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Table I. Cellular associations at each stage of the cycle of the seminiferous epithelium, and duration of each stage in hours

Stage of Cycle		1	2	3	4	5	6
spermatogonia	stem cells (A_s)	A_s	A_s	A_s	A_s	A_s	A_s
	proliferating	A_{pr},A_{al}	A_{pr},A_{al}	A_{pr},A_{al}	A_{pr},A_{al}	A_{pr},A_{al}	A_{pr},A_{al}
	differentiating	A_1	A_2	A_3	A_4	In	B
spermatocytes	1st layer	PL-L	L-P	P	P	P	P
	2nd layer	P	P	Dip,Dia,MI,SII,M-II			
spermatids	1st layer	7,8,9	10,11	11,12,1	1,2	3,4	5,6
	2nd layer	16		13	13,14	14,15	15
frequency of stage (percent)*		31	16	14	15	11	13
duration in hrs		64	33	29	31	23	27

PL pre-leptotene
P pachytene
Dip diplotene
Dia diakinesis
M-I First meiotic division
M-II Second meiotic division
SII Secondary spermatocyte
} spermatocytes

1-16 Spermatid stages (from Oakberg, 1956a)

*Based on a sample of 3,200 tubules; 200 from each of 16 mice.

Table 2. Duration of each cell type in hours, time required to develop into mature spermatids, and time required to reach the ejaculate in the mouse

Cell Type		Interval to release of mature spermatids from testis (days)	Interval to appearance of mature spermatozoa the ejaculate (days)
Spermatogonia	Life-span (days)		
A_s	total reproductive span	~42*	~49*
A_{pr}, A_{al}	8.6*	35-42*	42-49*
A_1	2.7	33-35	40-42
A_2	1.4	32-33	39-40
A_3	1.2	31-32	38-39
A_4	1.3	30-31	37-38
In	1.0	29-28	36-37
B	1.0	28-29	35-36
Spermatocytes**			
preleptotene	1.3	26-28	33-35
leptotene	1.3	25-26	32-33
pachytene	~9.0	16-25	23-32
diplotene	0.9	15-16	22-23
meiotic divisions	0.8	14-15	21-22
spermatids	14	0-14	7-21
Spermatozoa			0-7

*The exact times required for transformation of A_s into spermatogonia A_{pr} and A_{al}, and for the A_{pr} to form A_1 spermatogonia, is not known, but it is assumed that at least one cycle of the seminiferous epithelium is required.

**Zygotene has been omitted from Tables 1 and 2 because recent data indicates that the synaptonemal complex is present at the time of preleptotene DNA synthesis (37,38). Since contraction of the chromosomes is gradual, the division between leptotene and pachytene is arbitrary.

Table 3. Survival of A_s spermatogonia 120 and 207 hrs after exposure to 100-1000 R x-rays

Dose - R	Percentage Survival	
	120 h	207 h
0 (c)	-	-
100		70.7
300	22.9	47.6
500	11.1	21.2
600	13.6	13.2
1000	2.6	1.6
500 + 500	5.0	2.1

Table 4. Genetic and fertility effects of chemicals on the male

Chemical	minant Lethals	Translocations	Mutations in stem cells	Fertility effects
Triethylenemelamine (TEM)	Yes	Yes	Yes	Transient sterility
Nitrogen mustard	Inconclusive	Yes		Semi-sterile
Cyclophosphamide	Yes	Yes	No	Short sterile period
Ethyl methanesulfonate	Yes	Yes	No	Transient sterility
Methyl methanesulfonate	Yes	Yes	No	Transient sterility
Mitomycin C	Yes	Yes	Yes	Transient sterility
Ethylnitrosourea (ENU)	Yes	Yes	Yes	Long period of sterility
n-Propylmethanesulfonate	Inconclusive		No	
Isopropylmethanesulfonate	Yes	Only at negligible frequencies	No	Transient sterility
6-Mercaptopurine	Yes	No	No	
Tris(1-aziridinyl)phosphine sulfide (Thio-TEPA)	Yes	Yes	No	Transient sterility
Tris(1-aziridinyl)phosphine oxide (TEPA)	Yes	Yes	No	Transient sterility
Natulan (Procarbazine)	Yes	Yes		Transient steril

ls on the male

nslocations	Mutations in stem cells	Fertility effects	Spermatogonia killing	Reference
Yes	Yes	Transient sterility	Yes	21, 33, 47, 97
Yes		Semi-sterile		24
Yes	No	Short sterile period	Yes	21, 54, 96
Yes	No	Transient sterility	Yes	5, 10, 21, 35, 36
Yes	No	Transient sterility		8, 53
Yes	Yes	Transient sterility	Yes	21, 26, 53
Yes	Yes	Long period of sterility	Yes	26, 92
	No			21, 22
Only at egligible requencies	No	Transient sterility	Yes	21, 22, 31
No	No		Yes	28, 76
Yes	No	Transient sterility	Yes	28, 53
Yes	No	Transient sterility	Yes	27, 30, 53
Yes		Transient sterility	Yes	21, 23, 27, 95

Table 5. Survival of A_s spermatogonia 3-16 days after 50 and 1) mg/kg ethylnitrosourea

Dose mg/kg	Time after injection (days)	Percentage of control
0	-	-
50	3	43.5
50	5	36.0
50	8	27.8
50	12	65.6
50	16	102.4
100	3	32.8
100	5	14.5
100	8	8.3
100	12	49.3
100	16	77.8

Table 6. Classification of follicles in the adult mouse ovary

Follicle Stage	Characteristics	Illustration
1	0 to 3 or 4 follicle cells visible	Fig. 26
2	1 complete layer of flattened follicle cells	Fig. 27
3a	single layer of cuboidal cells, no zona	Fig. 28
3b	single layer of cuboidal or low columnar cells, zona formation beginning	Fig. 29
4a	1 to 1 1/4 layers of follicle cells, zona complete but thin	Fig. 30
4b	1 1/4 to 2 1/4 layers of cells, zona completely surrounds oocyte but still not fully developed	Fig. 31
5a	2 1/4 to 3 1/4 follicle cell layers	Fig. 32
5b	>3 1/4 follicle cell layers, oocyte at mature size, zona fully developed	Fig. 33
6	many layers of follicle cells, antrum formation initiated	Fig. 34
7	large follicle, 1 or 2 small antra	Fig. 35
8	mature Graafian follicle with large antrum and thin wall (normal stage 8 follicles occur only in proestrus)	Fig. 36

Table 7. Genetic and fertility effects of chemicals in the female

Chemical	Presumed Dominant lethal effect	Mutations	Fertility effects
Benzo[a]pyrene	No		Reduced fertility
Cyclophosphamide			Sterility after prenatal or postnatal exposure
Azathioprine			Sterility to female if exposed in utero
6-Mercaptopurine			Sterility to female if exposed in utero
Ethyl methanesulfonate	Yes, for some strains	Yes	Large reduction of litter size; later onset
Methyl methanesulfonate	Yes, for some strains	Yes	Slight litter size reduction
Triethylenemelamine	Yes	Yes	Permanent sterilizing effect
Dimethylbenzanthracene (DMBA)			
3-methylcholanthrene		Yes	Sterility
Isopropyl methanesulfonate	Yes	Yes	Later onset sterility
Myleran (1,4 di-methanesulfonoxybutane)	Yes	Yes	Permanent sterility

chemicals in the female

ed lethal t	Mutations	Fertility effects	Oocyte killing	Reference
		Reduced fertility	Yes	28, 57, 58
		Sterility after prenatal or post-natal exposure	Yes	56
		Sterility to female if exposed in utero	No	56
		Sterility to female if exposed in utero	No	56
r some ns	Yes	Large reduction of litter size; later onset	No	26, 29, 32
r some ns	Yes	Slight litter size reduction	No	26, 29, 32
s	Yes	Permanent sterilizing effect	Yes	29, 32
			Yes	50
	Yes	Sterility	Yes	39, 57
s	Yes	Later onset sterility	Yes	29, 30, 32
s	Yes	Permanent sterility	Yes	29, 32

FIGURE LEGENDS

Fig. 1. Schematic representation of spermatogonial stem cell renewal (Oakberg and Huckins, 1976).

Figs. 2-10. Stem and A_{pr} spermatogonia of the mouse, and labeled spermatogonia 207 hrs after ^{3}H-TdR injection. Figs. 2-4 from whole mount, 5-10 from sections. Fig. 2, A_s spermatogonium in stage 7 among B gonia; Fig.3, A_{pr} spermatogonium in stage 6 with B gonia; Fig. 4, one A_s and two A_{pr} spermatogonia in division; Fig. 5, A_s spermatogonium in tubule section; Fig. 6, A_{pr} spermatogonia; Fig. 7, 2 degenerating spermatogonia; Fig. 8, two labeled spermatogonia, 1 heavy; Fig. 9, labeled metaphase; Fig. 10, labeled A_{pr} spermatogonia. Key to symbols for Figs. 2-22. A_s, A_s-spermatogonia; A_1-A_4, A_1-A_4-spermatogonia; In, In-spermatogonia; B, B-spermatogonia; PL-preleptotene spermatocyte; EP-early pachytene spermatocyte; P, pachytene spermatocyte; S- I, secondary spermatocyte; S, Sertoli cell; Sptd-spermatid.

Figs. 11-16. Differentiating spermatogonia of the mouse as seen in tubule whole mounts. A_1, A_2, A_3, A_4, In and B mark respective classes of differentiating spermatogonia; PL, preleptotene spermatocytes; P, pachytene spermatocytes; S, Sertoli cells.

Figs. 17-22. Differentiating spermatogonia of the mouse as seen in tubule cross sections. Sptd-2, 5, 6, and 14, steps 2, 5, 6, and 14 of spermiogenesis. A_1, A_2, A_3, A_4, In and B mark respective classes of

differentiating spermatogonia; A_s, spermatogonial stem cell; EP, early pacytene, P, pachytene; Sptd-2, Sptd-5, Sptd-7, Sptd-14, different steps of spermiogenesis.

Fig. 23. Survival of A_s spermatogonia 207 hrs after irradiation. ●, Expt. 1; ○, Expt. 2 [from Oakberg (72)].

Fig. 24. Frequency of labeled spermatozoa in the ejaculate 28.5-40.5 days after ^{3}H-thymidine injection in controls and in experimental mice given 150 mg/kg 6-mercaptopurine intraperitoneally 1 hr after ^{3}H-TdR [from Oakberg et al. (75)].

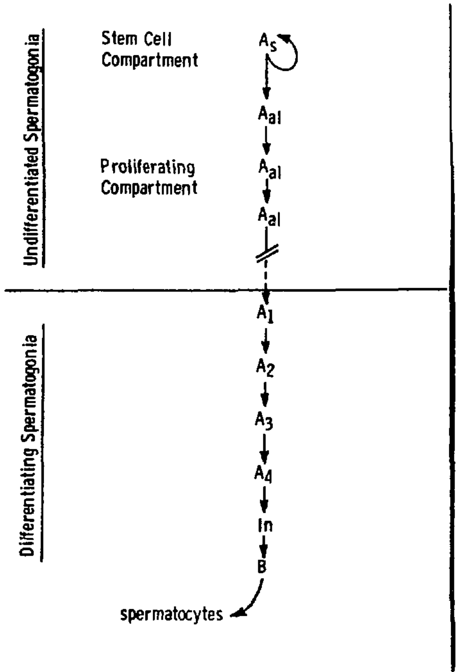
Fig. 25. The effect of 25 R x-rays at 10 days of age on decrease in oocyte number with age in 101 × C3H female mice [from Oakberg (68)].

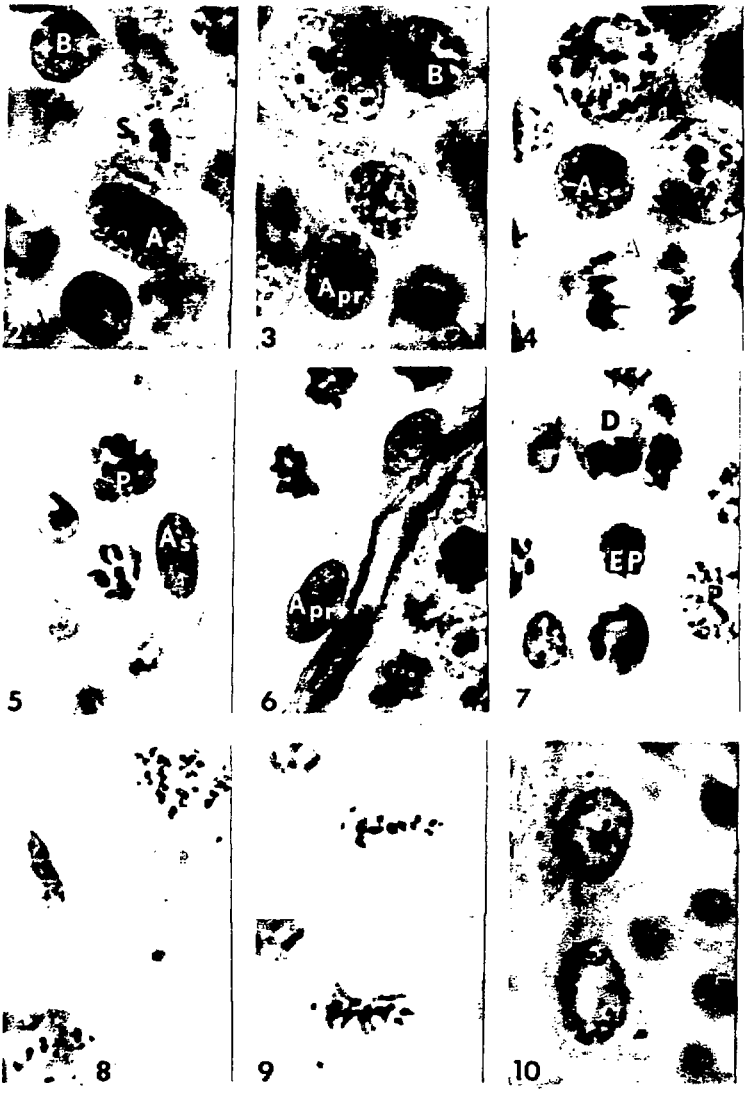
Figs. 26-32. Stages 1-5a in oocyte development of the mouse (Table 6). 26, stage 1; 27, stage 2; 28, stage 3a; 29, stage 3b; 30, stage 4a; 31, stage 4b; 32, stage 5a. All follicles normal. Figs. 26-29, X970; Fig. 30, X700; Figs. 31-32, X400.

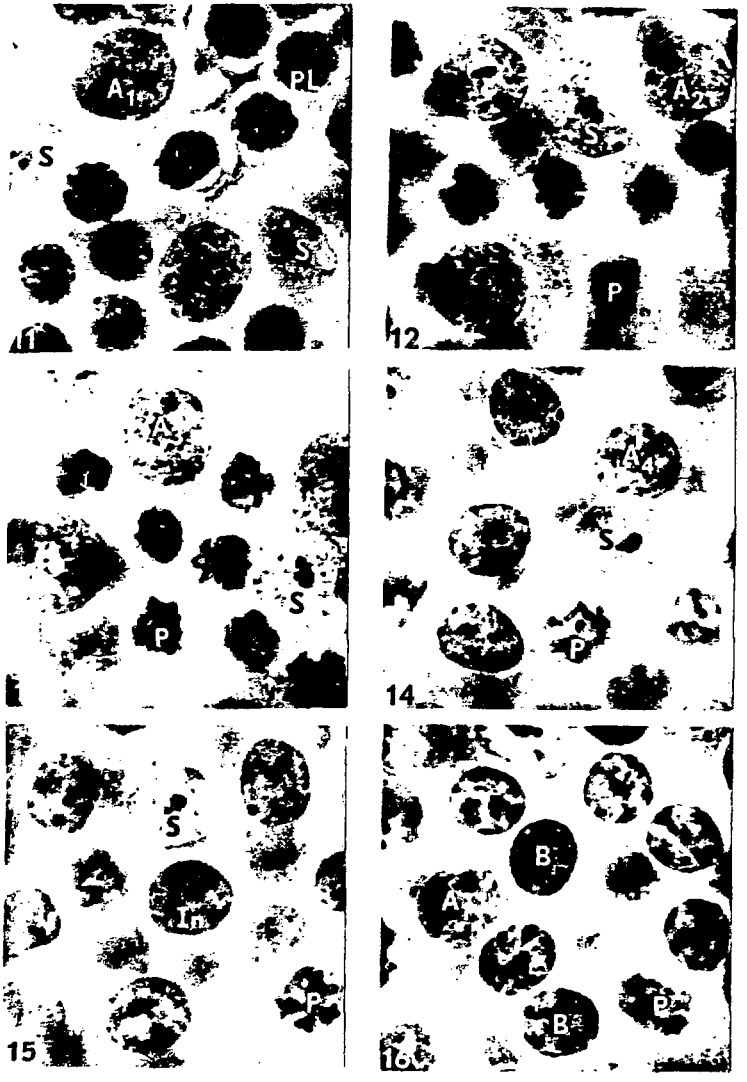
Figs. 33-36. Stages 5b-8 in oocyte development of the mouse (Table 6). Fig. 33, stage 5b; 34, stage 6; 35, stage 7; 36, stage 8. All follicles normal. Fig. 33, X400; Fig. 34, X300; Figs. 35-36, X200.

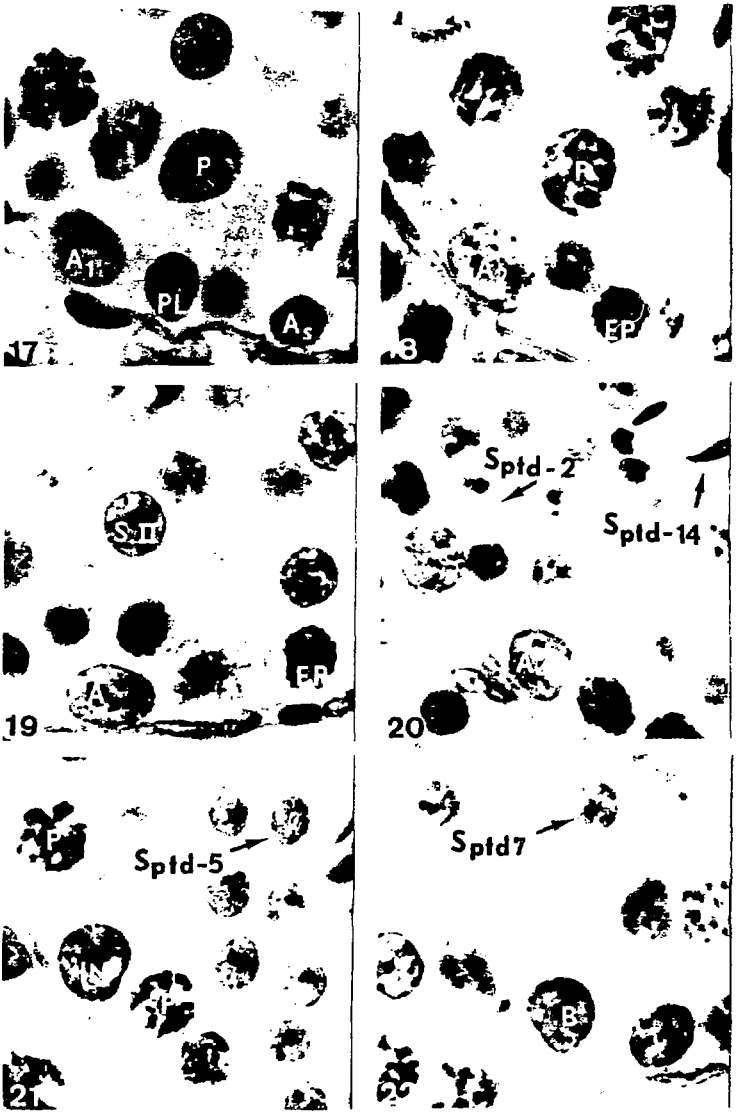
Fig. 37. Gamma-ray sensitivity of stage 1 and 2 oocytes in 10-day-old 101 × C3H female mice [from Oakberg (68)].

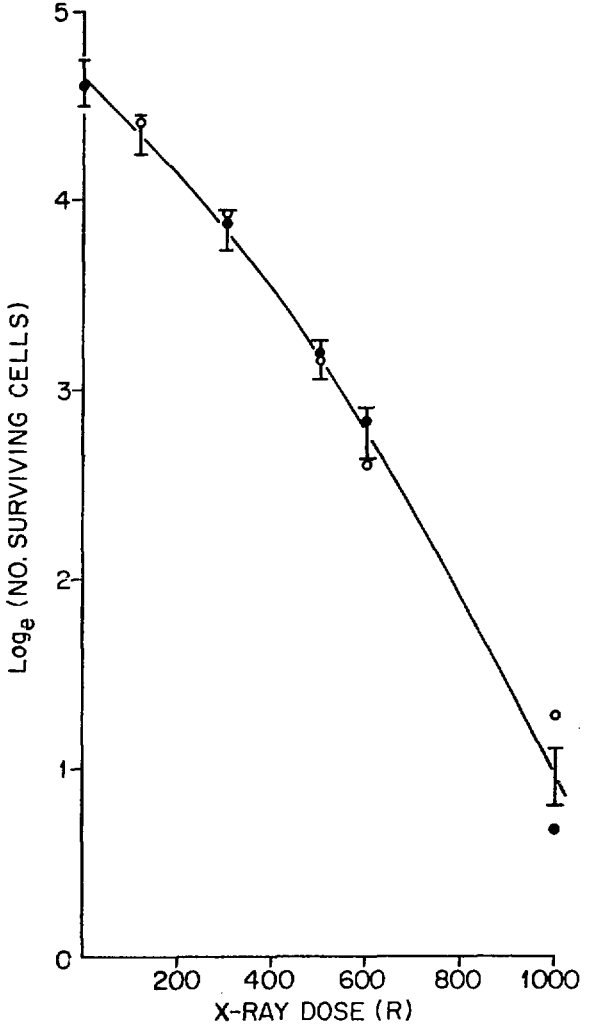
Fig. 38. Effect of 25 R x-rays at 10 days of age on litter size and reproductive span of 101 × C3H hybrid mice [from Oakberg (68)].

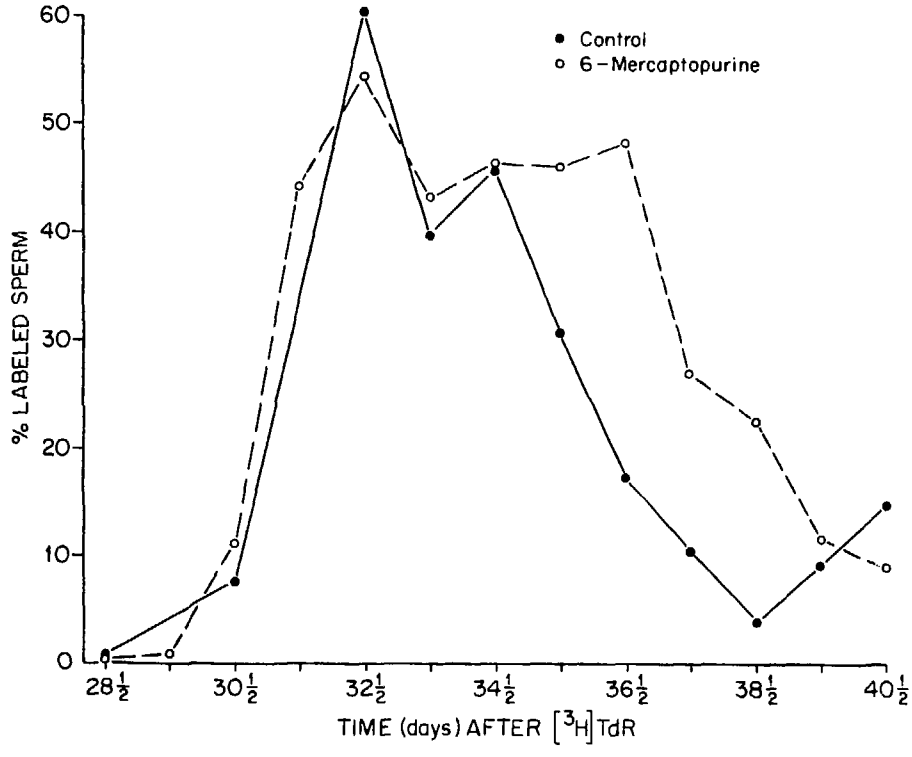

Undifferentiated Spermatogonia
Stem Cell
Compartment
As
Aal
Proliferating
Compartment
Aal
Aal
A1
Differentiating Spermatogonia
A2
A3
A4
In
B
spermatocytes


B
S
A
2
B
S
Apr
3
S
As
A
4
P
As
5
Apr
6
D
EP
P
7
8
9
10


A1
PL
S
S
11
A2
S
P
12
A
S
P
13
A4
S
P
14
S
In
P
15
B
A
B
P
16

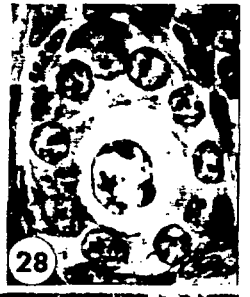

P
A_T
PL
A_S
17
EP
18
S_T
A_T
EP
19
S_{ptd-2}
S_{ptd-14}
20
P
S_{ptd-5}
21
S_{ptd7}
B


5
4
3
2
1
0
Log$_e$ (NO. SURVIVING CELLS)
200
400
600
800
1000
X-RAY DOSE (R)

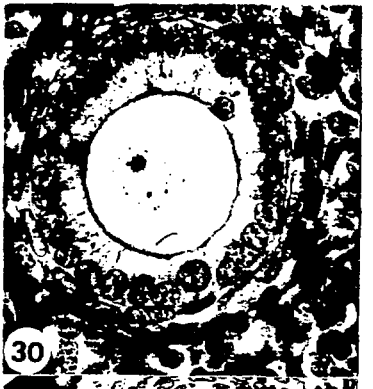

60
50
40
30
20
10
0
% LABELED SPERM
Control
6-Mercaptopurine
28½
30½
32½
34½
36½
38½
40½
TIME (days) AFTER [3H]TdR


26


27


28


29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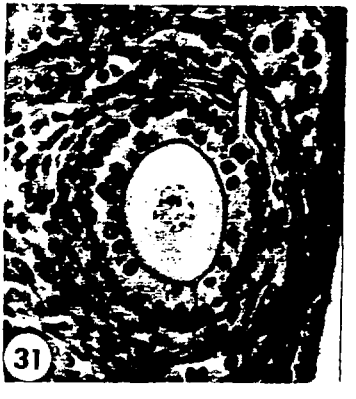
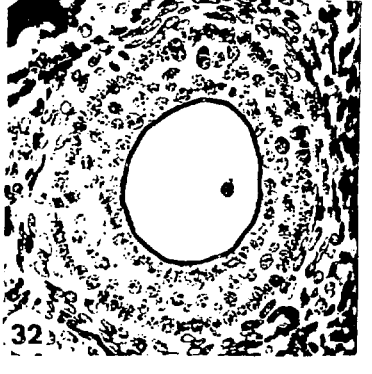
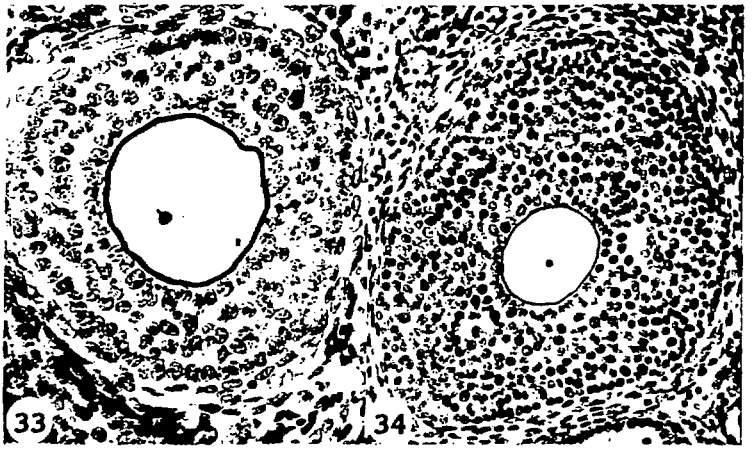
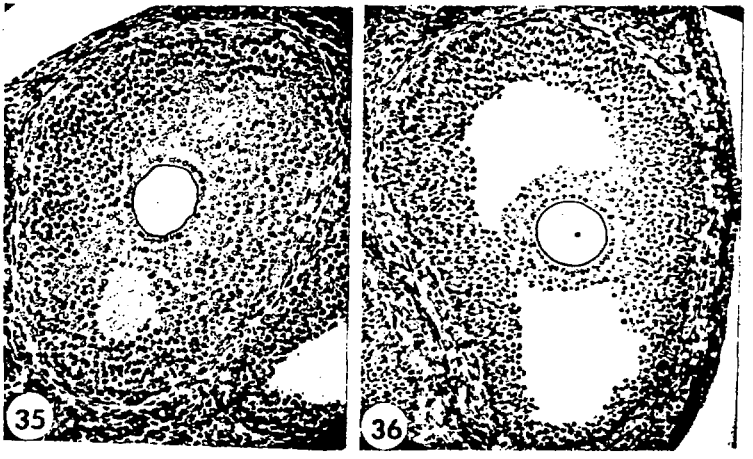
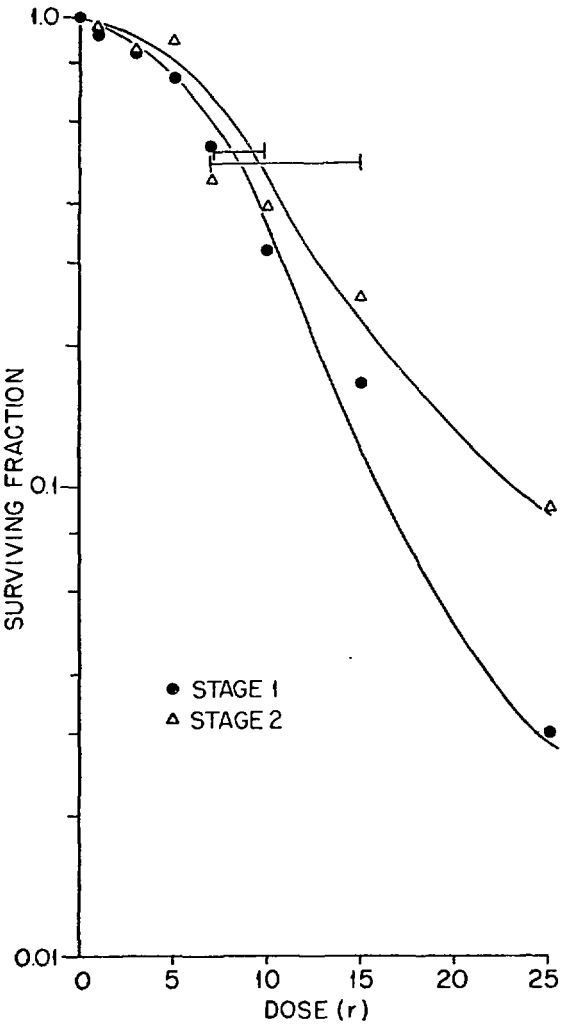
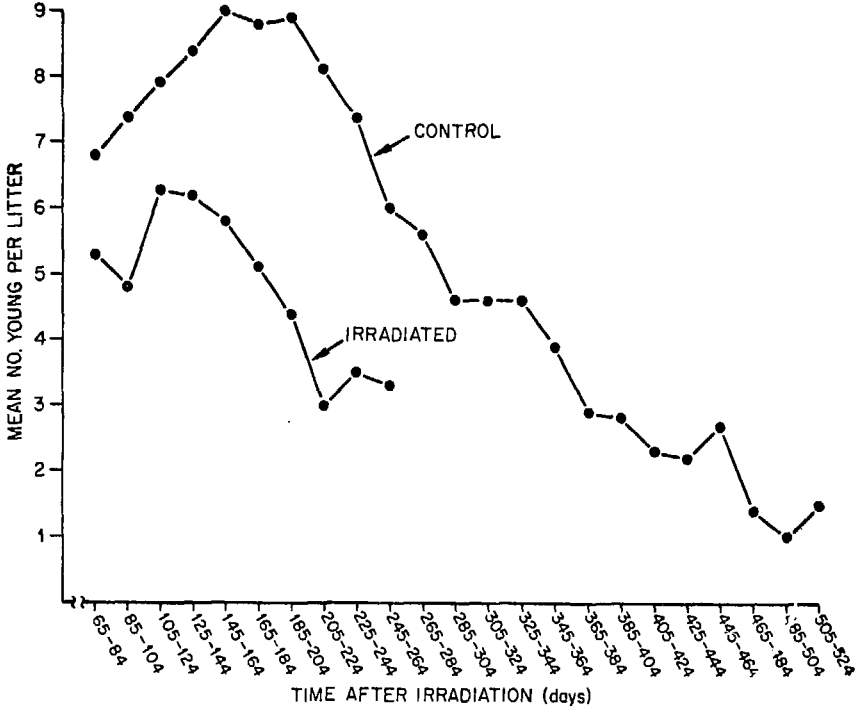

31


32


33
34


35
36


1.0
0.1
0.01
SURVIVING FRACTION
STAGE 1
STAGE 2
0
5
10
15
20
25
DOSE (r)


MEAN NO. YOUNG PER LITTER
9
8
7
6
5
4
3
2
1
CONTROL
IRRADIATED
65-84
85-104
105-124
125-144
145-164
165-184
185-204
205-224
225-244
245-264
265-284
285-304
305-324
325-344
345-364
365-384
385-404
405-424
425-444
445-464
465-484
485-504
505-524
TIME AFTER IRRADIATION (days)