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A NOTE ON THE ABSENCE OF THYROID STIMULATING HORMONES IN TOXIC AUTONOMOUS GOITER

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IMPROVED BIOASSAY for thyrotropic hormone (TSH) and long acting thyroid stimulator (LATS), has provided new support for the long held concept of the non-thyroidal origin of Graves' disease. The term "toxic dependent goiter", recently introduced for this condition, is an acknowledgment of our better understanding of its pathophysiology.¹ Simultaneously, we have improved our knowledge of toxic autonomous goiter, the hyperthyroidism first described by Plummer in 1913.² One form of this latter disease, the solitary toxic nodule, is easily identified by the I-131 scintigram. Another form, that represented by conglomeration of many such nodules is more difficult to diagnosis. This type of thyrotoxic patient has a large goiter which antedates his disease, often with a generalized although patchy distribution of I-131 on the scintigram. It has been suggested that such patients usually represent Graves' disease super-imposed on an old multinodular goiter, the areas of lesser activity representing tissue incapable of stimulation.³ This opinion has received support from an assay for LATS done on an elderly patient whom McKenzie considered typical of toxic nodular (autonomous) goiter.⁴ The assay was positive, although the same test was negative when performed on the serum of a patient with solitary toxic nodule.

The authors have recently hypothesized that many large goiters in thyrotoxic patients represent the high end of the spectrum of toxic autonomous goiter. This is an old observation but one never proved using the investigative tools of the past 15 years. In an attempt to make this theory currently acceptable, three recent patients with thyrotoxicosis and large goiters of long duration have been extensively studied. The purpose of this report is to call attention to the results of the analyses for TSH and LATS done on these patients. All were mild to moderately thyrotoxic, gave a history of thirty to forty years of goiter, and complained primarily of the cardiac manifestations of the disease. All had physical findings diagnostic of thyrotoxicosis and none had eye signs of any description or the neuromuscular excitability characteristic of Graves' disease. All had an elevated protein-bound iodine but none had an elevated I-131 uptake. (The latter may have been influenced by the geometry

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involved in counting the large goiters.) The uptake in all was considerably increased by the administration of 10 units of TSH. The laboratory findings are summarized in Table 1.

Table 1

Case	Age	Thyroid Weight	PBI	24 hour I-131 Uptake	Uptake after TSH	LATS	TSH
1	58	195 gm.	14.2	20%	65%	neg.	neg.
2	75	240 gm.	11.2	35%	70%*	neg.	neg.
3	61	340 gm.	9.6	22%	65%**	neg.	neg.

*Estimated from 24 hour urinary excretion of 15%.

**Estimated from 24 hour urinary excretion of 20%.

The appearance of the initial scintigram in each was somewhat dissimilar and the post-TSH scintigram was also. In Figure 1 the scintigram from Case 1 shows several areas of decreased uptake which do not change in B, the post-TSH scintigram. In Case 2, (Figure 2) the effect of TSH is evident in that the hot area in the left lower lobe has disappeared, that is, the surrounding tissue increased in uptake while the hot area did not. It reappeared on a subsequent scintigram. The scintigram of Case 3 (Figure 3) presents a more uniform generalized uptake than the other two, but there is a suggestion of altered distribution of the more active areas after TSH.

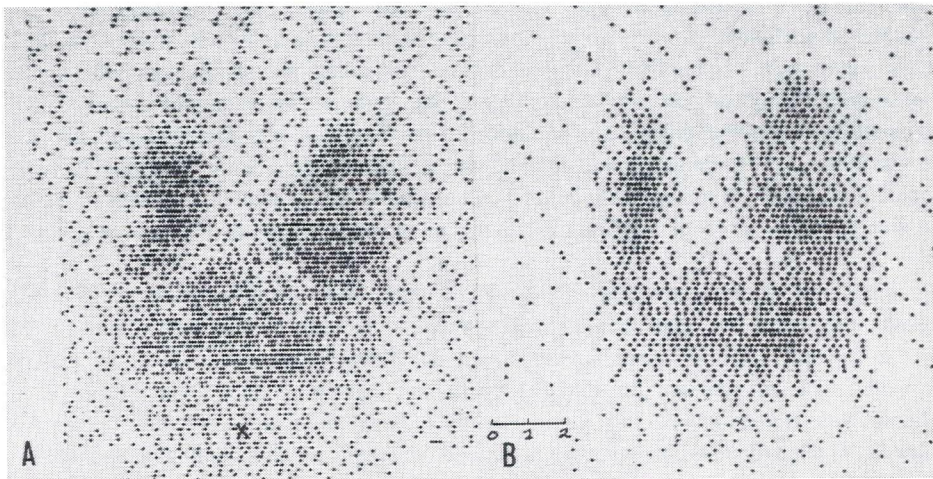


Figure 1

Scintigram of the thyroid, Case 1.
A. Before TSH. B. After TSH.

Serum was withdrawn while the patients were still thyrotoxic, immediately frozen and sent in this state to Bio-Science Laboratories, Los Angeles, California. TSH and LATS were determined by Dr. Orville Golub using the mouse assay method of McKenzie.⁴ The serums of all three were reported as negative for both hormones.

THYROID STIMULATING HORMONES

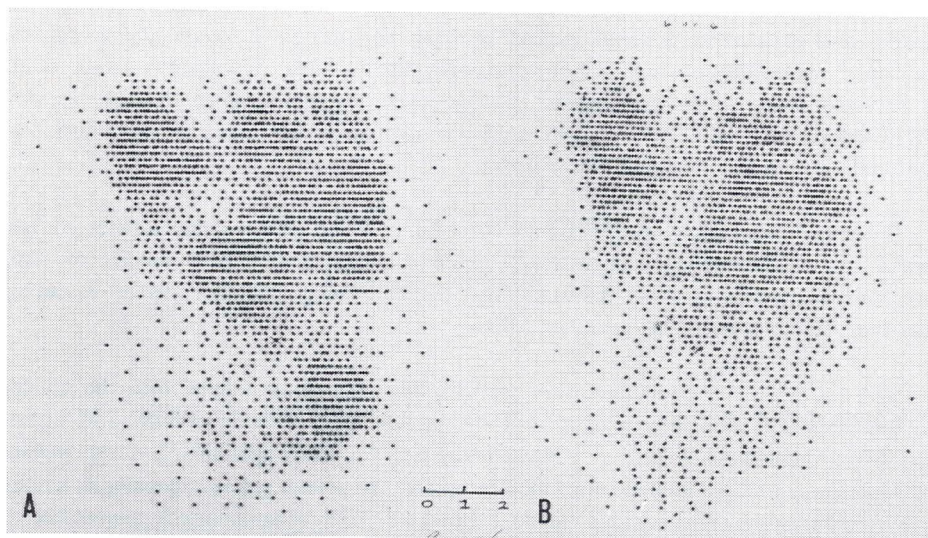


Figure 2

Scintigram of the thyroid, Case 2.

A. Before TSH.

B. After TSH.

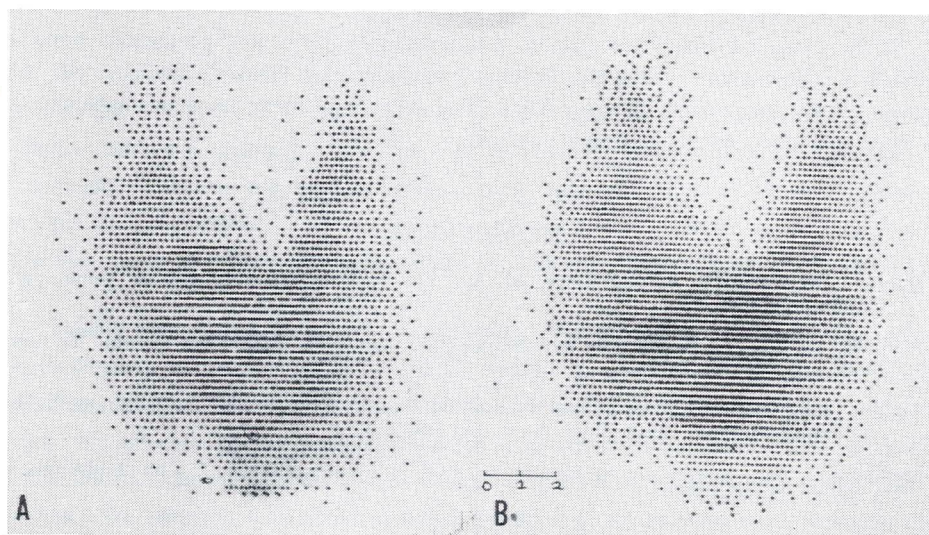


Figure 3

Scintigram of the thyroid, Case 3.

A. Before TSH.

B. After TSH.

Preparation for surgery consisted of methimazole, 100-125 mg. daily, for 2-3 months, and supportive adrenal steroid therapy beginning 12 hours pre-operatively. The latter was continued for 48 hours postoperatively. Case 1 was also given iodides for seven days as insurance against an incorrect diagnosis, even though previous administration of iodides had been said to aggravate her cardiac condition. No beneficial or detrimental effect was noted.

Extensive autoradiographic studies were done which will be the subject of later reports, but neither these nor ordinary tissue sections from 13-17 blocks of tissue per gland suggested Graves' disease. The histopathology did not differ essentially from that of large nontoxic nodular goiters.

The entire clinical and laboratory picture, therefore is consistent with the concept that this disease is similar in pathophysiology to the solitary toxic nodule, and distinct from toxic dependent goiter, or Graves' disease. In these patients a large volume of poorly functioning autonomous tissue eventually produces an unphysiologic amount of thyroid hormone, and toxicity ensues. Pituitary TSH is suppressed, as verified by the assay, and exogenous TSH may stimulate uptake either in suppressed normal tissue or in the autonomous tissue itself. The absence of LATS in the serum further documents the autonomy of the thyroid in this disease. It is not suggested that all large pre-existing goiters in thyrotoxic patients represent the same entity, for Graves' disease may be superimposed on any stage of sporadic or endemic goiter.

SUMMARY

Three cases of toxic autonomous multinodular goiter are presented, none of which had clinical or laboratory findings suggestive of Graves' disease. All had negative serum assays for LATS and TSH. The absence of these hormones substantiates the diagnosis made by more simple methods.

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