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Primary Site of Gene Action in Anterior Pituitary Dwarf Mice

Abstract. The transplantation of anterior pituitary glands of normal mice into hypophysectomized dwarf littermates has resulted in mice that are normal in appearance and growth rate. In contrast, the anterior pituitary gland of dwarf animals, when placed in the sella of hypophysectomized normal littermates, failed to promote the growth of these animals. These results indicate that the primary site of gene action in dwarfism lies in the anterior pituitary itself rather than in the hypothalamus.

The dwarf mouse has been used extensively in a variety of endocrine studies. Snell (*1*) demonstrated that the dwarfism is the result of a single recessive gene that is not sex-linked. The immediate cause of dwarfism is the failure of the anterior pituitary gland to function in the production of growth hormone. Smith and MacDowell (*2*) were the first to suggest this cause after observing the hypoplastic nature of the anterior pituitary lobe, the sexual glands, and the adrenal cortex. These two investigators produced dwarf mice that were normal in growth and appearance following daily implants of normal rat pituitaries. Kemp and Marx (*3*) demonstrated normal growth and appearance of dwarf mice following daily injections of anterior pituitary extracts. Francis (*4*) studied the cytology of the pituitary of the hereditary dwarf in some detail and confirmed earlier studies which related the dwarfism to an absence of typical acidophiles and a deficiency of growth hormone. Current interest in hypothalamic-anterior pituitary interrelationships directed our attention to the possibility that the primary site of gene action might lie in the hypothalamus rather than in the anterior pituitary per se.

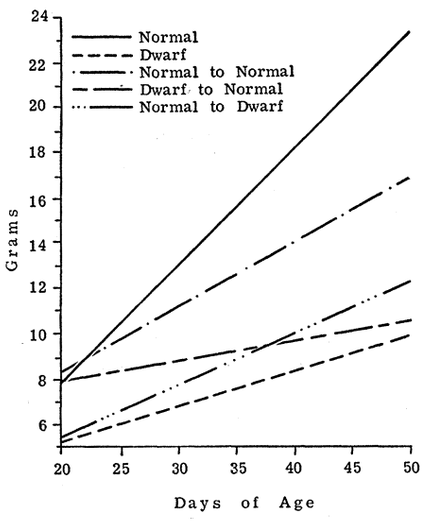

Fig. 1. Growth curves of intact and pituitary graft-bearing mice of the genetic dwarf strain. Each curve represents pooled data obtained from a group of five animals.

In order to answer this question we have transplanted anterior pituitary glands between normal and dwarf members of litters whose parents were heterozygous for the dwarf gene. Our experiments were so designed that the activity of the anterior pituitary homografts could be observed by daily weighings and resultant growth curves. Using littermates, we hypophysectomized normal mice (14 to 18 days old) by the parapharyngeal method. A dwarf littermate of like sex was killed, and its pituitary was placed immediately into the sella of the hypophysectomized normal littermate. The transplanted pituitaries were held in place against the hypothalamus by Gelfoam sponge (Upjohn), and the incision was closed with silk sutures. In this manner, transplants were made from dwarf mice to normal mice, from normal mice to dwarf mice, and from normal mice to normal mice. There were five animals in each of these groups. The growth of these animals and that of five unoperated dwarf and five unoperated normal mice was determined by daily weighings for a 30-day period (20th day through the 50th day). Growth curves representing these five groups of mice were then made.

Our observations were as follows (Fig. 1). (i) Unoperated normal mice gained 15.5 gm. (ii) Unoperated dwarf mice gained 4.4 gm. (iii) Hypophysectomized normal mice bearing transplants from normal mice gained 8.7 gm. (iv) Hypophysectomized normal mice bearing transplants from dwarf mice gained 2.8 gm. (v) Hypophysectomized dwarf mice bearing transplants from normal mice gained 6.7 gm.

More important than the total weight gain is the rate of weight gain. The rate of weight gain in hypophysectomized dwarf mice bearing pituitaries of normal mice was almost equal to the rate of growth of hypophysectomized normal mice bearing pituitary transplants from normal mice. On the other hand, the rate of weight gain of hypophysectomized normal mice bearing pituitaries of dwarf mice was even less than the rate of growth of unoperated dwarf mice.

These results indicate that the hypothalamus of the hereditary dwarf mouse is capable of stimulating a pituitary graft from a normal animal to function at a level comparable to that seen in normal animals bearing similar pituitary grafts. It is noteworthy that the dwarf mouse, when given a normal anterior pituitary as an intrasellar graft, comes to resemble a normal mouse in rate of growth and in physical appearance. Also, the evidence obtained indicates that the pituitary of the dwarf mouse is incapable of producing significant amounts of growth hormone, even when it is placed in contact with the hypothalamus of a normal animal. This shows rather clearly that the anterior lobe of the pituitary and not the hypothalamus is the primary site of gene action in the anterior pituitary dwarf mouse.

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Heterogeneity of Ion Exchange Resins

Abstract. The density gradient method of Linderström-Lang has been used to study density variations among swollen beads in batches of cation exchange resin. Solutions of salts such as sodium tungstate which have dense anions are used. Certain commercial resins appear to be very uniform in cross linking and sulfonation.

A report by Högfeldt (*1*) shows that individual beads in a batch of ion exchange resin can differ widely in their characteristics. Beads taken from a batch of sulfonated polystyrene resin with a nominal 4 percent of cross linking showed selectivities for silver ions against hydrogen ions which varied by a factor of more than 2. Parallel variations were found in the swelling. These could be due to differences in cross linking, sulfonation, or both.

In our laboratory we are studying the thermodynamics of ion exchange,