however, may be followed by varying degrees of developed refractoriness to the drug, as evidenced in some mice by a reappearance of normal estrous cycles. The anestrous condition in both strains is accompanied by atrophy of the ovaries and uteri, and atresia of the follicles. Possible modes of action of the *Lithospermum* are discussed.

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## Anesthesia. XXI. Anesthesia and the Steroid Hormones.*

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Selye[1-4] reported that the steroid hormones injected into certain species of laboratory animals produced anesthesia. In the generalization enunciated by Selye and referred to as "the fundamental law of steroid hormone anesthesia," this investigator states that "All compounds having a steroid-hormone action are capable of producing anesthesia while no compound devoid of hormone action possesses this power."[1] Indeed, Cashin and Moravek[5] had previously reported that they had anesthetized cats by injecting cholesterol suspensions intravenously. These experiments, in our opinion, appear to be inimical to the validity of Selye's generalization. In our studies on the effect of cholesterol on ether and pentothal sodium anesthesia, it appeared desirable to study further Selye's generalizations.

*Experimental.* Twenty-five rabbits received 2.5 cc/kg of 2% cholesterol suspension in a 25% solution of polyethylene glycol (Carbowax 1500) intravenously. Most of these animals appeared depressed. Six of them became unconscious and died promptly of acute pulmonary edema.

Fifteen dogs treated in a similar manner all manifested depression. Ten of these animals lost consciousness and died within 5 minutes.

Our attention was directed next to the hormonal steroids. Using the dosage schedules established by Selye we used the following compounds: progesterone, methyl testosterone, stigmasterol, estrone, benzestrol and diethylstilbestrol. Owing to the fact that in the "cat assay" of digitoxin, this glycoside in toxic quantities, produces a depression of the animal so that the anesthetic (ether) may be discontinued, we also used digitoxin in the series. In doses of 50 mg per rat weighing 92-205 g (average 158 g) not any of the foregoing compounds except progesterone and digitoxin produced "anesthesia."

Twenty-six animals, 8 male and 15 female, were used. None of the animals receiving digitoxin recovered from the comatose state produced by the drug. Three of the 9 animals receiving progesterone died.

Neither in the animals which died of progesterone nor with those that recovered was there ever a period in which the animal did not respond promptly to pain stimuli (pinching tail with hemostat). This syndrome cannot correctly be referred to as anesthesia when the sensory pathways are not blocked. In the rat, 6 mg/kg of

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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 Evans[1] 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] Ascheim[4] and Zondek[5] have demonstrated the role of the anterior pituitary gland in maintaining ovarian function. Smith[6] described the profound atrophy of the gonads which invariably follows surgical removal of the anterior pituitary gland of the rat. Moreover, Fee and Parkes[7] 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 Evans[1] have shown, the beginning of

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