

Mitotic Activity in Male and Female Rat Hypophyses After Combined Injections of Androgen and Estrogen.*

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Since mitotic activity in the hypophysis of female rats is increased significantly after injections of the female hormone estrogen,¹ the question arises whether the male hormone might not likewise affect the proliferative activity in the hypophysis of either male or female animals. There is some evidence that androgen inhibits the activity instead of stimulating it. Wolfe and Hamilton² found that the pituitaries of rats were only slightly increased in weight after 10 daily injections of both testosterone-acetate and estrone whereas the increase was considerable after the same number of injections of estrone alone.

In the present experiments combined injections of androgen and estrogen were likewise made into rats to see if there is a modification in mitotic activity of the anterior hypophysis. Also the mitotic activity of male rats is compared with that of female rats after equivalent injections of estrogen.

In determining the mitotic activity, all dividing cells are counted in one or more 3 micra coronal sections of the hypophysis and the number present per square mm of section is calculated. The androgen and estrogen used is testosterone propionate and alpha-estradiol benzoate, respectively, both of which were dissolved in sesame oil.[‡] All injections were made subcutaneously. The female animals were ovariectomized approximately one month previous to the time of injections.

The tabulation of the experiments shows the number of animals, the average age of the animals in each group, the hormones injected and the mean and standard error of the mean of the mitoses per sq mm of section. Injections of estrogen were made either 48 and 72 hours before killing the animals or, as in Groups 5, 6, and 7, they were made 28, 36, 52, and 60 hours before killing. In Groups 2 and 3 the androgen was injected 24, 48, and 72 hours before killing, and in Group 6 it was injected at the same times as the estrogen.

The number of dividing cells in the hypophysis of ovariectomized females and in that of normal males is uniformly low in animals 3 months of age or older (Groups 1 and 8). Only 2 or 3 mitotic figures are usually seen and at the most 5 to 10 occur in an entire section that includes 5 or 6 square mm.

Injections of estrogen result in a considerably increased mitotic activity in both ovariectomized females and normal males (Groups 4, 5, and 7). In all 3 groups the average number of mitoses is about 20 per sq mm. Statistically there is no significant difference in the mitotic activity of the male Group 7 and female Group 5, both of which received estrogen ($P = .8$).[§] In the males there is no evidence that the testicular androgen modifies the activity of the injected estrogen. The male hypophysis thus appears to respond to the estrogen about the same as that of the female. However, in the male there is a higher percentage of chromophil cells undergoing division than there is in the female, although, as in the female, the majority of divisions occur in the chromophobes.

Injections of androgen into ovariectomized

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¹ Hunt, T. E., *Anat. Rec.*, 1947, **97**, 127.

² Wolfe, J. M., and Hamilton, J. B., *Endocrinology*, 1937, **21**, 603.

‡ The estrogen (Progynon-B) and androgen (Oreton) were kindly furnished by the Schering Corporation, Bloomfield, N.J.

§ Fischer's table of P was used to determine statistical significance. P must have a value of less than .05 before a difference can be considered as possibly significant.

TABLE I.
Mitotic Activity in the Hypophysis of Rats.

Group	No. of animals	Age mean	Sex	Inj. of androgen and/or estrogen μ g	Mitoses per mm ² Mean $\pm$ S.E.
1	5	117	♀		1.20 $\pm$ 0.25
2	4	102	♀	3x500A	1.17 $\pm$ 1.07
3	6	101	♀	3x500A + 2x25E 3x1000A + 2x25E	17.0 $\pm$ 2.76
4	10	97	♀	2x25E	20.0 $\pm$ 1.94
5	10	91	♀	4x17E	21.3 $\pm$ 1.55
6	6	94	♂	4x500A + 4x17E	18.7 $\pm$ 4.20
7	6	93	♂	4x17E	20.8 $\pm$ 2.00
8	9	92	♂		.52 $\pm$.13

females does not change the mitotic activity in the hypophysis (Group 2). The glands of only 4 animals were examined but since in all of these the activity is uniformly low, it seemed unnecessary to extend the series.

In the males and females which received both androgen and estrogen (Groups 3 and 6) the average mitotic activity does not differ significantly from either the male or female groups which received estrogen alone. In comparing Group 3 with 4 statistically, $P = .35$, and 6 with 7, $P = .65$. The animals in Group 3 that had injections of 500 μ g of androgen show a somewhat lower activity

than those which had 1000 μ g, but the difference is not believed to be important.

Summary. The estrogenic hormone, alpha-estradiol benzoate, stimulates mitotic division in the cells of the anterior hypophysis of both male and female rats and, provided the animals are about the same age, an equal amount injected results in approximately the same mitotic activity. When the androgen, testosterone propionate, is injected with the estrogen in either male or female rats, the mitotic activity is not significantly different from that resulting from injections of estrogen alone.

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Increased Susceptibility of Mice to Swine Influenza as a Result of Methionine Injections.*

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In recent years numerous experiments have been reported on the effects of various dietary constituents on the susceptibility of animals to viral infections. I reported in 1942 that methionine decreased the susceptibility of the rabbit to vaccinia.¹ It seemed advisable however to repeat these experiments in the mouse using swine influenza as the virus. When

mice on an adequate diet are injected with methionine there is a slight increase rather than decrease in susceptibility to swine influenza. But, if methionine were given to mice on a low protein diet, a marked increase in susceptibility occurs. This paper is to report such experiments.

Since poor or malnutrition from many causes will result in an increase in the animal's resistance to viral infections² it was thought

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¹ Sprunt, D. H., *Proc. Soc. Exp. Biol. and Med.*, 1942, **51**, 226.

² Sprunt, D. H., *J. Exp. Med.*, 1942, **75**, 297; Foster, C., Jones, J. H., Henle, W., and Dorfman, F., *J. Exp. Med.*, 1944, **80**, 257.