

approach would appear to have a logical basis if the recent work of Hall [4] with thyroid stimulators, demonstrating that T.S.I. (Thyroid Stimulating Index) [5] falls immediately postoperatively [6], withstands further evaluations. This work provides the first clear evidence that surgery makes a definitive change in the function of the toxic thyroid gland remnant. Therefore, blood supply, or lack of it, may play an important role in the later development of hypothyroidism.

I agree with the follow-up program outlined by Michie *et al*. Patients must be strongly encouraged to undertake their follow-up, even those taking thyroid hormone. They should have both clinical and laboratory review, and thyrotrophin estimations should be part of the basic follow-up requirement.

Hypothyroidism occurs for the reasons outlined and others yet to be revealed to future investigators. To do the best by our patients, in the current state of the art of surgery for hyperthyroidism, long-term follow-up is mandatory. This should include clinical and laboratory assessment and introduction of treatment when appropriate. This is the best insurance against hypothyroidism that can be provided at this time, as the authors suggest.

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## Invited Commentary

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Michie and coworkers have done a very comprehensive study of the incidence and possible causes of hypothyroidism following subtotal thyroidectomy for thyrotoxicosis. Their impressive series of 554 patients, acquired during a decade (1965–1974) in which radioactive iodine was widely used in treating adult patients with Graves' disease, contributes significantly to our knowledge about the end results of subtotal thyroidectomy. Their detailed follow-up, including both clinical and laboratory evaluation of thyroid function, in all of their patients is commendable. Often, mild hypothyroidism is subclinical and not detected unless there is a specific search for evidence.

The authors' concern that hypothyroidism may be a common problem following subtotal thyroidectomy is verified by recent reports showing an incidence ranging from 25 to 70%. Their study shows that the incidence of hypothyroidism is clearly related to the size of the thyroid remnant but may be influenced by the prevalence of thyroiditis and environmental factors. The specific environmental factor they have identified as being significant is the iodine intake. They also emphasize that approximately 15% of patients treated surgically will develop hypothyroidism regardless of technique and remnant size because of the natural history of the disease.

The currently available evidence shows that the 2 traditional goals of subtotal thyroidectomy for thyrotoxicosis, permanent cure and prevention of hypothyroidism, are mutually exclusive. It has been our opinion that the occurrence of hypothyroidism should not be considered a complication of an operation done to cure thyrotoxicosis, but rather as recently stated by Utiger, "a common consequence of effective surgical therapy" [1]. We consider the primary goal of an operation for thyrotoxicosis to be the excision of sufficient thyroid tissue to alleviate the disease and prevent recurrence. Recurrent hyperthyroidism, a more difficult problem to manage, is considered a significant complication and a consequence of inadequate therapy. Definitive treatment of recurrent thyrotoxicosis by reoperation is generally considered hazardous, since such procedures are associated with a complication rate estimated to be at least 3 times that of a primary thyroid operation. The alternative is to recommend  $^{131}I$  even though originally considered unacceptable by the patient or referring physician. Because of these factors, many surgeons accept a high incidence of hypothyroidism, providing that the incidence of recurrence is negligible. The early recognition and appropriate timing of replacement therapy for those patients who develop permanent hypothyroidism, therefore, is of considerable clinical importance.

In a review of 285 thyroidectomies done at the University of Michigan for thyrotoxicosis between 1950 and 1965, Olsen *et al*. found that 25% developed

hypothyroidism and 7% had recurrences when evaluated [2]. In this series, 232 had Graves' disease, treated at a mean age of 24 years, and 53 patients had toxic nodular goiters treated at a mean age of 53 years. The 13 patients (7%) developing recurrences did so from 3 to 9 years after operation (mean 5 years). Fifty of the 200 patients followed for 2 or more years after a subtotal thyroidectomy developed hypothyroidism. The mean time at which this diagnosis was established was 3 months after operation. Only 6 patients in the entire series developed hypothyroidism 6 months or more after operation and only 2 became hypothyroid (1%) after the first 2 years. It was concluded that the critical time for establishing the diagnosis of hypothyroidism was by the sixth month (88%) in most patients, although continued follow-up studies were required after the second year to identify the rare patient with late onset of hypothyroidism and/or evidence of recurrent hyperthyroidism.

Because hypothyroidism is not entirely preventable after subtotal thyroidectomy and attempts to do so result in an increased incidence of recurrence, some surgeons have advocated total thyroidectomy for the treatment of all patients with thyrotoxicosis. For example, Perzik [3] reported that there were no deaths or permanent recurrent laryngeal nerve injuries, and only 1 patient with permanent hypoparathyroidism following this procedure in 326 patients with Graves' disease. There were, of course, no recurrences. Additional benefits claimed were that no patients developed or had progression of existing ophthalmopathy and that the operations eliminated occult or microscopic papillary carcinomas found in 7% of the patients. Exogenous thyroid hormone was given to all patients immediately after operation. The extremely low morbidity rate for total thyroidectomy reported by Perzik in the treatment of benign thyroid disease is unlikely to be equaled by any but very experienced thyroid surgical specialists. In an assessment of the over-all results of thyroid operations in the United States based upon the data from 24,108 thyroid operations performed in 1970, Foster [4] showed that of those patients with toxic nodular goiters, 12% had total thyroidectomies with more frequent complications than the 88% having subtotal thyroidectomies. For patients with Graves' disease having total thyroidectomies (10%), the incidence of complications was not significantly different from those having subtotal thyroidectomies, with the exception of recurrent laryngeal nerve injury which was 7 times more frequent. However, a 3% incidence of hypoparathyroidism following subtotal thyroidectomy seems excessive.

Currently, the majority of patients with thyrotoxicosis referred for surgical treatment at the University of Michigan are 25 years of age or younger. Most

patients 35 years of age or older elect  $^{131}\text{I}$  therapy when offered the choice, although we continue to believe that subtotal thyroidectomy, unless contraindicated because of severe unrelated disease, is good treatment in older adults. We have not done total thyroidectomies for thyrotoxicosis in adult patients, although we have been leaving smaller remnants (4 g) in order to prevent recurrences.

Recently, we have reevaluated our experience with children and adolescents treated surgically for Graves' disease during the period 1969–1976 [5]. In this group of 41 patients with a mean age of 13.3 years, an effort was made to prevent recurrence rather than to prevent hypothyroidism. A remnant estimated to be no larger than 4 g was left in each patient. In many patients the remnant was believed to be only 2 g, and in 7, a total thyroidectomy was performed. The incidence of hypothyroidism in the group treated by subtotal thyroidectomy was 60%. Many of these children did not appear hypothyroid and would not have been detected without the benefit of biochemical studies which included serum thyroxine, triiodothyronine, and thyrotropin (TSH) assays. There was only 1 recurrence in this group, a 2-year-old child who developed a visible goiter 6 months after subtotal thyroidectomy at which a thyroid remnant of 4 g was left. In evaluating our total experience in 85 children having thyroidectomies for Graves' disease from 1945 through 1976, only 1 other patient, also under 10 years of age, developed recurrence. Because none of the children older than 10 years of age have developed recurrence and 40% are euthyroid without replacement therapy, we will continue to do subtotal thyroidectomies, leaving a minimal remnant, in this age group. In those younger than 10 years of age, we have been doing either total or near-total thyroidectomies with the goal of eliminating recurrences altogether because of the need for either years of antithyroid drug therapy or use of  $^{131}\text{I}$ , neither of which is considered satisfactory treatment in this age group. We have had no difficulty in treating hypothyroidism in the pediatric age group and patient compliance has not been a problem after hypothyroidism has been detected. Similar results in children having subtotal thyroidectomies for Graves' disease were recently reported by Wesley et al. [6]. They found that 25 of 43 children (58%) operated upon between 1964 and 1975 at the University of Southern California became hypothyroid, despite a mean remnant size of 4.3 g. Their only recurrence was in a 13-year-old girl who became symptomatic 6 months after operation. They also were encouraged by the relative ease with which hypothyroidism can be treated by thyroid supplements. Consistent with a goal of curing hyperthyroidism, they concluded that the amount of gland left behind should be determined by the margin necessary to protect the integrity of

the parathyroid glands and the recurrent laryngeal nerves, and not on the amount to prevent postoperative hypothyroidism.

From a practical clinical viewpoint, one of the most important aspects of the study of Michie *et al*. is the finding that the PBI levels at 1 and 4 months after operation were of value in predicting the ultimate outcome of thyroid function. They found that when both values were low ( $< 4 \mu\text{g}\%$ ), all patients were permanently hypothyroid and required replacement therapy. Significantly, only 2 of their patients developed hypothyroidism more than a year after operation, confirming the impression that the late insidious development of hypothyroidism following subtotal thyroidectomy is uncommon. We are in agreement with the authors in believing that the diagnosis of permanent hypothyroidism can usually be made by the fourth month after operation. However, a note of caution in this regard has been expressed by Toft *et al*. [7] who found that 20% of their patients were temporarily hypothyroid when studied at 3 months. Only 14% showed evidence of hypothyroidism at 1 year, in contrast to the 34% who would have been considered hypothyroid had not further studies been done at 6 months. Perhaps it would be best to wait for 6 months in an asymptomatic patient before making a final determination as to the need for permanent replacement therapy.

Michie and his coworkers are commended for

their continuing efforts to assure that patients treated surgically receive optimal care. Their continuing follow-up of all patients subjected to thyroidectomy for thyrotoxicosis, through a pioneering computer-assisted program, is a major contribution to the long-term management of these patients.

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