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Experimental Menstruation in the Monkey after Removal of Ovaries and Adrenals.

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Menstruation is preceded by vasoconstriction of endometrial vessels and hemostasis which begins 6 to 12 hours before menstruation and may persist throughout the first day. This observation was made by Markee[1] in living endometrium of the monkey transplanted to the anterior chamber of the eye. Bartelmez[2] had previously emphasized the part played by the spiral arteries in menstruation and the recent study of these vessels in the monkey by Daron[3] has focussed attention on this aspect of the menstrual cycle.

It has long been known that double ovariectomy is followed in a few days by menses and then by disappearance of menstruation and atrophy of the uterus. Experimental menstrual cycles can be induced in the ovariectomized monkey by injections of ovarian follicular hormone (theelin, oestrin). This hormone produces an effect upon the uterus in 6 to 10 days which is followed by menstruation (Allen,[4, 5] Morrell, Powers, Varley and de Frates,[6] and others). Eighty to 150 rat units of theelin in 6 to 10 days is the menstrual threshold for adults, larger doses are required for immature monkeys, but 350 rat units in 10 days will produce menstruation in infantile monkeys of 1500 gm. body weight (Allen, Diddle, Burford and Gardner[7]). The thyroid gland can be completely removed without affecting the ovarian hormone threshold necessary to produce experimental menstruation (Burford, Allen, Diddle[8]).

Assuming that premenstrual vasoconstriction and hemostasis may be essential in producing the hemorrhage and desquamation which follow, the secretion of the adrenal medulla might be a factor con-

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2 Bartelmez, G. W., *Carnegie Inst. Wash.* No. 443, *Contrib. to Embryol.*, **24**, 141-186.

3 Daron, G. H., *Am. J. Anat.*, 1936, **58**, 349.

4 Allen, E., *Anat. Rec.*, 1926, **32**, 226.

5 Allen, E., Contrib. to Embryol., Carnegie Inst. of Washington, 1927, **19**, 1.

6 Morrell, J. A., Powers, H. H., Varley, J. R., and de Frates, J., *Endocrinology*, 1930, **14**, 174.

7 Allen, E., Diddle, A. W., Burford, T. H., and Gardner, W. U., *Am. J. Physiol.*, 1936, **117**, 381.

8 Burford, T. H., Allen, E., and Diddle, A. W., 1936, **20**, 635.

tributing to the onset of menstruation. The present preliminary experiments were made to test the effect of removal of all suprarenal medullary tissue on experimental menstruation induced by theelin† in ovariectomized monkeys.

Adrenalectomy was done in 2 stages, several weeks elapsing between removal of right and left glands. On the day following removal of the last suprarenal, injection of cortical extract was begun. This extract was prepared and standardized by Dr. Swingle. Doses ranging from 1.7 to 3.0 cc. given twice daily were adequate to prevent adrenal cortical deficiency.

Theelin was injected twice daily for 10 days, 50 r.u. per day in monkey No. 50, and 60 r.u. in monkey No. 62. A marked increase in the redness of the "sexual skin" was noted. A latent period of 5 days followed the last injection and then menstruation began in both animals. The flow was profuse on the second and third days and menstruation lasted for 5 days in monkey No. 50 and for 7 days in monkey No. 62.

There was enough cortical extract to last for 21 days. The monkeys were then observed for onset of cortical deficiency. During this period monkey No. 50 was injected with theelin, 60 r.u. daily for 11½ days. There followed a latent period of 4 days and then 4 days of menses.

Thus 3 experimental menstrual periods were obtained in 2 ovariectomized monkeys following doses of 500, 600 and 690 r.u. of theelin and after removal of all adrenal medulla. These menses differed in no way from the usual course of events previously observed in ovariectomized animals with intact suprarenals under similar hormone treatment.

Signs of adrenal insufficiency appeared as expected in monkey No. 62 but not in No. 50, and at autopsy a nodule of cortical tissue one cm. in diameter was found adherent to the vena cava in the right suprarenal region in the latter. Since this contained no medullary tissue, it had little bearing on the main objective of the experiment.

Summary. Both ovaries and suprarenals were removed from 2 monkeys which were then injected with cortical extract (Swingle). Three experimental menstrual periods were then induced by injections of theelin—total doses ranging from 500 to 690 r.u. in 10 to 11½ days. Latent periods of 4 to 5 days followed the last injections and then menstrual periods of 4 to 7 days. The adrenal medulla is not essential to experimental menstrual periods induced by theelin.

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