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## Effect of Growth-Promoting Extracts of Bovine Anterior Hypophysis on Hypophyses of Castrated Albino Rats.*

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In view of the reports of Smith[1] and of Evans and Simpson[2] on the prevention of the peripheral action of the gonad-stimulating complex of the anterior pituitary by the simultaneous administration of anterior pituitary growth-promoting extracts, it was thought that the latter might have some influence on the increase in gonad-stimulating potency of the anterior pituitary which has been shown to follow castration.[3]

A growth-promoting extract was prepared from bovine anterior lobe tissue according to the method of Bugbee, Simond, and Grimes.[4] The extract contained also a slight amount of gonad-stimulating substance since a single intravenous injection of 7 cc. produced ovulation in the rabbit, and 0.5 cc. daily for 6 days caused a slight increase in weight of the ovaries and uteri of immature female rats.

The work of Evans and Simpson was confirmed on a group of 12 immature female rats, 4 litters of 3 littermate sisters each. Two females from each litter received 3 glands apiece from littermate male donors daily for 4 days; and to one of these females was administered simultaneously 0.5 cc. of the growth-promoting extract twice daily, subcutaneously, for the 4 days. The females were killed 48 hours after the last implantation, the ovaries and uteri were removed and weighed. The largest ovaries and uteri were found in the group receiving the implantations alone; in the group receiving the implantations plus the extract, the organs were definitely smaller than in the preceding group, indicating a nullification of the action of the implants; yet the organs were definitely larger than in the case of the untreated control group, hence the nullification of the

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[1] Smith, P. E., *J. Am. Med. Assn.*, 1927, **88**, 158.

[2] Evans, H. M., and Simpson, M. E., *J. Am. Med. Assn.*, 1928, **91**, 1337.

[3] Engle, E. T., *Am. J. Physiol.*, 1929, **88**, 101; Evans, H. M., and Simpson, M. E., *Am. J. Physiol.*, 1929, **89**, 371.

[4] Bugbee, E. P., Simond, A. E., and Grimes, H. M., *Endocrinology*, 1931, **15**, 41.

action of the implants was not complete, as reported by Evans and Simpson. This difference can, of course, be explained on the basis of relative dosage.

The extract having thus been shown to be essentially similar to the one employed by Smith and by Evans and Simpson, the following experiment was set up: A total of 120 male albino rats was accumulated, of 30 groups, 4 littermates to a group. Each group of littermates was weaned on the 21st day of life and castrated on the same day. Injections were started the same day, or the day following, and were given subcutaneously, 0.5 cc. twice daily. One animal in each group received the growth-promoting extract; the second animal received the inactive beef-muscle extract; the other 2 animals remained as untreated controls. The injections were continued for about 40 days, or until the animals were approximately 60 days old. At this time, 3 animals from each group were killed. These consisted of the one receiving the growth-promoting extract; the one receiving the beef-muscle extract; and that one of the untreated controls which weighed the most; this latter control thereby served as an age control. The smallest untreated control was allowed to grow until it had reached approximately the same gross weight as its littermate receiving the growth-promoting extract, at which time it was also killed; this control thereby served as a weight control.

When the hypophyses were removed, it was found that both on an absolute and relative weight basis, both the anterior and posterior lobes of the glands from the animals receiving the growth-promoting extract were smaller than in the case of the glands from the 3 control groups; whereas the weights of the glands in the control groups did not differ significantly from one another. Nevertheless, on implantation into immature females, the anterior lobes from the "growth" treated group showed no significant lessening of potency to stimulate the genital system as indicated by ovarian and uterine weights. The significance of the data was arrived at by statistical treatment by the method of paired comparisons.[5]

It is concluded that growth-promoting extracts of the nature described above, when injected for approximately 6 weeks following castration do not prevent the increase of gonad-stimulating potency of the hypophysis, as revealed by the implantation technique, yet do cause a marked diminution in weight of both the anterior and posterior lobes.

[5] Fisher, R. A., Statistical Methods for Research Workers, 3rd ed., 1930, 104.