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Failure to Induce Ovulation in Constant Estrous Guinea Pigs.*

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Ovulation may be induced in the rabbit, which normally ovulates only following copulation, by injecting a dilute solution of copper acetate either intravenously[1] or else into the third ventricle.[2] This reaction fails to occur after transection of the hypophysial stalk.[3] Acetylcholine, on the other hand, induces ovulation in the rat regardless of whether the stalk is intact or not.[4]

Guinea pigs with large lesions in the anterior hypothalamus at the caudal border of the optic chiasma fail to ovulate post-operatively.[5] The vaginal membranes of these animals remain constantly open and the genitalia increase markedly in size. The ovaries resemble those of the pre-copulatory rabbit, *i.e.*, ovarian follicles develop but ovulation does not occur spontaneously and corpora lutea are not formed. This disturbance of genital function appears to be due to the failure of the pituitary to release luteinizing hormone. When this hormone is administered artificially, the ovarian follicles rupture, corpora lutea are formed and the vaginal membrane closes. A single injection of luteinizing hormone is sufficient to cause this reaction. The vaginal membrane remains closed for an entire cycle (13-16 days) once luteinization is effected.[6]

Experiments were undertaken to determine whether luteinization might be induced in guinea pigs with this type of disturbance by injecting acetylcholine or copper acetate.

Eight mature female guinea pigs were utilized in this study. Large electrolytic lesions were placed in the anterior hypothalamus of each animal by means of the Horsley-Clarke stereotaxic instrument. Following this procedure, the animals developed the condition of constant estrus. The injection experiments were begun some 3 weeks after the onset of this condition. In one animal, 7.5 mg of copper acetate in normal saline (10 mg/cc) was injected into the jugular vein; in 2 animals, 0.05 mg of copper acetate (in 0.01 cc of saline) was injected into the third ventricle; and in a fourth animal, 0.05 mg of the drug (in 0.01 cc of saline) was injected directly into the pituitary gland. In the 4 remaining animals, a mixture of acetylcholine and physostigmine (10 γ acetylcholine plus 5 γ physostigmine in 0.002 cc saline) was injected directly into the pituitary gland. Following these injections, the animals were observed daily for a period of 9 to 12 days and the condition of the vaginal membrane was recorded. The animals were sacrificed at the end of this period and the ovaries were prepared for microscopic study.

The vaginal membrane of only one of the 4 animals injected with copper acetate closed post-operatively. In this animal, the drug had been injected directly into the hypophysis. The animal became quite ill following the injection and it was killed 7 days later. The vaginal membranes of each of the 4 animals injected with acetylcholine were reduced to a slight tear 4 days after the injections, but they opened widely again within 3 days. The ovaries of all the animals utilized in the experiment were studied microscopically and no evidence of ovulation or corpus luteum formation was found.

These experiments indicate that neither copper acetate nor acetylcholine is capable

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of inducing the liberation of luteinizing hormone in the constant estrous guinea pig. The closure of the vaginal membrane in the one animal injected with copper acetate and the partial closure in the 4 animals injected with acetylcholine was probably due to the debilitating effects of the injections rather than to a specific action of the drugs since no evidence of ovulation nor of luteinization could be found in the ovaries.

Summary. Lesions of the anterior hypothalamus of the female guinea pig may prevent the secretion of luteinizing hormone. The ovaries of these animals undergo marked follicular development but ovulation and luteinization fail to occur. Injections of copper acetate and of acetylcholine failed to induce the liberation of luteinizing hormone in these animals although several routes of injection were employed.

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Treatment of Circulatory Collapse of Experimental Venous Occlusion: Use of Adrenal Cortical Extract and Saline Solution.

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The appearance of a shock-like syndrome and a high mortality rate has been demonstrated in untreated dogs subjected to occlusion of the venous drainage in one leg.[1,2] It has been reported, moreover,[3] that pre-treatment with desoxycorticosterone acetate (DCA) or with adrenal cortical extract (ACE) lengthened the survival time and, in a number of cases, resulted in complete recovery. Post-operative treatment with DCA, so far as recovery was concerned, proved relatively ineffective.[4]

The crucial problem, however, in an experimental attack upon the control of shock would appear to lie, not in the pre-treatment of incipient shock-like states, but in the contravention of such crises once they have set in. The present report deals with the postoperative use of ACE and of physiological saline, administered only after unmistakable signs of collapse have appeared.

Methods. Animals subjected to venous occlusion in one hind limb by suitable ligation and by injection of lampblack,[2] under pentobarbital anesthesia, were followed during their postoperative course for signs of a failing circulation and of systemic distress; mean arterial pressure (femoral puncture), respiratory rate, pulse, and rectal temperature were recorded at intervals. Symptoms of prostration appeared within a postoperative period ranging from 2 to 8.5 hours (Table I); the mean arterial pressure, for example, had fallen to levels as low as 27 mm Hg., and several of the animals were comatose. The therapy then instituted consisted of intravenous administration of ACE (Eschatin*), 3 cc per kg body weight, supplemented by subcutaneous injection of physiological saline, 4% of body weight.

Results. In a series of 18 experiments there were significant increases in the survival time in 6 animals (Table I, animals 2, 3, 5, 6, 8, 10). Of these, 4 were sacrificed after a 2-3-day survival period, at which time they were in good condition. Although no actual measurements were made, the legs with venous drainage occluded appeared to have undergone some reduction in size. Animal 10 was a complete survival, and 3 weeks after operation was in excellent condition; the limb with venous occlusion had returned to normal size. The survival times

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