

Uterine Bleeding of the Interval Type in Macacus Monkey During Injections of Extracts of Pregnancy Urine.*

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Uterine bleeding in the spayed or immature macacus monkey is known to occur from an interval type endometrium about 6 days after cessation of an adequate treatment with oestrin (Theelin, Allen¹, Maddux²;) (Amniotin, Morrell *et al.*³). These observations have been repeatedly confirmed in this laboratory. Uterine bleeding in the adult also occurs after bilateral ovariectomy (Allen; Van Wagenen and Aberle⁴) or occasionally after unilateral ovariectomy (VanWagenen and Aberle). (Uterine bleeding indicates a hemorrhage of uterine origin macroscopically visible on the external genitalia of the monkey, but which may not be homologous with menstruation). Saiki⁵ has shown that uterine bleeding may be induced in immature macaques 4 to 9 days after the cessation of 8-17 days treatment with an extract of anterior lobe (P. D. & Co.). Our work confirms these results. However, if water soluble extract of pregnancy urine or the "luteinizing hormone" (P. D. & Co.) be administered in adequate doses for from 19 to 22 days, in 2.8 to 4 kg. animals, bleeding occurs *during the course of treatment*. If the injections are continued, bleeding stops in 4 to 6 days, after an apparently normal flow.

Injections of extracts of pregnancy urine have failed to cause reddening of the sexual skin, or induce the turgose, pachydermatous condition of the circumgenital and anal area which is obtained by injections of oestrin or is seen after ovarian stimulation by means of water soluble fraction of pyridine extract (Hisaw, Fevold and Leonard⁶). No follicular cysts, nor any determinable growth of the ovarian follicle occurs after such injections. Modification of

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¹ Allen, E., *Cont. to Embryol., Carnegie Inst.*, 1927, 19.

² Maddux, W. P., *PROC. SOC. EXP. BIOL. AND MED.*, 1930, **27**, 873.

³ Morell, J. A., *et al.*, *Endocrinol.*, 1930, **14**, 174.

⁴ VanWagenen, G., and Aberle, S. B. D., *Am. J. Physiol.*, **99**, 271.

⁵ Saiki, S., *Am. J. Physiol.*, **100**, 8.

⁶ Hisaw, F. L., Fevold, H. L., and Leonard, S. L., *PROC. SOC. EXP. BIOL. AND MED.*, 1931, **29**, 204.

the structure of large atretic follicles may be obtained after continued intravenous injection of pregnancy urine, but no structures which are clearly corpora lutea have as yet been obtained with this substance, although luteinization in the rat is a pronounced result after prolonged subcutaneous intraperitoneal or intravascular injections.

In the female monkey the only well recognized phenomena which occurs after treatment of normal intact animals with pregnancy urine extracts is this uterine bleeding. The ovaries, although they show no morphological change as yet recognizable, are essential in this mechanism for bleeding, as no results were obtained in an ovariectomized animal even after 30 days of treatment. In no case has the endometrium shown the degree of development which is obtained by means of oestrin, or after stimulation with the water soluble pyridine extract of anterior pituitary. Bleeding in every case studied has occurred from an interval type endometrium, with poor glandular development and with relatively little tissue destruction.

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Prevention of Experimental Uterine Bleeding in Macacus Monkey by Corpus Luteum Extract (Progestin).*

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Since uterine bleeding was shown to follow cessation of follicular treatment, the many observations on experimental menstruation in the monkey have not given adequate consideration to the rôle of the corpus luteum. Experiments were designed to study this question. Adult or subadult animals, all beyond the first menstruation (3700 to 5150 gm. B.W.) were injected with the follicle stimulating water soluble fraction of sheep pituitaries (Pyridine method of Fevold, Hisaw and Leonard) for 10 to 14 days. Coincident with the last 4 of these injections oestrin (Theelin) was also given in large doses (100 R.U. per diem)**. The uterus at the end of the treatment

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