

Temporary Suppression of Estrous Cycles in the Rat by Prolactin.

ERNEST L. LAHR AND OSCAR RIDDLE.

From Carnegie Institution, Station for Experimental Evolution, Cold Spring Harbor, N. Y.

Though prolactin was early shown to induce a speedy and extreme atrophy (decrease in weight) of the gonads of adult birds,^{1,2} of both sexes, this hormone was found to have no influence whatever upon the weights of testes of adult rats.³ Because of the relation of this hormone to lactation it has nevertheless seemed probable that the "lactation anestrus" of mammals is associated with this pituitary hormone—and most plausibly with its proved depressant action on the gonads of some animals (birds). The present study, following that of Dresel,⁴ demonstrates that daily injections of prolactin temporarily suppress those ovarian functions which are expressed by estrus. In addition, it is here shown that a dosage of progesterone which (in another study) appears to have an influence on maternal behavior in the non-parous rat has no appreciable influence on the estrous cycles of these rats.

In mature non-parous mice Dresel briefly reported that "prolactin suspends the estrous cycle for about 3 weeks, after which a prolonged estrum sets in lasting from 4 to 8 days in spite of further continued injections." These observations led to the suggestion that the suspension of the estrous cycle during lactation is caused by prolactin, rather than by the corpus luteum hormone.

Smears were made by us once daily on mature non-parous rats, and the vaginal material was obtained by pipette. Observations were made on 3 series of prolactin-injected rats. First, a preliminary series of 4 rats 172 days old at first injection. Previously smeared for 16 days, the cycles of 3 of these 4 rats had been found quite regular and normal; thereafter they each received 4 units of prolactin daily for 15 days, and each rat showed partial or nearly complete suppression of 1 or 2 cycles followed by resumption of quite normal cycles. In the partial or "mixed" smears which some-

¹ Riddle, O., and Bates, R. W., *Endocrin.*, 1933, **17**, 689.

² Bates, R. W., Lahr, E. L., and Riddle, O., *Am. J. Physiol.*, 1935, **111**, 361.

³ Riddle, O., Lahr, E. L., Bates, R. W., and Moran, C. S., *Proc. Soc. Exp. Biol. and Med.*, 1934, **32**, 509.

⁴ Dresel, I., *Science*, 1935, **82**, 173.

times replaced the normal cycles there were few or no squamous cells. The cycles of two control rats of this series were normal and unmodified during this period. Second, a series of 9 rats whose response is shown in Fig. 1. The cycles of the 4 control rats (not

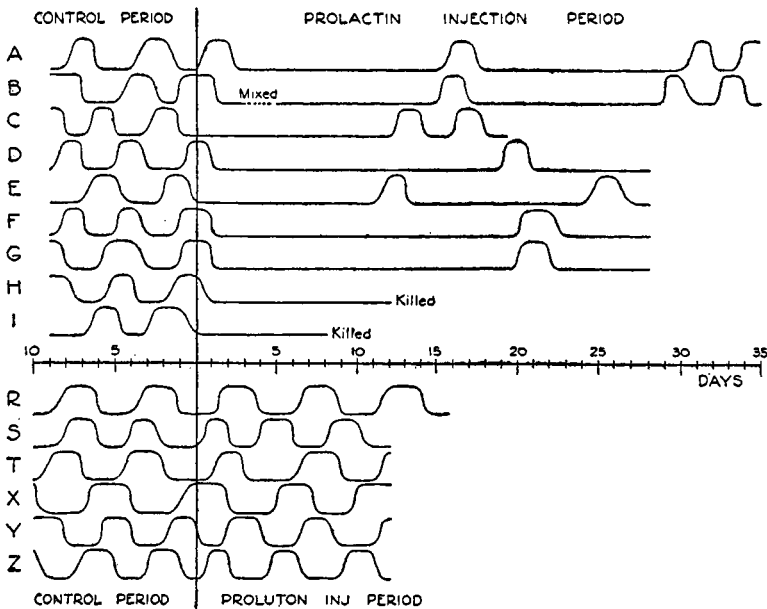


Fig. 1.

figured) of this series remained nearly or quite regular and normal. Of the 9 treated rats, aged 148-186 days, 3 (here called A-C) were injected with 30 units of prolactin daily for 35 days (19 days for 1). About 3 cycles were suppressed in each rat, but despite continued injections quite normal cycles recurred between the 13th and 16th day of treatment; in the two rats treated for 35 days the 3 next following cycles also were completely suppressed, after which quite normal cycles occurred although injections were being continued. Rats D-I received 15 units of prolactin daily; in 3 of the 4 rats treated for 28 days, about 4 cycles were completely suppressed (in the other rat only 2 or 3 cycles), and thereafter a single normal cycle was followed by a further suppression of cycles in all 4 cases. Two rats (H, I) received only 8 and 12 such injections, and were killed at these periods for a special study of their ovaries which, in both cases, disclosed the retention of large corpora with large cells apparently not in stages of degeneration. A third series is formed from random observations on a number of rats injected with pro-

lactin for shorter periods and with variable dosage. On these rats the infrequency of cycles under such treatment has been confirmed.

It can be observed that prolactin dosage was initiated at all of the various stages of the cycle in one or another of the 9 rats recorded on Fig. 1. All prolactin preparations used on those 9 rats, and on the 4 rats of the preliminary series, had been heated to 60° C. for 5 hours after previously testing free from follicle-stimulating and thyrotropic hormones (dove testis and dove thyroid tests). Injections were made once daily and subcutaneously. It is particularly notable that after stopping the injections there was almost immediate resumption of normal estrus in all cases.

The 6 rats (Fig. 1) receiving progesterone* were 156-172 days old at the beginning of treatment. The dosage was 0.03 mg. daily, subcutaneously, for 12 to 16 days. The rhythm of the cycles was *not* interrupted, and the character of the smears remained normal. At a dosage level 10 times higher (0.3 mg. daily) we noted slightly prolonged diestrus (remained normal in 2 controls), and Selye, Browne and Collip⁵ have already reported the suppression of estrus in the rat with huge doses (4 mg. daily) of progesterone.

It is of course possible that prolactin suppresses estrous cycles through diminishing the release of F.S.H. from the rat's own pituitary; but a direct and antagonistic action of these two hormones on the gonads of birds has not been excluded. Whatever the mechanism involved in its action in both mice and rats, prolactin has been found capable of temporarily suppressing ovarian cyclic activity; and, curiously enough, in both cases cycles are later resumed under continued injections. Whether increasing daily doses would prevent this resumption of cycles is still unknown. In the case of the rat the anestrus period induced by prolactin seems always to be rather shorter than the gestation or the lactation period. The retained large corpora found at 8 and 12 days of prolactin treatment suggest an active output of progesterone, but the failure of low or moderate amounts of this hormone to suppress cycles is here definitely indicated.

Conclusions. In the regulation of the ovarian activity of rats prolactin is shown to be capable of playing a part, directly or indirectly. Prolactin can not be summarily omitted from lists of pitu-

* Proluton, crystalline progesterone dissolved in oil, was supplied for these tests through the courtesy of Dr. Erwin Schwenk of the Schering Corporation, Bloomfield, N. J.

⁵ Selye, H., Browne, J. S. L., and Collip, J. B., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **34**, 472

itary principles having action on the gonads of mammals. The suggestion of Dresel that lactation anestrus in mice is induced by prolactin is supported by these tests on mature non-parous rats. But under effective prolactin dosage the corpora of rats remain large, and at the age of 10-12 days their large cells show no clear evidence of degeneration. The failure of daily injections of low or moderate doses of progesterone to affect the estrous cycles of rats suggests that in this rodent, though the corpus luteum hormone plays its part, it is perhaps not the hormone primarily responsible for the anestrus of either gestation or lactation.

8827 P

Removal of Corpora Allata on Egg Production in the Grasshopper, *Melanoplus Differentialis*.*

ISABELLE G. WEED. (Introduced by J. H. Bodine.)

From the Department of Zoology, State University of Iowa, Iowa City.

It has been shown by Wigglesworth¹ that in *Rhodnius prolixus* the corpora allata secrete a hormone which is necessary for the production of eggs. In order to determine whether these glands have a similar function in the grasshopper, females were operated as shown in Table I. For comparison, unoperated adults were killed at intervals from one to 42 days after moulting. Camera lucida drawings were made of the largest eggs in each of the above animals, egg length was measured, and the oviducts were examined to determine whether the secretion produced by the anterior portions of the oviducts was present. This secretion forms the ootheca.

There was great variation in the development of the ovary in unoperated adults autopsied from 28 to 42 days after moulting. However, of the 43 specimens examined, 35 contained eggs which were more than 1 mm. in length. Of these, the eggs of 8 were fully developed and had passed into the oviducts. The operated controls at autopsy also contained eggs exceeding 1 mm. in length and in one instance the fully developed eggs had entered the oviducts.

The eggs of the animals from which both corpora allata had been removed, however, were less than .9 mm. in length at autopsy in all

* Aided by a grant from the Rockefeller Foundation for work on cellular biology.

¹ Wigglesworth, V. B., *Nature*, 1935, **136**, 338.