gradual decline with the advance of the lactation period in both species.

Summary. In the case of both the rabbit and the guinea pig the lactogen content of the AP does not increase during early pregnancy and very little during late pregnancy. After parturition a distinct increase is noted in both species although the rise in the case of the rabbit is much higher than in the guinea pig. On the other hand, the increase seems to be somewhat slower and more gradual in nature in the rabbit than in the guinea pig which seems to reach its peak almost immediately after parturition.

In both species there is evidence that the absence of nursing results in an increased lactogen content of the AP whereas following nursing the pituitary contains less lactogen. It has been suggested previously that the stimulus of nursing in some way causes a discharge of lactogen from the pituitary.[1]

10947

Effect of Testosterone Propionate on Genital Tract of Adrenalectomized and Ovariectomized Immature Female Rats.

IRA T. NATHANSON AND RULON W. RAWSON. (Introduced by J. C. Aub.)

From the Laboratories of the Collis P. Huntington Memorial Hospital of Harvard University.

In an earlier communication the effect of testosterone upon the genital tract of ovariectomized and hypophysectomized immature female rats was reported.[1] The essential findings were (a) a direct effect upon the vagina, producing premature opening and an estrous response; (b) a direct effect upon the uterus; and (c) an indirect effect upon the ovary through stimulation of the anterior pituitary. The nature of the vaginal and uterine response to testosterone was not clear, since it has not been shown that this hormone has estrogenic properties. Conversion of testosterone to an estrogen by the adrenal was considered as a possibility. Consequently, in this experiment the effect of testosterone on the genital tract was studied in immature female rats that had been adrenalectomized or both adrenalectomized and ovariectomized. These experiments were per-

[1] Nathanson, I. T., Franseen, C. C., and Sweeney, A. R., Jr., PROC. SOC. EXP. BIOL. AND MED., 1938, **39**, 385.

formed on immature rats weighing between 55 and 65 g. Maturity generally occurs at a weight of from 110 to 120 g.

Experiment No. 1. Twelve intact immature female rats were given a single injection of 5.0 mg of testosterone propionate* in sesame oil to serve as controls for the subsequent experiments.

Result: All animals had vaginal opening within 96 hours, uterine enlargement and ovarian stimulation, which was in accord with our previous findings.

Experiment No. 2. Ten immature female rats were bilaterally adrenalectomized and ovariectomized in one operation. They were given a total of 5 cc of 0.9% NaCl subcutaneously in divided doses daily. In addition, 5 of these received 6 dog units of cortin† subcutaneously once within 6 hours after operation. Twenty-four hours following operation 5.0 mg of testosterone propionate were given to each of these 10 animals.

Result: (a) Vaginal opening occurred within 120 hours in all animals. In 7 of these it occurred within 96 hours. Microscopic examination revealed mucification and cornification of the vaginal epithelium. (b) Uterine enlargement and edema was noted in all animals. Microscopic examination showed an increase in the stroma, in vascularity, and in the number of uterine glands.

Treatment with saline was discontinued in all animals immediately after vaginal opening. Weight curves and the survival period were taken as criteria of complete adrenalectomy. All animals except one died within 144 hours after cessation of treatment. The one animal which survived was believed to have sufficient adrenal tissue remaining to maintain life.

Experiment No. 3. Six immature female rats were submitted to bilateral adrenalectomy and were then given 5 cc of 0.9 NaCl subcutaneously in divided doses daily. Six dog units of cortin were given subcutaneously to each animal only once within 6 hours after operation. Twenty-four hours after operation 5.0 mg of testosterone propionate were given subcutaneously.

Results: (a) Vaginal opening occurred in all animals within 96 hours. Microscopic sections showed the changes described above. (b) Uterine changes were also similar. (c) The ovaries showed definite follicle stimulation and in one instance evidence of early corpus luteum formation.

Treatment with saline was discontinued as soon as vaginal opening

* We are indebted to Doctors Gregory Stragnell and Max Gilbert of the Schering Corporation for a generous supply of testosterone propionate (Oreton).

† Eschatin—Parke, Davis & Co.

was noted. All animals died within 72 hours after cessation of this treatment.

Experiment No. 4. Five immature female rats were submitted to bilateral adrenalectomy and were then given 5 cc of 0.9 NaCl subcutaneously in divided doses, daily. No other treatment was given. The animals were sacrificed 7 to 9 days after the operative procedure.

Results: Vaginal opening did not occur in any animal. Histological examination of the vagina, uterus, and ovaries did not reveal any perceptible alteration from the normal untreated controls.

It appears from the results summarized above that testosterone propionate will act directly upon the vagina and uterus of the adrenalectomized, and adrenalectomized and ovariectomized immature female rats. It is also capable of stimulating the ovary by way of the hypophysis[1] even in the absence of the adrenals. The cortin given only once post-operatively may have aided this reaction, but it does not seem probable, since the reaction occurred in 5 rats which had not been so treated. One cannot be absolutely certain that all adrenal tissue was removed, even though a careful autopsy was performed on all the animals. At any rate, they all showed definite adrenal insufficiency with the exception of the one animal. Death occurred invariably during a convulsion. It does not seem probable, therefore, that sufficient adrenal tissue remained to change the chemical structure of testosterone if it could not maintain life.

In general, the animals which had bilateral adrenalectomy and ovariectomy survived longer than those which had bilateral adrenalectomy only.

Conclusions. Testosterone propionate acts directly upon the uterus and vagina and indirectly upon the ovary *via* the hypophysis in operatively adrenal-insufficient immature female rats.‡

‡ We are indebted to Dr. Joseph C. Aub for valuable suggestions in carrying out this experiment.