716229

EFFECTS OF IONIZING RADIATION ON THE
TESTICULAR FUNCTION OF MAN
AT (45-1) 1780
RENEWAL PROPOSAL: 8/1/72 - 7/31/73

Carl G. Heller, M.D.,Ph.D.
Division of Reproductive Physiology
Pacific Northwest Research Foundation
Seattle, Washington 98104

3001301

May 26, 1972

Frank T. Brooks
Division of Biology and Medicine
HQ

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

Enclosed are progress reports and a renewal proposal for the subject program entitled "Effects of Ionizing Radiation on the Testicular Function of Man". Principal Investigator, Dr. Carl G. Heller requests an AEC support level of $98,792 for the project for the period August 1, 1972 through July 31, 1973.

ORIGINAL SIGNED BY
N. W. FRASER

Nell W. Fraser
Contract Administrator Representative
Contract Administration Division

Enclosures:
1. Renewal Proposal (3)
2. One-Year Progress Rpt. (3)
3. Nine-Year Progress Rpt. (3)
4. NRP Form (3)

bcc: Official File
CAD Rdg. File
NWF Rdg. File

3001302

OFFICE ▶	CAD					
SURNAME ▶	FRASER					
DATE ▶	5/26/72					

Revised Budget: AEC Contract AT(45-1)1780 - 8-1-72 thru' 7-31-73

		P/R Taxes	Total
Personnel	33,483.	3,269.	36,752. same personnel + effort cut in
Collaborators			1,250.
Supplies			6,100.
Travel			3,500.
Miscellaneous			2,762.
Penitentiary Costs			5,104.
Indirect Costs (43.4% S&W)			14,532.
			70,000.
Cost sharing from non-Federal funds by grant from The Population Council, received in August, 1972			4,468.
Total project funds for period: 8-1-72 thru' 7-31-73			$74,468.

3001303

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, 1972 - July 31, 1973

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.
	Eighth year	120,000.
	Ninth year	101,118.
	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.
President & Director, Pacific Northwest Research Foundation

3001304

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I. OBJECTIVES

The objectives stated in this proposal will not be changed from those stated in the current year's research objectives. These are: 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 times; 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.

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).

II. CHARTS (pages 2 thru' 9)

A. BIOPSY TIMES FOLLOWING IRRADIATION
B. PARAMETERS MEASURED AND RESPONSE RECORDED DURING RECOVERY
C. PARAMETERS MEASURED AND RESPONSE RECORDED DURING DEPLETION

3001306

25wk	30wk	40wk	50wk	60wk	80wk	100wk	120wk	140wk	160wk	180wk	200wk	220wk	240wk
		31wk											
		32wk											
		39wk			70wk								
	30wk			51wk	79wk								
					76wk								
	27wk	35wk			61wk	84wk		121wk					
		39wk			77wk								
									151wk				
								123wk					
	29wk		50wk										

[redacted]

001307

A. 1

PRIVACY ACT MATERIAL REMOVED

DOSE	SUBJECT	1 day	1wk	2wk	3wk	4wk	6wk	8wk	10wk	15wk	20wk
8r											
8r											
8r											17wk
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											
20r				11d		26d					

h hour
d day
wk week

800 1308

25wk	30wk	40wk	50wk	60wk	80wk	100wk	120wk	140wk	160wk	180wk	200wk	220wk	240wk
	30wk												
	29wk			60wk									
	27wk				69wk	84wk							
								121wk					
						85wk	109wk						
21wk													
25wk		42wk	50wk	54wk									
24wk													
		37wk											

3001309

PRIVACY ACT MATERIAL REMOVED

Fig. 2

DOSE	SUBJECT	1 day	1wk	2wk	3wk	4wk	6wk	8wk	10wk	15wk	20wk
20r										15wk	
20r		½h				25d		47d			
25r		6h				24d	40d				
25r	+	24h			15d		29d		64d		18wk
50r		4½*/ 7*h				24d	40d				
50r											
50r											
50r	+										20wk
55r											17wk
78r											
78r											
78r			3d		17d	24d					18wk
78r											

h hour
d day
wk week

(N.C.) No control biopsy
* Cannot be quantitated
+ Second irradiation

3001310

5wk	30wk	40wk	50wk	60wk	80wk	100wk	120wk	140wk	160wk	180wk	200wk	220wk	240wk
	30wk			51wk		113wk	118wk						
		36wk			70wk								
						87wk	104wk	125wk	153wk		183wk		232wk
	28wk					81/ 99wk	109wk	129wk					
		37wk			61wk			125/ 135wk					
			45wk										
		31wk											
		35wk											
23wk			43wk	55wk		82wk							
		31wk	47wk										

[redacted]

3001311

PRIVACY ACT MATERIAL REMOVED

DOSE	SUBJECT	1 day	1wk	2wk	3wk	4wk	6wk	8wk	10wk	15wk	20wk
78r		½h				26d					
100r		24h		2wk		25d		7wk			16wk
100r	(N.C.)	16h*					32½d*	46½d*	62d*		
100r	(N.C.)	4*/ 6½*h					31d*				
100r										15wk	
100r										11wk	
100r										11wk	
100r	+	24h			15d		29d		64d		17wk
100r											
100r		24h		2wk			35d				17wk
200r	(N.C.)	13h*			14½d*			46½d*			
200r		22½h			14½d		29d			13wk	
200r											

h	hour	(N.C.)	No control biopsy
d	day	*	Cannot be quantitated
wk	week	+	Second irradiation

3001312

25wk	30wk	40wk	50wk	60wk	80wk	100wk	120wk	140wk	160wk	180wk	200wk	220wk	240wk
								139wk				203wk	
	27wk			54wk	67wk	81wk	102/ 119wk	136wk		165wk			
21wk		41wk		59wk									
	29wk		46/ 50wk		69/ 81wk								
22wk	30wk												
		40wk											
			44wk	53wk	70wk	89wk	111wk						
					71wk	90wk		123wk					
		38wk											
21wk		38wk											
24wk		35wk	41wk		70wk			121wk		169wk		209wk	
21wk	27wk												

3001313

PRIVACY ACT MATERIAL REMOVED

DOSE	SUBJECT	1day	1wk	2wk	3wk	4wk	6wk	8wk	10wk	15wk	20wk
200r											
200r											19wk
200r				11d		26d					
200r	+			11d				8wk			
200r				11d		26d					
200r					17d	24d					
200r											
200r											
200r											
200r		½h				26d					
300r	(N.C.)	15h					33/ 40½d	62½d			
300r							40d				
400r		4½/ 6h				24d	40d				

h hour
d day
wk week

(N.C.) No control biopsy
+ Second irradiation

30013 4

A. 5

PRIVACY ACT MATERIAL REMOVED

DOSE	SUBJECT	1 day	1wk	2wk	3wk	4wk	6wk	8wk	10wk	15wk	20wk
400r										72d	
600r		4h				26d		44d		13wk	
600r		22½h			14½d		29d			12wk	
600r											20wk
600r											
600r											
600r		18 min				24d		8wk			
600r		16 min				24d			9wk		
600r			1wk					46d		13wk	
600r	++		1wk				6wk			13/ 15wk	
600r	+						5wk			15wk	
600r							5wk			15wk	
600r			3d		17d						

h hour
d day
wk week

(N.C.) No control biopsy
* Cannot be quantitated
+ Second irradiation
++ Third irradiation

300 1315

25wk	30wk	40wk	50wk	60wk	80wk	100wk	120wk	140wk	160wk	180wk	200wk	220wk	240wk
			42wk	55wk	69/ 77wk	87wk	104/ 119wk						
		33wk	42wk						148/ 160wk	179wk		209/ 219wk	246wk
23wk		36wk	46wk		63wk	81wk							
	29wk												
22wk		31wk											
						99wk			154wk				
22wk		37wk*	45wk	58wk			101/ 119wk		144/ 154wk	175wk			
22wk		37wk*	45wk	57wk	67wk	89wk	106wk	125wk	146wk	177wk			
	26wk			51/ 57wk	67wk	89wk	106wk	127wk	141/ 148wk				
									148wk	161wk			
			45wk	60wk		83/ 99wk							
		33wk	47wk		71wk								
		33wk	48wk										

[redacted]

3061316

3001317

260wk	290wk
260wk	272wk

PRIVACY ACT MATERIAL REMOVED

DOSE	SUBJECT	1 day	1wk	2wk	3wk	4wk	6wk	8wk	10wk	15wk	20wk
600r			3d		17d	24d					
600r											
600r		½h				26d		8wk			

h hour
d day
wk week

3001318

5wk	30wk	40wk	50wk	60wk	80wk	100wk	120wk	140wk	160wk	180wk	200wk	220wk	240wk
		32wk	41wk	52wk									
1wk		35wk	48wk	59wk	80wk								
4wk		39wk											

3001319

B. PARAMETERS MEASURED AND RESPONSE RECORDED DURING RECOVERY

	Dose	Number of Subjects	CYTOL				
			GERMINAL CELL RECOVERY				
			Start of Histo-logical Recovery	First Sperm OR First Increase of Sperm in Seminal Fluid	Complete Recovery	Germinal Cell Ultra-structure	Sperm Concen-tration i Seminal Fluid
Current status of all samples collected to date	8-25r	18	Incom-plete	Complete	Incom-plete	Incom-plete	Complete
Current status of all samples collected to date	50-100r	23	Incom-plete	Complete	Incom-plete	Incom-plete	Complete
Current status of all samples collected to date	200-300r	16	Incom-plete	Complete	Incom-plete	Incom-plete	Complete
Current status of all samples collected to date	400-600r	17	Incom-plete	Complete	Incom-plete	Incom-plete	Incom-plete

NO ADDITIONAL IRRADIATIONS REQUIRED TO COMPLETE ANALYSIS OF EACH OF THE ABOVE PARAMETERS

0 3 0 1 3 2 0

ICAL		HORMONAL						
		URINARY				PLASMA		
Leydig Cells	Sertoli Cells	ICSH	FSH	Estrogen	Testosterone & Epitestosterone	ICSH	FSH	Testosterone
Incomplete	Incomplete	Complete	Complete	Complete	Complete	Complete	Complete	Incomplete
Incomplete	Incomplete	Complete	Complete	Complete	Complete	Complete	Complete	Incomplete
Incomplete	Incomplete	Incomplete	Incomplete	Complete	Complete	Complete	Complete	Incomplete
Incomplete	Incomplete	Incomplete	Incomplete	Complete	Complete	Complete	Complete	Incomplete

3001321

C. PARAMETERS MEASURED AND RESPONSE RECORDED DURING DEPLETION

	Dose	Number of subjects	CYTOL				
			GERMINAL CELL QUANTITATION				
			Sperma togonia	Sperma-tocytes	Sperma-tids	Germinal Cell Ultra-structure	Sperm Concen-tration in Seminal Fluid
urrent status of all samples collected to date	8-25r	18	Complete	Complete	Complete	Incom-plete	Complete
urrent status of all samples collected to date	50-100r	23	Complete	Complete	Complete	Incom-plete	Complete
urrent status of all samples collected to date	200-300r	16	Complete	Complete	Complete	Incom-plete	Complete
urrent status of all samples collected to date	400-600r	17	Complete	Complete	Complete	Incom-plete	Complete

NO ADDITIONAL IRRADIATIONS REQUIRED TO COMPLETE ANALYSIS OF EACH OF THE ABOVE PARAMETERS

3001322

CAL		HORMONAL						
		URINARY				PLASMA		
ydig lls	Sertoli Cells	ICSH	FSH	Estrogen	Testosterone & Epitestosterone	ICSH	FSH	Testosterone
complete	Incomplete	Complete	Complete	Complete	Complete	Complete	Complete	Incomplete
complete	Incomplete	Complete	Complete	Complete	Complete	Complete	Complete	Incomplete
complete	Incomplete	Complete	Complete	Complete	Complete	Complete	Complete	Incomplete
complete	Incomplete	Complete	Complete	Complete	Complete	Complete	Complete	Incomplete

3001323

III. RESULTS

A. HISTOLOGICAL

We have observed an increase in the number of Leydig cells following irradiation with 600r using the Leydig cell/Sertoli cell ratio method (Heller, Lalli, Pearson and Leach, 1971). The data suggest this rise begins approximately 90-95 days post-irradiation. Thus far, five subjects show an increase in Leydig cell numbers and one subject shows a slight decrease; however, his later biopsies must still be quantitated.

Although a total of 15 subjects have received 600r of irradiation only 12 have sufficient biopsies taken after 90 days to ascertain if an increase has taken place. Of these there is only one subject that has been followed for a long enough time to begin to show a recovery in Leydig cell numbers - this being roughly 1,900 days. His Leydig cell/ Sertoli cell ratios are shown in the following:

Subject #199
LC/SC Ratios

	Right Testis	Left Testis
Control	.45	.47
26 days	.44	-
92 days	.53	-
232 days	-	.52
295 days	.63	-
1022 days	.55	-
1120 days	-	.75
1253 days	.49	-
1722 days	-	.88
1904 days	-	.61

3001324

The number of men that will be available after this amount of time has elapsed can only be postulated. At this time seven subjects who have received 600r are actively participating in the irradiation program and five have biopsies after 700 days post-irradiation.

We shall continue to follow these subjects for as long as possible after irradiation. Hopefully, until they again reach control levels.

If indeed, we do find that there is a significant rise in Leydig cells in the population of subjects who have received 600r, we shall then begin quantitation of biopsies from subjects who have received lower doses of irradiation. Should increases in Leydig cells be found at these doses then we shall determine if these increases correspond with those at 600r. Questions we shall be answering are: 1) are the increases at these lower doses, if they do occur, as statistically significant as those at 600r, i.e., are the increases as great, 2) are the intervals of time to notice an increase and to notice recovery the same, 3) is there possibly a dose-response relationship involved?

Quantitation of the germinal epithelium has proceeded by accumulating more data for adequate statistical analysis. No "new" findings can be reported although initial findings are being further substantiated. Examples of results at different dose levels by tubule counts (Rowley and Heller, 1971) are as follows:

	Ad	Ap	B	R	L	Z	P	Sa	Sb	Sc	Sd
	Spermatogonia			Spermatocytes				Spermatids			
Control	0.93	0.80	0.49	0.42	0.76	0.11	2.56	1.56	3.09	2.67	2.45
25r											
6hrs	0.68	0.63	0.25	0.09	0.45	0.01	2.87	1.78	2.62	1.13	1.54
24days	0.74	0.64	0.29	0.05	0.14	0.02	2.85	2.65	2.00	0.27	0.35
40days	0.28	0.23	0.03	0.02	0.04	0	0.20	0.30		1.16	
201days	0.36	0.28	0.07	0.03	0.04	0	0.31	0.21		0.41	
420days	0.96	0.88	0.30	0.45	0.25	0.25	3.31	0.99	2.45	3.49	
Control	0.71	0.53	0.28	0.24	0.43	0.06	1.99	1.43	1.29	1.29	1.00
100r											
24hrs	0.62	0.44	0.14	0.14	0.33	0.02	1.32	0.72	0.79	0.71	0.74
14days	0.59	0.06	0.003	0	0.009	0	1.05	0.55	0.59	0.73	0.49
25days	0.20	0.08	0.04	0.02	0	0	0.27	0.81	1.06	0.75	0.73
49days	0.27	0.12	0.02	0.03	0.04	0	0.20	0.17		0.32	
112days	0.06	0.02	0	0	0	0	0.03	0.02		0.06	
210days	0.06	0.06	0.005	0	0	0	0.06	0.03		0.02	
Control	0.56	0.44	0.29	0.33	0.61	0.01	2.60	1.58	2.20	1.83	1.60
600r											
22hrs	0.47	0.24	0.07	0.07	0.74	0.04	2.90	1.88	2.24	2.22	1.68
14days	0.28	0.23	0.004	0	0.01	0	1.39	0.44	0.99	0.71	0.72
29days	0.21	0.14	0.01	0	0	0	0.01	1.34		2.37	
84days	0.01	0.002	0	0	0	0	0	0	0	0	0
151days	0.002	0	0	0	0	0	0	0	0	0	0
252days	0.006	0	0	0	0	0	0	0	0	0	0
[illegible]days	0.003	0.01	0.02	0.005	0	0	0.05	0.04		0.01	
477days	0.001	0	0	0.006	0	0	0.01	0	0	0	0

We have been examining and charaterizing the ultrastructural features of Leydig cells in control biopsies before carefully examining those after irradiation. Preliminary ultrastructural examination indicates Leydig cells are affected by irradiation within two days. With the aid of the electron microscope we shall continue to study the morphological changes of the Leydig cells which cannot be seen with the light microscope following irradiation. Again we are attempting to answer questions concerning dose-response relationships of the morphological effects of X-ray irradiation on the Leydig cell.

Ultrastructural examination of the germinal epithelium has revealed many morphological changes, some of which we have not seen in either normal or otherwise altered testis. For example, at 24 days after irradiation at 600r, we have found macrophages traveling through the basal lamina into the tubules. We believe they pick up damaged cellular material and then move into the lumen. The Sertoli cells, however, also act as disposals for damaged tissue releasing acid phosphatase into the cell to break it up and then acting as a transporting medium for the broken-up cells to pass through into the lumen.

Although much progress has been made we have really only scratched the surface. Because of the number of biopsies taken and the wealth of information available in each biopsy, much of the material has not yet been examined.

B. HORMONAL

Plasma testosterone is being measured by the method of Murphy (1970). This method consists of extraction of steroids from plasma with diethyl ether, isolation of testosterone with the use of a column of Sephadex LH-20, and quantitation by competitive protein binding using L.P.P. and charcoal uptake.

Although there are many methods currently available in the literature, the above method seems most suitable due to its relative speed and simplicity. The other methods are characterized by the extensive solvent preparation and multi-stage isolation steps (often both thin-layer and paper chromstography).

The normal male control value obtained in this laboratory (36 plasma samples) is 515 $\pm$ 164 (S.D.) ng/100ml with a range of 212 - 896 ng/100ml. Preliminary data from two subjects at 600r and two subjects at 200r indicate no statistical change in plasma testosterone following irradiation. More plasma samples will have to be assayed at all dose levels so that a valid conclusion may be reached as to the effect of irradiation on plasma testosterone. We shall continue to collect samples from those subjects who remain on the irradiation program and assay them along with the samples we have already collected.

The methods that we use for the radioimmunoassay of plasma FSH and ICSH are modifications of methods by Odell, et al. (1967), and Midgley (1966). We use the NIH standard LER 907. The method involves iodinating 2μg of highly purified HLH (or 1μg of FSH with 2mc of ^{131}I by the modified method of Greenwood, Hunter and Glover

(1963). The iodinated hormone is separated from the inorganic ^{131}I by passing the sample through a G-75 Sephadex column. The trailing edge of the earliest peak is used in the assay. The specific activity ranges from 200 to 600µc per µg.

The buffer system and assay procedure differ from that of Odell in incubation and concentration of rabbit serum. After adding the buffer, EDTA, plasma and antibody, we incubate for one day, add iodinated hormone and further incubate for four days. We prefer this because the sensitivity of the assay is increased by the creation of a non-equilibrating system. The plasma ICSH control value (50 men) is 9.04 $\pm$ 2.65 (S.D.) µg LER 907/100ml, RIA with a range of 4.74 to 15.25 µg LER 907/100ml. The plasma FSH control value (34 normal adult males) is 34.4 $\pm$ 8.55 (S.D.) µg LER 907/100ml with a range of 22.0 to 45.4 µg LER 907/100ml.

Measuring plasma FSH has confirmed those results we have found in the urine. Namely, no change at 8r; a slight increase at 20r; and highly significant increases were seen at 78 - 600r. Measuring plasma ICSH by radioimmunoassay has produced contrasting results to those which we found in the urine. Only two doses (8r and 20r) revealed no change while at the higher doses there were definite increases in plasma ICSH especially at 600r.

One man has had most of the collected samples completed (other samples are run randomly to insure our double blind system). His values are shown as an example of the data being collected.

6-30-70	8.0	77.5	----	----
7-20-70	21.3	87.5	7-10-70	0
10-20-70	21.2	85.0	10-26-70	0.1
11-20-70	17.2	82.0	11-20-70	0.2
1-21-71	13.5	77.5	2-5-71	4
2-19-71	15.3	70.0	3-29-71	6
3-20-71			4-5-71	0.3
4-20-71				
5-20-71				
6-20-71				
7-20-71				
8-20-71	12.8	50.7	8-30-71	12
9-20-71			10-1-71	8
10-20-71			10-22-71	18
11-20-71			11-1-71	21
12-20-71				
1-20-72				

3001330

PLASMA ICSH AND FSH DETERMINED BY RADIOIMMUNOASSAY. SPERM COUNTS ARE GIVEN FOR APPROXIMATE PLASMA COLLECTION DATES FOR REFERENCE.

Collection Date	ICSH µgLER 907/ 100ml	FSH µgLER 907/ 100ml	Collection Date	S.F. Count M/cc
1-20-68	11.4	23.7	1-16-68	157
2-3-68	7.0	31.2	1-30-68	126
2-17-68	7.0	33.8	2-13-68	258
5-5-68	9.5	25.0	4-23-68	213
5-12-68	8.7	33.3	5-14-68	160
10-8-68	8.9	32.3	10-7-68	236
11-14-68	9.0	30.3	11-4-68	125
11-14-68	600r			
11-28-68	10.2	45.8	11-25-68	87
12-20-68	18.6	95.0	12-16-68	94
1-8-69	21.7	101.3	1-10-69	27
1-10-69	18.7	112.3	1-24-69	10
1-22-69	16.3	81.3	1-31-69	1.5
2-18-69	16.3	106.3	2-7-69	0.3
4-25-69	11.4	86.3	2-28-69	0
5-12-69	9.9	91.3	5-16-69	0
5-29-69	16.9	86.3	5-23-69	0
6-30-69	13.0	92.5	6-20-69	0
8-5-69	14.7	80.0	7-24-69	0
8-22-69	9.7	76.9	8-21-69	0
9-29-69	21.6	110.0	9-18-69	0
10-28-69	14.5	115.0	10-9-69	0
11-29-69	18.0	75.3	11-26-69	0
12-29-69	10.6	79.4	12-29-69	0
1-30-70	20.4	106.3	1-18-70	0

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We shall continue to collect plasma samples on all irradiated subjects who are currently on the program. These samples will be assayed for both plasma FSH and ICSH along with the 250 plus samples that have been collected from irradiated subjects but have not been assayed. These data will then be grouped according to X-ray dosage and statistically evaluated to determine the dose-response relationship.

Concerning urinary hormones (FSH, ICSH) we are still in the process of re-analyzing the vast amount of data we have accumulated. Each assay is being carefully evaluated both personally and with the aid of a computer. This analysis will continue for some time because of the time involved in evaluating each response that has been obtained in all subjects who have received irradiation. After this careful analysis has been completed it will be inspected further and the same questions applied as before, is there a dose-response, etc.

C. SEMINAL FLUID

Sperm counts and sperm morphological examination will continue to be done on a weekly basis. Analysis of sperm count will be done on a dose irradiated basis to determine a possible dose-response effect and length and degree of effect for each dose.

D. CHROMOSOMAL ANALYSIS

During the past two months, Dr. J. G. Brewen of Oak Ridge National Laboratories has been collecting testicular tissue for

chromosomal analysis. We shall continue to supply Dr. Brewen with tissue from all biopsies done on subjects who have received testicular X-ray.

E. REFERENCES

Albert, A., Rosemberg, E., Ross, G. T., Paulsen, C. A. and Ryan, R. J.: Report of the National Pituitary Agency collaborative study on the radioimmunoassay of ICSH and FSH. J. Clin. Endo. & Metab., 28:1214-1219, 1968.

Gandy, H. M. and Peterson, R. E.: Measurement of testosterone and 17-ketosteroids in plasma by the double isotope dilution derivative technique. J. Clin. Endo. & Metab., 28:949-977, 1968.

Greenwood, F. C., Hunter, W. M. and Glover, J. S.: The preparation of I^{131}-labelled human growth hormone of high specific radioactivity. Biochem. J., 89:114-123, 1963.

Hales, C. N. and Randle, P. E.: Immunoassay of insulin with insulin-antibody precipitation. Biochem. J., 88:137-146, 1963.

Heller, C. G., Lalli, M. F., Pearson, J. E. and Leach, D. R.: A method for the quantification of Leydig cells in man. J. Reprod. Fert., 25:177-184, 1971.

Heyns, W., Verhoeven, G., Van Baelen, H. and DeMoor, P.: Measurement of testosterone in plasma by competitive protein binding. Ann. d'Endocr., 30(1b):153-158, 1969.

Maeda, R., Okamoto, M., Wegienka, L. C. and Forsham, P. H.: A clinically useful method for plasma testosterone determination. Steroids, 13:83-99, 1969.

Mayes, D. and Nugent, C. A.: Determination of plasma testosterone by the use of competitive protein binding. J. Clin. Endo. & Metab., 28:1169-1176, 1968.

Midgley, Jr., A. R.: Radioimmunoassay: A method for human chorionic gonadotrophin and human luteinizing hormone. Endocrinology, 79:10-18, 1966.

Murphy, B. E. P.: Methodological problems in competitive protein binding techniques: The use of Sephadex column chromatography to separate steroids. Acta Endocrinol., suppl. 147:37-60, 1970.

Odell, W. D., Ross, G. T. and Rayford, P. L.: Radioimmunoassay for luteinizing hormone in human plasma or serum: physiological studies. J. Clin. Invest., 46:248-255, 1967.

Rosenfield, R. L., Eberlein, W. R. and Bongiovanni, A. M.: Measurement of plasma testosterone by means of competitive protein binding analysis. J. Clin. Endo. & Metab., 29:854-859, 1969.

Rowley, M. J., Berlin, J. D. and Heller, C. G.: The ultrastructure of four types of human spermatogonia. Z. fur Zellforsch., 112: 139-157, 1971.

Rowley, M. J. and Heller, C. G.: Quantitation of the cells of the seminiferous epithelium of the human testis employing the Sertoli cell as a constant. Z. fur Zellforsch., 115:461-472, 1971.

Sherwood, L. M., Mayer, P., Potts, S. T. and Aurbach, G. D.: Determination of parathyroid hormone in ovine plasma by radioimmunoassay. The Endocrine Society Program, 47th Annual Meeting, 1965, p. 23 (abstract).

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PRIVACY ACT MATERIAL REMOVED

IV. QUALIFICATIONS OF SCIENTIFIC PERSONNEL

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

Birthdate:

Birthplace: , New York

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 in the 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.

1970, Guest Lecturer, Workshop Conference on the Human Testis, Positano, Italy, April 23-24, 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.

1971, Advisor, Conference on Research Strategies on the Control of Male Fertility, World Health Organization Headquarters, Geneva, Switzerland, May 27-29.

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	Director, Division of Reproductive Physiology, Pacific Northwest Research Foundation, Seattle, Washington

CARL G. HELLER, M.D., Ph.D.

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, Endocrinol., 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, Endocrinol., 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.: Gonadotropic hormone: Clinical application of extraction methods for assay purposes, Endocrinol., 24:319, March, 1939.

Heller, C. G., Lauson, H., 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, Endocrinol., 24:34, January, 1939.

Heller, C. G.: Metabolism of the estrogens: The effect of liver and uterus upon estrone, estradiol and estriol, Endocrinol., 26:619, April, 1940.

Heller, E. J., Heller, C. G. and Sevringhaus, E. L.: Gonadotropic hormone: Assay of human male urine, Endocrinol., 29:1, July, 1941.

3001337

Heller, C. G.: Gonadotrope 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? Endocrinol., 30:309, 1942.

Heller, C. G., Farney, J. P., Morgan, D. N. and Myers, G. B.: Relation of gonadotropic hormone to oophorectomy, climacteric symptoms and diethylstilbestrol therapy in women, Endocrinol., 30:S1031, 1942 (abstract).

Heller, C. G. and Chandler, R. E.: Gonadotropic hormone: Modification of the alcohol-precipitation assay method, J. Clin. Endocrinol., 2:252, April, 1942.

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, Endocrinol., 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, Endocrinol., 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. P., 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, J. 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.

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, Endocrinol., 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.

3001340

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.: Antihormone 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 lutectrophin 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., Pearl, C. L. and Heller, C. G.: Suppression of urinary chorionic gonadotrophin, symptoms and pulmonary metastases in choricepithelioma 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.

3001341

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.

Mortimore, G. E., Paulsen, C. A. and Heller, C. G.: The effect of steroids and lactone derivatives on hypophyseal gonadotrophin content, Endocrinol., 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 Supplementum, 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. New York 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, Endocrinol., 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, Supple. 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, Supple. 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)Diamines, Experimental and Molecular Pathology, Suppl. 2, 2:107, December, 1963.

Heller, C. G.: The Male and Female Sex Organs, Clinical Physiology, A. Grossman, Chap. 27 (1956), Chapter 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, Science, 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, 1964.

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, 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).

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., 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, 1968, Vol. 2.

Radiobiological Factors in Manned Space Flight, Report of the Space Radiation Study Panel of the Life Sciences Committee, Space Science Board National Academy of Sciences, National Research Council, 1967 - Wright H. Langham, editor. (C.G.Heller committee member)

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., 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., 35,2:493, 1968 (abstract).

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, in Progress in Endocrinology, (Proceedings of the III International Congress of Endocrinology, Mexico City, June 30-July 5, 1968), Carlos Gual and F. J. G. Eblin (eds.), Excerpta Medica Foundation (Amst.) 1969, pp. 1012-1018.

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.

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. R. 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, G. V. and Heller, C. G.: The effects of clomiphene citrate on the normal human male reproductive system, Clin. Res., 16:143, 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., 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., 30:196-207, 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, in Advances in Experimental Medicine and Biology, Vol. 10, "The Human Testis" (Proceedings of the Workshop Conference on the Human Testis, Positano, Italy, April 23-25, 1970), E. Rosemberg and C. A. Paulsen (eds.), Plenum Publishing Corporation, New York, New York, pp. 249-259.

Rowley, M. J., Teshima, F. and Heller, C. G.: Duration of transit of spermatozoa through the human male ductular system, Fertility and Sterility, 21:390-296, 1970.

IBID
Urology Digest, 9:62, 1970 (abstract).

Heller, C. G., Morse, H. C. and Rowley, M. J.: The effect of testosterone on the normal testis, Proceedings of the 52nd Annual Meeting of The Endocrine Society, St. Louis, Missouri, June 10-12, 1970, pp. 50 (abstract).

Rowley, M. J. and Heller, C. G.: Embryology, anatomy and histology of the male sexual organs, in Fertility Disturbances in Men and Women, pp. 48-64, Karger/Basel, 1971.

Rowley, M. J., Berlin, J. D. and Heller, C. G.: The ultrastructure of four types of human spermatogonia, Zeitschrift für Zellforschung, 112: 139-157, 1971.

Heller, C. G., Lalli, M. F., Pearson, J. E. and Leach, D. R.: A method for the quantification of Leydig cells in man, J. Reprod. Fert., 25:177-184, 1971.

Heller, C. G. and Leach, D. R.: Quantification of Leydig cells and measurement of Leydig-cell size following administration of human chorionic gonadotrophin to normal men, J. Reprod. Fert., 25:185-192, 1971.

Rowley, M. J. and Heller, C. G.: Quantitation of the cells of the seminiferous epithelium of the human testis employing the Sertoli cell as a constant, Z. fur Zellforsch., 115:461-472, 1971.

Rowley, M. J. and Heller, C. G.: The testosterone rebound phenomenon in the treatment of male infertility, Accepted for publication in Fertility and Sterility.

Morse, H. C., Leach, D. R., Rowley, M. J. and Heller, C. G.: Effect of cyproterone acetate on sperm concentration, seminal fluid volume, testicular cytology and levels of plasma and urinary ICSH, FSH and testosterone in normal men, submitted to the Journal of Reproduction and Fertility.

PRIVACY ACT MATERIAL REMOVED

Mavis J. Rowley

Born: , California

Nationality:

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, Postgradate 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-present Senior Investigator, Division of Reproductive Physiology, Pacific Northwest Research Foundation, Seattle.

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.

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 Medical 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., 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.

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 Medica Foundation, International Congress Series, Progress in Endocrinology, pp. 1012, 1969.

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., 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, 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, in Advances in Experimental Medicine & Biology, Vol. 10, "The Human Testis", Eugenia Rosemberg and C. A. Paulsen (eds.), Plenum Publishing Corporation, New York, 1970, pp. 249-259.

Rowley, M. J., Teshima, F. and Heller, C. G.: Duration of transit of spermatozoa through the human male ductular system, Fertil. & Steril., 21:390-396, 1970.

IBID: Urology Digest, 9:62, 1970 (abstract).

Heller, C. G., Morse, H. C. and Rowley, M. J.: The effect of testosterone on the normal testis, Proceedings of the 52nd Annual Meeting of The Endocrine Society, St. Louis, Missouri, June 10-12, 1970, pp. 50 (abstract).

Rowley, M. J. and Heller, C. G.: Embryology, anatomy and histology of the male sexual organs, in Fertility Disturbances in Men and Women, pp. 48-64, Karger/Basel, 1971.

Rowley, M. J., Berlin, J. D. and Heller, C. G.: The ultrastructure of four types of human spermatogonia, Z. fur Zellforschung, 112: 139-157, 1971.

Rowley, M. J. and Heller, C. G.: Quantitation of the cells of the seminiferous epithelium of the human testis employing the Sertoli cell as a constant, Z. fur Zellforsch., 115:461-472, 1971.

Heller, C. G., Lalli, M. F., Pearson, J. E. and Leach, D. R.: A method for the quantification of Leydig cells in man, J. Reprod. Fert., 25:177-184, 1971.

Heller, C. G. and Leach, D. R.: Quantification of Leydig cells and measurement of Leydig-cell size following administration of human chorionic gonadotrophin to normal men, J. Reprod. Fert., 25:185-192, 1971.

Rowley, M. J. and Heller, C. G.: The testosterone rebound phenomenon in the treatment of male infertility, accepted for publication in Fertility and Sterility.

Morse, H. C., Leach, D. R., Rowley, M. J. and Heller, C. G.: Effect of cyproterone acetate on sperm concentration, seminal fluid volume, testicular cytology and levels of plasma and urinary ICSH, FSH and testosterone in normal men, submitted to the Journal of Reproduction and Fertility.

PRIVACY ACT MATERIAL REMOVED

Howard C. Morse, Ph.D.

Born: , Idaho

Nationality:

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, 1964-66

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, G. C., Su, M. and Rowley, M. J.: The role of FSH, ICSH and endogenous testosterone during testicular suppression by exogenous testosterone in normal men, in Advances in Experimental Medicine & Biology, Vol. 10, "The Human Testis", Eugenia Rosemberg and C. Alvin Paulsen (eds.),(Proceedings of the Workshop Conference on the Human Testis, Positano, Italy, April 23-25, 1970), Plenum Publishing Corp., New York, New York, pp. 249-259, 1970

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.

Morse, H. C., Leach, D R., Rowley, M. J. and Heller, C. G.: Effect of cyproterone acetate on sperm concentration, seminal fluid volume, testicular cytology and levels of plasma and urinary FSH, ICSH and testosterone in normal men, Submitted to the Journal of Reproduction and Fertility.

PRIVACY ACT MATERIAL REMOVED

David R. Leach

Born: Texas

Nationality:

Education:

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

Experience:

1967-present Research Associate, Division of Reproductive Physiology, 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).

Heller, C. G., Lalli, M. F., Pearson, J. E. and Leach, D. R.: A method for the quantification of Leydig cells in man, J. Reprod. Fert., 25:177-184, 1971.

Heller, C. G. and Leach, D. R.: Quantification of Leydig cells and measurement of Leydig-cell size following administration of human chorionic gonadotrophin to normal men, J. Reprod. Fert., 25:185-192, 1971.

Leach, D. R. and Heller, C. G.: Effect of cyproterone acetate on testicular histology, sperm count, and levels of urinary and plasma gonadotropins and testosterone in the normal human male, Presented to the 53rd Annual Meeting of The Endocrine Society, San Francisco, California, June 24-26, 1971, Proceedings of The Endocrine Society, #206, p. A-145.

Morse, H. C., Leach, D. R., Rowley, M. J. and Heller, C. G.: Effect of cyproterone acetate on sperm concentration, seminal fluid volume, testicular cytology and levels of plasma and urinary ICSH, FSH and testosterone in normal men, submitted to the Journal of Reproduction and Fertility.

PRIVACY ACT MATERIAL REMOVED

Jo Lynn Miller

Born: , Montana

Nationality:

Education:

1971 B.A. - Chemistry & B.A. - Biology, Pacific Lutheran University, Tacoma, Washington

Honors:

Pacific Lutheran University Scholarship, Magna cum laude

Experience:

August 1971 to present Research Technician, Division of Reproductive Physiology, Pacific Northwest Research Foundation, Seattle, Washington.

PRIVACY ACT MATERIAL REMOVED

Florence Teshima

Born: , Washington

Nationality:

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-present Research Assistant, Division of Reproductive Physiology, 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 Biosciences 4, Schering Symposium on Mechanisms Involved in Conception, Berlin, 1969, Pergamon Press, pp. 121-131.

Rowley, M. J., Teshima, F. and Heller, C. G.: Duration of transit of spermatozoa through the human male ductular system, Fertil. & Steril., 21:309-396, 1970.

Rowley, M. J., Teshima, F. and Heller, C. G.: Duration of transit of spermatozoa through the human male ductular system, Urology Digest, 9:62, 1970 (abstract).

PRIVACY ACT MATERIAL REMOVED

Neil Horike

Born: , Idaho

Nationality:

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

Michael H. H. SU

Born: China

Nationality:

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-present	Research Associate, Division of Reproductive Physiology, 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, in Advances in Experimental Medicine & Biology, Vol. 10, "The Human Testis", Eugenia Rosemberg and C. A. Paulsen (eds.), Plenum Publishing Corporation, New York, 1970, pp. 249-259.

3001360

PRIVACY ACT MATERIAL REMOVED

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.
1946-68	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, Medical Service, Oregon State Penitentiary, Salem, Oregon.
1956-66	Division Surgeon, Oregon National Guard.

Yoshiko Osborne

Born: , Japan

Nationality:

Education:

High School - Hiranuma School, Yokohama, Japan
Graduated, 1949.

Experience:

1965-67	Photographic Assistant, Pacific Northwest Research Foundation, Seattle, Washington.
1967-present	Photographic Assistant and Histology Technician, Division of Reproductive Physiology, Pacific Northwest Research Foundation, Seattle, Washington.

3001361

PRIVACY ACT MATERIAL REMOVED

Glenn A. Warner, M.D.

Born: , Washington

Nationality:

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-present	Staff, Tumor Institute of The Swedish Hospital Medical Center, Seattle, Washington
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).

V. 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 thru' July 31, 1972

Grant award: $357,370.00

National Institute of Child Health & Human Development: "Human testis: study of Leydig and Sertoli cell cycles".

Grant period: February 1, 1972 thru' January 31, 1974

Grant award: $28,883.00

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 two meetings: The Society for the Study of Reproduction and the 1973 Endocrine Society Meeting. We consider these to be the most important annual meetings in our field occurring during this grant year.

VI. FACILITIES

The Oregon State Penitentiary at Salem, Oregon, is our source of 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 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 conduct the experiments personally, spending six to eight days per month at the prison.

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, BSP, 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.

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) room for radioimmunoassay procedures; (f) steroid analysis laboratory; (g) larger general laboratory used for gonadotropin analysis, rat autopsy and general chemical analysis; (h) small office; (i) laboratory for frozen sectioning and ultra-structural technique work; (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.

Major permanent equipment available includes the following: Two Zeiss Model WL binocular research microscopes: two Zeiss Photo-microscopes equipped to allow us to use phase contrast, darkfield, brightfield, and polarized illumination. A Zeiss Model GL micro-scope with accessories and a Wild M-5 stereo-microscope 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 American Optical Model 820 microtome, paraffin embedding oven, etc.; a Mettler analytical balance, Harvard trip double-beam

balances, and Roller-Smith Torsion balances for bioassay purposes; Spinco Duostat and Durrum electrophoretic cell; Spincraft automatic speed filters; International centrifuges and a Corning pH meter; Kahn-type automatic shaker, Burrell wrist-action automatic shaker, Beckman Model B spectrophotometer, Labine incubator, Rotovapor, water baths, hot plates; drying oven, Gilson volumetric fractionator, Brinkmann equipment for thin-layer chromatography, automatic pipette washer and continuous flow extraction apparatus for steroid determinations; refrigeration and freezing 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 also have 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.

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 (Model CTI) and a Packard Tri-Carb Liquid Scintillation Spectrometer.

3001366

VII. ITEMIZED BUDGET

BUDGET OUTLINE

A.	SALARIES		
	Personnel	$ 52,308.	
	Professional Collaborator	1,250.	$ 53,558.
B.	EQUIPMENT		-0-
C.	SUPPLIES		6,130.
D.	TRAVEL		3,500.
E.	MISCELLANEOUS		2,762.
F.	PENITENTIARY COSTS		10,140.
		TOTAL DIRECT COSTS	76,090.
G.	INDIRECT COSTS		22,702.
		GRAND TOTAL	$ 98,792.

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PRIVACY ACT MATERIAL REMOVED

ITEMIZED BUDGET (Continued)

A. SALARIES

Personnel		% Time Devoted to AEC project	Prorated Yearly Rate	P/R Taxes & Fringe Benefits	Total
Heller, Carl G.	Principal Invest.		$		
Rowley, Mavis J.	Senior Invest.				
Morse, Howard C.	Senior Invest.				
Teshima, Florence	Research Assoc.				
Su, Mike H.H.	Research Assoc.				
Horike, Neil	Research Assoc.				
Leach, David R.	Research Assoc.				
Savage, Grace*	Secty/Clerk				
Osborne, Yoshiko	Research Tech.				
Marty, Carole M.*	Admin. Assist.				
					$

Professional Collaborator

Daniel DiIaconi, M.D., Surgeon	$
	$ 53,558.

* Part-time employee

PENSION PLAN AND MEDICAL PLAN HAVE BEEN INCLUDED IN FRINGE BENEFITS WHERE APPLICABLE

3001368

PRIVACY ACT MATERIAL REMOVED

ITEMIZED BUDGET (Continued)

B.	EQUIPMENT		
	(None)		$ -0-
C.	SUPPLIES		
	One diamond knife	$ 550.	
	For EM including tissue preparation & photographic supplies	1,000.	
	Histological preparation - light microscope	500.	
	Radioimmunoassay		
	FSH & ICSH immunoassay $100/12 samples for both FSH and ICSH	2,400.	
	$50/month to Tumor Institute Division of Nuclear Medicine	600.	
	Testosterone-plasma-protein binding $7.50/sample	1,080.	$ 6,130.
D.	TRAVEL		
	Oregon State Penitentiary		
	Twice per month - 2 days each time Carl G. Heller, M.D., Ph.D. /trip		
	Annual Meeting of The Endocrine Soc.		
	One person	600.	
	Society for the Study of Reproduction		
	One person	500.	$

E.	MISCELLANEOUS		
	Freight charges for transporting urine, blood, and seminal fluid from Salem, and return of empty reefers	250.	
	Service contracts	1,012.	
	Communications	500.	
	Publications, reprints, lantern slides, journals, books	1,000.	$ 2,762.
F.	PENITENTIARY COSTS		
	Yearly meritorious pay ($100/year)	1,900.	
	Monthly pay ($15/month)	3,420.	
	Biopsy payment ($35/biopsy)	2,660.	
	2 inmate technicians ($90/month)	2,160.	$ 10,140.
	TOTAL DIRECT COSTS		$ 76,090.
G.	INDIRECT COSTS		
	43.4% Salaries and Wages, current "provisional" rate, DHEW agreement for research grants dated 10-29-71	22,702.	22,702.
	GRAND TOTAL		$ 98,792.

VIII. MISCELLANEOUS

A. REGULATIONS GOVERNING RESEARCH INVOLVING HUMAN SUBJECTS

See attached form letter from D. T. Chalkley, Ph.D. (p. 57)

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.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

MAR 10 1972

29

William B. Hutchinson, M.D.
President and Director
Pacific Northwest Research Foundation
1102 Columbia Street
Seattle, Washington 98104

Dear Dr. Hutchinson:

In association with its responsibilities regarding the review and acceptance of assurances on the use of human subjects, this office periodically issues a cumulative list of institutions which have filed acceptable general assurances.

Since many institutions are involved in cooperative activities, the enclosed copy of the "Forty-third Cumulative List. . ." will facilitate determining if cooperating institutions have filed acceptable general assurances and have committees with which you can work.

We are also using this letter to advise you of the current status of your own institution. Our records indicate that:

- [ ] Your revised assurance of compliance with Department of Health, Education, and Welfare policy has been accepted and you have been so notified.
- [x] Your revised assurance of compliance with DHEW policy has been received and is under review.
- [ ] Your committee structure only has been submitted.
- [ ] You have not submitted a substantive response to previous memoranda requesting compliance with DHEW policy.

The code designations (2)-(9) immediately preceding the institution's name indicate your assurance status as of February 11, 1972. If you note any discrepancy between your understanding of your status and the code listing, please let us know.

The DHEW policy permits us to interpret assurances of compliance with the older Public Health Service policy as temporarily meeting the Departmental requirements. However, institutions not in compliance with DHEW policy as of July 1, 1972, will be deleted from the cumulative list.

Sincerely yours,

D. T. Chalkley

D. T. Chalkley, Ph.D.
Special Assistant to the Director
Division of Research Grants

Enclosure 3001372

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

BOX: 046264

FOLDER: 1780 - HELLER PACIFIC NW RES. FOUNDA.

ASSIGNED NUMBER: RLHTS 94-0028

300/372-A