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A Search for Neurological Mechanisms in Ovulation.*

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There is no doubt that the nervous system is involved in producing the ovulation which follows copulation in the rabbit. The observations here presented represent one phase of our attack upon this problem.

Ascheim and Zondek[1] found that a substance (Prolan) in the urine of pregnant women produces effects similar to the sex hormone in the anterior lobe of the hypophysis. Friedman[2] induced ovulation in the rabbit by the intravenous injection of the urine of pregnant women. The utility of this reaction depends upon the fact that ovulation does not occur spontaneously in the rabbit (Heape,[3] Ancel and Bouin,[4] Hammond and Marshall[5]). We have utilized the Friedman phenomenon to produce ovulation at will in the rabbit. Evidence has been presented that prolan and the sex hormone from the anterior lobe of the hypophysis are not identical (Parkes and Hill,[6] Reichert, Pencharz, Simpson, Meyer and Evans,[7] Evans, Meyer and Simpson,[8] Wallen-Lawrence and Van Dyke,[9] and Loeb[10]). We have been concerned in finding out whether or not any of the efferent pathways from the central nervous system are involved in the ovulation that follows the injection of pregnancy urine into the rabbit. Although ovulation has occurred in transplanted ovaries in many species including man (Knauer,[11] Grigo-

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2 Friedman, M. H., *Am. J. Physiol.*, 1929, **89**, 438.

3 Heape, W., *Proc. Roy. Soc. London*, (Series B), 1905, **76**, 260.

4 Ancel, P., and Bouin, P. J., *J. de physiol. et de path. gen.*, 1911, **12**, 1.

5 Hammond and Marshall, Reproduction in rabbits. 1925. Oliver and Boyd, Edinburgh and London.

6 Parkes, A. S., and Hill, M. J., *J. Physiol.*, 1930, **69**, 23.

7 Reichert, F. L., Pencharz, R. I., Simpson, M. E., Meyer, K., and Evans, H. M., PROC. SOC. EXP. BIOL. AND MED., 1931, **28**, 843.

8 Evans, H. M., Meyer, K., and Simpson, M. E., PROC. SOC. EXP. BIOL. AND MED., 1931, **28**, 845.

9 Wallen-Lawrence, A., and Van Dyke, H. B., *J. Pharmacol. and Exp. Therap.*, 1931, **43**, 93.

10 Loeb, L., *Endocrinol.*, 1932, **16**, 129.

11 Knauer, E., *Z. f. Gynäk.*, 1896, **20**, 524.

rieff,[12] and Frank[13]), this is the first study in the rabbit of induction of ovulation in ovaries completely isolated from the influence of the central nervous system.

Virgin rabbits, weighing 2 to 3 kilos, were isolated in individual cages for 3 weeks. Ovulation was induced in each case by the injection of 8 to 10 cc. of the urine of pregnant women, and the ovaries were examined approximately 20 hours following the injection. An autopsy was done to control the experimental procedures in each of the experiments.

In a series of 5 animals transected at the level of the 10 T spinal cord segment, the 4 into which urine was injected 4 days following the transection, showed ovulation with 3 to 9 rupture points in the 2 ovaries. The one used as a control without the injection of urine showed no ovulation. In one rabbit sectioned at the 4 T segment and in 2 sectioned through the 5 T segments, the ovaries showed 6 rupture points in each case.

Ovulation with 5 rupture points was present in one animal in which the spinal cord was completely removed from 5 T to below the 3 L segment. The spinal cord was removed caudal to the 1 S segment so that all of the sacral nerves were sectioned in one animal and caudal to the 5 L segment in another. Six rupture points were found in the former and 5 in the latter following the injection of pregnancy urine.

Inasmuch as the experiments so far had shown that ovulation occurred even after complete excision of the thoracolumbar segments giving rise to the preganglionic thoracolumbar sympathetic fibers on the one hand and the total absence of the sacral segments of origin of the preganglionic sacral parasympathetic fibers on the other, it was deemed necessary to completely sever the nervous pathways from the central nervous system which might exert an influence upon the ovary. The experiments devised to accomplish this were performed in 3 stages. First, the thoracolumbar cord was completely removed under ether anesthesia. Three days later the animals were again anesthetized with ether and the sacral cord was removed. Following these 2 procedures, the animals ate, drank and defecated. They were in excellent condition. Bilateral section of the vagus in the neck was performed under ether anesthesia after another interval of 5 days. The urine was injected immediately after the last operation. Three animals were used and it seems advisable to describe the autopsy findings individually. In

[12] Grigorieff, W., *Z. f. Gynäk.*, 1897, **21**, 663.

[13] Frank, L., *Z. f. Gynäk.*, 1898, **22**, 444.

one animal in which 2 rupture points were present, the spinal cord was removed from the 4 T through the 2 L inclusive and caudal to the 6 L segment; both vagi were completely sectioned. In another in which 4 rupture points were observed, the cord removal extended from the 4 T through the 2 L segments and caudal to the 6 L segment; both vagi were sectioned. In a third animal, immediately after vagotomy, 10 cc. of urine from a non-pregnant woman was injected. Twenty-four hours later when an exploratory operation was performed, ovulation had not occurred. Immediately 10 cc. of pregnancy urine was injected. The animal died during the night but one follicle had ruptured. Autopsy showed that the spinal cord had been removed from the 4 T through the 2 L segment and caudal to the 5 L segment; both vagi were cut in the neck. Microscopic observations confirmed the occurrence of ovulation where rupture points had been observed grossly.

These experiments conclusively show that ovulation induced by the injection of pregnancy urine does occur in the complete absence of the visceral afferent and efferent vagal pathways to the ovary, and of those which pass to and from the thoracolumbar and sacral segments of the spinal cord. The efferent pathways were certainly completely removed; thus rendering impotent the effect which any few remaining afferent pathways might exert.

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The Protein-Crystalloid Complex as an Antigenic Unit.*

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It was implied in all classical theories of specific immunity that the alien protein molecule functions as a single antigenic unit, stimulating the production of a single antiprotein substance or function. Within the last decade, however, this early theory has been challenged, several European theorists denying the assumed antigenic unity and postulating that the protein molecule is little more than an immunologically inert mechanical "carrier" of potentially antigenic superficial crystalloids. Each of these superficial "determinants," "coefficients," or "unit characteristics," is pictured as func-

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