

by any method, have lost precisely those lymphocytes which disappear in the lymphopenic reaction, characterizing the state of stress in normal mice. Irrespective of the origin of lymphopenia, the alarm reaction<sup>6-8</sup> was anomalous in mice with an absolute lymphocyte count of about 1000, and in addition to the disturbance of immunological adaptation other adaptational disturbances could be observed. It seems that the organism cannot adapt itself appropriately to changed conditions unless the lymphoid system is sound and properly functioning, and the disturbance of the latter is indicated by the anomalous alarm reaction. The present results point to the importance of the lymphoid system in processes other than immunological adaptation.

**Zusammenfassung.** Nachweis, dass Mäuse nach i.v. oder i.p. Injektion homologer Milzzellen eine Lymphopenie, verbunden mit Gewichtsverlust, entwickeln. Diese Tiere

reagieren nachher auf einen Stress in Form von Abkühlung oder Schütteln nicht mehr mit einem weiteren Lymphozytenabfall.

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<sup>6</sup> H. SELYE, *Nature* 138, 32 (1936).

<sup>7</sup> H. SELYE, *Endocrinology* 21, 169 (1937).

<sup>8</sup> C. M. HARLOW and H. SELYE, *Proc. Soc. exp. Biol. Med.* 36, 141 (1937).

## The Effects of X-Irradiation, Applied in Infancy to the Head Region, on the Reproductive System of Female Rats

Recently, we have demonstrated that the whole body exposure of infant female rats to X-rays delays the onset of puberty; this statement was equally applicable to both the animals bearing hypothalamic lesions and to just irradiated ones<sup>1</sup>. In this work we intend to describe the reaction of the reproductive tract of female rats to X-irradiation limited to the head region only. The effects of microcoagulation in the hypothalamus in head-irradiated rats are left for a later publication.

**Material and methods.** The head region of a number of 8-day-old female rats was irradiated with 400, 500, 600, 700 or 800 R of X-rays from a Siemens set (200 kV, 16 mA, filter Cu 0.5 mm, FSD — 34 cm, dose rate 103 R/min) or from a Philips set (200 kV, 16 mA, filter Cu 0.5 mm + Al 1 mm, FSD — 34 cm, dose rate 194 R/min). During the irradiation procedure the animals were anaesthetized with Kemital (thialbarbitone sodium). The number of young per mother was restricted to 6 in all experimental groups and in their controls. A certain number of animals from each of the above groups were mated with normal males.

**Results and discussion.** In all the experimental groups the opening of the vagina, taken as an index for puberty,

took place at about the same time as in non-irradiated controls. At that time the mean body weight of the experimental animals was slightly below that of the controls (see Table I). As the animals grew older the gain in body weight of the irradiated groups of rats and of the controls proceeded at about the same rate. In connection with this result of ours it is of interest to note that 600 R of X-rays applied to the head only of the neonatal rat produced stunted growth, which could not be repaired by hormone treatment<sup>2,3</sup>. Stunted growth was also obtained in our strain of random-bred rats when the dose of 600 R of X-rays was applied to the head region of 2-day-old rats<sup>4</sup>.

<sup>1</sup> P. N. MARTINOVITCH, O. K. IVANIŠEVIĆ and J. V. MARTINOVIĆ, *Experientia* 24, 839 (1968) and references cited therein.

<sup>2</sup> H. D. MOSIER JR. and R. A. JANSON, *Growth* 37, 139 (1967).

<sup>3</sup> H. D. MOSIER JR. and R. A. JANSON, *Proc. Soc. exp. Biol. Med.* 128, 23 (1968).

<sup>4</sup> N. SAVKOVIĆ, J. KAČAKI, R. ANDJUS and K. MALČIĆ, *Strahlentherapie* 130, 432 (1966).

Table I. The occurrence of opening of the vagina and the litter size of 8-day-old head-irradiated rats

Dose of irradiation	Opening of the vagina			Litter size		
	No. of rats	Age (days)	Body weight (g)	No. of rats	No. of litters	No. of new-borns per litter
400 R	22	44.1 ± 5.74	103 ± 9.5	14	14	8.4 ± 2.16
500 R	17	42.8 ± 1.77	101 ± 5.5	4	4	10.2 ± 0.83
600 R	14	43.0 ± 2.90	97 ± 12.5	7	10	8.2 ± 2.32
700 R	17	45.2 ± 6.79	99 ± 11.0	12	15	7.5 ± 2.00
800 R <sup>a</sup>	17	46.2 ± 8.76	100 ± 12.5	6	6	9.0 ± 3.44
Total irradiated	87	44.3 ± 6.01	100 ± 10.6	43	49	8.3 ± 2.45
Non-irradiated	95	44.0 ± 4.57	107 ± 14.0	27	27	8.7 ± 2.01

<sup>a</sup> The difference in the mean age at vaginal opening of this group compared with normal controls was not significant at 5% level.

Table II. Weight of corpora lutea in pregnant rats

	No. of animals	No. of ovaries	No. of corpora lutea	Mean weight of corpora lutea $\pm$ standard deviation	Weight of corpora lutea (mg)									Range
					Below 2.6			2.6–5.5			Over 5.5			
					No. of rats	No. of corpora lutea	% corpora lutea	No. of rats	No. of corpora lutea	% corpora lutea	No. of rats	No. of corpora lutea	% corpora lutea	
Irradiated														
400 R	3	3	14	4.7 $\pm$ 0.94	0	0	0	3	10	71.4	2	4	28.6	2.7–6.1
500 R	7	8	46	4.1 $\pm$ 1.29	2	8	17.4	7	35	76.1	2	3	6.5	0.6–6.4
600 R	7	8	40	4.5 $\pm$ 1.04	1	1	2.5	7	34	85.0	2	5	12.5	1.8–7.2
700 R	10	11	53	4.7 $\pm$ 1.17	2	3	5.7	9	38	71.7	5	12	22.6	1.5–6.9
Total	27	30	153	4.5 $\pm$ 1.19	5	12	7.8	27	117	76.5	11	24	15.7	0.6–7.2
Controls	24	33	173	4.1 $\pm$ 0.69	3	4	2.3	24	169	97.7	0	0	0	1.5–5.4

At occasional laparatomies and at killing of the non-pregnant rats belonging to all groups of irradiated rats, luteal bodies were always found in the ovaries. This observation also applies to the control group. Their number per ovary was, on the average, about the same as in the controls, i.e., up to 20 at most. An exception to this was seen in 3 experimental rats with 25, 25 and 32 luteal bodies respectively.

A striking difference between irradiated and non-irradiated animals was recorded in regard to the weight of corpora lutea in the ovaries of pregnant rats (Table II). The results obtained on the weight of corpora lutea in the ovaries of pregnant rats belonging to the 800 R irradiated group were close to those obtained for normal controls, indicating that the 800 R may be a limiting dose for the appearance of large-sized luteal bodies. Since results with the 800 R dose require confirmation, we have decided not to include them in the statistical studies presented in Table II and in the Figure. From Table II it can be seen that, from a group of 27 irradiated pregnant rats, 11 had ovaries with one or more luteal bodies weighing over 5.6 mg, or 15% of their total number. The largest corpus luteum recorded, measuring 2.15 mm in diameter,

weighed 7.2 mg. No corpora lutea over 5.4 mg in weight were found in the ovaries of 24 controls. On the other hand, small luteal bodies (below 2.6 mg) were present in the ovaries of both categories of animals. The histogram and the distribution of luteal bodies around the mean weight is given in the Figure.

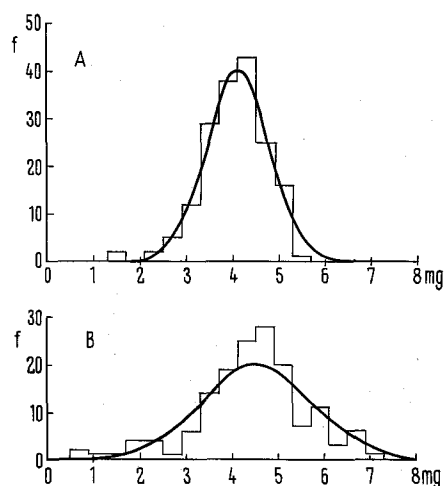
Relatively high doses of X-rays affected the weight of the pituitary. Thus, the mean weight of 83 pituitaries of normal mature animals was  $14.5 \pm 2.18$  mg, whereas 14 glands from adult rats belonging to the 600 R experimental group weighed  $7.5 \pm 2.03$  mg, and 5 glands from 800 R irradiated rats  $8.05 \pm 2.39$  mg.

Although some animals which received high doses of X-rays (700 and 800 R) looked unhealthy (weak, poor milk producers and with markedly small heads), no difference in reproducibility between the normal and the experimental animals could be detected. Daily vaginal smears, examined for longer periods, revealed more or less regular oestrus cycles (4–5 days) in all experimental groups of animals. The litter size of irradiated animals was also not affected (Table I). One fact which deserves attention was a disproportion, sometimes very pronounced, between the number of corpora lutea per ovary or irradiated pregnant animal and the number of embryos in the corresponding uterine horn. Thus, in the 500 R irradiated group, one unilaterally ovariectomized animal had 19 corpora lutea in its right ovary, only 8 of them weighing more than 3 mg, and 6 embryos plus one resorption in the uterine horn. We have been assuming that the small-size corpora lutea must be left-overs from the cycles which preceded the pregnancy state<sup>5</sup>.

*Résumé.* Les rats femelles de 8 jours, dont la tête a été irradiée à une dose atteignant 800 R croissent et se reproduisent normalement. L'ouverture du vagin s'affectue au même moment que chez des témoins. Quelques'un des corporea lutea des femelles gravides irradiées dépassent la taille et le poids maximum.

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Histogram and normal curve for the weight of corpora lutea of pregnant rats. (A) Non-irradiated controls; (B) irradiated (all doses except 800 R).

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