ease[22] and nontoxic multinodular goitre[23]. Thus, TSH-receptor antibodies do not necessarily lead to thyroid cell stimulation in all cases. This finding seems paradoxical, but might be explained by complete target cell destruction in Hashimoto's thyroiditis and variations in affinity and specificity of thyroid receptor antibodies in ophthalmic Graves' disease[22] and nontoxic multinodular goitre[23]. Further studies, evaluating a possible influence of MHC genes (including Ia type alloantigens) on persisting TSH-receptor antibody production in those Graves' disease patients who tend to relapse frequently, seem to be essential.

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An immunohistochemical and ultrastructural comparison of the effects of 2-bromo-α-ergocryptine on intrasellar and transplanted rat pituitaries

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Summary. Following 2 weeks of administration of 2-bromo-α-ergocryptine, a marked decrease was observed in prolactin immunoreactivity of the grafted pituitaries, whereas no reduction was noted in the intrasellar pituitaries. No evidence of crinophagy was revealed by electron microscopy in prolactin cells of 2-bromo-α-ergocryptine-treated rats.

The drug, 2-bromo-α-ergocryptine (bromocryptine), a dopaminergic agonist is known to cause a reversible suppression of pituitary prolactin secretion[2-4]. Controversy still exists as to whether the action of the drug is mediated through the hypothalamus[5] or directly on the prolactin cells of the pituitary[6,7]. This study investigates the effects of bromocryptine on the immunohistochemical and ultrastructural features of prolactin cells in the intrasellar and ectopic pituitary transplanted beneath the renal capsule.

Materials and methods. 35 male R-Amsterdam rats, maintained on Purina Chow and tap water, ad libitum, were divided into 4 groups. Groups 1 and 2 contained nontransplanted animals. Groups 3 and 4 were comprised of hypophysectomized animals with portions of the anterior pituitary grafted under the renal capsule. Groups 1 and 3, consisting of 9 and 8 animals, respectively, served as controls and remained untreated. Groups 2 and 4, both with 9 animals each, were given bromocryptine (Parlodel®, Sandoz) in a dose of 0.5 mg/100 g b.wt, through a gastric tube, once a day for 2 weeks.

6 animals from groups 1, 2 and 4 as well as 5 animals from group 3 were decapitated and the intrasellar and grafted pituitaries were removed, fixed in formalin and embedded in paraffin for light microscopy. For the immunohistochemical demonstration of prolactin, the antiperoxidase technique was used as described previously[8]. The prolactin antibody was kindly donated by Dr A.F. Parlow, through the NIAMDD Rat Pituitary Hormone Distribution Program.

For electron microscopy, pieces of adenohypophyses were removed from 3 animals in each group, fixed in glutaraldehyde, postfixed in OsO_4 and embedded in Durcapan.

Results. Only the cells of the grafted pituitaries showed a marked decrease in immunoreactive prolactin content following bromocryptine administration (figure 1). No recognizable difference in ultrastructural morphology was noted in the intrasellar pituitaries of untreated and bromocryptine-treated rats. However, in the grafts of the hypophysectomized animals, treatment has resulted in involution of prolactin cells (figures 2 and 3).

Discussion. Previous investigations of the mechanism of action of bromocryptine in the rat have shown a rise of pituitary prolaction content with a parallel reduction of serum prolactin levels[9-11] and it was claimed that the discharge of prolactin and not its synthesis was inhibited by bromocryptine. Another study demonstrated that estrogen-stimulated pituitary prolactin secretion can be inhibited by bromocryptine[9]. More recent investigations found no sig-

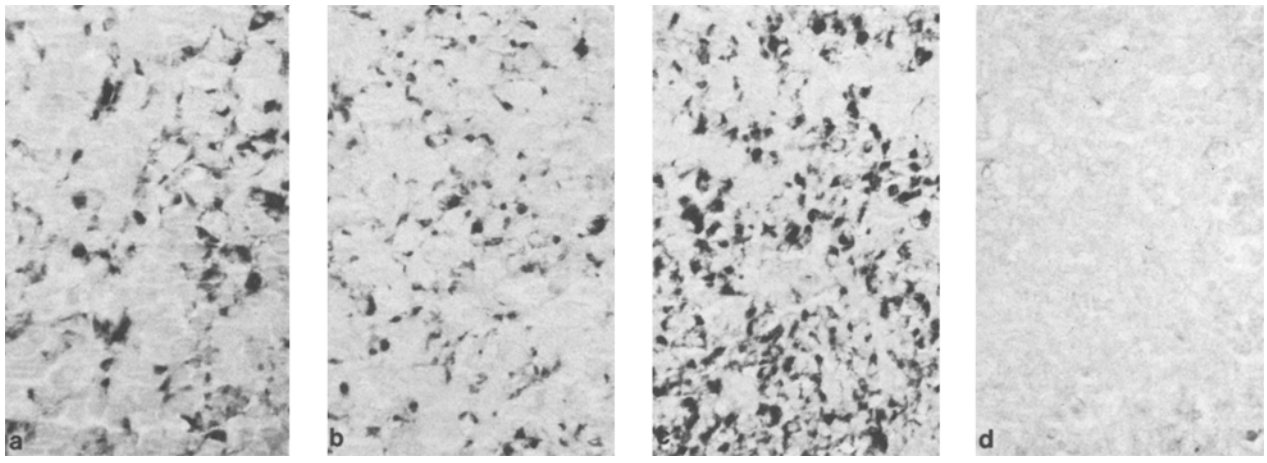

Fig. 1. Immunostaining for prolactin on paraffin embedded sections (× 1000). The adenohypophysis of a control rat (a) is indistinguishable from that of a bromocryptine-treated animal (b). There is an increased prolactin immunopositivity in the grafted pituitary (c); however, there is a marked decrease in the graft following bromocryptine treatment (d).

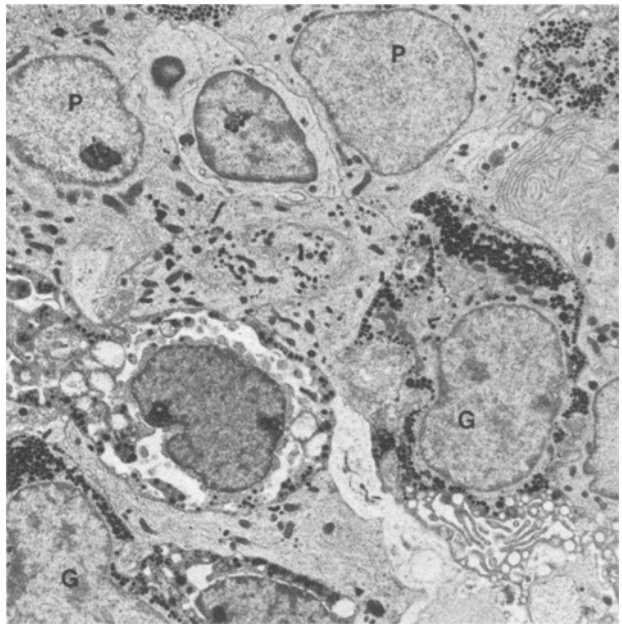

Fig. 2. Electron micrograph of a grafted adenohypophysis, showing growth hormone cells (G) and sparsely granulated prolactin cells (P). × 4900.

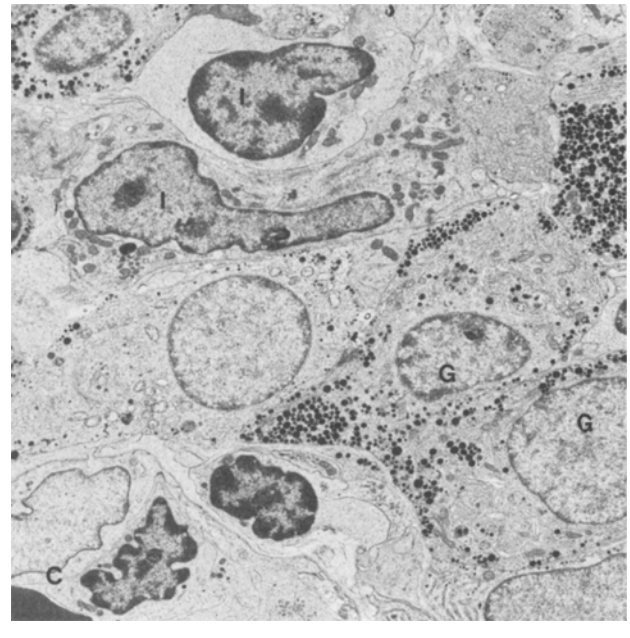

Fig. 3. Electron micrograph of a grafted adenohypophysis of a bromocryptine-treated rat. Growth hormone cells (G) are apparent. There are many unidentifiable cells (I) and no visible prolactin cells. A capillary (C) is also present. × 4800.

nificant change in pituitary prolactin content after bromocryptine treatment, although serum levels were reduced[12]. The drug was also found to cause a marked increase in granule size and number in prolactin cells of lactating animals, but with no evidence of crinophagy[2].

Our study provided evidence that bromocryptine decreases prolactin content in the grafted anterior pituitary, indicating that prolactin cells not directly connected with the median eminence are responsive to and even more susceptible to the effects of bromocryptine than those of the intrasellar pituitary.

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