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An Apparent Sex-Specificity in the Action of Progesterone on Adrenalectomized Cats.

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Stewart[1] first called attention to what he considered an unusual prolongation of the life-span of pregnant cats following adrenal removal. Later, Stewart and Rogoff,[2] working with dogs, reported similar findings and suggested the corpus luteum as the life-maintaining tissue in such animals. The writer[3] was subsequently unable to substantiate these claims in a study of an extended series of pregnant and lactating cats. Recent reports of prolonged survival in adrenalectomized pseudopregnant dogs,[4, 5] rats,[6, 7] and ferrets,[8, 9] together with the availability of progesterone in synthetic form, have led to a revival of interest in this phase of adrenal physiology.

Eight female and 2 male cats were adrenalectomized, and injections of progesterone ("Proluton"*) were begun at the first appearance of definite symptoms of cortico-adrenal insufficiency (anorexia, weakness, uncertain gait). The concentration of the blood glucose was followed throughout all experiments, and terminal determinations of the serum sodium, chloride, potassium and urea were made, as well as liver, muscle and cardiac glycogen.

The results obtained from the injection of progesterone into male animals indicated that the hormone served as an adequate replacement therapy in the absence of the adrenal cortex. Particularly notable was the restoration of normal carbohydrate levels following post-adrenalectomy depletion. The recovery of male cats from definite

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[2] Stewart, G. M., and Rogoff, J. M., PROC. SOC. EXP. BIOL. AND MED., 1925, **22**, 394.

[3] Corey, E. L., *Physiol. Zool.*, 1928, **1**, 147.

[4] Rogoff, J. M., and Stewart, G. N., *Am. J. Physiol.*, 1928, **86**, 20.

[5] Swingle, W. W., Parkins, W. M., Taylor, A. R., Hays, W. H., and Morrell, J. A., *Ibid.*, 1937, **119**, 675.

[6] Emery, F. E., and Schwabe, E. L., *Endocrinol.*, 1936, **20**, 550.

[7] Cavanaugh, C. J., and Gaunt, R., PROC. SOC. EXP. BIOL. AND MED., 1937, **37**, 226.

[8] Gaunt, R., *Cold Spring Harbor Symp. Quant. Biol.*, 1937, **5**, 395.

[9] Gaunt, R., and Hays, H. W., *Am. J. Physiol.*, 1938, **124**, 767.

* "Proluton"—synthetic, crystalline progesterone, furnished through the generosity of the Schering Corporation, Bloomfield, N. J.

symptoms of cortical insufficiency was rapid, and similar to that seen in cats treated with cortico-adrenal extract. The blood chemistry at this time was found to be essentially normal. The injection of progesterone was stopped 21 days after operation when both animals were in excellent condition. They subsequently succumbed, with typical symptoms of adrenal insufficiency and careful examination failed to reveal any trace of adrenal tissue.

Non-pregnant female cats, on the other hand, showed no favorable reaction to progesterone injection. All succumbed, indeed, within the usual life-span of untreated animals and with typical symptoms of adrenal insufficiency, despite increased progesterone dosage. The blood and tissues showed the usual abnormal chemical values characteristic of untreated adrenalectomized animals.

Gaunt[8] has shown that in the ferret the symptoms of adrenal insufficiency are accentuated by the injection of estrone. The possibility that the cats used in the present experiments, adrenalectomized in the spring, possessed a sufficiently high estrone content in their blood to vitiate the progesterone therapy should be considered as an explanation of the apparent sex-specificity noted herein.

One pregnant animal, restored from symptoms of adrenal insufficiency, survived 17 days during progesterone treatment. It then succumbed, however, with typical symptoms, although the dosage of progesterone was increased from 10 to 12 mg per day. The abnormally extended survival period of this animal may be accounted for on the basis of additional progesterone secretion from the corpora lutea present in its ovaries, as well as the absence of estrone. These probably favorable conditions, however, failed to maintain life indefinitely.

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Relation of Spermatogenesis to the Factor in the Testis Which Increases Tissue Permeability.

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The ability of aqueous extracts of the mammalian testis to increase the dermal spread of particulate matter has been demonstrated by