Discussion. The two strains of golden hamsters used by the authors differ considerably in their susceptibility to the Lansing strain virus and in the titer of the hamster passage virus. One of the strains (MDH) is clearly not suitable for experimental research with the Lansing strain virus, and the other (TF) which gave considerably more favorable results, also is in every respect inferior to both the white mouse and the cotton rat.

The immunization of the hamster with active Lansing strain virus resulted in fairly good titers of neutralizing antibody, provided cotton-rat passage or mouse passage virus was used for immunization. In view of the small size of the hamster, use of this animal for serological work with the Lansing strain virus does not seem to present any particular advantage.

Summary and conclusions. Golden hamsters (*Cricetus auratus*) from two different sources were found to present marked differences in their susceptibility to the Lansing strain of poliomyelitis virus. Both strains were found to be markedly inferior to the white mouse and to the cotton rat as experimental animals for poliomyelitis research.

The adjustment of the inoculum at a low pH did not increase the titer of the hamster passage virus consistently. The use of the autolyzed normal mouse brain technic did not increase the infectivity of the virus for the hamster.

The intraperitoneal inoculations of mouse-passage and cotton-rat passage virus resulted in higher titers of neutralizing antibody in the golden hamster than when hamster passage virus was used.

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17161. Relation of Pregnancies to Induction of Ovarian Tumors by X-rays.

JACOB FURTH.

From the Veterans Administration Hospital and Southwestern Medical College, Dallas, Texas.

Two forces are now postulated in the genesis of ovarian tumors: direct delayed x-ray effect and a hormonal "imbalance." Ova are highly sensitive to x-rays. Their destruction disrupts the normal development of the ovarian follicles. It is believed that new formation of ova occurs in young female mice, therefore, it can be assumed that the hormonal imbalance induced by x-rays in very young mice as well as that caused by small doses of x-rays is slight and under such conditions ovarian tumors are less likely to occur. These were the thoughts that led to the pilot experiments here described.

Irradiation of Mice at 1-3 Days of Age: Earlier experiments have shown that a single exposure to 87r or more at 5-10 weeks of age will produce tumors in most mice when they reach adult age.[1]

In the first experiment reported here, mice were irradiated with 150r at 1-3 days of age and were reared by their non-irradiated mothers and allowed to live until natural death or about 20 months of age. At about 4-6 weeks of age they were weaned and a few weeks later mated with normal males. When pregnant they were separated, allowed to nurse their babies after which they were returned to the mating cage. Table Ia indicates that about 30% of these mice became pregnant and some had as many as 4 pregnancies. Ovarian tumors developed in 76%. One-half of those that were pregnant remained free from ovarian tumors as compared to 8% of those that were completely sterilized by x-rays. However, even multiple pregnancies failed to prevent the development of ovarian tumors. The time of appearance of these neoplasms is not significantly shorter than that in mice irradiated at 4-6 weeks of age.[1]

[1] Furth, J., and Boon, M. C., *Cancer Research*, 1947, **7**, 241.

TABLE Ia.
Effect of Irradiation of 1-3-Day-Old Mice (Rf/Ak) with 150r.

Length of life (mo.)	No. in group	No. pregnant	No. of pregnancies 1	2	3	4	Neoplasms Ovary	Lung	Leukemia
7	2	1	1						
8-13	5	2	2				2	1	
14-18	13	6	3	2	1		9	3	3
19-23	39	9	3	2	2	2	34	15	1
Total	59	18	9	4	3	2	45	19	4
%		30.5%					76.3%	32.2%	6.8%

Factors of irradiation were as follows: 140 kv., 5 m. amp., 25 cm target skin distance, with an inherent filtration of 1 mm of aluminum, machine delivering 120r per minute.

TABLE Ib.
Controls.

Length of life (mo.)	No. in group	Neoplasms Ovary	Lung	Leukemia
7	1	0	0	0
8-13	2	0	0	0
14-18	7	0	1	0
19-22	28	0	9	1
Total	38	0	10	1
%			(26.3%)	(2.6%)

A group of 38 closely related mice were set aside as controls for the incidence of ovarian and other tumors. No pregnancy records were kept on these mice but it may be assumed that they were fertile. None developed ovarian tumors as shown in Table Ib.

While this slight increase in the incidence of leukemia and lung tumors in x-rayed mice may not be significant, the figures are in line with those observed in earlier larger experiments.[2-5]

The brothers of the female mice irradiated at 1-3 days of age with 150r were also observed until natural death or about 20 months of age. Only one developed a testicular interstitial cell tumor.

Ten Ak mice received 150r at the advanced stage of pregnancy. The females born 1 to 5 days after irradiation were autopsied at 7 to 15 months of age. None had grossly detectable ovarian tumors. Three examined microscopically have shown changes as those seen in x-rayed animals.

Irradiation of Mice with 25-200r at 5 Weeks: In these experiments C3H mice obtained from the L.C. Strong were used. All other stocks of mice tested earlier were highly susceptible to the induction of ovarian tumors and it was thought that the use of C3H mice susceptible to breast cancers might disclose additional facts.

Table II shows that with increase of the irradiating dose the number of pregnancies is reduced while the ovarian tumor incidence is increased. The only figure out of line of this statement is the lower percentage of ovarian tumors in mice irradiated with 100r. Loss from intercurrent disease was high among these mice. The overall low tumor incidence and the above irregularity may be due in part to poor health and early death of many mice.

A summary analysis of all pertinent data is in Table III.

Comments. The data here recorded indicate that mice x-rayed at 1-3 days or 5 weeks of age can have one or several normal pregnancies although they are destined to develop ovarian tumors at a later age. The data do not answer the question which group is more liable to develop ovarian tumors, the x-rayed sterile or x-rayed fertile group. Should induction of ovarian tumors be solely due to a hormonal "imbalance" produced by x-rays, one would expect a much lower incidence of ovarian tumors in mice that go through normal

[2] Furth, J., and Furth, O. B., *Am. J. Cancer*, 1936, **28**, 54.

[3] Kaplan, H. S., *Cancer Research*, 1947, **7**, 141.

[4] Lorenz, E., Heston, W. E., Eschenbrenner, A. B., and Deringer, M. K., *Radiology*, 1947, **49**, 274.

[5] Henshaw, P. S., Riley, E. F., and Stapleton, G. E., *Radiology*, 1947, **49**, 349.

TABLE II.
Effect of Irradiation of C3H Mice at 5 Weeks of Age.

Dose	Length of life (mo.)	No. in group	No. of mice pregnant	No. of pregnancies 1	2	3	Neoplasms: Ovary	Lung	Leukemia
25r	7	2	2	1	1			1	
	8-13	7	7	5	2			1	
	14-19	8	4	1	1	2	2	1	1
	Total	17	13	7	4	2	2	3	1
50r	9-13	7	4	2	2				1
	14-19	13	7	7			4	2	
	Total	20	11	9	2		4	2	1
100r	7	1							1
	8-13	5	1	1				1	
	14-18	7	1	1			2		
	19-23	3	1	1			1	1	
	Total	16	3	3			3	2	1
200r	9-13	16	3	1			4	1	2
	14-18	5	2	1			2		1
	19-23	5					4	1	
	Total	26	5	2			10	2	3

In addition the following number of mice had borderline or "pretumors";[6] 2 in the 25r; one in the 50r; and 4 in the 200r groups.

TABLE III.
Induction of Ovarian Tumors by Small Doses and Relation to Pregnancy.

Mice, stock	C3H								Rf/Ak
Age at irradiation:							4-6 weeks[7]		1-3 days
Dose:	25r	50r	100r	200r	25-200r*	50-200r*	87r	175r	150r
% x-rayed developing ovarian tumors	12%	30%	19%	39%	24%	31%	84%	94%	76%
Sterile mice, No.	4	9	13	21	47	43			41
No. developing ovarian tumors	2	2	2	7	13 (27.6%)	11 (25.6%)			37
Pregnant mice, No.	13	11	3	5	32	19			18
No. developing ovarian tumors	0	2	1	3	6 (18.7%)	6 (31.6%)			8

* Combined.

pregnancies than in those sterilized by x-rays. The immediate hormonal "imbalance" caused by small doses of x-rays is slight if any, yet the liability of these mice to develop ovarian tumors is great. X-rays are powerful mutagens and cause tumors in organs not under hormonal control. It seems that neither the skin nor the hemopoietic tissues wholly recover from even minor damage caused by x-rays.[8] The same seems true for the ovary and it is possible that a chromosomal change is a basic factor in the genesis of neoplasm induced by x-rays. However subsequent hormonal influences may eventuate or suppress the appearance of ovarian neoplasms.[9]

Data on the factors of induction of ovarian tumors by radiation are meager. It is known that they can be induced by very small doses. The present experiments show that the amount of x-rays required to induce ovarian tumors is about 25 to 50r if given in a single dose. In the experiments of Lorenz and associates[4]

[6] Butterworth, J. S., *Am. J. Cancer*, 1937, **31**, 85.

[7] Earlier experiments cited.[1]

[8] Stone, R. S., *Radiology*, 1947, **49**, 297.

[9] Li, M. H., and Gardner, W. V., *Cancer Research*, 1949, **9**, 35.

a single dose of 50r produced tumors in 70% of the mice. Daily exposure to 0.11r (from radium) with an accumulated total dose of 90r produced ovarian tumors in about 70% of the mice.[4] No hematological changes have been detected with a daily exposure of 0.1r of gamma radiation in animals that subsequently developed ovarian tumors.[10] An increase in the ovarian tumor incidence in mice exposed to single doses of 26n to 90n of fast neutrons is on record.[5] This is probably much above the minimal tumor producing dose. If mutation is the basis of tumor induction by x-rays, with an increase in dosage an increase in the number of tumors should be anticipated. The present experiments do not exclude this possibility in the range of about 25 to 200r while earlier experiments in the dose range above 87r[1] and those of Lorenz and associates[4] failed to show such a trend.

The relation of age to tumor induction was studied by Kaplan[3] who irradiated 2 weeks to 6 months old mice with 600r administered in daily doses of 50r on 12 consecutive days. The greatest ovarian tumor incidence occurred in mice irradiated at 1 month. None was noted in 7 mice irradiated at 2 weeks but intercurrent mortality was high in this group. The present studies show that mice are susceptible even at 1-3 days of age.

A follow-up of these pilot experiments is desirable, even though each requires about 3 years. The relation of the dose of x-rays and age of hosts to the rate of ovarian tumor induction requires a closer check. The hormonal state of mice preceding tumor development and the incidence of pregnancies and abortions should be determined more accurately. The histological changes in ovaries following irradiation ante- and postpartum deserve further consideration, particularly the alleged postnatal ovogenesis and the regenerative phase which leads to neoplasms. Does irradiation induce a chromosomal change and what initiates and sustains the hormonal imbalance are questions to be answered.

Summary. Mice exposed to 50-200r of x-rays can have one or several normal pregnancies and still be liable to the development of ovarian tumors in a stock in which this neoplasm is practically non-existent.

Irradiation at 1-3 days of life with 150r sterilized only 1/3 of the mice while ovarian neoplasms appeared in about 76%. Irradiation at 1-3 days did not hasten the onset of ovarian neoplasms as compared to irradiation at 4-10 weeks. In both groups the tumors developed in middle aged and old mice. The growth rate of the tumors was likewise slow, hardly interfering with the normal life span of these animals.

It is postulated that a specific delayed x-ray effect coupled with a hormonal imbalance provoked by x-rays leads to the development of ovarian tumors.

These experiments were begun at Cornell University Medical College and assisted by Thelma Weaver Mold.

[10] Jacobson, L. O., and Marks, E. K., *Radiology*, 1947, **49**, 286.

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17162. Correction of Steatorrhea in Bile Fistula Dogs by Frequent Return of Bile.*

G. W. SEARLE AND J. H. ANNEGERS.

From the Department of Physiology, Northwestern University Medical School, Chicago, Ill.

It was previously reported that 3 to 6 g daily doses of various bile acid preparations mixed with a fatty meal were at best only partially effective in correcting the steatorrhea of bile fistula dogs.[1] This was attributed to one or more of the following possibilities: *a*,

* Supported in part by a grant from G. D. Searle & Co., Chicago, Ill.

[1] Heersma, J. R., and Annegers, J. H., PROC. SOC. EXP. BIOL. AND MED., 1948, **67**, 339.