

Assessment of thyroid function during and after treatment of thyrotoxicosis

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Before treatment of thyrotoxicosis has started it is not possible at present to foretell which patients will experience a protracted illness and which will promptly recover. The aim of assessment during treatment of thyrotoxicosis is to define which course the disease is running and consequently whether antithyroid drugs or destructive therapy will be the more appropriate.

Basis of Plan of Management

Destructive therapy for thyrotoxicosis frequently results in hypothyroidism, necessitating life-long treatment with thyroxine. Antithyroid drug therapy is followed by remission in a considerable proportion of patients and subsequent clinical hypothyroidism is rare. There thus seems to be a strong case for the use of antithyroid drugs as the initial treatment in most thyrotoxic patients under the age of 45 years. Beyond the age of 45 or 50 years the risk of cardiac problems increases.

The plan of treatment proposed is an interim one based on data obtained in a prospective study of 105 patients followed for more than four years (Alexander, McLarty, Horton, and Pharmakiotis, 1973).

Thyrotoxicosis followed one of three courses: remission after one course of antithyroid drugs (group 1, 43 patients, 41%); persistent thyrotoxicosis (group 3, 43 patients, 41%), in these patients either the disease was active more than four years after the start of antithyroid drug therapy (36 patients) or thyrotoxicosis had persisted for two to four years before subtotal thyroidectomy (seven patients); an intermediate group (group 2, 19 patients, 18%).

We suggest, therefore, the use of antithyroid drugs in the majority of patients with Graves' disease under 45 years of age, coupled with repeated assessment of the response to treatment at six-monthly intervals (Alexander *et al.*, 1973; Goolden, Williams, and Thalassinis, 1973). Every six months a decision, based on clinical assessment together with evidence from the tests of thyroid function,

is taken to follow one of three courses of action: to continue with antithyroid drugs, to arrange destructive therapy, or to stop antithyroid drugs if the disease has remitted. In many patients the disease will remit as shown by a return of normal thyrotoxicity. In order to assess the development of thyrotoxicity, triiodothyronine (T_3) in a dose of 80 μg daily is given in conjunction with carbimazole.

In the interim plan described below the choice of the form of destructive therapy (surgery or radioiodine) is assumed to follow conventional lines (Wayne, 1960; McGirr, 1972).

Plan of Management for Thyrotoxic Patients under 45 Years of Age

WHEN THE PATIENT IS FIRST SEEN (FIG 1)

Carry out clinical examination and assess goitre size, measure 20-minute ^{132}I thyroid uptake, measure free thyroxine index (FTI), perform thyroid scan.

Either start treatment with antithyroid drugs and T_3 , or arrange destructive therapy (subtotal thyroidectomy or ^{131}I) if the patient has other serious disease, a large disfiguring goitre above 100 g^{1*} , relapse after thyroidectomy, thyrocardiac disease, or hyperthyroidism associated with functioning nodule(s). At subsequent six-monthly assessments repeat the 20-minute ^{132}I uptake, the FTI and the assessment of goitre size. In the first year FTI is also measured at three and nine months.

AFTER SIX MONTHS' TREATMENT WITH ANTI-THYROID DRUGS (FIG 2)

Change to destructive therapy if the 20-minute ^{132}I uptake has risen,² is above 30%,³ or has not suppressed by 50% of the control value⁴.

Continue with antithyroid drugs for a further six months if the 20-minute ^{132}I uptake has fallen by more than 50%⁵ of the control value, or is less than 8%.

*Superscripts refer to numerals in table.

20 MIN ¹³²I UPTAKE %

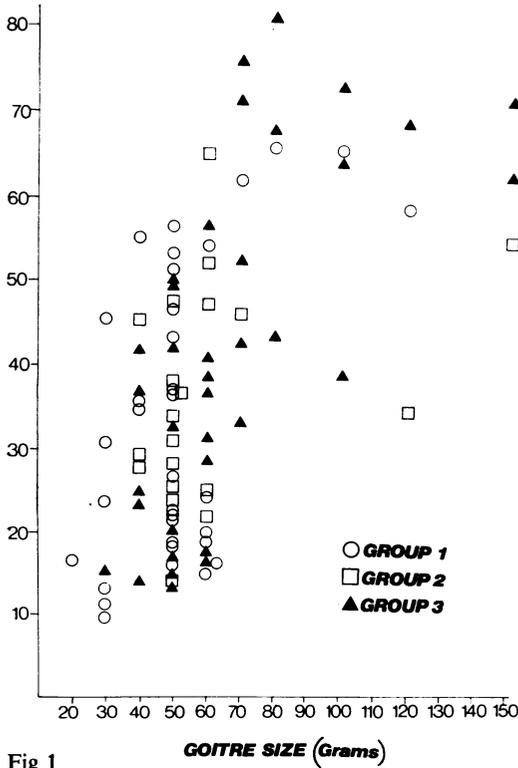


Fig 1

20 MIN ¹³²I UPTAKE %

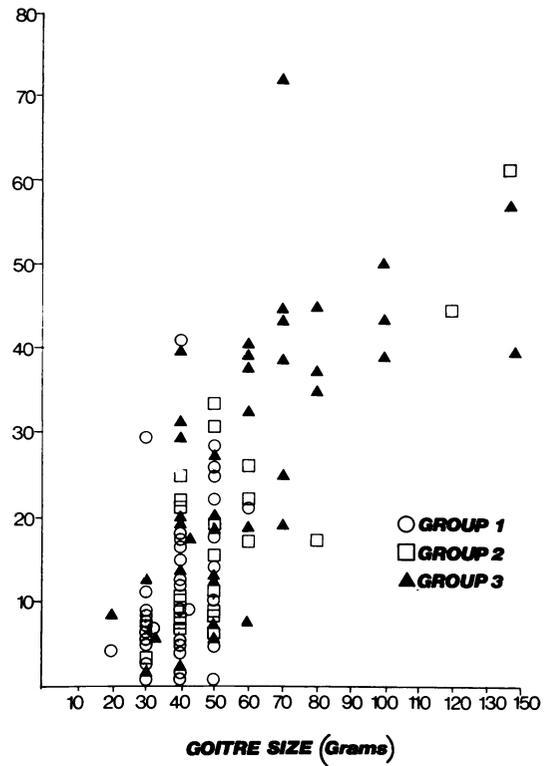


Fig 2

20 MIN ¹³²I UPTAKE %

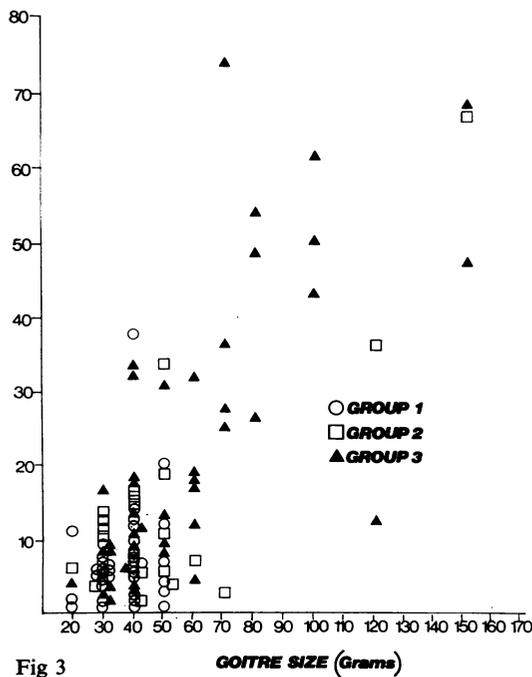


Fig 3

Fig 1 Relationship between goitre size and 20-minute ¹³²I uptake in groups 1, 2, and 3 before the start of treatment.

Fig 2 Relationship between goitre size and 20-minute ¹³²I uptake in groups 1, 2, and 3, six months from the start of treatment.

Fig 3 Relationship between goitre size and 20-minute ¹³²I uptake in groups 1, 2, and 3, 12 months from start of treatment.

AFTER 12 MONTHS' TREATMENT WITH ANTI-THYROID DRUGS (FIG 3)

Change to destructive therapy if the 20-minute ^{132}I uptake is above 15%⁶ and/or the goitre is more than twice the normal thyroid size⁷, measurement of circulating levels of thyroid hormone and enquiry reveal that the patient is not taking tablets regularly.

Continue with antithyroid drugs for a further six months if the 20-minute ^{132}I uptake is between 8 and 15%, and the goitre is not more than twice the normal thyroid size.

Stop antithyroid drugs if the 20-minute ^{132}I uptake is below 8%⁸.

AFTER 18 MONTHS' TREATMENT WITH ANTI-THYROID DRUGS

Change to destructive therapy if the 20-minute ^{132}I uptake is above 15%⁹. Continue with antithyroid drugs for a further six months if the 20-minute ^{132}I uptake is between 8 and 15%.

Stop antithyroid drugs if the 20-minute ^{132}I uptake is less than 8%.

AFTER 24 MONTHS' TREATMENT WITH ANTI-THYROID DRUGS

Change to destructive therapy if 20-minute ^{132}I uptake is above 15%¹⁰. Stop therapy otherwise.

When antithyroid drugs are discontinued after 12, 18, or 24 months, triiodothyronine (80 μg daily) is continued, to determine whether thyroïdal suppressibility continues or not. At this stage serial measurement of the free thyroxine index or PBI provides an adequate indication of the underlying functional state of the thyroid, and is continued six monthly for a further two years. Thereafter, assessment of thyroid status is carried out annually, since recurrence has been observed in one patient as long as 22 years after a first course of treatment with antithyroid drugs.

If hyperthyroidism recurs in those patients in whom thyroïdal suppressibility had returned, antithyroid drugs are restarted and a decision whether or not to change to destructive therapy, continue with antithyroid drugs or stop treatment is again taken every six months on the same plan as before. If relapse follows two courses of antithyroid drugs, destructive therapy is carried out.

Relapse occurred in eight patients in whom the 20-minute ^{132}I uptake had fallen to less than 8% and in whom treatment was discontinued before 12 months from the start of treatment. This suggests that even if the 20-minute uptake falls below 8%, it may be advisable to continue antithyroid drug therapy in such patients for 12 months.

This plan of management is an interim one, and

Text Reference No.	Group			Relapse after First Course	Probability of Relapse after First Course	
	1	2	3			
1	Pretreatment goitre size 100 g or more	2	2	8	10	0.83
2	Increase in 20-min uptake during first six months on carbimazole and T_3	0	3	4	7	1.00
3	20-Min ^{132}I uptake 30% or more after 6 months on carbimazole and T_3	1	3	18	21	0.95
4	20-Min uptake more than 50% of control value after 6 months on carbimazole and T_3	7	6	21	27	0.79
5	20-Min uptake less than 50% of control value after 6 months on carbimazole and T_3	27	11	11	22	0.45
6	20-Min ^{132}I uptake 15% or more after 12 months from the start of treatment	2	5	22	27	0.93
7	Goitre more than twice normal size at 12 months	0	4	19	23	1.00
8	20-Min ^{132}I uptake less than 8% 12 months from the start of treatment	29	9	10	19	0.39
9	20-Min ^{132}I uptake 15% or more 18 months from the start of treatment	1	11	24	35	0.97
10	20-Min ^{132}I uptake 15% or more 24 months from the start of treatment	0	6	13	19	1.00

Table Relation between selected features and probability of relapse in a series of 105 thyrotoxic patients (Alexander et al, 1973)

will require to be tested. Since also the normal radioiodine uptake may vary in different parts of the world and even within the same region (Stanbury, 1969; Pittman, Dailey, and Beschi, 1969), it may be necessary for each centre to establish 20-minute ^{132}I uptake values which correspond with those mentioned in this interim plan. Similar guidelines based on 20-minute $^{99\text{m}}\text{Tc}$ uptakes will also have to be established by those clinics who use it rather than ^{132}I . Measurement of the 20-minute uptake now makes it possible to follow the course of Graves' disease during treatment with antithyroid drugs and to plan treatment accordingly. We recommend that destructive therapy be carried out after two years if the thyroid gland has remained continuously hyperactive. However, since remission may occur beyond this period of time, some physicians might wish to continue antithyroid drugs beyond 24 months. This may be of particular relevance in children and adolescents, since the results of treatment with thyroidectomy and ^{131}I are unsatisfactory and associated with a high morbidity (Reeve, Hales, White, Thomas, and Hunt, 1969; Starr, Jaffe, and Oettinger, 1969). Since the results of antithyroid drug treatment are no different in older age groups, there may be a case for extending the age limit beyond 45 years in some cases, and making a decision whether or not to proceed with destructive therapy after a period of six months on antithyroid drugs.

Long-term Follow Up

Patients who have received treatment for thyro-

toxicosis may have a recurrence or develop hypothyroidism even after several years. Therefore periodic assessment of thyroid status is important and it should probably be life-long. Increasing experience of a computer-assisted follow-up system (using clinical examinations and PBI) has confirmed the initial impression that this simple arrangement achieves advantages for the patient, the general practitioner, and the hospital clinic (Boyle, 1974). Measurement of serum TSH may provide a useful additional index of hypothyroidism when its exact role has been better defined.

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