SOME OBSERVATIONS ON THE EFFECT OF *l*-TRI-IODOTHYRONINE ON ACNE VULGARIS*

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Although the cutaneous changes of myxedema and Grave's disease have been well documented, little is known of the role of the thyroid hormone in the physiology of the pilosebaceous apparatus. Our attention was focused on this problem by observations in five patients, aged 15 to 28, with Grave's disease (1). In these individuals, the first appearance of acne vulgaris or striking exacerbation of a previously mild acne occurred 1 to 4 months following induction of eumetabolism by anti-thyroid drugs. Bauer and Goodwin (2) in 1951 similarly reported the transient appearance of acne in a series of male patients with Grave's disease following therapy with carrier-free I^{131}. In recent years, 3-5-3′*l*-tri-iodothyronine (T-3), a naturally occurring thyroid hormone of greater activity and more rapid action than thyroxine, has become available. The ability of this hormone to induce acute alterations in metabolism has prompted further inquiry into the effect of thyroid hormone on acne. The results obtained with T-3 during the fall and winter months of 1957–59 in eleven intensively studied female patients with acne vulgaris form the basis of this preliminary report.

METHODS

Patients were selected as follows: All females with well-established moderate to severe acne who had no clinical or laboratory evidence of abnormal thyroid function and who were in good general health were considered for study. They were placed on a routine of mild topical therapy, consisting of soap and water, 2 per cent sulfur and 0.5 per cent resorcinol ointment, and astringent lotion, and observed at weekly intervals to establish a base line. Those who adhered to the routine and attended clinic for 4 to 9 consecutive weeks were then placed on 4–6 placebo tablets daily and again seen at weekly intervals for 4 to 11 weeks. Patients who showed significant improvement on either topical therapy alone or placebo tablets were excluded from further study. Eleven subjects did not respond to these regimens, but nevertheless faithfully returned for weekly visits to the clinic. In these eleven patients, *l*-tri-iodothyronine* in doses of 100 to 150 μgm daily was substituted for placebo. Observation continued at weekly intervals for 4 to 15 weeks, after which placebo was re-exhibited for 4 weeks.

At each visit, pulse, blood pressure, and weight were recorded and clinical evidences of metabolic status evaluated. Basal metabolic rates were obtained at suitable intervals. The skin was examined independently by two observers. Three separate and possibly unrelated components of the acne process on the face were selected for "quantitation." Oiliness was graded roughly 0 to 3-plus. Comedones were counted and graded: 0; less than 5 (1-plus); less than 10 (2-plus); and more than 10 (3-plus). Papules and pustules were counted and graded on the same scale as comedones. In addition, notations were made of cysts, deep nodules, seborrhea of the scalp, as well as texture and color of the skin.

In evaluating the results of these estimations, an arithmetic mean for each of these components was derived from the numerical grades for all observations in each of the four periods: observation, placebo, T-3, and placebo (see table). Because of the relative lack of scatter in the observations for any individual patient, significant improvement was arbitrarily selected to be a unit of 1.0 in the mean of either the placebo or T-3 over the observation period.

RESULTS

As can be seen from the table, no improvement was noted during the first placebo period except in one patient whose comedones were significantly reduced. During the T-3 period, oiliness improved in 7 patients, comedones in 8, and papules and pustules in 6. No patients showed worsening during this time. While seborrhea of the scalp could

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* *l*-Tri-iodothyronine (Cytomel) and identical placebo tablets were kindly furnished by Smith, Kline and French Laboratories.

TABLE 1

Observations in patients with acne vulgaris during treatment with tri-iodothyronine and placebo

Patient	Oiliness				Comedones				Papules and Pustules			
	Obs.	Pl.	T-3	Pl.	Obs.	Pl.	T-3	Pl.	Obs.	Pl.	T-3	Pl.
J. F.	2.5	2.0	1.8	2.3	1.7	0.6	0.7	2.0	2.2	2.0	1.4	2.7
J. B.	2.2	3.0	0.7	2.2	2.0	2.0	0.7	0.7	2.5	3.0	2.0	1.5
J. G.	2.8	2.7	1.6	2.0	2.0	2.3	0	0.5	2.7	2.3	0	1.7
F. M.	3.0	3.0	1.5	3.0	1.6	1.0	0.5	0.7	2.7	2.0	1.3	1.3
V. M.	2.0	1.7	2.2	2.9	2.5	2.3	2.0	2.2	3.0	3.0	3.0	3.0
P. P.	3.0	2.7	0.9	3.0	2.0	2.0	0.3	1.0	2.2	3.0	2.8	3.0
A. F.	3.0	3.0	1.0	3.0	3.0	2.3	0.5	0.8	3.0	3.0	1.7	2.2
J. M.	2.2	2.7	1.7	2.5	1.8	3.0	2.0	2.5	2.0	2.0	0.2	2.2
M. G.	1.7	1.5	0.2	2.8	2.2	1.8	0.2	0.6	3.0	2.6	1.9	2.3
K. K.	2.0	1.2	1.7	3.0	2.6	2.5	0.9	1.2	2.6	2.4	1.3	1.8
T. M.	3.0	2.5	2.0	2.5	2.1	2.1	1.5	2.1	3.0	2.5	2.3	2.5
Mean....	2.5	2.4	1.4	2.7	2.1	2.0	0.9	1.3	2.6	2.5	1.6	2.1

Obs. = Observation period, Pl. = Placebo period, T-3 = Tri-iodothyronine period. Each valuc is the arithmetic mean of all observations during that period (see text).

not be readily assessed, 8 patients were able to increase the interval between shampoos by 2 to 5 days and still maintain relatively oil-free scalp and hair. In six patients a definite softening and thinning of the skin, accompanied by heightened facial color, appeared 2 to 4 weeks after institution of a minimal dose of 125 μgm of T-3. One to two weeks after re-exhibition of the placebo pill, there was a return of oiliness in all patients with prior improvement; three of the six patients in whom papules and pustules had improved showed a flare in these lesions; no marked exacerbation of comedones occurred in any patient.

The pre-treatment basal metabolic rate average was −12 (range −22 to −2). On the maximal dose of tri-iodothyronine, basal metabolic rates averaged −3 (range −9 to +4). The average change was +9; only one patient failed to get any rise, while in 4 patients the rise was +15 or greater. During the 4 to 15 week period of T-3 treatment, no significant changes in pulse rate, blood pressure or weight were found. Side effects were limited to mild diarrhea and nervousness in one patient on 150 μgm of T-3, and increased dysmenorrhea with scanty menstrual flow in two others.

DISCUSSION

The present report constitutes one phase of a continuing inquiry into the intermediate metabolism of skin. It has been shown that in a small series of female patients, who were refractory to mild topical and placebo therapy, administration of tri-iodothyronine significantly diminished some of the features of acne vulgaris. In the past, thyroid hormone has been advocated for the treatment of acne vulgaris (3, 4, 5). More recently, the value of either desiccated thyroid (6) or even T-3 (7) has been disputed. Data in support of either thesis are scanty. The data presented here do not contribute to the resolution of this controversy and no inference that T-3 is a useful or even desirable adjunct to the therapy of acne can be drawn from them. The short-term studies provide no information about the sustained effectiveness of prolonged administration of T-3. Furthermore, in the doses used T-3 effects an acute increase in the delivery of thyroid hormone to the tissues, suppresses endogenous thyroid activity, presumably by suppression of the thyroid-pituitary axis, and eventually lowers the protein-bound iodine (8). It is obvious, therefore, that conjecture regarding the prolonged implications of such therapy is hazardous.

The present data justify no conclusions about the mode of action of T-3 in acne vulgaris: *i.e.*, whether it acts on the skin *per se* or primarily on the cutaneous vasculature or through other endocrine structures.

The authors do not intend to imply that thyroid abnormalities are involved in the pathogenesis of acne. However, the data may furnish

some clues to the metabolic derangements of acne vulgaris and justify further examination of thyronine derivatives in which systemic and focal metabolic effects (9) may be dissociated as well as the effectiveness of topically applied thyromimetic agents. Such studies are currently in progress.

SUMMARY

A series of 11 selected, eumetabolic female patients with acne vulgaris was treated with *l*-tri-iodothyronine under controlled conditions in a single-blind study. Administration of T-3 in doses of 100–150 μgm daily was accompanied by significant clinical amelioration of the disease.

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