

pentobarbital sodium intraperitoneally as well as 3 to 4 cc of ether by inhalation abolish response to these stimuli.

Conclusion. We question the suitability of the word anesthesia either in its restricted or in its extensional meaning as applied to the syndrome of cholesterol depression. Etymologically "anesthesia" means without

sensation, but usage confines it to a description of a reversible process; unless accidentally it becomes terminal. We hold, therefore, that when this syndrome of depression produced by these steroid compounds is described as anesthetic, that the use of the adjective lacks preciseness, and that this loose choice of the word is misleading.

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Effect of Hypophysectomy During Early Proestrus on Ovulation in the Rat.*

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Long and Evans¹ have described the cyclic changes in the ovary of the adult rat and correlated them with the changes in the vaginal smear and, more recently, Boling *et al.*² correlated the changes in the ovary with estrous behavior. Smith,³ Ascheim⁴ and Zondek⁵ have demonstrated the role of the anterior pituitary gland in maintaining ovarian function. Smith⁶ described the profound atrophy of the gonads which invariably follows surgical removal of the anterior pituitary gland of the rat. Moreover, Fee and Parkes⁷ showed that hypophysectomy in the rabbit will prevent ovulation, if the pituitary is removed within an hour after

copulation; if more than an hour intervenes between copulation and hypophysectomy, ovulation will proceed normally. Since ovulation in the rabbit occurs approximately 12 hours postcoitum the data of Fee and Parkes suggest that the rabbit ovary has an intrinsic latency of about 11 hours in its ovulatory response to hypophyseal stimulation.

In a spontaneously ovulating form such as the rat the secretion of hypophyseal gonadotrophin (LH) may take place over a considerable portion of the estrous cycle before the concentration is great enough to produce ovulation. The present experiments were undertaken to determine whether, within a 2-hour period after the beginning of proestrus, there is a sufficient quantity of gonadotrophin in the blood to cause ovulation within the following 46 hours.

Materials and Methods. The regularity of the estrous cycles of a group of 70 young adult female rats of the Sprague-Dawley strain was determined by making daily vaginal smears during 2 or 3 cycles. On the day preceding the next calculated estrus the vaginal smears were made every 3 hours to determine more closely the onset of the proestrous phase. This procedure makes for a maximum error of 3 hours in determining the beginning of proestrus. As Long and Evans¹ have shown, the beginning of

* This work was supported by a grant from the Wisconsin Alumni Research Foundation.

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¹ Long, J. A., and Evans, H. M., *Memoirs Univ. Calif.*, 1922, **6**, 1.

² Boling, J. L., Blandau, R. J., Soderwall, A. L., and Young, W. C., *Anat. Rec.*, 1941, **79**, 313.

³ Smith, P. E., *Proc. Soc. Exp. Biol. and Med.*, 1926, **24**, 131.

⁴ Ascheim, S., *Z. f. Geburtsh. u. Gynak.*, 1926, **90**, 387.

⁵ Zondek, B., *Z. f. Geburtsh. u. Gynak.*, 1926, **90**, 372.

⁶ Smith, P. E., *Am. J. Anat.*, 1930, **45**, 205.

⁷ Fee, A. R., and Parkes, A. S., *J. Physiol.*, 1929, **67**, 383.

TABLE I.

Animal No.	Operation	No. tubal ova	No. corpora lutea	No. preovulatory follicles
1	None	4	4	1
5	"	6*	6	2
6	"	4	4	0
7	"	5	5	0
8	"	4	5	0
9	"	5*	5	0
2	Sham hypophysect.	5	5	0
3	" "	6	7	0
4	" "	4	5	1
1	Hypophysect.	0	0	4
2	"	0	0	5
3	"	0	0	5
4	"	0	0	2
5	"	0	0	6
6	"	0	0	5
7	"	0	0	3
8	"	0	0	4
9	"	0	0	4

* Number of ova difficult to determine because of beginning fragmentation.

proestrus is marked by the appearance of large numbers of uniform nucleated epithelial cells in the vaginal smear, to the exclusion of all other cell types. We adhered closely to the latter specification and did not regard as proestrous animals any individuals showing any degree of cornification of the vaginal epithelium, as determined by the vaginal smear method. Thus, from a group of 70 animals observed over a period involving 3 to 7 cycles, 18 animals were obtained which were within 3 hours of the onset of proestrus at the time of selection for experimental use.

Of this group of 18 early proestrous animals, 9 were hypophysectomized by the parapharyngeal approach within 2 hours of the time of selection. Of the 9 remaining animals, 6 were retained as unoperated controls and 3 were submitted to a sham hypophysectomy which included trephining of the sphenoid bone and tearing the dura mater. All animals were autopsied 48 hours following the onset of proestrus. The completeness of the hypophysectomy was checked by careful examination of the sella under the binocular microscope. The oviducts of all animals were ligated with fine silk at the tubo-uterine junction and the ovaries and tubes were then fixed in Bouin's solution.

Serial sections of one ovary and oviduct

from each of the operated and control animals were stained with hematoxylin and eosin and prepared for microscopic study. The sections were examined carefully for the presence of incompletely formed corpora lutea, preovulatory type of follicles and for tubal ova.

Results and Discussion. The data are summarized in Table I. The ovaries of the animals which had been hypophysectomized in early proestrus all failed to ovulate, but from 4 to 7 follicles in the preovulatory phase were present.

In sham-operated and unoperated control animals microscopic study revealed from 4 to 7 tubal ova, a comparable number of incompletely formed corpora lutea and only an occasional preovulatory follicle. In some cases it was difficult to determine the exact number of tubal ova since their beginning fragmentation made it difficult to make an accurate count. Thus, in these cases, there was a slight discrepancy between the number of tubal ova and the number of incompletely formed corpora lutea.

The size of the residual cavity in the incompletely developed corpora of the sham-operated and control animals varied considerably. In some animals there was only a narrow rim of lutein tissue formed about a large follicular antrum, and in others there

was almost complete obliteration of the follicular cavity by newly formed lutein tissue. This variation in the development of the corpora lutea at a fixed time following the onset of proestrus is in keeping with the variation in the time of ovulation of different follicles within a single ovary.

The data support the conclusion that a hypophyseal hormone is required for ovulation and luteinization in the rat. It seems clear that this hormone must be secreted in sufficient quantities subsequent to the onset of proestrus, to produce ovulation and luteinization in the intact rat, as hypophysectomy in the early proestrus effectively prevents ovulation.

The procedure and results described in

this paper provide the basis for further studies of the factors concerned with ovulation and corpus luteum formation in the rat.

Summary. Hypophysectomy of adult female rats within 2 hours after the beginning of proestrus prevents ovulation from occurring within a 46-hour postoperative interval. Sham hypophysectomy does not prevent ovulation as shown by the presence of partially developed corpora lutea and tubal ova. It is concluded that a hypophyseal hormone (LH) is required for ovulation and luteinization in the rat and that the quantity of hormone needed to produce ovulation and luteinization is secreted subsequent to early proestrus.

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Further Studies on Galactose Paralysis in the Rat.

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The occurrence of paralysis has been observed in rats fed galactose on certain purified rations.¹ The purpose of the present experiment was to determine the effects of B vitamins on the incidence and severity of the above condition.

Procedure and Results. Female rats of the Sprague-Dawley strain were raised to maturity on a stock ration and selected for the present experiment at approximately 3 months of age and an average weight of 160 g (range 145 to 178 g). Four experimental rations were employed: diet I consisting of glucose alone; diet II of 50% glucose and 50% galactose; diet III of 50% glucose, 50% galactose and the following synthetic vitamins per kg of ration: thiamine hydrochloride 200 mg, riboflavin 400 mg, pyridoxine hydrochloride 20 mg and calcium pantothenate 200 mg; and diet IV of 40% glucose, 50% galactose and 10% yeast* pro-

viding the same amounts of the B vitamins as were present in diet III. Animals were placed in individual metal cages with raised screen bottoms to prevent access to feces, and sufficient food was administered to assure *ad lib.* feeding. Feeding was continued for 75 days or until death, whichever occurred sooner; and food and water intake determined daily for all rats.

Results are summarized in Table I. All animals fed galactose-containing diets developed a typical "galactose paralysis" consisting in early stages of an irregular and wobbly gait and progressing to the point of complete disuse of the hind limbs. One hundred per cent of the rats were affected, with severe paralysis developing in general by the 35th day. No significant differences in time of onset or severity of paralysis were observed on the various rations employed. Subsequent to the 35th day a rapid improvement occurred in the paralytic condition of rats fed the yeast-containing ration (diet IV); animals regained use of their limbs and by the 50th day no evidence of paralysis was observed in any of the surviving rats of this group. Recovery of paralyzed rats did not occur on the other rations

¹ Ershoff, B. H., *Am. J. Physiol.*, 1946, **147**, 13.

* Hi-Ribo No. 24, Anheuser-Busch, Inc., St. Louis, Mo. Each gram contained the following vitamin potencies according to the manufacturer: thiamine, 2 mg; riboflavin, 4 mg; pyridoxine, 100-170 µg; pantothenic acid, 200-250 µg; and nicotinic acid, 400-500 µg.