

Effects of Cortico-Adrenal Extract on the Estrus Cycle of Hypophysectomized Rats.*

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An adreno-hypophyseal interrelationship has been strongly indicated by numerous lines of evidence. The experiments of Smith,¹ Richter and Wislocki,² Atwell,³ and Cutuly⁴ have shown that extensive atrophy of the adrenal cortex follows complete hypophysectomy in the rat. Collip and his co-workers⁵ have established the elaboration of an adrenotropic hormone by the pituitary, and alterations in carbohydrate metabolism have been shown to follow the ablation of either or both glands.⁶⁻¹² Long¹³ has suggested that the hypophysis may control sugar formation from protein through the mediation of the adrenal. Furthermore, Swingle, *et al.*,¹⁴ report life-prolonging effects from the administration of hypophyseal and anterior-pituitary-like extracts to adrenalectomized cats and dogs. The work of Kitagawa,¹⁵ Wyman,¹⁶ Martin,¹⁷ Martin and Kroc,¹⁸ and Corey and Britton¹⁹ on the cessation of estrus following

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¹ Smith, P. E., *Am. J. Anat.*, 1930, **45**, 205.

² Richter, C. P., and Wislocki, G. P., *Am. J. Physiol.*, 1930, **95**, 481.

³ Atwell, W. J., *Endocrinology*, 1932, **16**, 639.

⁴ Cutuly, E., *Anat. Rec.*, 1937, **66**, 119.

⁵ Collip, J. B., Anderson, E. M., and Thomson, D. L., *Lancet*, 1933, **2**, 347.

⁶ Houssay, B. A., Biasotti, A., and Rietti, C. T., *Compt. rend. Soc. de Biol.*, 1932, **111**, 479.

⁷ Smith, P. E., Dotti, L., Tyndale, H. H., and Engle, E. T., *Proc. Soc. Exp. Biol. and Med.*, 1936, **34**, 247.

⁸ Phillips, R. A., and Robb, P., *Am. J. Physiol.*, 1934, **109**, 82.

⁹ Fisher, R. E., and Pencharz, R. I., *Proc. Soc. Exp. Biol. and Med.*, 1936, **34**, 106.

¹⁰ Chaikoff, I. L., Reichert, F. L., Larson, P. S., and Mather, M. E., *Am. J. Physiol.*, 1935, **112**, 493.

¹¹ Britton, S. W., and Silvette, H., *ibid.*, 1934, **107**, 190.

¹² Corey, E. L., and Britton, S. W., *ibid.*, 1937, **118**, 15.

¹³ Long, C. N. H., *Ann. Int. Med.*, 1935, **9**, 166.

¹⁴ Swingle, W. W., Parkins, W. M., Taylor, A. R., and Morrell, J. A., *Proc. Soc. Exp. Biol. and Med.*, 1936, **34**, 94.

¹⁵ Kitagawa, S. N., *Fujiuko. Gaz. Z.* 22, 1927 (Biol. Abstracts).

¹⁶ Wyman, L. C., *Am. J. Physiol.*, 1928, **85**, 414.

¹⁷ Martin, S. J., *ibid.*, 1932, **100**, 180.

¹⁸ Martin, S. J., and Kroc, R. L., *ibid.*, 1933, **105**, 71.

¹⁹ Corey, E. L., and Britton, S. W., *Proc. Soc. Exp. Biol. and Med.*, 1933, **30**, 592.

adrenalectomy and the restorative effects of cortico-adrenal extracts points in the direction of such an interrelationship.

The present study was designed to determine whether cortico-adrenal extracts possess any estrus-restoring properties when administered to hypophysectomized rats. Three dozen female rats were obtained from the colony of the Wistar Institute,[†] of which 24 were of pure "Wistar" stock and 12 of the "red-eyed-yellow" Castle strain. All animals were between 5 and 7 months of age. The periodicity of the cycles of all rats was established by the vaginal smear method of Long and Evans²⁰ for 2 to 6 weeks prior to operation. Twenty-six animals were completely hypophysectomized[‡] and a total of 34 individual tests were made. No test animal showed an estrous type of smear for more than 2 days following operation, and all reacted positively to the injection of 5 units of "Progynon-B" (estradiol benzoate). The test dosage of cortico-adrenal extract (made by a modified Swingle-Pfiffner technique²¹) was varied from 3 to 10 cc. per day. In the case of a "positive" response, injections were immediately discontinued and subsequent vaginal smears studied to check the possibility of an incomplete hypophysectomy. Otherwise the tests consisted in daily injections of increasing amounts of extract over a period of 7 days.

Of the 34 tests made, 28 were definitely negative and 6 were classified as "positive" (heavy smear—cornified cells only). One animal which showed a negative reaction to the extract alone exhibited the estrous type of smear on 2 successive days following 2 injections of one mg. of thyroxin plus 5 cc. of extract. Continued treatment yielded only negative results and the animal died in diestrus 6 days after beginning the injections.

In another case treatment was begun 35 days after operation and continued for 3 days. A smear of the estrous type was obtained on the day after the first injection, persisting for 4 days. The rat died 24 days later, having shown no subsequent smears indicative of estrus.

Four rats which received extract on the day following operation showed one "positive" smear four days later with no further indications of estrus until death (at an average of 14 days after ces-

[†] Obtained through the kindness of Dr. M. J. Greenman.

²⁰ Long, J. S., and Evans, H. M., *Univ. Calif. Memoirs*, 1922.

[‡] Completeness of hypophysectomy was judged in all cases by the daily vaginal smear record and by gross autopsy findings at the termination of the experiments (examination of the sella; presence of uterine and adrenal atrophy; loss of weight).

²¹ Britton, S. W., and Silvette, H., *Am. J. Physiol.*, 1931, **99**, 15.

sation of treatment). In none of the remaining tests (28) did indications of estrus appear, although some animals were subjected to repeated courses of injection.

From the quantitative standpoint, therefore, the results were negative, and similar to those previously obtained²² in tests of adrenal extracts on ovariectomized rats. In the latter experiments the estrous type of smear appeared in about 30% of cases, although the results were statistically negative. It is concluded that cortico-adrenal extracts of known life-maintaining potency possess no estrogenic value when administered to completely hypophysectomized rats.

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Non-specificity of Orchid Mycorrhizal Fungi.

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While isolating the mycorrhizal fungi from various species of native Wisconsin orchids, several features were noted which are at variance with the usually reported results of European investigators concerning the specificity of mycorrhizal infections. Thirty-three isolations have been made from temperate species, of which at least 16 are morphologically different. All of the strains* possess typical *Rhizoctonia* "spore-forms" as described by Bernard¹ for fungi from tropical and European orchids. One also has a perfect stage with basidia, but its exact taxonomic status has not yet been determined.

There is an apparent correlation between ecological habitat and fungus type, rather than between orchid species and fungus. For example, *Habenaria leucophaea* from a tamarack-sphagnum bog was infected with a different strain of *Rhizoctonia* from that found in the same orchid growing in an open prairie. The two fungus strains differed markedly in spore size, growth characteristics and physiological properties. On the other hand, 4 other orchid species from the above sphagnum bog, *Habenaria dilatata*, *H. hyperborea*,

²² Corey, E. L., and Britton, S. W., *ibid.*, 1934, **107**, 207.

* The word "strains" is here used to denote cultures differing markedly in both morphological and physiological characteristics.

¹ Bernard, Noel, *Ann. Sci. Nat. Bot.*, 1909, **9**, 1.