

the peritoneal fluid-serum calcium ratio increased to 83% and 91% with a constant or a falling serum calcium concentration suggests the possibility that the parathyroid hormone may increase the diffusible calcium at the expense of the nondiffusible serum calcium fraction under certain conditions. Why the production of these phenomena should be effected by the removal from the organism of such relatively small amounts of calcium as 183 and 201 mg under the conditions of the experiment cannot be stated at the present time.

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Influence of Testosterone Propionate on Vaginal Opening in the Immature Albino Rat.*

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Butenandt and Kudzusz¹ observed that androgenic substances administered to immature female rats produced premature vaginal opening. Since then Salmon² has attempted to determine whether this effect (vaginal opening) was the result of a direct action of the androgenic substance upon the genitals or whether the effect was secondary to a stimulating action of the androgen on the ovary. Because Salmon observed follicle stimulation or luteinization (or both) in his test animals, he concluded that the premature vaginal opening which he noted was due to the effect of the testosterone propionate and androstenediol (which he used) upon the ovary. Since this author did not use spayed animals it is difficult to see how a direct effect of the androgenic substance upon the genital organs can be ruled out. For this reason, the following experiments which utilized both non-castrate and castrate animals as test objects are reported.

Fifty-two female albino rats (*Mus norvegicus*—var. *alba*) of Wistar Institute stock 26 days of age were divided into 4 groups consisting of (1) 16 non-spayed test animals; (2) 10 spayed litter-mate test animals; (3) 16 non-spayed litter-mate controls; and (4) 10 spayed litter-mate controls. Castrations were carried out at 22

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¹ Butenandt, A., and Kudzusz, H., *Hoppe-Seyler's Z. Physiol. Chem.*, 1935, **237**, 75.

² Salmon, U. J., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **35**, 49.

days of age. The test animals were treated with injections of testosterone propionate (Perandren-Ciba) in a dosage of one mg daily (except Sunday) which were administered intraperitoneally beginning on the 26th day of age. The control rats remained uninjected. All animals were maintained under similar environmental conditions, being fed on purina dog chow (cubes) daily and green vegetables twice weekly. Water was constantly present.

Daily observations of all animals disclosed that vaginal opening occurred in the treated normal animals at 31 to 35 days of age, in the treated spayed animals at 32 to 35 days and in the normal controls at 40 to 48 days of age. While some of the spayed controls acquired spontaneous vaginal opening at 65 to 70 days, others failed to show this phenomenon at 75 days of age.

When the means of these observed ages are compared (Table I) it is seen that vaginal opening in the treated non-spayed and spayed animals occurred 11.7 ± 0.54 and 10.5 ± 0.60 days respectively earlier than in the normal controls, while the treated non-spayed animals showed this phenomenon only 1.2 ± 0.41 days sooner than the treated castrate group.

TABLE I.
Showing a comparison between the ages (variation and means) at which vaginal opening was noted. The differences between groups are compared and the ratios between the differences and their respective probable errors listed.

Group	No. of Animals	Age at Time of Vaginal Opening		Difference Noted	Critical Ratio
		Range	Mean $\pm$ P.E.		
Castrate test	10	32-35	33.8 ± 0.34	1.2 ± 0.41	2.92
Normal test	16	31-35	32.6 ± 0.23		
Normal control	16	40-48	44.3 ± 0.49	11.7 ± 0.54	21.66
" test	16	31-35	32.6 ± 0.23		
Normal control	16	40-48	44.3 ± 0.49	10.5 ± 0.60	17.50
Castrate test	10	32-35	33.8 ± 0.34		

It is interesting to note that vaginal smears made at the time of vaginal opening failed to reveal a full estrus picture in any of the animals examined.

From these results it is seen that testosterone propionate (Perandren-Ciba) had a marked stimulating effect on vaginal opening in both non-spayed and spayed immature animals. That this observation is in all probability highly significant can be appreciated from the high critical ratios (C. R.) noted in the table.

On the other hand, in spite of the fact that the critical ratio between the castrate and non-castrate test animals approaches "3"

(actually 2.92 in Table I) which would ordinarily lead one to suspect a probable significance in the difference noted, such significance is questionable for the following reasons. First, it will be noted (Table I) that while the vaginal opening of the treated non-castrate animals occurred in some cases a day earlier than in some of the treated castrate rats, the vaginas of all treated animals were open by the 35th day. Secondly, in some animals not included in the experiments herein reported, vaginal opening under similar conditions was seen to occur on the 30th day of age. Finally, in experiments reported elsewhere⁸ it was observed that the Graffian follicle under the influence of chronic injections of testosterone propionate was actually inhibited in growth and failed to ovulate.

Conclusions. Testosterone propionate (Perandren-Ciba) stimulates vaginal opening in both non-spayed and spayed immature female rats. This substance, therefore, does have an effect on the vaginal zone which is independent of the ovary. Because such direct effect has been noted and because the age at which vaginal opening occurs in the non-spayed and spayed test groups corresponds so closely it is believed that the intact ovary plays but a negligible part in the process under the conditions of these experiments.

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Effect of Sulfanilamide on Experimental Tuberculosis in the Guinea Pig.

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Sulfanilamide has been found by Rich and Follis¹ to exert a markedly inhibitory effect upon the development of experimental tuberculosis in the guinea pig. These authors noted that 100 mg of sulfanilamide in a single daily dose did not modify the tuberculous process, while 2 daily doses of 100 mg produced considerable inhibition. This was much more marked when 500 mg of sulfanilamide, divided into 4 doses, were given daily. In their experiments treatment was commenced 3 days before the subcutaneous injection of the human tubercle bacilli. Smithburn,² on the other hand, failed to

⁸ Rubinstein, H. S., *J. A. M. A.*, in press.

¹ Rich, A. R., and Follis, R. H., Jr., *Bull. Johns Hopkins Hosp.*, 1938, **62**, 77.

² Smithburn, K. C., *Proc. Soc. Exp. Biol. and Med.*, 1938, **38**, 574.