in patients receiving gonadotrophin therapy, *Acta Endocrinologica*, Suppl. 28:55, 1956.
- Heller, C. G.: Effect of Enovid and 17-Ethynyl-19-Nortestosterone on daily urinary gonadotrophin and estrogen excretion and on premenstrual tension and other menstrual disorders, *Proc. of A Symposium on 19-Nor Progestational Steroids*, Searle Research Laboratories, 1957.
- Marinosci, A., Nelson, W. O., Laidlaw, W. M. and Heller, C. G.: Spermatogenic activity and hypophyseal gonadotrophin content of the cryptorchid rat, *Folia Endocrinologica (Italy)*, 10:5, 1957.
- Heller, C. G., Laidlaw, W. M., Harvey, H. T. and Nelson, W. O.: Effects of progestational compounds on the reproductive processes of the human male, *Ann. N. Y. Acad. Sciences*, 71:649, July, 1958.
- Heller, C. G. and Laidlaw, W. M.: Physiology and pathologic physiology of the testis, *Postgrad. Med.*, 24:550, November, 1958.

- Rigas, D. A., Paulsen, C. A. and Heller, C. G.: Purification of gonadotrophins derived from urine and pituitary glands of human beings: Observations of their electrophoretic behaviour and biological activity, *Endocrinology*, 62:738, June, 1958.
- Heller, C. G., Moore, D. J., Paulsen, C. A., Nelson, W. O. and Laidlaw, W. M.: Effects of progesterone and synthetic progestins on the reproductive physiology of normal men, *Fed. Proc.*, 18: 1057, December, 1959.
- Heller, C. G., Paulsen, C. A. and Moore, D. J.: Alteration in spermatogenesis of normal men with synthetic and natural progestins, First International Congress of Endocrinology, Copenhagen, 1960, *Acta Endocrinologica*, Suppl., 51:925, 1960.
- Paulsen, C. A., Moore, D. J., Roscoe, R. T. and Heller, C. G.: Failure of progesterone administration to depress urinary gonadotrophin excretion in normal menstruating women, First International Congress of Endocrinology, Copenhagen, 1960, *Acta Endocrinologica*, 25:203, Suppl. 51, 1960.
- Heller, C. G.: The problem of the international reference preparation, Human Pituitary Gonadotrophins - A Workshop Conference, A. Albert, M.D. (ed.), Chas. C. Thomas, Springfield, Illinois, 1961.
- Heller, C. G., Moore, D. J. and Paulsen, C. A.: Suppression of spermatogenesis and chronic toxicity in men by a new series of Bis(chloroacetyl) Diamines, *Toxicol. and Appl. Pharmacol.*, 3:1, January, 1961.
- Heller, C. G.: Therapy of male infertility and hypogonadism: Endocrine dysfunction and infertility. Report of the 35th Ross Conference on Pediatric Research, S. J. Fomon, (ed.), Columbus, Ohio, Ross Laboratory, pp. 82, 1961.
- Moore, D. J., Roscoe, R. T., Matson, L. J. and Heller, C. G.: Increased gonadotrophin excretion induced by antispermatogenic agents, *Clin. Res.*, 10:(No.1), 1962 (abstract).
- Paulsen, C. A., Leach, R. B., Lanman, J., Goldston, N., Maddock, W. O. and Heller, C. G.: Inherent estrogenicity of Norethindrone and Norethynodrel: Comparison with other synthetic progestins and progesterones, *J. Clin. Endocrinol. & Metab.*, 22:1033, October, 1962.
- Heller, C. G. and Moore, D. J.: Dichotomy between total gonadotrophins (HPG) and ICSH excretion produced by clomiphene, *Clin. Res.*, 11:111, January, 1962 (Abstract).
- Heller, C. G., Flageolle, B. Y. and Matson, L. J.: Histopathology of the human testes as affected by Bis(Dichloroacetyl)Diamones, *Experimental and Molecular Pathology*, Suppl. 2, 2:107, December, 1963.

3000961

- Heller, C. G.: The Male and Female Sex Organs, Clinical Physiology, A. Growman, Chap. 27 (1956), Chap. 26 (1963), rev. 1962.
- Heller, C. G., Matson, L. J. and Moore, D. J.: Rate of spermatogenesis in man determined by incorporating tritiated thymidine into testes, Proc. of an International Symposium on the Effects of Ionizing Radiation in the Reproductive System, Colorado, U.S.A., 1962, Pergamon Press, July, 1963, pp. 263.
- Christoffers, H. J., Roscoe, R. T. and Heller, C. G.: A combined chemical-biological approach to the determination of urinary estrogens. International Workshop on Estrogens, Orcas Island, Washington, Proceedings (U. of W.) May, 1963.
- Heller, C. G. and Clermont, Y.: Spermatogenesis in man: An estimate of its duration, Sciences, 140:184, April 12, 1963.
- Heller, C. G., Roscoe, R. T. and Rowley, M. J.: Hormonal alterations in normal men and women receiving Delalutin: Their correlation with spermatogenesis and Leydig cell morphology or menstruation, Squibb Symposium on Delalutin in advanced endometrial cancer in women, Proceedings (in press).
- Heller, C. G. and Clermont, Y.: Kinetics of the germinal epithelium in man, Rec. Prog. in Hormone Res., 20:545, 1964.
- Heller, C. G. and Wootton, P.: Effect of graded doses of ionizing radiation on human testes, Clin. Res., 12:116, January, 1964. (abstract).
- Oakberg, E. F. and Heller, C. G.: Radiation response of the human testis, Proc. of the III International Congress of Radiation Research, Cortina d'Ampezzo, Italy, June 26-July 2, 1966 (abstract in publication).
- Heller, C. G.: Estrogen Assays in Clinical Medicine, Workshop on Estrogens, ed. C. Alvin Paulsen, M.D., U. of W. Press, 1965, pp. 120-123, 8, 55, 64, 72-73, 114, 118-119, 124-125, 134, 135, 153, 179, 184, 186, 191, 203, 215, 271-273, 275-277, 283-287.
- Heller, C. G.: Oliver Bird Lecture, International Planned Parenthood News, No. 142, December, 1965.
- Heller, C. G.: Control of Male Fertility, Annotations, The Lancet, October 30, 1965, pp. 892.
- Ford, L., Cacheiro, N., Norby, D. and Heller, C. G.: Identification and characterization of normal human pachytene chromosomes, Genetics, 52:443, August, 1965 (abstract).

3000962

- Rowley, M. J. and Heller, C. G.: The testicular biopsy: Surgical procedure, fixation and staining technics, *Fertil. & Steril.*, 17:177, March-April, 1966.
- Rowley, M. J. and Heller, C. G.: The duration of each cell association (stages) of the human testis, *Fed. Proc.*, 25:313, March-April, 1966. (abstract)
- Heller, C. G.: INTERVIEW "Birth control choices for men", *Humanist*, January/February, 1966.
- Heller, C. G., Wootton, P., Rowley, M. J. and Lalli, M. F. and Brusca, D.: Action of radiation upon human spermatogenesis, *Proc. VI Congreso Panamericano de Endocrinologia*, Mexico City, October 10-15, 1965. *Excerpta Medica International Congress Series*, No. 112, pp. 408, 1966.
- Heller, C. G., Lalli, M. F. and Rowley, M. J.: Factors affecting testicular function in man, III International Pharmacological Congress, Sao Paulo, Brazil, July 1966, Pergamon Press, Ltd., *Pharmacology of Reproduction*, E. Diczfalusy (ed.), pp. 61-73, Vol. 2., 1968.
- Heller, C. G. (Committee member): Radiobiological Factors in Manned Space Flight, Report of the Space Radiation Study Panel on the Life Sciences Committee, Space Science Board National Academy of Sciences, National Research Council, 1967 - Wright H. Langham, Editor.
- Brusca, D. R., Kastella, J. M. and Heller, C. G.: Proceedings of the U.S. Endocrine Society, Chicago, p. 142, 1966 (abstract).
- Heller, G. V., O'Keefe, K. B. and Heller, C. G.: Effects of follicle-stimulating hormone (FSH) on Sertoli cells in the hypophysectomized rat, *Clin. Res.*, 16:113, 1968 (abstract).
- Pearson, J. E. and Heller, C. G.: Human chorionic gonadotropin effect on Leydig cell number and size in normal men, *Clin. Res.*, 16:115, 1968 (abstract).
- Rowley, M. J. and Teshima, F. and Heller, C. G.: Duration of transport of spermatozoa through the ductular system, *Clin. Res.*, 16:150, 1968 (abstract).
- Rowley, M. J., O'Keefe, K. B. and Heller, C. G.: Decreases in sperm concentration due to testicular biopsy procedure in man. *J. Urol.*, 101:347, 1969.

3000963

- Heller, C. G., Heller, G. V. and Rowley, M. J.: An estimate of the duration of each cell association and of each cell type, Third International Congress of Endocrinology, June 30-July 5, 1968, Mexico City, Excerpta Medica Foundation, International Congress Series, Progress in Endocrinology, pp. 1012, 1969.
- Heller, C. G., Heller, G. V., Warner, G. A. and Rowley, M. J.: Effect of graded doses of ionizing radiation on testicular cytology and sperm count in man, *Rad. Res.*, 35;2:493, 1968 (abstract).
- Rowley, M. J. and Heller, C. G.: Embryology, anatomy and histology of the male sexual organs, Part I, Chapter II, Fertility Disturbances in Men and Women - Etiology, Diagnostic and Treatment, ed. C. A. Joel, S. Karger, AG, Basel (in press) 1969.
- Heller, C. G., Rowley, M. J. and Heller, G. V.: Clomiphene citrate: a correlation of its effect on sperm concentration and morphology, total gonadotropins, ICSH, estrogen and testosterone excretion, and testicular cytology in normal men, *J. Clin. Endo. & Metab.*, 29:638, 1969.
- Leach, D. and Heller, C. G.: A method for the quantitation of Leydig cells in man, *Clin. Res.*, 16:106, 1969 (abstract).
- Rowley, M. J. and Heller, C. G.: The use of the "rebound phenomenon" in the treatment of the infertile male, *Clin. Res.*, 16:109, 1969 (abstract).
- Heller, C. G., Teshima, F. and Rowley, M. J.: Duration of transport of spermatozoa through the ductular system, *Advances in the Biosciences 4*, Schering Symposium on Mechanisms Involved in Conception, Berlin 1969, Pergamon Press, pp. 121-131.
- Heller, G. V. and Rowley, M. J.: The effect of clomiphene citrate on spermatogenesis in normal men, Soc. Study of Reproduction, 2nd Annual Meeting, University of California, Davis, California, September 8-10, 1969 (abstract).
- Rowley, M. J. and Berlin, J. D. and Heller, C. G.: The fine structure of human spermatogonia, Soc. Study of Reproduction, 2nd Annual Meeting, University of California, Davis, California, September 8-10, 1969 (abstract).
- Heller, G. V. and Heller, C. G.: Quantitation of normal and abnormal germinal cells following administration of clomiphene citrate in normal men, *J. Clin. Endo. & Metab.*, 30:196, 1970.
- Rowley, M. J., Teshima, F. and Heller, C.G.: Duration of transit of spermatozoa through the human male ductular system, *Fertil. & Steril.*, (Accepted for publication in April 1970 issue).

3000964

Heller, C. G., Morse, H. C., Su, M. and Rowley, M. J.: The role of FSH, ICSH and endogenous testosterone during testicular suppression by exogenous testosterone in normal men, Proceedings of the Workshop Conference on the Human Testis, Positano, Italy, April 23-25, 1970, Eugenia Rosemberg and C. Alvin Paulsen (eds.), Plenum Publishing Corporation, New York, New York.

Heller, C. G., Morse, H. C. and Rowley, M. J.: The effect of testosterone on the normal testis, Presented to the 52nd Annual Meeting of The Endocrine Society, St. Louis, Missouri, June 10-12, 1970, published in the Proceedings of The Endocrine Society.

3000965

05

Mavis J. Rowley

Born: 1939 - Porterville, California

Nationality: U.S. Citizen

Education:

- 1961 B.S. - Biology-chemistry, Pacific Lutheran University, Parkland, Washington
- 1962 ASCP - Histology-cytology, The Swedish Hospital Medical Center, Seattle, Washington
- 1963-66 Postgraduate courses, The University of Washington, Seattle, Washington

Honors:

- Carl Raymond Gray Scholarship
- Union Pacific Railroad Scholarship
- Captain Carl Beard Trophy and Scholarship
- National Honor Society Scholarship
- Women of the Moose Science Scholarship
- Invitational speaker, Postgraduate Seminar of the American Fertility Society, San Francisco, California - March 27-30, 1968.
- Winner. Wyeth Exchange Lectureship, Canadian Fertility Society, June 1969, Toronto, Canada

Experience:

- 1960-61 Clinical Histology, The Swedish Hospital Medical Center, Seattle, Washington
- 1961-62 Electron microscopy, The Swedish Hospital Medical Center, Seattle, Washington
- 1963- Senior Investigator, Division of Reproductive Physiology, Pacific Northwest Research Foundation, Seattle, Washington.

Personal Publications:

Heller, C. G., Roscoe, R. T. and Rowley, M. J.: Hormonal alterations in normal men and women receiving Delalutin: their correlation with spermatogenesis and Leydig cell morphology or menstruation. Squibb Symposium on Delalutin in Advanced Endometrial Cancer in Women, 1964.

PRIVACY ACT MATERIAL REMOVED

3000966

- Rowley, M. J. and Heller, C. G.: An analysis of the effect of one or more testicular biopsies upon sperm count. Proc. Northwest Soc. Clin. Med., 1965 (abstract).
- Heller, C. G., Wootton, P., Rowley, M. J., Lalli, M. F. and Brusca, D. R.: Action of radiation upon human spermatogenesis. Proc. VI Congreso Panamericano de Endocrinologia, Excerpta Medica International Congress Series, No. 112, pp. 408-410, 1966.
- Rowley, M. J. and Heller, C. G.: The duration of each cell association (stages) of the human testis, Fed. Proc., 25:313, 1966 (abstract).
- Rowley, M. J. and Heller, C. G.: The testicular biopsy: surgical procedure, fixation and staining technics, Fertil. Steril., 17:177, 1966.
- Rowley, M. J. and Heller, C. G.: The depletion of the human germinal epithelium by x-irradiation: a study of the timing of spermatogenesis, Clin. Res., 15:127, 1967 (abstract).
- Heller, C. G., Lalli, M. F. and Rowley, M. J.: Factors affecting testicular function in man. II. International Pharmacological Congress, Pharmacology of Reproduction, Vol. 2., pp. 61-73, Pergamon Press, E. Diczfalusy, (ed.), 1968.
- Rowley, M. J., Teshima, F. and Heller, C. G.: Duration of transport of spermatozoa through the ductular system, Clin. Res., 16:150, 1968 (abstract).
- Heller, C. G., Heller, G. V., Warner, G. A. and Rowley, M. J.: Effect of graded doses of ionizing radiation on testicular cytology and sperm count in man, Rad. Res., 35:493, 1968 (abstract).
- Rowley, M. J. and Heller, C. G.: Embryology, anatomy and histology of the male sexual organs, Part I. Chapter II, Fertility Disturbances in Men and Women - Etiology, Diagnostic and Treatment, ed. C. A. Joel, S. Karger, A.G., Basel (in press), 1969.
- Rowley, M. J., O'Keefe, K. B. and Heller, C. G.: Decreases in sperm concentration due to testicular biopsy procedure in man, J. Urol., 101:347, 1969
- Rowley, M. J. and Heller, C. G.: The use of the "rebound phenomenon" in the treatment of the infertile male, Clin. Res., 17:109, 1969 (abstract).
- Heller, C. G., Rowley, M. J. and Heller, G. V.: Clomiphene citrate: a correlation of its effect on sperm concentration and morphology total gonadotropins, ICSH, estrogen and testosterone excretion, and testicular cytology in normal men, J. Clin. Endo. & Metab., 29:638, 1969.

3000967

- Heller, C. G., Heller, G. V. and Rowley, M. J.: Human spermatogenesis: an estimate of the duration of each cell association and of each cell type, III International Congress of Endocrinology, Excerpta Medical Foundation, International Congress Series, Progress in Endocrinology, pp. 1012, 1969.
- Rowley, M. J., Berlin, J. D. and Heller, C. G.: The fine structure of four types of spermatogonia in the human male, Submitted to Amer. J. Anat., 1969.
- Heller, C. G., Teshima, F. and Rowley, M. J.: Duration of transport of spermatozoa through the ductular system, Advances in the Biosciences IV, Schering Symposium on Mechanisms Involved in Conception, Berlin 1969, Pergamon Press, pp. 121-131.
- Heller, C. G. and Rowley, M. J.: The testosterone rebound phenomenon in the treatment of male infertility, Fertil. Steril, April, 1970.
- Heller, C. G., Morse, H. C., Su, M. and Rowley, M. J.: The role of FSH, ICSH and endogenous testosterone during testicular suppression by exogenous testosterone in normal men, Proceedings of the Workshop Conference on the Human Testis, Positano, Italy, April 23-25, 1970, Eugenia Rosenberg and C. Alvin Paulsen (eds.), Plenum Publishing Corporation, New York, New York.
- Heller, C. G., Morse, H. C. and Rowley, M. J.: The effect of testosterone on the normal testis. Presented to the 52nd Annual Meeting of the Endocrine Society, St. Louis, Mo., June 10-12, 1970, Proceedings of the Endocrine Society.

3000968

Howard C. Morse, Ph.D.

Born: 1938 - Orofino, Idaho

Nationality: U.S. Citizen

Education:

- 1961 B.S. - Biology, George Fox College, Newberg, Oregon
- 1963 M.S. - Zoology-cytology, Oregon State University, Corvallis, Oregon
- 1967 Ph.D.- Cytology-Biochemistry, Oregon State University, Corvallis, Oregon

Honors:

National Science Foundation Graduate Fellow, 1964-1966

Experience:

- 1963-64 Research Associate, Department of Biochemistry, Oregon State University
- 1964-66 Graduate Student, Oregon State University
- 1966-69 Professor of Biology, Northwest Nazarene College, Nampa, Idaho
- 1969-present Research Associate, Division of Reproductive Physiology, Pacific Northwest Research Foundation, Seattle, Washington

Personal Publications:

- Coffey, R. G., Morse, H. and Newburgh, R. W.: The synthesis of nucleic acid constituents in the early chick embryo, *Biochim. et Biophys. Acta*, 114:547, 1966.
- Morse, H. C., Harris, P. and Dornfeld, E.: Pacifastacus Leniusculus: fine structure of arthrobranch with reference to active ion uptake, *Trans. Amer. Microsc. Soc.*, 89:12, 1970.
- Heller, C. G., Morse, H. C., Su, M. and Rowley, M. J.: The role of FSH, ICSH and endogenous testosterone during testicular suppression by exogenous testosterone in normal men, *Proceedings of the Workshop Conference on the Human Testis, Positano, Italy, April 23-25, 1970*, Eugenia Rosemberg and C. Alvin Paulsen, eds., Plenum Publishing Corporation, New York, New York.
- Heller, C. G., Morse, H. C. and Rowley, M. J.: The effect of testosterone on the normal testis. Presented to the 52nd Annual Meeting of the Endocrine Society, St. Louis, Mo., June 10-12, 1970. *Proceedings of the Endocrine Society.*

PRIVACY ACT MATERIAL REMOVED

3000969

Kathleen B. O'Keefe, Ph.D.

Born: 1923, Lynn, Massachusetts

Nationality: U.S. Citizen

Education:

1946 A.B. - University of California, Berkeley, California
1948 M.A. - University of California, Berkeley, California
1959 Ph.D.- University of California, Berkeley, California

Experience:

1946-48 Research Assistant, Statistical Laboratory, University
of California, Berkeley, California
1949-50 Research Assistant, Department of Labor Economics,
University of Washington, Seattle, Washington
1950-52 Research Assistant, Department of Poultry Husbandry,
University of California, Berkeley, California
1952-54 Research Assistant, Statistical Laboratory, University
of California, Berkeley, California
1953-57 College Teaching, Mathematics and Statistics, College of
the Holy Names, Oakland, California
1957-59 College Teaching, Mathematics and Statistics, Hunter
College, New York
1959-67 Assistant Professor of Mathematics, University of
Washington, Seattle, Washington
1967- Bio-statistician, Division of Reproductive Physiology,
Pacific Northwest Research Foundation, Seattle,
Washington

Selected Personal Publications:

- O'Keefe, K. B.: A property of the differential ideal (y^P) , Trans.
Amer. Math. Soc., 94:483, 1960.
- O'Keefe, K. B.: A symmetry theorem for the differential ideal (uv) .
Proc. Amer. Math. Soc., 12:654, 1961.
- O'Keefe, K. B.: On a problem of J. F. Ritt, Pac. J. Math., 17:149,
1966.
- O'Keefe, K. B.: Unusual power products and the ideal (y^2) ,
Proc. Amer. Math. Soc., 17:257, 1966.

3000970

- Hillman, A. P., Mead, D. G., O'Keefe, K. B. and O'Keefe, E. S.:
Ideals generated by products, Proc. Amer. Math. Soc., 17:717,
1966.
- Hillman, A. P., Mead, D. G., O'Keefe, K. B. and O'Keefe, E. S.:
A dynamic programming generalization of xy to n variables, Proc.
Amer. Math. Soc., 17:720, 1966.
- O'Keefe, K. B. and O'Keefe, E. S.: The differential ideal (uv),
Proc. Amer. Math. Soc., 17:750, 1966.
- Heller, G. V., O'Keefe, K. B. and Heller, C. G.: Effects of follicle-
stimulating hormone (FSH) on Sertoli cells in the hypophysectomized
rat. Clin. Res., 16:113, 1968 (abstract).
- Rowley, M. J., O'Keefe, K. B. and Heller, C. G.: Decreases in sperm
concentration due to testicular biopsy procedure in man. J.
Urol., 101:347, 1969.

3000971

Florence Teshima

Born: 1924, Seattle, Washington

Nationality: U.S. Citizen

Education:

1943-45 William Smith College, Geneva, New York, Major in
Biology and Minor in Chemistry

Experience:

1946-48 Physicians Medical Laboratory, Technician, Portland,
Oregon
1948-51 Technician to Archie R. Tunturi, Ph.D., University of Oregon
Medical School; Portland, Oregon
1951-62 Technician for Department of Anatomy, University of
Oregon Medical School, Portland, Oregon
1964- Research Assistant, Division of Reproductive Physiology,
present Pacific Northwest Research Foundation, Seattle,
Washington

Personal Publications:

Rowley, M. J., Teshima, F. and Heller, C. G.: Duration of transport
of spermatozoa through the ductular system, Clin. Res., 16:150,
1968 (abstract).

Heller, C. G., Teshima, F. and Rowley, M. J.: Duration of transport
of spermatozoa through the ductular system, Advances in the Bio-
sciences, Schering Symposium on Mechanisms Involved in Conception,
Berlin, 1969, Pergamon Press, pp. 121-131, 1969.

3000972

Michael H. H. Su

Born: 1938, Taiwan, China

Nationality: China - U.S. Permanent Resident

Education:

1958-62 B.A., National Taiwan University, Teipei, Taiwan
1963-65 B.S., Chemistry, University of South Carolina, Columbia,
South Carolina
1965-67 M.S., University of Washington, Seattle, Washington

Experience:

1965(summer) Research Assistant, Department of Chemistry,
University of South Carolina, Columbia, South
Carolina (NIH Grant).
1965-66 Teaching Assistant, Department of Chemistry, University
of Washington, Seattle, Washington
1966-67 Research Assistant, Department of Chemistry, University
of Washington, Seattle, Washington (NIH Grant).
1967-68 Research Technologist, University of Washington Medical
Center, Seattle, Washington
1968- Research Associate, Division of Reproductive Physiology,
present Pacific Northwest Research Foundation, Seattle,
Washington

Personal Publications:

Heller, C. G., Morse, H. C., Su, M. and Rowley, M. J.: The role of
FSH, ICSH and endogenous testosterone during testicular suppression
by exogenous testosterone in normal men, Proceedings of the
Workshop Conference on the Human Testis, Positano, Italy,
April 23-25, 1970, Eugenia Rosemberg and C. Alvin Paulsen (eds.),
Plenum Publishing Corporation, New York, New York.

3000973

David R. Leach

Born: 1944, San Antonio, Texas

Nationality: U.S. Citizen

Education:

1967 B.A. - Biology, University of Texas, Austin, Texas

Experience:

1967- Research Associate, Division of Reproductive Physiology,
present Pacific Northwest Research Foundation, Seattle,
 Washington

Personal Publications:

Leach, D. R. and Heller, C. G.: A method for the quantitation of
Leydig cells in man, Clin. Res., 17:106, 1969 (abstract).

3000974

Neil Horike

Born: 1943 - Hunt, Idaho

Nationality: U.S. Citizen

Education:

1965 B.S. - Chemistry, University of Washington, Seattle, Washington
1965-67 Graduate Study, Brown University, Providence, Rhode Island

Honors:

National Merit Commendation

Experience:

1964- June-August Undergraduate Research Participant (National Science Foundation), Oregon State University, Corvallis, Oregon
1964-65 Undergraduate Research Assistant, Department of Chemistry, University of Washington, Seattle, Washington
1968-present Research Associate, Division of Reproductive Physiology, Pacific Northwest Research Foundation, Seattle, Washington

PRIVACY ACT MATERIAL REMOVED

3000975

Glenn A. Warner, M.D.

Radiological Consultant

Born: 1919, Orting, Washington

Nationality: U.S. Citizen

Education:

1948 M.D. - George Washington University, Washington, D.C.

Experience:

1949 Internship, Southern Pacific Hospital, San Francisco, California
1950 Residency, County Hospital, San Mateo, California
1951-53 General Practice, Othello, Washington
1953-56 Residency-Surgery, Westside Veterans Administration Hospital, Chicago, Illinois
1956-59 Surgical Practice, Yakima, Washington
1959-60 Residency, Tumor Pathology, The Swedish Hospital Medical Center, Seattle, Washington
1960-63 Fellowship, Radiation Therapy, Tumor Institute of The Swedish Hospital Medical Center, Seattle, Washington
1963-65 Fellow, National Cancer Institute, Project: Chemotherapy of Malignant Disease
1966- Staff, Tumor Institute of The Swedish Hospital Medical Center, Seattle, Washington
present
1966 Diplomat, American Board of Radiology

Personal Publications:

Heller, C. G., Heller, G. V., Warner, G. A. and Rowley, M. J.:
Effects of graded doses of ionizing radiation on testicular cytology and sperm count in man, Rad. Res., 35:493, 1968 (abstract).

3000976

Daniel E. DiIaconi, M.D.

Surgical Consultant

Education:

1942 M.D. - Marquette University Medical School, Milwaukee,
Wisconsin

Experience:

1942-43 Rotating Internship, St. Francis Hospital, Pittsburgh,
Pennsylvania
1943-46 U.S. Army Medical Corps - European Theater, Captain
M.C.
1946-48 General Surgery Residency, Mt. Carmel Mercy Hospital,
Detroit, Michigan
1948-53 Surgeon, Veterans Administration Hospital, Vancouver,
Washington .
1953 Fellow American College of Surgeons
1953-56 Private Practice, General Surgery, Salem Memorial
Hospital Staff and Salem General Hospital Staff
1966 Secretary-Treasurer, Staff Salem Memorial Hospital,
Salem, Oregon
1958-59 Secretary-Treasurer, Salem Surgical Society
1959-66 Director of Medical Services, Oregon State Penitentiary,
Salem, Oregon
1956-66 Division Surgeon, Oregon National Guard

VI. FINANCIAL INTERACTIONS

A. OTHER RESEARCH SUPPORT

The Ford Foundation: " Hormonal and chemical agents as contraceptives in men - An investigation of their effectiveness and mechanism of action ".

Grant period: August 1, 1968 through July 31, 1971

Grant award: \$357,370.00

B. TRAVEL

It has been our pattern for Dr. Heller to go to the Oregon State Penitentiary at least twice a month, usually spending two working days each time. Transportation to Salem may be by own car (12¢/mile) or more usually by airplane, renting a car in Portland or Salem. If plane transportation is used, the cost per trip is more expensive.

We are requesting travel funds for three meetings: The Laurentian Hormone Conference in Mt. Tremblant, to which Dr. Heller has been invited, the 1971 Endocrine Society meeting, and the Society for the Study of Reproduction meeting in Columbus, Ohio, to which we have submitted three abstracts. We consider these to be the most important annual meetings in our field.

C. STIPENDS FOR INMATE VOLUNTEERS AT THE OREGON STATE PENITENTIARY

We are requesting \$270 per individual subject to pay for exposure to radiation, submission to several subsequent testicular biopsies, the collection of urine for hormone studies, the collection of weekly

3000978

samples of seminal fluid and for vasectomies. The volunteers are paid \$10.00 per month while on the program. This includes, at times, many months of control studies. They receive \$10.00 for each testicular biopsy (including control), \$10.00 for each thymidine-H³ injection and \$150.00 bonus for satisfactory completion of the program. At Christmas and on other occasions the subjects who are cooperating well are advanced money against their anticipated bonus. Occasionally additional "bonus" payments are made. Incidental costs at the Penitentiary laboratory are also taken from this fund.

D. INDIRECT COST ALLOCATION RATE

We propose that the 20% indirect cost rate be continued. Based on figures established by Benson & McLaughlin, Auditors for the Pacific Northwest Research Foundation, the indirect cost rate for the fiscal year ending June 30, 1969 is 23.5% of total direct costs. Therefore, for our institution, the 20% rate appears to be equitable to government agency sponsors. Further substantiating data can be furnished if required.

3000979

VII. FACILITIES AVAILABLE

A. The Oregon State Penitentiary at Salem, Oregon, is our most unique and prized facility, for only here can we find normal subjects who are willing to have repeated observations made on samples of seminal fluid, urine and testicular tissue, who are willing to take experimental drugs and who, of course, are available for such observations over a period of years. Since 1957 excellent rapport has been established between our group and the administrative officers, the medical staff and the hospital staff. Salem, though 221 miles distant from Seattle, is readily reached by plane, train or automobile, so that the investigators can and do conduct the experiments personally, spending 6 to 8 days per month at the prison.

Also at the Oregon State Penitentiary hospital we have available a completely equipped modern operating room, the hospital beds we need (biopsy patients are all hospitalized for 24 hours or more) and a complete staff of inmate nurses, orderlies, surgical assistants, etc. In addition, a well-equipped routine laboratory is available for performing routine urinalyses and hematological studies and liver functions tests, such as cephalin flocculation, B.S.P., thymol turbidity, transaminase, blood sugar, urinary PABA, etc. These tests are used to protect the subjects from any untoward or unanticipated toxic reaction from any of the medications administered.

B. Facilities available at the Pacific Northwest Research Foundation in Seattle: The Reproductive Physiology Division has laboratories in a former nurses' dormitory comprising a total of 3,294 square feet. These include: (a) a completely equipped histological laboratory; (b) a light microscopy room; (c) an electron microscope room with adjoining dark room for developing photomicrographs and radioautography; (d) small animal room; (e) hydrolysis and extraction room for steroids; (f) steroid analysis laboratory; (g) larger general laboratory used for gonadotropin analysis, rat autopsy and general chemical analysis; (h) small office; (i) cytochemical laboratory for frozen sectioning and enzyme localization; (j) a completely equipped photographic dark room containing, in part, a 45H Bessler Manual Model enlarger, Schneider Componon lenses, 1620 A loadmaster print washer; A-25 Arkay electric print dryer; and a macro photography unit that can be attached to the Bessler Enlarger. All these are for our exclusive use and do not include joint facilities of the Foundation.

C. Major permanent equipment available includes the following: Two Zeiss Model W1 binocular research microscopes; two Zeiss Photomicroscopes equipped to allow us to use phase contrast, darkfield, bright-field, and polarized illumination. A Zeiss Model GL microscope with accessories and a Wild M-5 stereomicroscope Model 1250 are also available. We also have a Norelco Closed Circuit Television Camera and Receiver for use with one of our microscopes. This instrument facilitates teaching, and also speeds scanning of tissue sections.

Other equipment includes a complete micro-technique set-up including an A.O. Model 820 microtome, paraffin embedding oven, etc.; a Volland analytic balance, Harvard trip double-beam balance, triple-beam balances, and a Roller-Smith Torsion balance for bioassay purposes; Spinco Duostat and Durrum electrophoretic cell; Spincraft automatic speed filter; International centrifuge and Beckman Zeromatic pH meter for gonadotropin processing; Kahn-type automatic shaker, Burrell wrist-action automatic shaker, Beckman Model B spectrophotometer, Labine incubator, Rotovapor, water baths, hot plates, crying oven, Gilson volumetric fractionator, Brinkmann equipment for thin-layer chromatography, automatic pipette washer and continuous flow extraction apparatus for steroid determinations; refrigeration facilities for storing urine and seminal fluid specimens; biopsy racks and an autoclave for their sterilization; two Monroe calculators, a typewriter and miscellaneous other small equipment.

We have recently added an R.C.A. electron microscope EMU 3B, improved, and an Automatic Reichert Ultramicrotome OMU 2. A Packard Instrument Company Model 7201 Radiochromatogram Scanning System complete with automatic localization of radioactivity on paper strip chromatograms or thin layer plates is also available.

D. The Foundation provides for our joint use with other investigators a Barnstead still and a Beckman Model L-2 Ultracentrifuge, a Vir-Tis tissue homogenizer and additional paper chromatography apparatus, a Blackstone Ultrasonic cleaner, an International Equipment Company Cryostat and a Packard Tri-Carb Liquid Scintillation Spectrometer.

VIII. ITEMIZED BUDGET

BUDGET OUTLINE

| | | | |
|----|-----------------------------------|------------|--------------------|
| A. | SALARIES | | |
| | <u>Personnel</u> | \$ 73,671. | |
| | <u>Professional Collaborators</u> | 1,950.* | |
| | | | <u>\$ 75,621.</u> |
| B. | EQUIPMENT | | <u>945.*</u> |
| C. | SUPPLIES | | <u>13,376.</u> |
| D. | TRAVEL | | <u>5,374.</u> |
| E. | MISCELLANEOUS | | <u>4,612.</u> |
| F. | PENITENTIARY COSTS | | <u>9,930.*</u> |
| G. | INDIRECT COSTS | | <u>19,407.</u> |
| | | TOTAL | <u>\$ 129,265.</u> |

* Items excluded for the basis of indirect cost calculation

3000982

4 31,888 / yr

ITEMIZED BUDGET (Continued)

| A. | Salaries | % Time Devoted to AEC project | Pro-rated Yearly Rate | P/R Taxes & Fringe Benefits | Total |
|----|------------------------------------|-------------------------------|-----------------------|-----------------------------|-------------------|
| | <u>Personnel</u> | | | | |
| | Heller, Carl G. Principal Invest. | 45 | | | |
| | Rowley, Mavis J. Senior Invest. | 50 | | | |
| | Morse, Howard C. Senior Invest. | 50 | | | |
| * | O'Keefe, Kathleen Bio-statistician | 17 | | | |
| | Teshima, Florence Research Assist. | 50 | | | |
| | Su, Mike H.H. Research Assoc. | 50 | | | |
| | Leach, David Research Associ. | 50 | | | |
| | Horike, Neil Research Assoc. | 50 | | | |
| * | Savage, Grace Secty/Clerk | 45 | | | |
| | Osborne, Yoshiko Research Tech. | 50 | | | |
| | Ruthroff, Gordon Research Tech. | 50 | | | |
| | Butler, John Research Tech. | Hourly | | | |
| | Technician | 50 | | | |
| | | | | | <u>\$ 73,671.</u> |

Professional Collaborators

| | |
|---|------------|
| Glenn A. Warner, M.D. Radiotherapist | \$ |
| Daniel DiIaconi, M.D. Surgeon | \$ 75,621. |

* Part-time employees

Pension Plan and Medical Plan have been included in Fringe Benefits where applicable

3000983

ITEMIZED BUDGET (Continued)

B. EQUIPMENT

| | | |
|----------------------|-------------|---------|
| 1 diamond knife | \$ 500. | |
| pH meter - Photovolt | <u>445.</u> | |
| | | \$ 945. |

C. SUPPLIES

| | | |
|--|-------------|------------|
| For EM including tissue preparation and photographic supplies | 3,500. | |
| FSH bioassay - cost per week for 5 men \$32.40 x 40 weeks | 1,296. | |
| Testosterone - urinary - cost per sample \$30 x 60 samples | 1,800. | |
| ICSH bioassay - cost per week for 5 men men - \$128 x 10 weeks | 1,280. | |
| Testosterone - plasma - protein-binding \$30 per sample x 40 samples | 1,200. | |
| <u>Radioimmunoassay.</u> | | |
| \$50 per month to Tumor Institute | 600. | |
| ICSH plasma - 12 samples per month | 1,200. | |
| FSH plasma - 12 samples per month | 1,200. | |
| Histological preparation - light microscope | 750. | |
| Freight charges for transporting urine, blood, and seminal fluid from Salem, Oregon, and return of empty reefers | <u>550.</u> | |
| | | \$ 13,376. |

3000984

D. TRAVEL

Oregon State Penitentiary

Twice per month, 2 days each time
Carl G. Heller, M.D., Ph.D., \$100 each \$ 2,400.

Society for the Study of Reproduction

September, 1970 - Columbus, Ohio
Three people 1,374.

Laurentian Hormone Conference

August, 1970 - Mt. Tremblant, Canada
Stopover at McGill University, Montreal
Carl G. Heller, M.D., Ph.D. 600.

Endocrine Society 52nd Annual Meeting

June, 1971 - Two people 1,000.

Handwritten scribble

\$ 5,374.

E. MISCELLANEOUS

Communications: Seattle-Salem calls,
telephone and telegrams 1,000.

Publication costs, reprints, photographs
and lantern slides, journals, books 2,000.

Service Contracts

Scientific Supplies Co. microscopes (50%) 75.
Calculators (50%)
M501 30.
Epic .2000 63.
RCA Electron microscope (50%) 844.
General repairs and sharpening of diamond
knives 600.

\$ 4,612.

F. PENITENTIARY COSTS

| | | |
|--|---------------|-----------|
| Cost of shipping biopsy specimens; chemicals and small laboratory supplies for Oregon State Penitentiary | \$ 750. | |
| Payments to Oregon State Penitentiary Inmates - 30 inmates at \$120 per year plus \$150 bonus each upon completion | 8,100. | |
| Inmate Technicians - \$45/month | <u>1,080.</u> | |
| | | \$ 9,930. |

G. INDIRECT COSTS

It has been the policy of the AEC to allow a rate of 20% excluding penitentiary costs, professional collaborators fees and permanent equipment. These items have again been excluded for the basis of indirect cost calculation

| | | |
|--|-------------------|------------|
| | <u>\$ 19,407.</u> | |
| | | \$ 19,407. |

| | |
|-------------|--------------------------|
| GRAND TOTAL | <u><u>\$129,265.</u></u> |
|-------------|--------------------------|

IX. MISCELLANEOUS

A. REGULATIONS GOVERNING RESEARCH INVOLVING HUMAN SUBJECTS

The policy of the Pacific Northwest Research Foundation with regard to research involving human subjects is currently being revised. Our Review Committee is being expanded to include paramedical and lay individuals and the policy itself is being outlined in much greater detail than in the past. This new policy will be finalized as of June 1st, 1970 and a copy will be forwarded to you at that time.

Also attached is a copy of the minutes of the Meeting of the Review Committee for Human Experimentation of the Pacific Northwest Research Foundation, September 16, 1969, at which our project was evaluated in detail and approved.

B. We agree to the general provisions as provided: "Equal Employment Opportunity" clause (HEW-386) - Revised December 1968, Clause 6. "Patent Rights" (July 1967) Clause 20.

3000987

MINUTES OF THE MEETING OF THE REVIEW COMMITTEE FOR HUMAN EXPERIMENTATION OF THE PACIFIC NORTHWEST RESEARCH FOUNDATION

September 16, 1969

The regular meeting of the Review Committee for Human Experimentation of the Pacific Northwest Research Foundation, was held at 4:00 p.m., Tuesday, September 16, 1969 in Room 105, Eklind Hall.

Members present:

John L. Bakke, M.D., F.A.C.P., Principal Investigator, Endocrinology, Pacific Northwest Research Foundation
Carl G. Heller, M.D., Ph.D., Principal Investigator, Reproductive Physiology, Pacific Northwest Research Foundation
Carteret Lawrence, M.D., Principal Investigator, Ophthalmology, Pacific Northwest Research Foundation
Vernon T. Riley, D.Sc., Principal Investigator, Microbiology, Pacific Northwest Research Foundation
Sherman W. Day, M.D., F.A.C.S., Co-Principal Investigator, Surgery, Pacific Northwest Research Foundation
Orliss Wildermuth, M.D., Radiotherapist, Diplomat of the American Board of Radiology, Director of the Tumor Institute of The Swedish Hospital Medical Center
William B. Hamlin, M.D., Pathologist, Diplomat of the American Board of Pathology, Director of the Department of Pathology of The Swedish Hospital Medical Center
Carl D. F. Jensen, M.D., Ophthalmologist, Diplomat of the American Board of Ophthalmology, Chairman of the Medical Research Board of the Pacific Northwest Research Foundation
William B. Hutchinson, M.D., F.A.C.S., Surgeon, Diplomat of the American Board of Surgery, President of the Board of Trustees of the Pacific Northwest Research Foundation
Reverend Richard Johnson, Chaplain, The Swedish Hospital Medical Center

Member absent:

Allan W. Lobb, M.D., F.A.C.S., Surgeon, Diplomat of the American Board of Surgery, Medical Director, The Swedish Hospital Medical Center

3000988

Included during the meeting was a review of an Atomic Energy Commission Contract application submitted by Dr. Carl G. Heller, with regard to research involving human subjects. Dr. Heller outlined the methods used to obtain volunteers for the experiments, the tests and interviews involved in screening the volunteers, possible effects of the experiments proposed, and results obtained during clinical and experimental observation.

A lengthy discussion followed in which details of the research, methods, patient health and risks were enlarged upon. Particular emphasis was placed in two areas, i.e.:

1. Informed consent and volunteer motivation for being on an experimental program.
2. Dosage of radiation to be used during the coming year (6 men at 600r, 10 men at 200r and perhaps others at lower doses.) and experimental procedures (collection of samples, etc.).

The Review Committee was particularly impressed with the thoroughness shown in these two areas and voted unanimous approval of all aspects of the application.

The meeting adjourned at 5:00 p.m.

Respectfully submitted,

Grace E. Plummer

(M rs.) Grace E. Plummer
Secretary

REPOSITORY: DOE-RICHLAND
COLLECTION: GSS HUMAN TEST SUBJECTS STUDIES
PRISONER STUDY

BOX: 046264

FOLDER: 1780 - HELLER PACIFIC NW RES. FOUNDA.

ASSIGNED NUMBER: RLHTS 94-0022

3000989-A