

She has always been an emotional, insecure woman. For years she had anxiety about the health of her husband, who suffered from chronic heart disease and mental disorder until his death in August, 1947. She continues to be over-anxious and is easily upset emotionally. She suffers from paroxysmal auricular fibrillation and often complains of varying symptoms of a functional character.

Discussion

The above case histories are typical of the whole series and illustrate the important psychological features present in every patient. It would appear that emotional difficulties not only play an all-important part in precipitating a thyrotoxic state but also account for the differences in response to treatment and the tendency to relapse in certain cases. Accordingly it seems essential that in the treatment of thyrotoxicosis attention must be focused on the psychiatric aspects. In most cases the acute symptoms have to be controlled with thiouracil before the patient becomes responsive to simple psychotherapy, but the latter may, as in Case 1, prove the most important part of treatment. Admittedly the emotional problem may be difficult to solve and the thyrotoxic symptoms be kept in control only by continued therapy. Nevertheless, the discovery of the psychological disturbance may explain why a patient is unable to abandon thiouracil without relapsing and make it possible to give at least some advice and guidance, which often proves beneficial. It seems particularly desirable that examination of the psychological aspects should be attempted before any decision is made on thyroidectomy, as it might be possible in some cases to improve the patient without operation, while it might cause rejection as unsuitable of those cases which subsequently relapse and which then prove so difficult to control with thiouracil.

In conclusion, reference must be made to the second group in this series. These patients were nervous and had thyroid enlargement, but they were not thyrotoxic, at any rate at the time when examined. Yet four of the 93 patients had had thyroidectomy and a considerable number had in the past been treated with thiouracil without benefit. It is to be noted that, as shown in Fig. 1, these patients belonged to the younger age groups and that they gave a family history of thyrotoxicosis almost as high as that of the thyrotoxic group—11.8% compared with 15.3%. It seems an irresistible conclusion that these nervous goitrous patients are potential sufferers from thyrotoxicosis within the next 10 to 20 years. In view of what has been said above, it would appear desirable that such patients should have early psychiatric treatment in the hope that thereby this serious complication may be averted.

Summary

Examination was made of 265 patients suspected to be suffering from thyrotoxicosis. In only 144 cases was this diagnosis accepted.

Over 60% of thyrotoxic patients gained, and possibly at least 75% will ultimately gain, remission of symptoms after treatment with methyl-thiouracil. Patients who had previously undergone thyroidectomy often required a maintenance dose for an indefinite period and proved particularly liable to relapse if the drug was discontinued.

Inquiry into the psychiatric history revealed in every case disturbances which seemed of great importance in precipitating thyrotoxicosis, in accounting for relapse after either thiouracil therapy or thyroidectomy, and in explaining the necessity for continuing a maintenance dose. An attempt to deal with the emotional factor is regarded as an essential part of the treatment of thyrotoxicosis.

Attention is drawn to a group of patients complaining of nervousness and showing some thyroid enlargement but who

were not regarded as thyrotoxic. It is suggested that such patients may be prone to develop toxic goitre in the future and that psychiatric treatment might be of prophylactic value.

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BODY WEIGHT IN GRAVES'S DISEASE

BY

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Loss of weight is one of the classical features of Graves's disease. It is recognized, however, that sometimes the loss may be insignificant, and occasionally weight may even rise while the disease is still active. Thus Joll (1939) said that "rarely the patient for a time actually gains weight, even very considerably." Linnell, Keynes, and Piercy (1946) pointed out the error of regarding loss of weight as a constant feature of thyrotoxicosis and observed that "maintenance, or even an increase, of weight is not very uncommon even in patients with primary toxic goitre."

Means (1948) noted that the nutritional state in Graves's disease varies greatly but in the average case weight loss is not evident. He added that occasionally a patient actually gains weight while thyrotoxic. A "plump" type of the disease was described by Trotter and Eden (1941). They studied eight patients who were plump in appearance and had gained weight before or after admission to hospital. Apart from the increase in weight these cases had several other features in common, and it was considered that they constituted a special type of Graves's disease. Moreover, differentiation of this type was found to be of practical importance because operative treatment gave unsatisfactory results.

The object of the present investigation was to study the nutritional state in Graves's disease, and the findings are based on 50 cases observed and treated during the past three years. Patients with hyperfunctioning adenoma of the thyroid (Plummer's disease) are not included.

Material and Methods

The series consisted of 47 women and 3 men; their ages varied from 22 to 54 years. Patients were accepted for the investigation only if the diagnosis was undoubted and complications, such as diabetes, were absent; otherwise

they were unselected. The following information was obtained about each case.

Basal Metabolic Rate (B.M.R.).—A considerable number of estimations were made at short intervals until a constant result was obtained. This "level" was usually reached in 10–14 days.

Initial Weight.—This was expressed as a percentage of the expected weight, obtained from age, height, and sex tables, and compared with the patient's own estimate of weight alteration since the onset of symptoms.

Calorie Value of the Diet.—A full dietary history was taken and the daily calorie intake calculated for the period immediately before admission to hospital.

Energy Requirement.—The method described by Wright (1945) was used, allowance being made for the increased B.M.R. A typical day's activity was analysed, with emphasis on the nature of the occupation, the amount of exercise, and the use of leisure. The daily calorie requirement was assessed on the basis of three eight-hour periods of sleep, work, and leisure.

The difference between the theoretical energy requirement and the calculated calorie intake was noted.

Results

The incidence and range of the initial weights is shown in Fig. 1. Seven patients were definitely heavier and 33 lighter than their expected weight; 10 approximated very

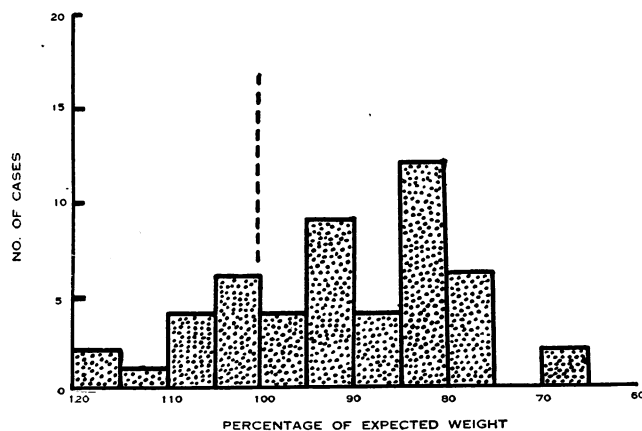


FIG. 1.—Distribution of the initial weights (expressed as a percentage of expected weight) of 50 cases of active Graves's disease.

closely to it. There was a fairly close correspondence in individual cases between the subjective estimate of weight alteration and the measured variation from the expected weight. Thus two patients who could be described as "plump" complained of getting too fat, 12 noticed no change, and 30 had experienced loss of weight of varying degree. Despite a few marked discrepancies—for example, one patient who said that her weight had been steady was only 80% of her expected weight—it was considered that, overall, the calculated percentage of expected weight was a good guide to the actual weight changes (Table I).

The level of the B.M.R. bore no relation to the degree of alteration in weight. The B.M.R. was between +25% and +30% in nine patients whose weights varied from 109%

TABLE I.—Comparison of Subjective Weight Change and Percentage of Expected Weight

Subjective Weight Change	No. of Cases	Average Percentage of Expected Weight
Loss greater than 1 st. (6.3 kg.)	12	83
Loss up to 1 st.	18	88
Nil	12	95
Increase up to 1 st.	6	108
Increase greater than 1 st.	2	118

to 67% of their expected weight. One patient who was acutely ill with all the classical clinical signs of Graves's disease, including marked loss of weight, had a B.M.R. of only +9%.

Age may be of some significance in determining the body's reaction to thyrotoxicosis. With one exception all patients who were heavier than expected were under the age of 30; on the other hand, all over 45 were considerably underweight.

In most cases the balance of daily calorie requirement over intake fell within the range +1,000 to -500 calories. No significance was attached to this degree of difference because of the obvious sources of error in assessing the two figures; when the same methods of calculation were applied to 10 normal adult subjects the range was +700 to -600 calories. The results were striking, however, in the cases at the extremes of the weight range (Table II). The two

TABLE II.—The Difference Between the Daily Calorie Requirements and Intakes Compared with the Initial Weights (Expressed as a Percentage of Expected Weight)

	Balance of Daily Energy Requirements over Dietary Intake (Calories)	No. of Cases	Percentage of Expected Weight	
			Range	Average
Positive	2,500-2,000	2	69-67	68
	2,000-1,500	3	76-75	76
	1,500-1,000	2	102-96	99
	1,000-500	13	107-79	90
	500-0	12	113-81	93
Negative	0-50	14	108-78	92
	500-1,000	1	—	90
	1,000-1,500	1	—	99
	1,500-2,000	2	120-117	118

plump patients (120% and 117% of expected weight) were ingesting 1,850 and 1,600 calories respectively more than they theoretically required. At the other end of the scale all five patients who were 76% or less of their expected weight had a balance of requirement over intake of more than 1,500 calories.

Appetite was stated to be ravenous in 3 cases, increased in 35, unchanged in 11, and poor in one. The estimated value of the diets varied from 4,250 to 1,600 calories a day. The patient who was only 67% of her expected weight admitted having lost about 3 stone (19 kg.) and was taking the lowest diet of all. The figures for the two plump patients were the highest obtained—4,250 and 4,010 calories.

The Plump Cases

Some clinical details are shown in Table III. In Case 15 the adiposity was most marked on the upper back, anterior abdominal wall, and thighs—there were fresh striae in the latter site. This selective distribution was not obvious in the other patient, who just appeared to be moderately overweight. Biopsy of the abdominal wall showed in both instances normal adipose tissue and there was no clinical evidence of excessive fluid retention. The patients were

TABLE III.—Clinical Features of the "Plump" Cases

	Case 15	Case 23
Sex	Female	Female
Age	23	25
Duration of symptoms	4 months	6 months
B.M.R.	+25%	+30%
Percentage of expected weight	120	117
Complaint	Nervousness; goitre; "getting too fat"	Dyspnoea; prominent eyes; goitre; "getting too fat"
Menstrual periods	Regular	Regular
Enlarged tonsils	Absent	Absent
Appetite	Ravenous	Ravenous

considerably incapacitated by symptoms of severe thyrotoxicosis, and emotional instability was very pronounced. There was no menstrual upset.

The family history of Case 15 was of considerable interest. Her elder sister, now aged 36, was treated for Graves's disease by x rays in the Western Infirmary, Glasgow, in 1933. When interviewed, the sister said that during her illness she had a voracious appetite and became "puffy all over." The hospital record states that she was slightly obese and her weight was 139 lb. (63 kg.). At present she is very well and weighs 113 lb. (51.3 kg.). Compared with her younger sister she thought that her own obesity developed more slowly and was more generalized. There was nothing of significance in the family history of Case 23.

Methyl thiouracil alone was used in treatment, and satisfactory remissions were obtained. The drug was administered, in gradually decreasing dosage, for 18 months in Case 15 and for 15 months in Case 23; during the period of therapy they lost 16 lb. (7.3 kg.) and 12 lb. (5.4 kg.) respectively.

The slow reduction in weight was a very striking feature and compares closely with the post-operative finding of Trotter and Eden (1941). The fall in weight was accompanied by a gradual diminution of appetite, and the calorie values of the diets, originally 4,250 and 4,010 calories a day, were 2,350 and 2,200 calories respectively one year after the beginning of treatment. The classical thyrotoxic symptoms such as nervousness, dyspnoea, and tachycardia subsided within a few months. The follow-up has as yet been short; but neither patient has relapsed, and their weights have remained steady.

Fig. 2 shows the striking difference between the weight curves of Case 15 and a patient who was considerably underweight before the start of treatment.

Discussion

Those who are most familiar with toxic goitre in all its manifestations agree that there is no sign of classical Graves's disease which may not be absent. There are many atypical categories, and diagnosis depends on a careful appraisal of the presenting clinical complex. A B.M.R. within the normal range or absence of eye signs does not necessarily exclude active thyrotoxicosis. The same holds for maintenance or even increase of body weight. Provided that natural remission is not taking place, gain of weight reflects an increase in the consumption of food sufficient to counterbalance the raised metabolism.

The plump patients differed from the classical ones in their excessively large appetite. No explanation can be offered for the cause of this bulimia, but its disappearance after treatment probably means that it was specifically due to the hyperthyroidism and not to any chance circumstance. Its occurrence in two sisters suggests the possibility of a

familial influence. Whatever its pathogenesis, the large food intake acts in a protective manner and prevents the wasting which may be such a menacing feature of the disease. In the average case more food is eaten, probably in a vain attempt to counteract the nutritional effects of increased metabolism; occasionally the stimulation of appetite is so great that the attempt succeeds. As regards clinical severity, however, the well-nourished state of the plump patients was deceptive and their symptoms belied their appearance. They were no less seriously ill than more typical cases with an equivalent degree of thyrotoxicosis.

Trotter and Eden (1941) postulated that the plump type of Graves's disease was a specific entity; their patients were all young females who had pronounced signs but few symptoms; the incidence of lymphoid tissue overgrowth and amenorrhoea was higher than in ordinary cases and the results of operative treatment were unsatisfactory. The present investigation does not lend support to this theory. Apart from the gain in weight there were no gross differences between the plump patients and the classical ones. At one end of the scale were the fat patients, at the other the thin ones; between there was every nutritional grade. All were suffering from the same disease process—one which affects the balance of calorie intake and output; the latter usually exceeds the former, but the reverse may hold. The conception that weight is gained only in young women with a particular combination of physical signs seems hypothetical. The present study does support the contention that the set of circumstances causing increase in weight occurs exclusively in the young, but the series is small and only 11 patients were over the age of 40. It may be that the older patients have not the necessary resilience to protect themselves from the increased metabolism by excessive stimulation of appetite.

Thyroidectomy was performed on seven of the cases reported by Trotter and Eden (1941). Two died within a few hours and three had a recurrence. The authors considered that the operation was not only unsatisfactory but also dangerous, and suggested that medical treatment be preferred to surgical. This view was challenged by Linnell, Keynes, and Piercy (1946), whose experience of surgery in plump cases was no less satisfactory than in ordinary patients. If there remains any doubt about the wisdom of undertaking thyroidectomy, thiouracil treatment can be recommended.

Summary

The nutritional state has been studied in 50 cases of active Graves's disease. Their initial weights varied from well above to well below the expected weights. Two patients were plump in appearance.

The body weight depends on the balance between calorie intake and requirement. Appetite is specifically influenced by thyrotoxicosis and may overcompensate for the increased metabolic rate.

The fundamental disease process is the same in all patients whether they have lost or gained weight, and varies only in its relative effects on appetite and B.M.R.

The plump patients responded well to thiouracil therapy.

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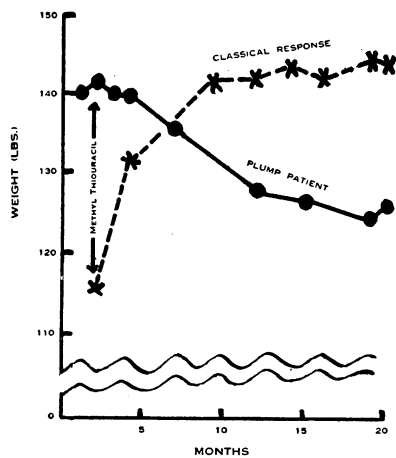


FIG. 2.—Weight curve of a plump patient compared with the classical response to thiouracil therapy.