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Clinical Studies with the Thyreotropic Pituitary Hormone.

PAUL STARR.

From the Thyroid Clinic, Northwestern University Medical School.

Schittenhelm and Eisler[1] reported the effect of a thyreotropic pituitary hormone in human beings in June, 1932. The metabolic rate of a healthy young woman rose 20%. Eitel and Loeser[2] studied the effect of a Schering-Kahlbaum thyreotropic preparation. From 200 to 300 guinea pig units per day in patients gave uncertain results, but a dosage of 600 units a day caused a rise from +15 to +42% in 7 days. Ten patients were referred to. The dosage values are to be compared with those indicated later. Schittenhelm and Eisler[3] later reported that a man with a postthyroidectomy myxedema sustained no rise in basal metabolic rate with 10 daily injections of 600 guinea pig units of thyreotropic hormone, but during this time the blood iodine concentration rose from 6 to 16 gamma %. In a puerperal obese patient, 4 series of injections led to no increase of metabolic rate but a loss of 10 pounds in weight occurred in a month. Müller[4] gave from 200 to 600 guinea pig units of the Schering-Kahlbaum preparation daily to several patients in the later months of pregnancy, with no observable effects. A thorough study of acute effects of Schering-Kahlbaum and of I. G. Farben industrie thyreotropic preparations was reported by Feuling.[5] Twenty-eight patients receiving 4 daily injections of Schering-Kahlbaum thyreotropic preparation sustained an average rise in basal metabolic rate of 15%; 29 patients receiving the I. G. preparation sustained an average rise of 19%. No prolonged experiments were conducted. Wachstein[6] reported 2 significant cases. A patient with myxedema was very susceptible to the first series of thyreotropic injections, moderately reactive to the second series a month later, but unresponsive to the third series of large doses given in the third month. This may be the first report of refractoriness to thyreotropic medication in a human being. A case of hypophyseal cachexia did not respond to the same medication. Thompson,[7]

[1] Schittenhelm and Eisler, *Klin. Wchns.*, 1932, **11**, 1092.

[2] Eitel and Loeser, *Klin. Wchns.*, 1932, **11**, 1748.

[3] Schittenhelm and Eisler, *Klin. Wchns.*, 1932, **11**, 1783.

[4] Müller, H. P., *Klin. Wchns.*, 1933, **12**, 1899.

[5] Feuling, M., *Deutsches Arch., f. Klin. Med.*, 1933, **176**, 90.

[6] Wachstein, M., *Klin. Wchns.*, 1934, **13**, 1434.

[7] Thompson, W., *J. Am. Med. Assn.*, 1935, **104**, 252.

using Squibb's growth hormone preparation and Wilson's Phyone found a rise of basal metabolic rate in 24 of 39 patients. He pointed out that the complete myxedema patients failed to respond, while the symptoms and metabolic rates of patients with hyperthyroidism were increased. Lederer[8] reported 2 cases of Simmonds' disease treated with a thyreotropic preparation, preglandol, Roche; the metabolic rate rose during treatment but from 3 weeks to a month after treatment fell to even lower levels than had been present originally.

The thyreotropic pituitary hormone preparation used in this study is prepared by Dr. O. Kamm of Parke, Davis and Company. It is described as an aqueous solution of bovine anterior pituitary gland, substantially free of growth, and gonadotropic hormones representing the thyreotropic principle in purified form. It is supplied for experimental purposes under the name Antuitrin T. It contains less than 1% total solids, has a pH close to 7, and is non-irritating. The potency is about 50 guinea pig units per cubic centimeter. Twenty-four patients have been treated with this preparation.

In 4 normal adults one, receiving 3 injections of 1 cc. sustained a rise of basal metabolic rate from 0 to +22 on the eighth day; a second sustained an exactly similar rise but received 8 injections and 21 days were required for the highest elevation of metabolism to be reached; the third and fourth, receiving 5 and 6 injections respectively, increased their metabolic rates 20% in 5 and 7 days. There is thus great individual variation of response in normal individuals.

In 4 castrate women, one receiving 7 injections had a rise of basal metabolic rate of only 3% in 21 days; a second, receiving 8 injections had a rise from —15 to +8% in 21 days; the metabolic rate of the third and fourth cases rose 24% with 4 and 7 injections respectively in 5 and 7 days. There is, thus, great individual variation to this material among castrate women and their responsiveness seems the same as that of normal persons.

Six patients with hypothyroidism, simple and complicated, have been treated with from 6 to 8 daily injections of 1 cc. The basal metabolic rate of one patient with pituitary deficiency of traumatic origin, partial Simmonds' disease, rose from —30 to —11%; 2 patients with congenital hypothyroidism and one with complete adult myxedema failed to respond with any elevation of rate; one mild myxedema and one adolescent hypothyroidism responded to the same degree as the normal adults.

[8] Lederer, J. A., *Rev. Belge des Sciences Med.*, 1935, **7**, 369.

Four adult female patients with large goiters have been treated with 6 daily injections. In one the basal metabolic rate rose from +10 to +34%, with no determinable change in the size of the goiter. In one, no change in metabolic rate was observed but there was a rapid diminution in size of the goiter. An acute variation of metabolic rate may have been missed. In 2 others no distinct changes were observed.

Six patients with hyperthyroidism have been treated. One received only 6 daily injections, sustaining a rise of metabolic rate from +32 to +58. One received 15 injections in 2 months; one received 35 injections in 4 months; one received 112 injections in 11 months. Of these 3 patients, none indicated the development of refraction to the medication or development of thyroid inhibition. Lugol's solution was given during some of this time. One patient, receiving 21 injections, divided into 6 series, during 3 months, failed to increase her metabolic rate with the injections, and after the last series has shown a fall of metabolic rate to normal. One patient received 63 injections during 4 months. During this time Lugol's solution has been administered. The metabolic rate fell to normal in 6 weeks and remains so under Lugol's solution. In 2 of these patients great increase in metabolic rate and symptoms was induced by the thyreotropic hormone; iodine obliterated this effect in the other patients.

Summary. A review of the published reports of the clinical application of the thyreotropic pituitary hormone is given. Our experience with 24 patients is outlined. In normal patients there is great individual variation in reactiveness to the material, as indicated by the basal metabolic rate. This is also true in castrate women. Some patients with low metabolic rates respond, whereas others do not. Patients with goiters respond with similar individual variation. In one, a diminution of the goiter was observed. Acute temporary exacerbation of hyperthyroidism has been produced in 2 patients; this has been prevented by iodine in others; in one patient with hyperthyroidism refractoriness to the medication seemed present before treatment, and treatment was followed by a fall in metabolic rate.