the 10 untreated rats was 150 g with a range of 134-163; the amounts of work performed averaged 1276 recorder revolutions with a range of 56-2399. Each recorder revolution is equivalent to approximately 400 g-cm of work. The values for body-weight and for work of the treated animals are presented in Table I.

As evidenced by the effect of these substances upon body-weight and upon work performance, the presence of a hydroxy group instead of a keto group on carbon 3 of the pregnene nucleus decreases but does not destroy these biologic effects of the compound. This compound was reported by Waterman and co-workers[4] to maintain the health of adrenalectomized dogs. The alteration of the molecule to the structure of substance C brought a still greater loss of activity so that substance C appeared to be biologically inactive in these tests. Earlier studies[5, 6] have demonstrated that although the work performance of adrenalectomized rats treated with substance A is improved over that of untreated animals, it remains very small as compared to sham operated animals. Similar values for work performance of animals treated with substance A were obtained in this study.

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Inhibition of Estrin-Deprivation Bleeding in Rhesus Monkey with Testosterone Derivatives Variously Administered.*

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Testosterone and its acetic and propionic acid esters have been shown to inhibit uterine bleeding in the castrate macaque primed with estrogens.[1] In the present experiments a similar effect was attained with methyl-testosterone and ethinyl-testosterone (pregneninolone) and with testosterone di-propionate administered in

[4] Waterman, L., Danby, M., Gaarenstroom, J. H., Spanhoff, R. W., and Uyldert, I. E., *Acta Brevia Neerlandica*, 1939, **9**, 75.

[5] Ingle, D. J., *Endocrinology*, 1940, **26**, 472.

[6] Ingle, D. J., *Endocrinology*, in press.

* The writer as well as the staff of the Carnegie Laboratory of Embryology whose hospitality the writer enjoyed, acknowledges with thanks the generosity of the Ciba Corporation for the generous supply of the testosterone compounds and to E. R. Squibb and Sons for keeping the laboratory supplied with Amniotin.

[1] Hartman, C. G., PROC. SOC. EXP. BIOL. AND MED., 1937, **37**, 87.

sesame oil. Some success also followed the oral administration of testosterone propionate given with bile salts, and of methyl and ethinyl testosterone. These experiments were carried out in the rhesus colony of the Carnegie Laboratory of Embryology, Baltimore, Maryland, in the spring of 1939.

1. *Testosterone dipropionate.* 5 mg daily injected into castrated monkey No. 584 for 16 days (June 12-27), after duly priming with estrogen (Amniotin-Squibb), inhibited bleeding and produced the usual[2] moderate proliferation of the endometrium, which measured up to 2.5 mm in thickness. The vaginal wall showed a fairly thick Dierks layer.

2. *Methyl Testosterone.* A. Administered parenterally. Monkey No. 596, a castrate, bled April 12, 1939 after injections of stilboestrol and was re-primed with the usual 100 R.U. of Amniotin for 9 days (April 17-25). From April 25 to May 20 incl., 5 mg of methyl testosterone in sesame oil were injected subcutaneously daily except Sunday; the animal was sacrificed on May 22. The proliferative action of the hormone was mild but bleeding was successfully inhibited.

B. *Hormone pellets placed subcutaneously.* In castrated monkey No. 584, after due priming with estrogen, eight 3 mg pellets of methyl testosterone were implanted subcutaneously at the end of the injections, April 22, 1939; 5 additional pellets on April 29. No bleeding had occurred by May 12 when biopsies were made. Results as in preceding.

C. *Hormone administered orally.* Beginning on the eighteenth day of a non-ovulatory cycle, 10 mg of methyl testosterone were fed to intact monkey No. 628 to see if the hormone might extend the cycle beyond the maximum of 31 days characteristic of this animal. Feeding was continued through day 46 of the cycle and no bleeding had occurred by day 52, when endometrial biopsies were taken. While bleeding was absent, the endometrium showed almost no proliferative activity, not a single mitotic figure being seen. The organ might almost be called atrophic.

3. *Ethinyl Testosterone (pregneninolone, anhydro-oxy-progesterone).* A. Administered parenterally. Monkey No. 613, a castrate, was primed from May 16-23, 1939, with 100 R.U. of estrogen (Amniotin) daily. From May 24 to June 10 five mg of ethinyl testosterone in sesame oil were injected daily. No bleeding had occurred by June 16 when the animal was sacrificed. In some areas of the well proliferated endometrium hematomata were noted.

[2] Hartman, C. G., *Endocrinology*, 1940, **26**, 449.

Apparently bleeding was imminent 6 days after the last injection of ethinyl testosterone. Estrogenic effects on uterus, cervix and vagina were marked.

B. *Hormone administered orally.* Castrated female No. 626 was primed the usual way with estrogen. She was then given one 20 mg tablet of ethinyl testosterone by mouth daily from May 24 to June 7. She began to bleed on the 15th day after the last injection of estrogen. She was sacrificed while still bleeding; while bleeding was not prevented it was probably postponed a few days above the usual maximal interval of 10 days following moderate treatment with estrone (Amniotin). Judging from the state of the uterine, cervical and vaginal mucosæ the effect of oral administration proved far less than that attained by one-fourth as large a dose administered subcutaneously.

4. *Testosterone Propionate given orally.* Monkey No. 591 had her endometrium almost totally removed on Jan. 18 and on Mar. 16 she received 50 mg daily of testosterone propionate. A uterine biopsy was made on May 11. She was castrated on June 9, then fed daily for 19 days two 10 mg tablets of testosterone propionate and one 100 mg tablet of bile salts. The bleeding which usually follows castration within 10 days or less did not occur. On the other hand, the endometrium showed no signs whatsoever of proliferation, measuring but 1 mm in thickness. The condition of the vagina and the cervix, likewise, proved that a minimal quantity of the absorbed hormone reached the systemic circulation.

Summary. 1. Testosterone di-propionate prevented estrin-privea bleeding in daily parenteral doses of 5 mg in sesame oil. 2. Methyl testosterone inhibited estrin-privea bleeding when administered subcutaneously in the form of pellets or dissolved in sesame oil. Orally in daily doses of 10 mg, methyl testosterone prevented menstruation but otherwise failed to exert the slightest visible estrogenic effects. 3. Ethinyl testosterone prevented estrin-privea bleeding in the monkey when administered parenterally in doses of 5 mg a day. Given orally, it delayed slightly but did not prevent bleeding in daily doses of 20 mg, with no other estrogenic effects. 4. Testosterone propionate when administered orally in 20 mg doses along with bile salts, prevented estrin-privea bleeding, but otherwise its estrogenic effects proved minimal. 5. It is apparent that oral administration of any of the testosterone derivatives here tested is most uneconomical as compared with parenteral methods.