Priming the Anestrous Cat for Reflex Discharge of Pituitary Ovulating Hormone.* (20503)

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The female cat, like the rabbit, ferret, mink and several other species, does not ordinarily ovulate spontaneously, but only after mating. Copulation in these forms initiates a reflex discharge of ovulating hormone from the adenohypophysis, which in turn leads to rupture of ovarian follicles. Although the nervous pathways involved in this reflex are incompletely understood, Greulich(1) demonstrated that in estrous cats prodding the uterine cervix with a glass rod was an effective stimulus for inducing ovulation.

In studies of neural control of the hypophysis and ovulation, although the rabbit has a number of advantageous characteristics that have resulted in its extensive use, the cat appears to have certain special advantages of its own as an experimental animal. Stereotaxic coordinates of the cat brain are available (2), the brain withstands lesions very well, and the behavorial afterreaction to vaginal stimulation in the estrous cat leaves no doubt that stimulation of higher nerve centers has been achieved. Unfortunately, however, the cat stays in heat for only a few days at a time, and for a long period from July to January(3), it remains completely anestrous. Earlier workers(4-6) using female sex steroids have induced estrous behavior in the anestrous cat without reference to ovulation. Others (7-11) have induced ovulation directly with the use of pituitary and placental gonadotrophins without involving nervous mechanisms. The present problem has been to prime the animal in such a way that neurogenic stimulation of her own hypophysis is necessary to induce ovulation. Only thus can ovulation be considered an indicator of successful stimulation of the hypophysis.

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The results are summarized in Table I. Estrogen refers to estradiol benzoate (0.83 mg/ml in oil)† and PMS to equine gonadotrophin (Anteron).† The vaginal stimulus was produced by several thrusts of a blunt glass rod, 5 mm in diameter, to the uterine cervix. Estrus implies that the cat not only raised her pelvis, deflected her tail and treaded in response to prodding the perineum, but that she responded to vaginal stimulation by a typical afterreaction—violent rolling, licking the vulva and rubbing the head and neck on the side of the cage.

Twelve cats received estrogen alone in divided subcutaneous doses totalling less than 0.3 mg over several days. While this resulted in complete behavioral estrus in 9 cats, laparotomy revealed ovarian stimulation in not one animal. Equine gonadotrophin in subcutaneous doses of 50 I.U. each on 2 consecutive days failed to stimulate either estrous behavior or ovulation in 5 cats. Incidentally, higher dosages of PMS (100 I.U.) on 3 successive days induced ovulation in 2 cats, independently of nervous stimulation, confirming Windle's(11) report. Fifteen cats received a standard regime of 0.04 mg estrogen and 50 I.U. PMS for 2 days and 0.08 mg estrogen alone on the third day without ovulating. They generally appeared to be in heat but were not given vaginal stimulation. Five similarly treated animals were subjected to vaginal stimulation without provoking an afterreaction and none ovulated. However, of 16 anestrous cats treated in this way and responding to cervical stimulation with the typical afterreaction, 9 out of 16 ovulated, presumably as a result of reflexly induced discharge of their own pituitary gonadotrophin.

In searching for the reason why the other 7 females did not ovulate, histological sections

† Kindly supplied by the Schering Corp., New Brunswick, N. J.

TABLE I. Effects of Estrogen and/or PMS in the Anestrous Cat on the Onset of Heat and Induction of Ovulation by Vaginal Stimulation.

No. of cats	Treatment			No. of cats reaching estrus	Ovulation	
	Estrogen	PMS	Vaginal stimulus		No.	%
			Anestrous			
12	+	—	+	9	0	0
5	—	+	+	0	0	0
15	+	+	—	—	0	0
5	+	+	+	0	0	0
16	+	+	+	16	9	56
			Estrous			
10	—	—	+	10	5	50

were made of several of the anovulatory ovaries. The latter contained unusually large follicles, more than 4 mm in diameter in 5 of the 7 cats and actually cystic in 2. The enlarged follicles revealed a thin granulosa, perhaps beyond the stage of responsiveness to ovulating hormone. In the ovulating animals some of the larger follicles luteinized without rupturing. The conditions recall the situation in which follicles overgrown in response to FSH failed to rupture in response to LH(9).

We have recently had the opportunity of observing cats in naturally occurring estrus and we have had similar results with them (Table I). Five out of 10 failed to ovulate in response to vaginal stimulation, and examination of their ovaries revealed similarly hypertrophied, almost cystic ovaries. Others (12,1) have reported that actually mating the cat does not insure ovulation under laboratory conditions. Perhaps left to her own devices in nature the female cat seeks out the male at the appropriate stage in the growth of her follicles, but under laboratory conditions the stimulus may arrive too late.

Estrogen without PMS is an effective priming agent for neurogenic stimulation of ovulation in the rat(13) and the rabbit(14). In anestrous sheep it has also been reported(15, 16) that injection of estrogen will often invoke ovulation. Possibly in the anestrous cat estrogen likewise facilitates hypothalamo-hypophyseal mechanisms, but the ovary cannot respond until growth of its follicles has been promoted by PMS.

Summary. The results indicate that the nervous-pituitary-ovarian conditions of the estrous cat may be simulated by estrogen-PMS priming, and that cats in such artificial estrus may be employed as favorable material in experimental studies on nervous control of the adenohypophysis.

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