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Luteinization of Ovary of Sexually Immature Monkey.*

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We reported the effects of aqueous pyridine extracts of sheep anterior pituitary on the ovaries of sexually immature *Macacus rhesus* monkeys.¹ We were able to produce marked follicular development in such ovaries, but in no case did definite luteinization occur. This was in agreement with the findings of E. Allen,² Hartman,³ Courrier,⁴ Saiki,⁵ and Engle.⁶

Nevertheless, intraperitoneal injections of anterior pituitary extracts into adult rats produce a greater degree of luteinization than comparable subcutaneous treatment. Similarly, Friedman⁷ showed, in the rabbit, that the type of ovarian response to the urine of pregnant women varies with the method of its administration; ovulation resulted from intravenous injections, whereas intraperitoneal treatment produced only the luteinization of the resulting corpora haemorrhagica. These observations suggested the possibility of altering the ovarian response of sexually immature monkeys by varying the injection procedure. We had previously found that a single intravenous injection of anterior pituitary preparation following numerous subcutaneous injections did not modify the effects obtained. Experiments were consequently devised in which a greater number of intravenous injections were given. We wish to report the response of 2 sexually immature monkeys to such treatment.

Both animals were first given a series of subcutaneous injections of a water soluble fraction of an aqueous pyridine extract of dried sheep pituitary† in doses equal to 0.5 gm. of the dried tissue at

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¹ Hisaw, F. L., Fevold, H. L., and Leonard, S. L., *PROC. SOC. EXP. BIOL. AND MED.*, 1930, **29**, 204.

² Allen, E., *Anat. Rec.*, 1928, **39**, 315.

³ Hartman, C. G., *PROC. SOC. EXP. BIOL. AND MED.*, 1930, **27**, 338.

⁴ Courrier, R., Kehl, R., Raynaud, R., *C. R. S. de Biol.*, 1929, **101**, 1093.

⁵ Saiki, S., *Am. J. Phys.*, 1932, **100**, 8.

⁶ Engle, E. T., personal communication.

⁷ Friedman, M. H., *Am. J. Phys.*, 1929, **90**, 617.

† The pituitary powder was kindly furnished by the Research Laboratories of Parke, Davis and Company.

12-hour intervals. Monkeys 8 and 9 received respectively 6 and 20 such subcutaneous injections. The initial treatment elicited the cornification of the vaginal epithelium and excessive development of the external genitalia and sexual skin as previously described.¹ At this point laparotomy on monkey 9 revealed ovaries of the following dimensions: right ovary, 2.2x1.8x1.8 cm.; left ovary, 1.9x1.9x1.9 cm. Subsequent findings indicate that the response of monkey 8 was much less extreme and the increased size of the ovaries was obviously proportional to the amount of pituitary material administered. The ovaries were constituted almost exclusively of immense translucent follicles and no signs of luteinization were observed.

Immediately following exploratory laparotomy monkeys 8 and 9 were given respectively 3 and 8 successive daily intravenous injections of 2 gm. equivalents of the same pituitary preparation previously applied subcutaneously. Throughout this period subcutaneous administrations of 0.5 gm. equivalents twice daily were continued. Thirty-six hours after the last injection both ovaries were removed and a biopsy of the uterus taken.

Marked luteinization was observed in the ovaries of Monkey 9, though only a few of the smaller follicles have been completely luteinized. The larger follicles still show clot-filled antra though in most instances the entire granulosa as well as the theca interna have been transformed to characteristic lutein tissue. In numerous cases the luteinized granulosa is separated from the lutein tissue derived from the theca interna by a considerable rim of connective tissue which surrounds the entire follicle.

The ovaries of monkey 8 showed numerous follicles possessing blood-filled antra and luteinized strata granulosa, but in no case had the luteinization extensively involved the theca interna. This limited effect is commensurate with the comparatively brief stimulatory treatment afforded this animal.

The endometrial samples showed clearly that the lutein tissue described above was physiologically functional. The histological picture in both cases is that which obtains in the lutein phase of the normal primate menstrual cycle, though the condition is obviously more exaggerated in the case of the more highly stimulated animal.

Several external influences associated with this induced luteinization were likewise noted. These are chiefly a decrease in redness of the sexual skin, a marked loss of turgidity in the labia majora and sexual skin, and a preponderance of leucocytes in the vaginal smear.

The pituitary preparations employed in these experiments were previously found to possess both follicular stimulating and luteinizing properties when injected subcutaneously into sexually immature rats. These findings show the extraordinarily high threshold of anterior pituitary material required for the luteinization of the primate ovary, and indicate the widely different responses to be obtained from subcutaneous and intravenous injections of the same preparation.

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Gonadotropic Action of Phyone on Juvenile Female Rabbit.*

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Van Dyke and Wallen-Lawrence¹ have prepared an extract of fresh beef pituitary tissue (phyone) possessing marked growth promoting properties on the hypophysectomized as well as on the normal immature rat. This preparation was without effect on the gonads of such test animals. Phyone was consequently thought to contain only the growth promoting hormone of the pituitary gland, and to be free of the sex-stimulating factors known to exist in this gland.

We have assayed 3 different batches of phyone† upon juvenile chinchilla female rabbits from 12 to 13 weeks of age. Four litters of 4 rabbits each were employed. In each litter one rabbit was retained as an uninjected control. Two of the members of each litter were given 0.5 cc. of phyone either intravenously or subcutaneously for from 3 to 5 days. Since Leonard² has shown that a female rabbit, if fully adult, will ovulate upon the intravenous injection of phyone, the remaining rabbit in each litter was given a single intravenous injection of 1 cc. of phyone from the batch used on its own litter-mates. This single injection was without effect upon the ovaries of the juvenile rabbits, but 1 cc. samples from any

* Aided by a grant from the National Research Council, Committee on Problems of Sex.

¹ Van Dyke, H. B., and Wallen-Lawrence, Z., *J. Pharm. and Exp. Ther.*, 1930, **40**, 413.

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