maximum work response was obtained.

The degree of stretch was divided into groups; the class interval being a 5% increase. Plotting average amount of work done by the muscle for each group (Fig. 1) indicates the maximum work response occurs at 30% stretch over the original length. This agrees closely with the mean of the maximum for each individual muscle strip, the mean being 26.9% with a standard deviation of 9.7.

Discussion. The average filling volume of the left atrium of the dog is stated(3) as 3.4 cc. Assuming that the atria are spherical, this gives a surface of 10.93 square cm. To increase this surface 30%, it is necessary to increase the volume to 5.03 cc. Calculations employing previously reported(3) volume elasticity curves of the left atrium indicate that this volume will result in an intra-atrial pressure of 150 mm of H_2O.

Such a theoretical analysis of the data indicate that maximum left atrial systolic work will occur at an atrial pressure of 150 mm of H_2O. Pressures higher than this will result in atrial failure with markedly reduced work output.

Summary. Strips of left atrial muscle from the dog heart were subjected to varying degrees of stretch, and the work performed during contraction was calculated. Maximum work occurred at approximately 30% stretch. A theoretical analysis of these data indicates that maximum left atrial systolic work occurs at an intra-atrial pressure of 150 mm of water.

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Received April 23, 1953. P.S.E.B.M., 1953, v83.

Effect of Pituitary Extracts on Radiation-Induced Testicular Atrophy in Rats.* (20326)

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Treatment of both local and total-body radiation injuries in man and experimental animals has, in general, produced disappointing results. One exception to such results has been the study of Momigliano and Essenberg (1) on the effect of pituitary extract on radiation-induced testicular atrophy in rats. They have reported that gonadophysin (Searle), an extract from sheep pituitaries which contains both follicle-stimulating and luteinizing hormone, hastens regeneration of the testes of albino rats when injections are begun shortly after radiation exposure and continued for several weeks.

This finding is at variance with the usual experiences in treating radiation injuries and because of the possible practical importance of this method of treatment in human cases it was considered worth while to repeat and extend this work.

Materials and methods. A total of 172 three-month-old and 48 thirty-day-old male Sprague-Dawley rats weighing 280 to 340 and 80 to 110 g, respectively, were used. The animals were maintained 5 or 6 to a cage and given water and Purina laboratory chow *ad libitum*. The details of the method of X-ray exposure have been given in a previous report(2). In the experiments in which body shielding was employed the animals were anesthetized with pentobarbital (40 mg/kg), their testes drawn into the scrotum, and their entire bodies, with the exception of the scrotum, shielded with 6.4 mm of lead during the X-ray exposures. Gonadophysin (Searle), containing both follicle-stimulating hormone (FSH) and luteinizing hormone (LH) which are stimulatory to the seminiferous tubules and interstitial cells of the testis, respectively, was injected subcutaneously twice a week.

* Work done under the auspices of the AEC.

TABLE I. Effect of Gonadotropins on X-Ray-Induced Testicular Atrophy in Adult Rats Exposed to 500 r Total Body X Radiation. 6 rats in each series.

Treatment	Time of sacrifice, wk after x-radiation	Body wt, g	Wt of testes, g/100 g body wt	Testes, % of control wt
None (controls)	4	366	.97	100
	6	372	.95	100
	8	379	.97	100
Unirradiated 12.5 RU gonadophysin biweekly	4	369	.96	99
	6	393	.91	96
	8	400	.80	82
500 r total-body X radiation	4	361	.62	64
	6	362	.39	41
	8	382	.42	43
500 r total-body X radiation plus 12.5 RU gonadophysin biweekly	4	352	.58	60
	6	354	.36	38
	8	376	.31	31

TABLE II. Effect of Gonadotropins on X-Ray-Induced Testicular Atrophy on Adult Rats Exposed to 400 r Total-Body X Radiation. 5 rats in each series.

Treatment	Time of sacrifice, wk after x-radiation	Body wt, g	Wt of testes, g/100 g body wt	Testes, % of control wt
None (controls)	4	329	1.09	100
	6	345	1.10	100
	8	401	.92	100
	12	388	.94	100
	16	391	.92	100
Unirradiated 12.5 RU gonadophysin biweekly for 4 wk	4	308	1.08	99
	6	340	.91	93
	8	384	.87	95
	12	412	.86	91
	16	377	.88	96
500 r total-body X radiation	4	267	.81	74
	6	318	.45	41
	8	310	.40	43
	12	357	.38	40
	16	327	.47	51
500 r total-body X radiation plus 12.5 RU gonadophysin biweekly for 4 wk	4	294	.61	56
	6	314	.37	34
	8	353	.34	37
	12	329	.40	43
	16	328	.54	59

At predetermined time intervals rats were killed with ether and their testes, ventral prostate, and seminal vesicles removed and weighed. Two groups of adult male rats were given a single total-body exposure to 500 r of X-rays. Immediately after exposure and biweekly thereafter the animals were given 12.5 RU (rat units) of gonadophysin subcutaneously. In one group the injections were continued to the time of sacrifice at 4, 6, and 8 weeks after radiation exposure. The second group received the injections for 4 weeks. Rats from this group were sacrificed at 4, 6, 8, 12, and 16 weeks. Two groups of immature rats were given 800 r in 3 equally divided doses 5 days apart, with the first dose given when the rats were 30 days old. In each exposure the entire body with the exception of the scrotum was shielded with lead. Immediately following the last exposure one of the groups was given biweekly injections of 10 RU of gonadophysin for 8 weeks. At the end of this time interval the rats were sacrificed. The second group of immature rats was given biweekly injections of 10 RU of gonadophysin beginning 8 weeks following the last X-ray

TABLE III. Effect of Gonadotropins on Testicular Atrophy and Regeneration following 800 r (Fractionated in 3 Equal Doses) to the Scrotum of Immature Rats. 6 rats in each series.

Treatment	Time of sacrifice, wk after last dose of x-radiation	Body wt, g	Wt of testes, g/100 g body wt	Testes, % of control wt
None (controls)	8	372	.95	100
Unirradiated 10 RU gonadophysin biweekly from time of X radiation to sacrifice	8	339	.91	96
800 r to scrotum in 3 doses beginning when rats were 30 days old	8	318	.41	43
Radiation as above. 10 RU gonadophysin biweekly from time of last X radiation to sacrifice	8	320	.36	38
None (controls)	16	380	.93	100
Unirradiated 10 RU gonadophysin eighth to 16th wk	16	354	.83	90
800 r to scrotum in 3 doses beginning when rats were 30 days old	16	339	.81	87
Radiation as above. 10 RU gonadophysin biweekly 8th to 16th wk following last dose of X radiation	16	347	.35	38

exposure and continuing for an additional 8 weeks. This latter group was included to test the effect of the hormones on regenerating testes. In all the above studies 3 control groups of rats were used. These included normal rats of the same age as the experimental animals, rats receiving a similar dose of X-rays but no injections, and rats receiving injections of gonadophysin but no X-ray exposure.

Results. No evidence was obtained in the present study that gonadophysin injections exerted any beneficial effect on testicular atrophy or regeneration in rats following X-radiation. The data are summarized in Tables I-III. In general the degree of atrophy appeared to be somewhat greater in the irradiated rats receiving gonadophysin than in those receiving only X-radiation. This finding seemed to hold for both the immature rats receiving fractionated radiation to the testes alone and for adult rats receiving a single total-body exposure. Regeneration of the testes was incomplete by 16 weeks following irradiation in the case of adult rats exposed to 500 r, although the data shown in Table II suggest that regeneration was progressing both in the animals exposed only to X-rays and in those exposed to X-rays and injected with gonadophysin. The small differences in degree of regeneration are not considered significant in view of the individual variations found between rats of the same group.

In the case of 30-day-old rats exposed to 800 r in fractionated doses, regeneration was practically complete by 16 weeks following irradiation. It is apparent from Table III that when gonadophysin was administered during the time when regeneration was occurring in the irradiated controls (8th to 16th week), such regeneration was completely inhibited in the gonadophysin-treated rats.

The weights of the accessory sex organs are not included in the tables since in no instance was there a significant difference between the weights found for gonadophysin-injected and uninjected rats. The changes in weight of these organs following X-radiation paralleled the changes seen in the testicular weights.

Gonadophysin alone was found to produce a slight but consistent degree of testicular atrophy in all the groups studied (Tables I-III).

Discussion. Injections of gonadophysin neither prevented atrophy nor increased regeneration in the testes of adult rats exposed to 500 r of X-radiation or of immature rats exposed to 800 r to the testes in divided doses. With each dosage schedule the gonadophysin

slightly intensified the atrophy. Regeneration of the testis was inhibited in the experiment in which gonadophysin was given during the period in which regeneration would normally occur. This observation is in disagreement with that of Momigliano and Essenberg, who found a beneficial effect from injection of these hormones(1). In that study, 30-day-old rats were given 800 r to the scrotum in 3 divided doses at the same intervals employed in the present experiments. The injections given were similar although the time intervals used by Momigliano and Essenberg differed slightly from those used here. From their description of the changes induced it is evident that far more degeneration was seen by them than was found in the present study. The reasons for these discrepancies are not apparent.

Five hundred roentgens delivered in single doses to the entire body of adult rats produced more severe testicular atrophy and slower regeneration than did 800 r in 3 divided doses delivered only to the testes of immature rats. It is not known as yet whether this effect is due to additional deleterious effects produced by total body irradiation, such as disturbance of other hormone systems, anemia, weight loss, etc., whether fractionating the dose simply produces less effect even though the total amount given is higher, or whether the age of the animals is responsible for the difference.

Neither dose of X-radiation was sufficient to produce sterilization. Microscopic sections which were taken in all cases indicated that some mature spermatozoa were present. It is not known whether gonadotropic hormones would exert any beneficial effect on rats given enough X-radiation to produce complete sterility. Such an effect seems doubtful in view of the fact that at lower doses atrophy is intensified by the injections.

The interstitial cells of the testes are generally believed to be relatively resistant to radiation damage(3-7). A number of investigators have prevented atrophy of the accessory sex organs following irradiation by injecting compounds rich in leuteinizing hormone(8-10). There have also been reports of questionable hyperplasia of interstitial cells following irradiation alone(4). In the present study there was no histologic evidence of radiation damage to the interstitial cells. It appeared, however, that there was a functional depression since the accessory organs which depend on androgens secreted by the interstitial cells for their maintenance of normal size become atrophic. Injections of gonadophysin, a compound containing luteinizing hormone, did not prevent atrophy of these accessory organs in X-rayed rats even though luteinizing hormone is believed to stimulate specifically the interstitial cells and increase the androgen output.

Summary. A study has been made on the effect of gonadophysin (Searle), an extract from sheep pituitaries which contains both follicle-stimulating and luteinizing hormone, on radiation-induced testicular atrophy in rats. Adult and immature male rats were given single exposures of 500 r total-body X-radiation and 800 r of X-radiation to the testes only in 3 fractionated doses, respectively. Gonadophysin was injected twice weekly for the first 4 to 6 weeks or from the 8th to 16th week following radiation exposures to evaluate the effectiveness of this agent on testicular atrophy and regeneration. Gonadophysin was found to increase slightly the degree of testicular atrophy and to inhibit testicular regeneration in rats.

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Received April 24, 1953. P.S.E.B.M., 1953, v83.