Summary. 1. The thymus gland of adrenalectomized male rats maintained for 45 days on sodium chloride does not undergo the involution characterizing the gland in normal untreated animals or those treated with sodium chloride. Sodium chloride as employed appears to exert no consistent effect *per se* on the thymus or lymphoid tissues of the unoperated control. 2. The systemic lymph nodes of adrenalectomized animals maintained on sodium chloride were heavier than those of normal untreated animals or normal animals given sodium chloride. It is notable that the mesenteric lymph nodes do not undergo a comparable gravimetric increase.

11650 P

Effects of Progesterone Upon the Uterus of the Mouse.*

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The fragmentary understanding of the involvement of the corpus luteum in various phases of reproductive activity in the rat and mouse seems in no small measure to be attributable to the inadequacy of the available criteria of activity of the corpus luteum. It seems that no morphologic uterine response to progesterone has been reported for the mouse, and in the rat apparently the only reported effect is mitosis in the epithelium.[1] In the course of a study of the healing of uterine wounds,[2] a definite morphologic response was observed in the uteri of ovariectomized mice receiving progesterone. The experiments described here were conducted to examine the possibility indicated by that observation.

Only young adult mice of the Strong NH strain were used. All the animals were ovariectomized and a period of 3 weeks elapsed between operation and the start of treatment. One group of 6 mice was given daily injections of 0.25 mg of progesterone,† and another group of 6 received 0.5 mg of progesterone daily. Three animals

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1 Hisaw, F. L., Greep, R. O., and Fevold, H. L., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 840.

2 Hooker, C. W., *Anat. Rec.*, in press.

† Supplied by Ciba Pharmaceutical Products, Inc., through the courtesy of Mr. R. C. Mautner.

were given 0.016 mg (500 I.U.) of estradiol benzoate‡ every second day. Three animals received 0.5 mg of testosterone‡ daily. Both progesterone and testosterone in daily doses of 0.5 mg each were given to 2 animals, while 2 other animals were given 0.5 mg progesterone daily and 500 I.U. of estradiol benzoate every second day. The hormones were in solution in sesame oil in such concentration that the injection dose was 0.05 cc. The animals receiving progesterone alone were killed for study after 3 to 6 days of treatment. The remaining animals were autopsied after 5 days of treatment. For comparison 5 animals were killed 26 days after ovariectomy; of these, 4 had received daily injections of 0.05 cc of the bland oil and one was untreated.

Upon gross examination the uteri of the mice given progesterone were slightly larger than the uteri of the untreated animals and were definitely hyperemic. The uteri of the animals receiving this hormone exhibited no contractility upon mechanical or thermal stimulation.

Microscopically the progesterone elicited responses in all the tissues of the uterus. The epithelium was somewhat taller than in the untreated castrates and contained occasional mitotic figures. Mitoses were also present in both layers of the myometrium. The tunica propria presented the most marked changes. This layer was somewhat thickened and slightly edematous, and its blood vessels were dilated and apparently more numerous especially in the basal portion. Numerous mitoses were present—often as many as 10 in a single high power field. The nuclei of the stroma cells had transformed from the rather fusiform, somewhat pyknotic type of the untreated castrate into larger, spherical, vesicular nuclei resembling nuclei of granulosa cells of the ovary. Although these nuclear changes in the stromal cells were the most characteristic response to progesterone. not all the nuclei were thus affected, and in basal portions many nuclei were affected slightly if at all. On the basis of the nuclear changes alone it is impossible to confuse such a uterus with that of an untreated castrate. The smaller dose of progesterone seemed as effective as the larger, and the response was almost as marked at 3 days as after 6 days of treatment.

The uteri of the estrogen-treated animals exhibited the characteristic hyperemia, distention, irritability, epithelial growth, and edema. The nuclei of the stromal cells, although widely separated, were fusiform and pyknotic as in castrates and did not resemble

‡ Furnished by the Schering Corporation through the kindness of Dr. E. Schwenk.

stroma cell nuclei after treatment with progesterone. In the animals receiving progesterone in addition to the estrogen the cellular changes in the tunica propria seen after progesterone alone were added to the typical estrogen effects.

In the androgen-treated animals the endometrium was more or less intermediate between that of the castrates and of the animals receiving progesterone. The tunica propria was slightly thickened and more fibrous than in the castrates; but the stromal nuclei did not become spherical and vesicular, nor were many mitoses in evidence. In the animals receiving both testosterone and progesterone the effects of both substances were seen in the stroma, although the progesterone characteristics were less marked than in animals receiving progesterone alone.

The tunica propria of the uteri of the few pregnant and lactating mice which have been examined also exhibited nuclei like those described in the castrates receiving progesterone. Apparently, therefore, both endogenous and injected progesterone elicit morphologic change in the uterus of the mouse. Moreover, the nuclear changes in the uterine tunica propria may constitute a specific response to progesterone in the mouse.

Summary. With or without concomitant treatment with estrogen, the daily injection of 0.25 or 0.5 mg of progesterone into mice ovariectomized 3 weeks previously evoked mitosis in all the tunics of the uterus. The nuclei of the cells of the uterine tunica propria became larger and transformed from the fusiform, pyknotic type into vesicular nuclei. The latter condition was also seen in pregnant and lactating mice. Neither estrogen alone nor androgen provoked this morphology.

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Effect of Desoxycorticosterone and Testosterone on Water and Chloride Metabolism.

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Selye, *et al.*,[1] showed that high doses of estrogens cause water retention in the rat and this has subsequently been confirmed in the dog by Thorn and Engel.[2] These latter investigators claimed,

1 Selye, H., Harlow, C. M., and Collip, J. B., *Endokrinol.*, 1936, **18**, 81.

2 Thorn, George W., and Engel, Lewis L., *J. Exp. Med.*, 1938, **68**, 299.