

THE MANAGEMENT OF RECURRENT THYROTOXICOSIS AFTER THYROIDECTOMY*

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SUMMARY

Thirty-six patients who suffered a recurrence of thyrotoxicosis after subtotal thyroidectomy have been retrospectively analysed. After 11 subsequent second operations, 7 further relapses occurred while 2 patients had permanent recurrent laryngeal nerve paralyses. Only 1 patient out of 18 treated with either long-term neomercazole or beta-adrenergic blockade remained in remission. Radio-active iodine is the treatment of choice in patients who relapse after surgery for thyrotoxicosis.

A significant percentage of thyrotoxic patients treated by subtotal thyroidectomy have a recurrence of the hyperthyroid state.¹⁻⁴ Attention has recently been focused on the management of such patients; in particular the poor results of surgery in such recurrent cases have been emphasized.⁵ This report concerns a retrospective analysis of the management of 36 thyrotoxic patients seen at Groote Schuur Hospital who had a recurrence of hyperthyroidism after thyroidectomy.

PATIENTS AND METHODS

Thirty-six patients (34 females and 2 males) had all been seen and at some stage followed up at the Endocrine Clinic of Groote Schuur Hospital after thyroidectomy for thyrotoxicosis. Recurrence was diagnosed on the usual clinical criteria and confirmed in all cases by elevation of the 6- and 24-hour ¹³¹I neck uptake, the protein-bound iodine (PBI) and the red cell uptake of tri-iodothyronine. While many of the patients were under regular follow-up at the Endocrine Clinic, a number who were living in other cities were not traced at the time of this study but had been previously investigated at Groote Schuur Hospital at the time of the recurrence of the disease. Current clinical status, where possible, was either assessed personally, or by means of a questionnaire sent to the patient and/or attending practitioner.

RESULTS

Time of Relapse After Thyroidectomy

The time of relapse after surgery is shown in Fig. 1. Twenty-one patients (60%) had relapsed within 4 years of subtotal thyroidectomy. In 4 cases this occurred within 6 months of operation. At the other end of the spectrum, 4 patients relapsed after 21 years or more.

Therapy Given for Recurrence

1. *Repeat thyroidectomy*: Ten patients had a second subtotal thyroidectomy and 1 of these subsequently had a third operation for a further relapse. There have been 7 further recurrences after these 11 operations. Four of these recurrences have occurred within 2 years, 1 within 4 years, 1 at 8 years and 1 at 13 years. Of the 4 patients in whom recurrence has not occurred after a second operation, follow-up has been for only 1 year in 2 cases, 2 years in a further case and 7 years in the last instance.

Following 2 of the 11 operations, recurrent laryngeal palsy developed. The incidence of hypoparathyroidism in this group could not be meaningfully assessed as serum calcium estimations were obtained in only 4 cases. In none was hypocalcaemia evident.

After the second relapse, 3 patients have been successfully treated with ¹³¹I and are euthyroid, while 3 of the remainder are currently controlled by antithyroid medication and are not in remission.

2. *Long-term neomercazole*. Eight of the 36 patients had their recurrence treated by neomercazole for a minimum of 6 months. Only 1 such patient was considered euthyroid by clinical and investigative criteria after this time. The remainder were either treated definitively with ¹³¹I (5 cases) or are being maintained on neomercazole (2 cases).

3. *Beta-adrenergic blockade alone*. Ten patients in relapse were treated solely with propranolol 40 mg *q.i.d.* which effectively controlled the signs and many of the symptoms in most cases. However, ¹³¹I uptake and PBI remained abnormal and on stopping propranolol, symptoms and signs returned in all cases. As a result, 9 of the 10 patients have subsequently received ¹³¹I therapeutically.

4. *¹³¹I therapy*. Eight patients received ¹³¹I therapy immediately after recurrence was diagnosed, 3 following recurrence after a second subtotal thyroidectomy, while a further 14 patients received this form of therapy after varying periods on either antithyroid medication or beta-adrenergic blockade.

The satisfactory control of the hyperthyroid state followed 4-10 millicuries of ¹³¹I in all but 1 case, who needed 16 millicuries. The period of time before euthyroidism was achieved varied from months in some cases to up to a year in others. The patient needing 16 millicuries was only controlled after 2 years. Follow-up period has been too short to assess the true incidence of hypothyroidism following the administration of radio-active iodine in these cases. However, 2 patients are already hypothyroid and are on permanent thyroxine replacement therapy.

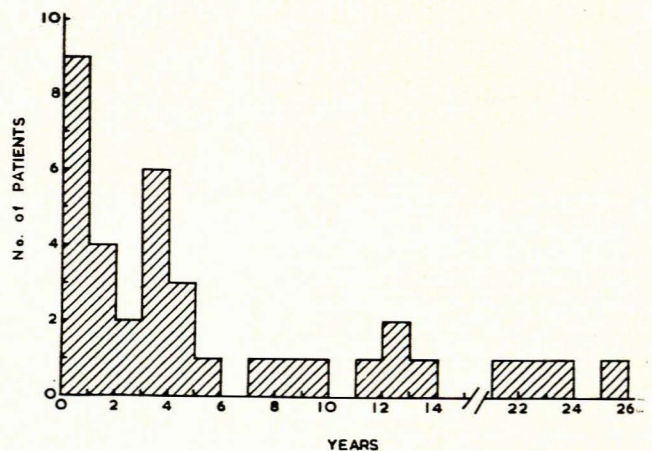


Fig 1. Time of relapse after thyroidectomy.

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DISCUSSION

There is a very wide variation from series to series in the incidence of recurrence of hyperthyroidism after subtotal thyroidectomy. While the average figure is around 5%,^{1,6,7} the incidence has varied from as low as 1.2%,⁸ to 27.9%.⁴

Sixty per cent of our patients relapsed within 4 years of operation, a percentage somewhat lower than that reported by Cattell *et al.*⁹ who found that 76% of recurrences after subtotal thyroidectomy were experienced within 3 years of the operation. McLarty *et al.*⁵ reported figures similar to ours: 55% of their patients relapsed within 5 years after surgery. Yet surveillance after subtotal thyroidectomy must continue indefinitely, for patients may relapse many years after the operation—as occurred in 4 patients in this series.

It was suggested by Taylor and Painter¹⁰ that recurrence after surgery was related to the volume of thyroid tissue left at operation. This is not the feeling of most authors as the incidence of recurrence is not related to a single operator⁵ (in this study many surgeons performed the thyroidectomies) and various volumes of thyroid tissue had been left by the different surgeons. Unfortunately the amount of the thyroid tissue left behind after the initial operation could not be meaningfully assessed in this retrospective study. While very early recurrence could possibly be explained by the size of the thyroid remnant, it is hard to believe that this is true of later recurrences. There appears to be a small but significant number of thyrotoxic patients in whom the stimulus to thyroid hyperplasia remains intense and prolonged. It is impossible at present to predict such patients in whom the removal of 80% or 90% of the thyroid gland will merely lead to an interim remission until such time as the remainder becomes hyperplastic enough for thyrotoxicosis to recur. On the other hand in some patients, for example those in our series who relapsed only after 10 years, recurrence was probably due to a fresh 'bout' of thyrotoxicosis as the cyclical nature of this disease has long been recognized.

It remains to discuss the rational therapy in this group of patients. The consensus of opinion that further attempts at subtotal thyroidectomy are fraught with considerable risk as regards damage to the recurrent laryngeal nerves (of which 2 examples are cited in this article) and parathyroid glands. The folly of such surgical intervention is heightened by the observation in this series (and in others) of the enormous incidence of further recurrence after the second operation. Seven of 11 such patients in our study showed a recurrence and all of 9 patients of McLarty *et al.*⁵ had a similar outcome. In the recent paper by Hedley *et al.*,¹ 5 of 6 patients suffered a recurrence under similar circumstances. Second operation can therefore rarely be justified in recurrent thyrotoxicosis. A possible exception may be severe compression of the trachea causing respiratory distress, when relief of obstruction becomes an urgent problem. Such a patient was recently seen by one of us (G.B.).

Antithyroid medication with or without beta-adrenergic blockade cannot be considered as definitive therapy in this situation as the very factors which tend to favour recurrence after surgery would favour relapse after withdrawal of antithyroid medication. Solomon *et al.*¹¹ con-

firmed that antithyroid drugs were less effective in obtaining permanent remission in patients with postoperative recurrence as opposed to those with primary hyperthyroidism. The experience of McLarty *et al.*⁵ confirms this observation while only 1 of 18 patients in this series on long-term neomercazole or adrenergic blockade obtained remission.

Ablation of the thyroid with radio-active iodine would seem to be the therapy of choice in this difficult situation. In all but 1 of our patients given from 4-10 millicuries of ¹³¹I, euthyroidism returned within a year. An exceptional patient needed a total of 16 millicuries given over 2 years before remission. In this series follow-up has been too short to assess the incidence of hypothyroidism. This has been reported to be high, possibly significantly greater in patients who have had a previous thyroidectomy.¹² Greig¹³ reported an incidence of 41% in a 1- to 8-year follow-up, while Nofal *et al.*¹⁴ found 51% in a somewhat longer surveillance. Thus vigilance after successful therapy with radio-active iodine must be as great as after any other form of therapy.

What is the risk of thyroid neoplasia in young people treated with radio-active iodine? This question is highly pertinent, as the majority of patients with recurrence after thyroidectomy are aged 20-35 years, a group considered by some authorities to be too young to receive ¹³¹I as definitive treatment in the first instance. In a number of major studies,¹⁵⁻¹⁷ the occurrence of late carcinoma in the thyroid has not been shown to be more frequent than could be accounted for by chance alone, although non-neoplastic nodules are described.¹⁵ Leukaemia has not been found. Furthermore, of 56 ¹³¹I treated young female patients reported in one series,¹⁶ 28 had 52 normal children, while 6 of 17 male patients had 17 normal children. There appears therefore to be no serious long-term risk of either malignancy or foetal abnormalities associated with the therapeutic use of ¹³¹I in hyperthyroidism. However, there is probably much more to be learned about its later hazards, so ¹³¹I should not be used as a routine in young people as the first line of treatment. However, in post-thyroidectomy recurrence of hyperthyroidism we regard it as the regimen of choice as other therapy has proved most unsatisfactory.

Do not close the 'casebook' on patients who have had what appears to be an immediately successful subtotal thyroidectomy for thyrotoxicosis. Quite apart from other complications of surgery which are not relevant to this report, the incidence of recurrent hyperthyroidism is significant. It must be anticipated in the individual case when rapid regrowth of the thyroid remnant occurs. Such patients must be carefully watched even though they might be euthyroid at the time. If recurrence does occur and has been confirmed by appropriate investigation, therapeutic ablation with 4-6 millicuries of ¹³¹I is recommended.

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