9618

Effect of Testosterone Propionate upon Gonadotropic Hormone Excretion and Vaginal Smears of Human Female Castrate.

UDALL J. SALMON.* (Introduced by R. T. Frank.)

From the Department of Laboratories of the Mount Sinai Hospital, New York City.

It has been previously shown that the excessive gonadotropic hormone excretion which occurs after castration in females can be controlled by the administration of adequate amounts of estrogenic substance.[1] Butenandt and Kudzus[2] have shown that testosterone, if given in sufficiently high doses, causes premature opening of the vagina in infantile rats.

The present investigation was undertaken to determine (a) whether the gonadotropic hormone can be made to disappear from the urine of a female castrate by the exhibition of male hormone and (b) whether at the same time an estrogenic effect can be demonstrated in the vaginal smears of the castrated patient.

The patient studied was 46 years of age and had had an hysterectomy and bilateral salpingo-oophorectomy 6 years before the present investigation. During a preliminary study of 20 days (started February 13, 1937) the urine was found to be constantly positive for G. H. (the excretion varying from 13 to 27 R.U. per day) and the vaginal smears were uniformly negative. (Fig. 1.)

The acetone precipitation method was used for G.H. determination in the urine.[3] The vaginal smears were prepared and graded according to the technic and classification previously reported,[4] reactions I and II representing "negative" smears and III and IV "positive" smears.

The patient was given 815 mg. testosterone propionate† in solution in sesame oil in divided doses intramuscularly over a period of 27 days. Individual doses varied from 10 to 50 mg. G.H. deter-

* Hiram N. Vineberg Research Fellow.

1 Frank, R. T., and Salmon, U. J., PROC. SOC. EXP. BIOL. AND MED., 1935, **33**, 311.

2 Butenandt, A., and Kudzus, H., *Hoppe-Seyler's Z.*, 1935, **237**, 75.

3 Frank, R. T., Salmon, U. J., and Friedman, R., PROC. SOC. EXP. BIOL. AND MED., 1935, **32**, 1666.

4 Salmon, U. J., and Frank, R. T., PROC. SOC. EXP. BIOL. AND MED., 1936, **33**, 612.

† For the testosterone used in this study we are indebted to Dr. Erwin Schwenk of Schering Corporation, Bloomfield, New Jersey.

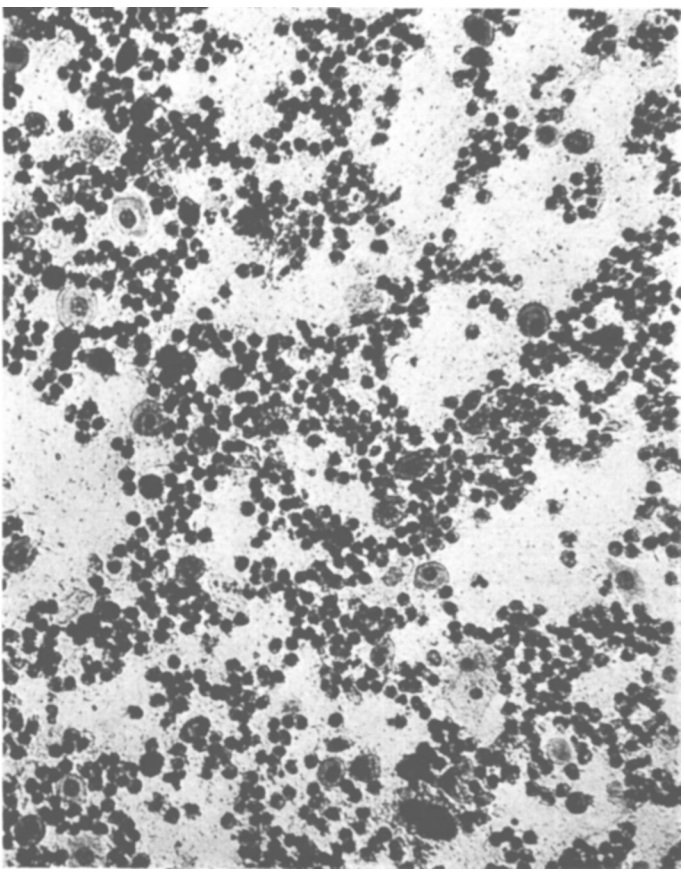


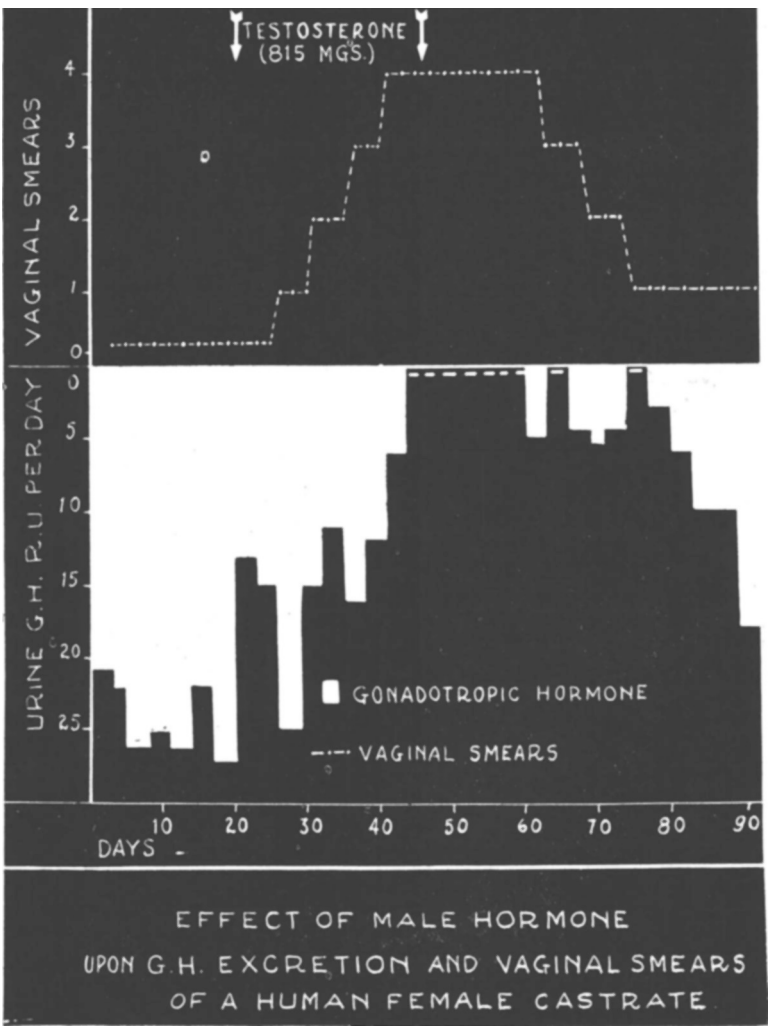
FIG. 1.
Preliminary "negative" smear exhibiting predominance of leucocytes with scattered, small epithelial cells.

minations and vaginal smears were performed throughout the period of observation of 92 days.

The results are represented in Graph 1.

The G.H. factors began to disappear from the urine after 465 mg. of testosterone had been administered. For a period of 18 days the urine remained negative for G.H. Following this, G.H. reappeared in the urine in increasing concentration. Coincident with the disappearance of G.H. from the urine large epithelial cells which exhibited various degrees of cornification appeared in the vaginal smears displacing completely the "compact cells" (Papanicolaou) and the leucocytes, thus representing a full estrogenic effect. (Fig. 2.)

The maximum effect on the smear lasted for 21 days, following



GRAPH 1.

Note the disappearance of gonadotropic hormone from the urine and the change in the vaginal smear reaction following the administration of testosterone propionate.

which a gradual return to the pre-treatment status occurred. The regression of the smear ran parallel with the reappearance of G.H. in the urine.

It is interesting to note that the patient began to experience relief of her symptoms (flashes, headaches, etc.) after 400 mg. of testosterone propionate had been administered. The amelioration of symptoms reached its maximum at the time when the smear exhib-

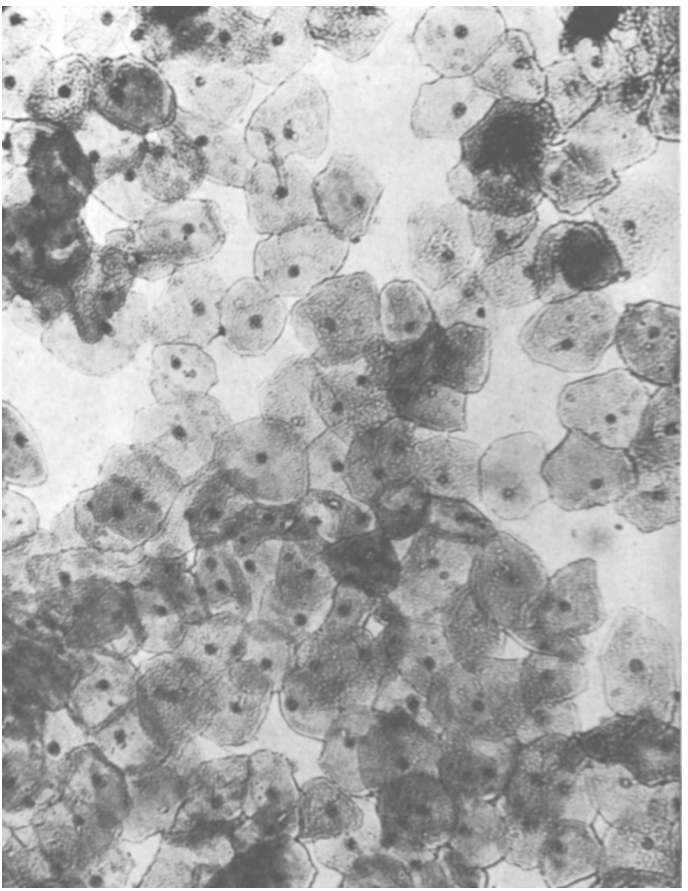


FIG. 2.
Estrogenic effect in vaginal smear following testosterone propionate.

ited a full estrogenic effect and the urine was negative for G.H. Symptoms recurred rapidly with the reappearance of G.H. in the urine and the regression of the smear to its pre-treatment status. Identical effects (as regards both G.H. excretion and vaginal smears) had been produced in the same patient 24 months previously with 16,000 R.U. of estradiol benzoate.

It would appear from this study that testosterone propionate when given in adequate dosage can inhibit the gonadotropic hyperactivity of the hypophysis in a female castrate and also produce a full estrogenic effect on the vaginal mucus membrane of a human castrate—thus paralleling two phases of biologic activity of the estrogenic substances.