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Effect of Choline on the Estrous Cycle of the White Rat.

EDWARD EAGLE. (Introduced by A. B. Luckhardt.)

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Moore and Price[1] presented the hypothesis that the hypophyseal hormones excite gonadal production of germ cells and hormone secretion, and that the gonad hormones of either sex suppress pituitary secretion. This hypothesis is in agreement with the conclusions of Ihrke and D'Amour[2] that injections of male hormone concentrates from bull testis-tissue prepared by Gallagher and Koch caused a suppression of the estrous cycle of female rats as determined by the vaginal smear. This effect on the cycle, immediately abolished by the addition of pituitary substance, was explained by Ihrke and D'Amour on the basis of a diminution of pituitary secretions and a resulting suppression of the normal gametogenic and hormonal activities of the ovaries.

1 Moore, C. R., and Price, D., *Am. J. Anat.*, 1932, **50**, 13.

2 Ihrke, I. A., and D'Amour, F. E., *Am. J. Physiol.*, 1931, **96**, 289.

In 1937, however, Duncan, Gallagher and Koch[3] reported that crude male hormone preparations from testis tissue inhibit the normal estrous cycle in rats, but that this response is not due to the inhibitory action of the male hormone on the hypophysis, but solely to the phospholipin fraction free from male hormone. They further stated that crude choline obtained by hydrolyzing the phospholipins, and pure choline prepared synthetically likewise produced the same inhibition, but that pure testosterone in doses 20 times those found in crude testis-tissue concentrate did not inhibit the estrous cycle. The papers by Robson,[4] and Browman,[5] however, show that testosterone does cause a suppression of the estrous cycle in both mice and rats. The present work was undertaken in the attempt to confirm the report of Duncan, Gallagher and Koch[3] that synthetically prepared choline causes an inhibition of the estrous cycle of the white rat.

TABLE I.
Summary of Rats Used.

	Series A	Series B	Series C	Total
Choline injected rats	29	25	13	67
Uninjected controls	9	17	—	26
Saline injected controls	—	5	—	5
Total No. rats used	38	47	13	98

In Series A, vaginal smears were done daily on 38 rats from January 16th to February 17th, after which 20 of the rats were injected intraperitoneally with 4 mg. of acetylcholine chloride (Hoffmann-LaRoche) and 9 rats were injected intraperitoneally with 8 mg. of the same preparation on the following days, immediately after the smear was taken: Feb. 17th, 22nd, 23rd, 24th, 25th, 26th, 27th and March 1st and 2nd. Vaginal smears continued daily from March 3rd to March 19th showed no evidence of an inhibition of the estrous cycle. The rats were then injected intraperitoneally with 40 mg. (and in 9 expts. with 80 mg.) of choline chloride (Hoffmann-La Roche) on March 20th, 22nd, 26th, 27th, 28th, and 29th. No indication of an interference with the estrous cycle was found, although the experiment was continued to April 21st.

In Series B, after a control period of daily vaginal smears lasting from July 26th to August 19th, subcutaneous injections of 29 mg. (and in 2 expts. 59 mg.) of choline (from choline-HCl, Eastman

[3] Duncan, D. R. L., Gallagher, T. F., and Koch, F. C., *Science*, 1937, **85**, 23.
[4] Robson, J. M., PROC. SOC. EXP. BIOL. AND MED., 1936, **35**, 49.
[5] Browman, L. G., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 205.

Kodak) were made on Aug. 19th, 20th, 21st, 22nd, 23rd, and 24th, immediately following the vaginal smear. This experiment lasted until Sept. 4th, yet no effect on the estrous cycle was noted. The rats in Series A and B were offspring of our active breeding colony, and littermate controls were used throughout.

In Series C, 13 adult rats with perfectly regular estrous cycles were selected from stock rats by a process of elimination and, after a preliminary control smear period of 16 to 44 days' duration, were all injected subcutaneously for 4 successive days (Dec. 15th to 18th) with 60 mg. of choline chloride (Hoffmann-La Roche) per 100 gm. body weight. The rats were then smeared daily for 17 days following the final injection. Even at this high dose-level none of the rats showed inhibition of the estrous cycle.

On the basis of 3 series of experiments on a total of 98 rats it is concluded, contrary to the findings of Duncan, Gallagher and Koch,[3] that estrous cycles in the rat are not modified by: (a) 4 or 8 mg. of acetylcholine chloride injected intraperitoneally, (b) 40 or 80 mg. of choline chloride injected intraperitoneally, (c) 29 or 58 mg. of choline injected subcutaneously, or (d) 60 mg. of choline chloride per 100 gm. body weight injected subcutaneously.

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Effect of Cysteine on Action of Insulin.

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An earlier paper[1] showed that alloxan produces hypoglycemia in normal rabbits. Alloxan is an oxidizing agent credited with special affinity for sulphydryl groups. If alloxan and insulin induce hypoglycemia through the same mechanism, and if alloxan's effect is produced through interaction with sulphydryl groups of tissues, then one might surmise that the normal hypoglycemic action of insulin could be diminished by the administration of sulphydryl compounds. Specifically, a quantity of sulphydryl groups equal in amount, reactivity and availability to those already in the tissues should diminish the hypoglycemic effect of a standard dose of insulin to one-half.

This paper presents the results of experiments in which cysteine

[1] Jacobs, H. R., PROC. SOC. EXP. BIOL. AND MED., 1937, **37**, 407.