Today's Treatment

Endocrine and metabolic diseases

Treatment of thyroid diseases—II. Goitre

D C EVERED

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A goitre is an enlargement of the thyroid gland, and is common in the general population, even in areas where iodine deficiency is not endemic (10-15% of women and 1-3% of men). Physiological thyroid enlargement commonly occurs at puberty and during pregnancy. It is not possible to detect any disturbance of thyroid function or discover any aetiological factor in most patients and no treatment is required other than reassurance. Thyroid enlargement may not be associated with any disturbance of thyroid function and this article will describe the management of those conditions which commonly present as goitre.

Thyroiditis

AUTOIMMUNE THYROIDITIS

The term autoimmune thyroiditis defines the group of conditions characterised by the presence of circulating thyroid antibodies and sometimes of immunologically competent cells capable of reacting with some thyroid constituents. This group includes those conditions which have been classified as Hashimoto's disease, lymphadenoid goitre, and lymphocytic thyroiditis. There is no specific treatment for autoimmune thyroiditis. Replacement treatment with thyroxine (T4) should be started only in patients with symptomatic hypothyroidism and those euthyroid patients with a raised serum thyrotrophin (TSH) concentration and a goitre which is causing pressure symptoms or placing the patient at a cosmetic disadvantage. The objective of treatment is to relieve symptoms and reduce thyroid size. Sufficient T4 should be given to suppress pituitary TSH secretion. There is no justification for treating asymptomatic patients with T4 and such treatment will not slow the progression of the thyroiditis. Surgical reduction of goitre is rarely required and should only be carried out if severe pressure symptoms are present.

SUBACUTE (DE QUERVAIN'S) THYROIDITIS

No treatment other than simple analgesics is required in mild cases. Most doctors agree that steroids are most effective in controlling symptoms in the more severe cases. The clinical response is rapid and the initial high dose of steroid (30-40 mg

prednisone or equivalent a day) can be rapidly reduced and discontinued after two to four weeks in most patients. It is alleged that relapses are more frequent if steroids are used but this probably only reflects their use in the more severe cases. It is also claimed that the addition of T4 or triiodothyronine (T3) may suppress pituitary TSH secretion, but this lacks proof and seems inherently unlikely since TSH will be suppressed by the rapid discharge of preformed hormone in the acute stages. Sulphonamides, antibiotics, iodine, antithyroid drugs, and irradiation have all been used. There is nothing to recommend any of them and irradiation almost certainly increases the risk of subsequent hypothyroidism.

The acute stage of the disease may be complicated by transient hyperthyroidism but this does not require treatment. Treatment would in any event present problems since the hyperthyroidism results from the discharge of previously synthesised hormone from the gland. Hypothyroidism if it occurs is treated with T4 (see part I of this paper).

INVASIVE FIBROUS (RIEDEL'S) THYROIDITIS

The treatment of Riedel's thyroiditis is primarily directed towards relieving pressure symptoms and most patients need partial thyroidectomy. The disease may become static later or may recur producing further pressure symptoms. No pharmacological preparation is of any value. Thyroid failure may occur if the disease is extensive and should be treated with T4 (see part I of this paper).

Tumours of the thyroid

Most thyroid tumours arise from the epithelial elements of the gland and neoplasms of mesenchymal origin are uncommon. The gross and histological features of both benign and malignant thyroid tumours show wide variations. Many classifications have tended to emphasise these differences, but there is little clinical or therapeutic justification for an elaborate taxonomy.

TUMOURS OF FOLLICULAR CELL ORIGIN

Adenoma

The major clinical importance of the thyroid adenoma lies in the need to distinguish between this lesion and carcinoma. The correct surgical procedure is excision biopsy.

Papillary and follicular carcinoma

There is no absolute agreement on the correct treatment of differentiated thyroid carcinoma. Total thyroidectomy should

probably be carried out in all patients since at least 60% of these tumours can be shown to be multicentric. Good results may be obtained by hemithyroidectomy in some patients but small foci of carcinoma in the other lobe are often invisible to the naked eye and this procedure cannot be generally recommended (and is associated with a considerably reduced survival time). The major complications of total thyroidectomy are damage to the external laryngeal nerves, recurrent laryngeal nerve injury, and hypoparathyroidism. The patient should then be started on replacement treatment with T4 or T3 if no secondary deposits are present. The treatment should restore euthyroidism and suppress pituitary TSH secretion. The TSH level must be suppressed since many well-differentiated tumours are dependent on TSH.

If present, cervical node metastases are generally mobile and should be excised. The patient with lymph node metastases should be left without replacement treatment for the first two months. The patient should become hypothyroid during this time and endogenous TSH levels will rise. A high-dose (200-500 μ Ci) 131 I scan should be carried out after further stimulation with exogenous TSH (10 units intramuscularly). If there are any areas of localised uptake of 131 I the patient should be given a therapeutic dose of 100-150 mCi of radioiodine. One week after treatment or immediately after the scan if no functional tissue has been shown the patient should start replacement treatment with (T3) in sufficient quantities (60 mcg/day) to suppress TSH secretion. Treatment should be stopped annually or earlier if there is clinical or radiological evidence of recurrence and a further scan (200-500 μ Ci) carried out. A further large dose of 131 I may be given before restarting replacement treatment. The advantage of T3 is that it has a shorter half-life than T4 and the patient is, therefore, subjected to the symptoms of hypothyroidism for a shorter period each year.

The management of the patient with skeletal or pulmonary metastases should follow similar lines. Thyroidectomy should be followed by radioiodine treatment (100-150 mCi) after about two months. The patient should subsequently receive replacement treatment with T3, but it may be desirable to give the patient further therapeutic doses of 131 I at intervals of a few weeks to a few months in the early stages of treatment. (131 I scans in patients with distant metastases should be done using at least 1 mCi.) No rigid schedule can be specified for patients in the early stages and T3 should be stopped and a scan performed, with subsequent treatment if indicated, on the basis of regular clinical and radiological assessment. Annual assessment may be instituted when 131 I uptake has been reduced to negligible proportions and no residual tumour can be detected radiologically or clinically. There are few major problems associated with 131 I treatment and the number of cases of leukaemia reported is only just into double figures. The overall five-year survival rate for well-differentiated carcinoma is 75-80%.

Anaplastic and other poorly differentiated tumours

Surgery has little to offer in the management of these tumours, which infiltrate widely and rapidly into adjacent tissues. Many anaplastic tumours are relatively radioinsensitive and the major objective of external beam irradiation is palliation. Reduction in tumour mass, the prevention of obstruction, ulceration, or haemorrhage will all help to make the patient's terminal phase more comfortable. The overall five-year survival rate is less than 20%. Radioiodine plays no part in the management of the undifferentiated tumour.

TUMOURS OF PARAFOLLICULAR CELL ORIGIN

Most medullary carcinomata are slow growing and surgery offers the best chance of cure. Total thyroidectomy should be carried out since many of these tumours are multifocal in origin.

Lymph node metastases should also be excised if possible. Partial resection should be attempted if the complete neoplasm cannot be removed since this may lead to partial relief of symptoms. External beam irradiation should be applied if it is not possible to resect the tumour fully, although this is not always effective. The treatment's success and patient's progress should be monitored by serial measurements of the calcitonin levels. The patient must be given replacement doses of T4 after ablative treatment. The mean survival time from diagnosis is about five years.

The management of coincidental hyperparathyroidism or pheochromocytoma should follow standard lines. Diarrhoea may be troublesome and does not always respond to standard remedies. Therapeutic success with indomethacin and nutmeg have been reported recently.

TUMOURS OF MESODERMAL AND MIXED ORIGIN

Lymphoma—Treatment for lymphoma of the thyroid should be by external beam irradiation. Thyroidectomy is carried out in some patients before the diagnosis is made histologically. Surgery should always be followed by external beam treatment. Replacement treatment with T4 will be required by most patients. The five-year survival rate is about 20%.

Teratoma is very rare. It is almost invariably benign in childhood but is generally malignant if detected in adult life (presumably the result of malignant change in a small and previously undetected teratoma). Surgery is the only treatment available.

Other tumours—Fibrosarcoma, mixed osteogenic and chondrogenic tumours, and the extremely rare haemangioendothelioma of the thyroid are all highly malignant and not generally amenable to treatment.

Endemic goitre

Endemic goitre and endemic cretinism rank among the world's most common major health problems. The role of iodine deficiency in causing endemic goitre is unquestioned, although local factors (such as ingested goitrogens) may play a contributory part in some areas. Treatment of affected communities can be achieved by iodisation of water or salt or by the injection of iodised oil, which provides a depot of iodine that is sufficient for several years. These methods are cheap and simple to apply and thus the problems of endemic goitre and endemic cretinism are potentially eradicable.

Dyshormonogenetic goitre

Dyshormonogenetic goitre is rare. Patients invariably have a goitre (which is TSH dependent) but do not always show the clinical features of hypothyroidism. Treatment should be with T4 in sufficient doses to suppress pituitary TSH secretion. There will be a substantial reduction in the size of the goitre unless irreversible degenerative changes have occurred in the gland. Treatment must be started as soon as the diagnosis is made in the infant or child to prevent permanent impairment of cerebral function or retardation of bone growth.

Is it safe to mix and then give intramuscular tetanus toxoid and intramuscular penicillin through the same hypodermic needle into the same site?

The answer is "no" to both questions. The effects of such a mixture have not been studied in clinical practice and mixing the drugs cannot be recommended. Nevertheless, in animal studies Knight¹ has reported that the effectiveness of adsorbed tetanus vaccine was not reduced when mixed with procaine penicillin before injection.

¹ Knight, P A, in *Symposium on Tetanus in Great Britain*. Leeds, the General Infirmary at Leeds, 1967—quoted in Martindale 26th edn 1972.