# Serum Beta-Glucuronidase in Thyroid Disease[1] (34889)

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The induction by thyroxine of metamorphosis in amphibia is associated with increased activity of several lysosomal enzymes in the resorbing tail, presumably in endocytic cells (1). One of these enzymes, beta-glucuronidase, has been shown to increase approximately 20-fold during metamorphosis (1, 2). Were thyroid hormone to have similar effects on mammalian tissues, changes in the amount or distribution of enzyme might be paralleled by changes in the activity of beta-glucuronidase in the sera of patients with diseases of the thyroid. Patients with hyperthyroidism might be expected to show increases in serum activity of the enzymes, myxedematous patients to show decreased activity; in either group, appropriate therapy should return these values to control levels. We should like to submit data indicating that the activity of beta-glucuronidase in the serum of humans does, in fact, appear to vary with the state of activity of the thyroid gland.

*Materials and Methods.* The beta-glucuronidase activity of fresh serum was determined by the method of Fishman *et al.* (3). Samples, 0.2 ml, were incubated with 2.0 ml of acetate buffer, pH 4.5, and 0.1 ml of a 0.01 *M* solution of phenolphthalein glucuronidate. The chromogen was developed after 18 hr incubation at 37°.

Diagnosis was on clinical grounds, and was verified in each case by determination of protein-bound iodine, uptake of $^{131}I$, or determination of protein-bound $^{131}I$ at 72 hr. Patients with equivocal thyroid status were not included in the study, nor were patients with frank liver disease, jaundice, or renal failure. Thyroiditis was diagnosed clinically by signs and symptoms of inflammatory disease of the gland accompanied by an elevated erythrocyte sedimentation rate; each case responded to anti-inflammatory steroid therapy.

*Results.* The data in Fig. 1 show that patients with hyperthyroidism had greater levels of beta-glucuronidase activity in their

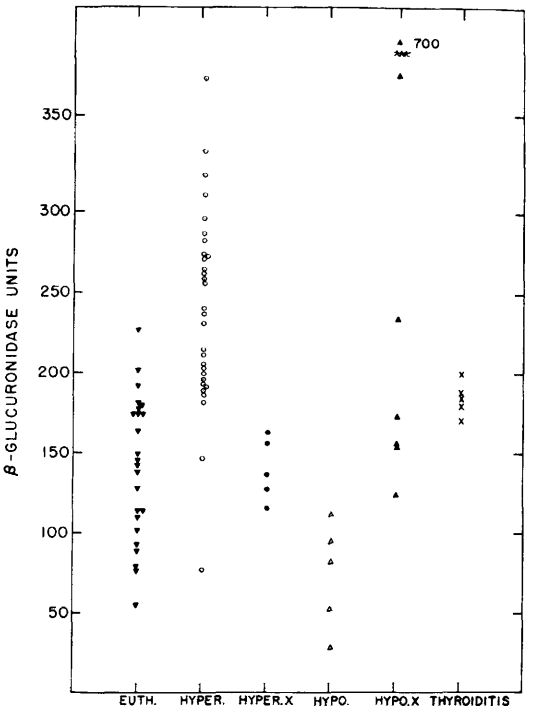


FIG. 1. Serum beta-glucuronidase levels in humans. Euth. = eurhyroid patients; Hyper. = patients with hyperthyroidism; Hyperx. = patients with treated hyperthyroidism; Hypo. = patients with hypothyroidism; Hypox. = patients with treated hypothrodism. The two highest values were in patients given triiodothyronine. X = patients with thyroiditis.

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serum than did euthyroid controls. When hyperthyroidism was brought under clinical control by treatment with $^{131}I$ (three cases) or propylthiouracil (two cases), these elevated levels reverted to normal. Patients with myxedema had lower serum beta-glucuronidase activity than did euthyroid individuals; upon treatment with thyroid extract these levels rose as their clinical status became more nearly normal. The two highest values were obtained with sera from patients treated with triiodothyronine. Patients with thyroiditis did not show significant elevations of serum beta-glucuronidase. None was hyperthyroid at the time of testing.

To exclude the presence of nonspecific inhibitors or activators of the enzymes, sera of hyperthyroid patients was mixed in equal volumes with normal sera. In each of four pairs of sera so mixed, the resultant activity was the arithmetical mean (± 6%) of the two sera before mixing. Similar results were obtained when sera from hypothyroid patients were mixed with normal sera.

*Discussion.* The source of enzyme activity, either in normal subjects, or in patients with hyperthyroidism, remains unknown. Although in most mammalian tissues beta-glucuronidase is sequestered within lysosomes, under some circumstances, a portion of beta-glucuronidase is found in the cysternae of endoplasmic reticulum (4). There is no evidence available indicating a direct effect of thyroid hormone on these particles in mammals. Numerous experiments in our laboratory (unpublished data) have failed to demonstrate any effect of thyroxine, triiodothyronine, or related compounds on lysosomes present in particulate fractions prepared in 0.25 *M* sucrose from a variety of tissues. Stimulation of the thyroid gland by thyrotropin results in endocytosis of thyroglobulin, its subsequent hydrolysis by lysosomal proteases, and release of free thyroxine into the circulation (5). No definite evidence is available as to whether bulk exocytosis, or release of lysosomal enzymes, accompanies this activity. It is furthermore unlikely that the thyroid gland itself is the source of enzyme, since administration of triiodothyronine yielded the highest levels of serum enzyme activity. Increased serum levels of beta-glucuronidase may, therefore, represent increased synthesis in, or release of enzyme from, tissues that have been rendered hypermetabolic by the hormone. Nor would the determination of serum beta-glucuronidase appear to be useful in the specific diagnosis of thyroid disease. Increased serum beta-glucuronidase activity is present in patients given androgens, or with acute pancreatitis, hepatitis, and in frank renal failure. However, the serial determination of serum beta-glucuronidase activity would seem to offer a quantitative means of following the therapeutic response of individual patients with thyroid disease. This might prove of value when the administration of iodone-containing compounds or other drugs has rendered conventional tests of thyroid function inaccurate.

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