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**Difference Between Human Anterior Pituitary Extract and Prolan.\***

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Numerous investigations in the last few years have indicated that the effect of administering anterior hypophyseal substances is different from that with the gonadotropic substances found in pregnancy urine. The tests are many: differential morphological changes in mice ovaries (Engle); limitation of the size of the immature rat ovary irrespective of dosage of prolان (Evans); negative response of prolان in birds (Riddle, Schockaert, Reiss); differential effect on hypophysectomized animals (Reichert, Kraul, Smith and Leonard, White and Leonard, Collip and Selye, Wade); and the relative ovulating doses in rabbits (Leonard). In all cases heretofore, the action of prolان was compared with that of the hypophysis of species other than human, namely, the cow and sheep. Recently, it was shown that the human hypophysis was unlike prolان when tested by the ovulation test method (Leonard<sup>1</sup>) in which the minimal ovulating dose in rabbits in terms of rat units equalled  $\frac{1}{4}$  R.U., whereas with prolان it equalled 2 R.U. In this paper it will be reported that the human hypophysis is unlike prolان when tested by other methods.

There is a limit of response to increasing doses of prolان in ovarian enlargement in immature rats which is about 60 mg. (Evans). Twenty immature female rats were injected with doses from 1 mg. to 10 mg. equivalent of dried human anterior pituitary for 5 days. In all cases, the vaginas opened with marked oestrus effects and on the largest doses, the ovaries weighed up to 187 mg. Contrasting to this, 100 to 400 R.U. of prolان produced ovaries weighing only 45 mg. According to this test method, the action of the human hypophysis resembles the hypophyseal action of other species and is different from prolان.

Birds which appear to be non-responsive to pregnancy urine have been shown by others to be very responsive to hypophyseal extracts

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<sup>1</sup> Leonard, S. L., *Anat. Rec.*, 1933, **55**, 26.

of beef and sheep. Six immature white leghorn cockerels, 5 weeks old, were injected with doses of 20, 30, and 50 mg. of alkaline human A.P. extract for 10 days. These doses were not sufficient to increase the weight of the testes markedly, but on histological examination, the tubules were greatly enlarged and contained many mitotic figures. The response with the smaller doses was almost negligible, resembling the controls, but 30 to 50 mg. doses gave a very pronounced histological change. Testes of birds in the same group were unaffected following treatment with prolan.

Thus by 3 different test methods has the human hypophysis been found to be different in its physiological action from prolan.

The human pituitaries were obtained through the kindness of Dr. Kurzrok, of the Department of Obstetrics and Gynecology of the College of Physicians and Surgeons, and Mt. Sinai Hospital.

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### Increased Skeletal Effects in A. P. Growth-Hormone Injections by Administration of Thyroid in Hypophysectomized, Thyro-Parathyroidectomized Rats.

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It has been shown (Smith<sup>1</sup>) and confirmed by a number of investigators that the injection of beef A.P. growth preparations, or the daily implantation of rat pituitaries caused a resumption of growth in rats dwarfed by hypophysectomy. Thyroid administration does not cause growth in the absence of the A.P. (Smith, Greenwood, and Foster<sup>2</sup>). It has been further shown (Flower and Evans<sup>3</sup>) that the A.P. growth hormone induces growth in rats dwarfed by thyroidectomy, a finding in harmony with the fact that A.P. extracts cause growth in hypophysectomized rats even though they may not repair the atrophied thyroids. It thus seems clear that of these 2 glands the A.P. only is essential for growth.

These findings, however, do not demonstrate that the thyroid may not normally aid the growth action of the pituitary or may

<sup>1</sup> Smith, P. E., *J. Am. Med. Assn.*, 1927, **88**, 158; *Am. J. Anat.*, 1930, **45**, 205.

<sup>2</sup> Smith, P. E., Greenwood, C. F., and Foster, G. L., *Am. J. Path.*, 1927, **3**, 669.

<sup>3</sup> Flower, C. F., and Evans, H. M., *Anat. Rec.*, 1925, **29**, 383.