Clinical Algorithms

Thyroid enlargement

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Thyroid enlargement, or goitre, is common and present in roughly 10% of women in areas not deficient in iodine. Although throughout the world most goitres result from iodine deficiency, it is the numerous other forms of thyroid enlargement that present in practice and may cause difficulty in diagnosis and management. In some cases, however, the diagnosis is obvious. For example, few would fail to recognise malignancy due to lymphoma or anaplastic carcinoma in a patient with a hard asymmetrical goitre enlarging rapidly over a few weeks, fixed to surrounding tissues, and possibly associated with stridor, recurrent laryngeal nerve palsy, and cervical lymphadenopathy. Similarly, a diagnosis of Graves' disease should be easily apparent in a patient with clinical evidence of hyperthyroidism and exophthalmos and that of medullary carcinoma in a patient with a solitary thyroid nodule who has multiple mucosal neuromas and a history of adrenal-ectomy for pheochromocytoma (multiple endocrine neoplasia, type IIb). In most patients with goitre, however, these helpful clinical features are not present, and it is valuable to begin the diagnostic process by determining by palpation whether the thyroid enlargement is diffuse, due to a solitary nodule, or

multinodular. The following algorithms are based on this subdivision and should be interpreted in conjunction with the accompanying notes.

Diffuse goitre

(1) *Subclinical hypothyroidism* is the term applied to the combination of normal thyroid hormone concentrations with raised concentrations of thyroid stimulating hormone in asymptomatic patients.

(2) *Drugs*—Lithium carbonate, which is widely used in the treatment of manic depressive psychosis, has an antithyroid action, and raised thyroid stimulating hormone concentrations have been recorded in 30% of patients at some stage during treatment. Overt hypothyroidism develops in fewer than 5% and in some patients may be associated with goitre, particularly in those in whom thyroid autoantibodies were present in the serum before the start of lithium treatment. Long term treatment with the iodine containing antiarrhythmic drug, amiodarone, or with iodides, usually

in the form of proprietary expectorants, may also cause goitrous hypothyroidism.

(3) *Dyshormonogenesis* is a rare condition in which there is a genetically determined defect in thyroid hormone synthesis. In its most common form there is a partial lack of the intrathyroidal peroxidase enzyme necessary for oxidation of iodide to iodine before it can be bound organically to tyrosine. Affected patients usually present in childhood or adolescence with goitre and varying degrees of thyroid failure depending on the relative severity of the enzyme defect. The combination of peroxidase deficiency and congenital nerve deafness is known as Pendred's syndrome.

(4) *Simple diffuse goitre* is most commonly found in young women in their teens or 20s. The natural history of this form of goitre in some patients is progression to multinodular goitre over 10-20 years.

(5) *Exophthalmic Graves' disease*—This term is used to describe patients exhibiting the ocular manifestations of Graves' disease in the absence of hyperthyroidism or a history of hyperthyroidism. A goitre may be present. Plasma thyroid hormone concentrations are usually normal but may be low. The thyrotrophin releasing hormone stimulation test yields abnormal results in 75% of cases, the most common abnormality being an absent or subnormal response of thyroid stimulating hormone. Antibodies to thyroid microsomes or thyroglobulin are present in the serum of over 50% of patients. There is an appreciable risk of developing overt hyperthyroidism or hypothyroidism, and annual review is advisable.

(6) *Subacute (de Quervain's) thyroiditis* is the result of a viral infection of the thyroid. It is commonly seen in general practice but is often wrongly diagnosed as an upper respiratory tract infection and treated with antibiotics. The hyperthyroid phase usually lasts for six to eight weeks and is mild. Symptoms are adequately controlled as a rule with simple analgesics and a β adrenoceptor antagonist such as propranolol. The hyperthyroidism is characteristically followed by a similar period of thyroid failure, which is often asymptomatic. In a small proportion the hypothyroidism is permanent.

(7) There are various causes of low iodine uptake hyperthyroidism with goitre. Exogenous iodine in the form of x ray contrast media, iodination programmes, or drugs such as

amiodarone may induce hyperthyroidism in susceptible patients in whom there is autonomous thyroid function such as multinodular goitre or Graves' disease in remission. Recently a condition was described with a clinical course similar to subacute thyroiditis but without pain and immunologically mediated. This form of autoimmune thyroiditis commonly develops post partum. It is important to recognise the disorder, previously known as painless subacute thyroiditis, as the prescription of destructive treatment or antithyroid drugs for 12 to 18 months is inappropriate.

Solitary nodule

(1) Half of all nodules considered to be single by clinical examination are subsequently shown at surgery to represent a solitary palpable nodule in a multinodular goitre. Pain associated with the appearance of a thyroid nodule, or enlargement of part of a multinodular goitre, usually indicates haemorrhage into a cyst. The discomfort settles within a few days, the thyroid enlargement slowly regresses, and further investigation is not usually necessary.

(2) *Isotope scanning*—The terms "cold," "neutral," and "hot" refer to the uptake of isotope (technetium-99m, iodine-131, iodine-123) by the nodule in relation to the rest of the thyroid gland. Little or no isotope is concentrated by a cold nodule; a neutral nodule is not apparent by scanning; and the isotope is exclusively concentrated by a hot nodule, the rest of the gland being suppressed.

(3) *Cold nodules*—Roughly 10% of solitary cold nodules are malignant, and it is reasonable to refer all patients with such lesions for surgery. If ultrasound scanning of the thyroid is available it will be possible to identify cold nodules that are pure cysts and that, if less than 4 cm in diameter, can be assumed to be benign. Treatment is either observation or aspiration of cyst fluid. If the cyst has not appreciably reduced in size or disappeared by three months or if the fluid has reaccumulated after aspiration surgery is advisable. Examination of fine needle aspiration biopsy specimens from solitary nodules has been shown to correlate well with the histology of the resected lesion and may avoid the need for surgery in some patients. The technique, however, requires the services of a highly skilled cytologist and is not widely available.

(4) *Euthyroid patients with a solitary hot nodule*—In these patients

thyroid hormone concentrations are in the upper part of the normal range and there is no plasma thyroid stimulating hormone response to thyrotrophin releasing hormone stimulation testing (subclinical hyperthyroidism). About 20% of such patients presenting with a nodule greater than 3 cm in diameter will develop hyperthyroidism within five years.

Multinodular goitre

(1) The diagnosis of multinodular goitre either on clinical grounds or unexpectedly by isotope or ultrasound scanning of a supposedly solitary nodule is reassuring as for practical purposes such a goitre is benign. Rapid painless enlargement of a long-

standing multinodular goitre, however, raises the possibility of malignant change and is an indication for surgery.

(2) *Annual review*—The natural history of simple multinodular goitre in some patients is the development of hyperthyroidism as the amount of autonomous tissue increases. Indeed, 25% of patients with euthyroid multinodular goitre show evidence of subclinical hyperthyroidism. It is this subgroup that is likely to develop overt hyperthyroidism, often of the T3 (triiodothyronine) variety within a few years.

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MATERIA NON MEDICA

An unusual x ray film

Events such as the 40th anniversary of VE Day inevitably bring back memories to those of us who were involved in any way and who are fortunate enough still to be around. One of the more light hearted is of the occasion when the advanced blood bank on the Eighth Army front in Italy, having been carried along in the rapid advance towards the Austrian frontier, paused in the little town of Oderzo, north of the Piave, to find that the board bearing the unit insignia of a vampire bat, normally erected by the roadside to disclose our whereabouts, had disappeared in the move. The creation of a new board entailed stencilling the outline of the vampire in red on a white background, and the necessary stencil was usually made from an old x ray film scrounged from a friendly military hospital, but these had all been left miles behind in the advance.

We found, however, that there was a small civilian hospital in the town, and George Stoddart and I were deputed to try to obtain an old film from this source. We were given a courteous reception by the elderly nun who greeted us and we stated our requirements in our best (but still execrable) Italian, roughly as follows: "Buon giorno, Sorella; e possibile, per favore, d'ottenere una pittura vecchia x ray?"—realising that, as we had not got the foggiest idea of the Italian for x ray, the only course of action was the traditional British method when dealing with foreigners of speaking the words slowly and loudly in English.

We thought the good sister looked a bit foxed but she rallied gamely and we were invited into the parlour where we were hospitably received, wine and small cakes were produced, and a variety of nuns tiptoed in to view these visitors from another world. Time wore on, and conversation was floundering a bit when the door opened with a flourish and a couple of nuns staggered in bearing a large framed portrait of the recently deposed King Victor Emmanuel III, and this was ceremoniously presented to us. It took a little while for us to realise the pitfall into which our linguistic incompetence had led us . . . x ray . . . ex-Re . . .

The only thing to do was to put a brave face on it, utter profuse thanks, and emerge into the outside world bearing our trophy. I imagine the good sisters are wondering to this day what we wanted with a picture of their ex-king. I can't remember what we did about the sign for the advanced blood bank.—A L TULK, retired general practitioner, Cheshire.

He saw his own funeral

I met him last year at a party. He is now a young looking grandfather, but when I was billeted during the war in his mother's house in Cambridge he was a pilot in the RAF and had just been reported missing. At the party I heard the whole story.

He was one of a crew of seven in a Lancaster bomber which was on a night bombing raid on Germany, and it had been brought down over northern Italy. The plane was a complete wreck, but as it happened the crew escaped almost undamaged. It was only after the initial jubilation died down that the Germans realised that there were no bodies. The airmen had been hidden away at separate safe houses. This was easy, as at that time there was no real love between the northern Italians and the Germans. It required much quick thinking, as a house to house search would have discovered the airmen, with the usual retribution on the Italians who had hidden them. Rapidly seven graves were dug, and seven coffins ordered from the local undertaker. Two parish priests conducted the sad cortège of the coffins and a few mourners down the main street—I suppose it was really a case of "rentacrowd." The heavy coffins, filled with stones, were decorated with a few flowers; a final prayer was said at the graveside, and everyone was happy—no one more so than my friend Watty who, hidden behind heavy curtains, had witnessed his own funeral.—SIR IAN FRASER, Belfast.