DESICCATED THYROID AND *l*-TRIIODOTHYRONINE ADMINISTRATION IN HYPOMETABOLISM WITHOUT THYROIDAL DEFICIENCY

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NINETEEN patients having hypometabolism of nonthyroidal origin were studied to compare the therapeutic effects of desiccated thyroid and *l*-triiodothyronine. The ages of the patients ranged from 8 to 49 years. There were 6 females and 13 males.

Symptoms

The incidence of symptoms was as follows: obesity, 17 patients; fatigue, 10; drowsiness, 7; loss of hair and dry coarse hair, 3; suspicion of retarded sexual development, 3; mild mental depression, 2; headache, 2; hoarseness, 2; intolerance to cold, 1 patient; muscular and joint pain, 1; mild oligomenorrhea, 1; edema, 1. The relationship between the most common symptoms, obesity and fatigue, and the hypometabolism is not clear. They may appear as the most frequent symptoms in these patients only because they were the complaints that prompted the ordering of a metabolism test. The hypometabolism may have aggravated a tendency to obesity but apparently did not cause the fatigue.

The symptoms in these patients are of little value in ascertaining whether nonthyroidal hypometabolism or true hypothyroidism is present. Consequently, determinations of serum protein-bound iodine (PBI) concentrations, serum cholesterol concentrations, and thyroidal radioiodine† (I^{131})-uptake values were done.

Laboratory Findings Before Treatment

Basal metabolic rates ranged between —15 and —30. Sixteen of the 19 patients had basal metabolic rates of —20 or lower.

Serum cholesterol concentrations ranged from 104 to 257 mg. per 100 ml., the average being 178 mg. per 100 ml.

Serum PBI concentrations were determined in 16 of the patients. The values ranged between 4.0 and 9.0 μg. per 100 ml., the average being 5.8 μg. per 100 ml.

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†*The radioactive material was obtained on authorization of the United States Atomic Energy Commission.*

Thyroidal I^{131}-uptake was determined in 18 patients. Six-hour uptakes ranged from 13 to 26 per cent, the average being 18.9 per cent. Twenty-four hour uptakes ranged from 22 to 48 per cent, the average being 33 per cent.

Effect of thyroid-stimulating hormone (TSH) on thyroidal I^{131}-uptake. In each of five patients in whom the six-hour thyroidal I^{131}-uptake had been previously measured, 5 units of TSH was given subcutaneously. Fifteen hours after the injection of TSH, I^{131} was again administered and the six-hour thyroidal uptake was measured. Four of the five patients demonstrated an increase of 100 per cent or more in I^{131}-uptake after the administration of TSH. In the fifth patient the uptake was increased only from 14 to 18 per cent; this low I^{131}-uptake response may have resulted from the patient's inadvertently taking desiccated thyroid in a dose of 2 gr. daily up to the date of the test.

Treatment

Each patient received *l*-triiodothyronine* in divided doses totaling from 50 to 150 μg. daily, and desiccated thyroid,† from 2 to 6 gr. daily. The hormones were given in separate courses. Twenty-five micrograms of *l*-triiodothyronine was considered approximately equivalent in potential effect to 1 gr. of desiccated thyroid. Basal metabolic rates were determined in all patients at intervals of from one month to two months, and in some the thyroidal I^{131}-uptake, serum PBI, and serum cholesterol values also were determined. The symptoms of all patients were re-evaluated at intervals of approximately one month. The lengths of follow-up ranged from five months to three years.

Results

Table 1 records the basal metabolic rates in the 19 patients before and after treatment with desiccated thyroid and *l*-triiodothyronine, as well as a comparison of the effectiveness of the drugs.

Thirteen patients had no improvement in symptoms. In six patients there was slight improvement; in five of these, improvement was limited solely to a subjective sense of slightly increased energy. In the sixth patient, menses, mildly irregular before treatment, became normal after treatment.

In five of the six patients who experienced improvement in symptoms, the effects of the two drugs were equal. In the sixth patient, desiccated thyroid was more beneficial than *l*-triiodothyronine. In none was *l*-triiodothyronine more effective than desiccated thyroid.

In some patients the basal metabolic rate could be elevated by large doses of *l*-triiodothyronine (100 to 150 μg. daily) or desiccated thyroid (4 to 6 gr.

**Cytomel (liothyronine, synthetic l-triiodothyronine), furnished through the courtesy of Smith, Kline & French Laboratories.*

†Tablets of desiccated thyroid U.S.P., uncoated, Armour Laboratories.

daily). However, most of the basal metabolic rates remained at low pretreatment levels. In general, there was a striking absence of response of both the symptoms and the basal metabolic rates even to large doses of either hormone.

Table 1.—*Results of treatment of nonthyroidal hypometabolism with desiccated thyroid and l-triiodothyronine**

Patient	Dosage		Length of follow-up, months	Basal metabolic rate			Symptomatic improvement	Drug more effective
	Desiccated thyroid, gr. daily	l-Triiodothyronine, μg. daily		Before treatment	After treatment: Desiccated thyroid	After treatment: l-Triiodothyronine		
1	4	100	9	—20	—11	—27	None	—
2	2	50	9	—21	—23	—24	Slight	Equal
3	2	50	6	—27	— 9	—16	None	—
4	3	150	12	—32	—26	—29	None	—
5	3	100	8	—23	—21	—24	None	—
6	6	150	26	—28	—11	—17	Slight	Equal
7	2	50	9	—27	—26	—26	None	—
8	3	50	12	—23	—18	—15	None	—
9	4	100	18	—22	—27	—24	None	—
10	4	100	24	—26	— 5	—11	Slight	Equal
11	6	75	32	—24	—18	—17	None	—
12	4	75	8	—25	—10	—24	None	—
13	3	75	6	—17	—16	—18	None	—
14	2	50	5	—21	+ 9	+ 2	Slight	Equal
15	3	75	7	—24	—16	—14	None	—
16	2	100	10	—29	—29	—25	None	—
17	6	150	8	—23	+ 5	—14	Slight	Thyroid
18	3	50	36	—15	— 8	—16	Slight	Equal
19	3	75	10	—19	—14	+ 8	None	—

*The hormones were given in separate courses.

Discussion

"Metabolic insufficiency,"[1] and "nonmyxedematous hypometabolism,"[2,3] are controversial terms that have been used by some authors in an attempt to denote a variety of symptoms (the most frequent being obesity and fatigue) and an abnormally low basal metabolic rate in the presence of normal results of other tests of thyroid function, including serum PBI, thyroidal I^{131}-uptake, and serum cholesterol determinations. It has been stated that *l*-triiodothyronine is more effective than desiccated thyroid in treating "metabolic insufficiency,"[1-5] but this

condition has been demonstrated not to depend upon a deficient production of thyroxin, and there are no data to support the contention that it results from a lack of *l*-triiodothyronine.

The biologic half-life of radiothyroxin was found by Lasker and Ryan[6] to be normal in three of four patients having "metabolic insufficiency"; and it has been suggested that the reason for the low basal metabolic rates is a disproportion between the mass of metabolizing cells and the mass of fat.[3] In another report[7] radiothyroxin was stated to be eliminated from the blood more slowly in patients having nonmyxedematous hypometabolism than in those having normal metabolism.

In four of our five patients to whom TSH was administered the response was active, indicating that the hypometabolism is not the result of primary thyroid failure. To our knowledge, TSH assays have not been reported as abnormal in this disorder.

The fact that our 19 patients tolerated relatively large doses of desiccated thyroid and *l*-triiodothyronine without overdosage manifestations suggests strongly that their symptoms were not the result of hypothyroidism. Thyroid-replacement therapy was peculiarly ineffective in these 19 patients. When there are an adequate concentration of thyroid hormone in the blood and a lack of cellular response, clinical myxedema should be present; but in these patients it is not. Further study is required to determine whether a basal metabolic rate that is only mildly or moderately depressed is truly abnormal for the individual involved, and, if it is abnormal, to ascertain its cause.

We agree with Keating[8] that to consider "metabolic insufficiency" as a disease entity or as a syndrome is erroneous. The well-controlled studies of Levin,[9] Sikkema,[10] and Goldberg[11] support such a view.

Summary

A group of 19 patients who had symptoms suggestive of hypothyroidism and low basal metabolic rates, but in whom other tests of thyroidal function were normal, did not respond significantly to the administration of *l*-triiodothyronine or equivalent doses of desiccated thyroid.

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