

### INTRODUCTION

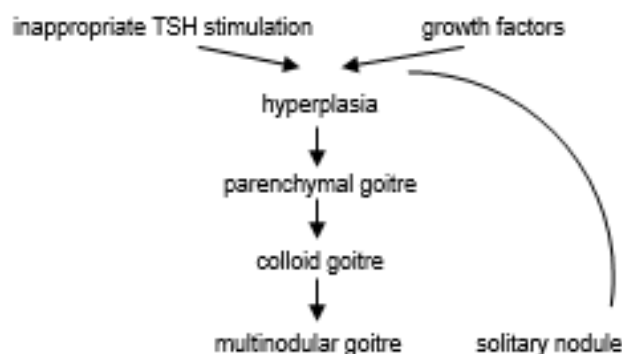
Thyroid problems are commonly encountered in general practice. In most instances they will be minor ones of physiological enlargement or simple goitre (the term goitre refers to any diffuse, smooth or nodular thyroid enlargement). In certain circumstances, however, the practitioner must be able to recognise features of potentially dangerous compression, or signs of malignancy. The features of thyroid malfunction, thyrotoxicosis or hypothyroidism, should also be recognised for appropriate referral.

### EUTHYROID GOITRE

**Physiological goitre** has the clinical features of an asymptomatic gland which is soft, diffusely enlarged, and both visible and palpable. It may be found in both sexes during puberty, and in women is common during the second and third decades, and during pregnancy and lactation. Reassurance is all that is required and medication is unnecessary and may be harmful.

**Simple goitre** is common in certain areas - Greece, Italy, and Spain for example - where iodine is in low concentration in drinking water and iodination of table salt not compulsory. This type of goitre is referred to as endemic goitre. The widespread iodination of salt in most Western countries has made this type of disease a rarity; the phenomenon having virtually disappeared in Switzerland, Derbyshire and the north-western Cape where it was common. When simple goitre is encountered in non-endemic areas (sporadic goitre), the pathogenetic mechanism is not clear.

The most widely accepted explanation is that the enlargement is due to long standing stimulation of the gland by TSH during periods of suboptimal



thyroid hormone production. There is no evidence of abnormality when TSH, T4 or T3 are measured, however. It would seem likely that the initial phase is one of diffuse enlargement that progresses through a process of cyclical changes of hyperplasia and colloid formation to multinodularity. These areas of activity are heterogeneous and apparently uncoordinated within the gland. On occasions, one area may outstrip the others and present as a clinical single nodule. This may be a cyst or an “adenomatous” (adenoma-like, but not a neoplasm) nodule. There is some evidence that growth factors - for example: GSI, IGF and EGF - may be involved.

Certain types of goitre are very rare and have known causes, including *genetic disorders* (familial goitre, an autosomal dominant, and the Pendred Syndrome where the goitre is associated with deafness) and *goitrogens* (anti-thyroid drugs, PAS, sulphonylureas, iodine containing medications, cobalt). Other than the use of iodine in endemic areas, there is no medication for these disorders. Thyroxin administration is pointless as the patients are euthyroid, and regression after administration most unusual. Thyroxin would, however, need to be prescribed in cases of proven hypothyroidism. Investigation and treatment may be necessary when malignancy has to be excluded, as in

the case of a single nodule or when the gland has caused compressive complications.

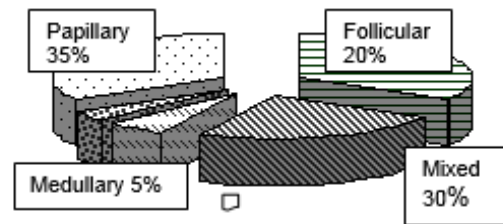
### THYROIDITIS

Inflammatory processes may, on rare occasions, involve the thyroid. Most present with diffuse thyromegaly, which may be firm or even multinodular. Pain and tenderness are a common feature with de Quervain<sup>1</sup> thyroiditis where fever, sore throat and dysphagia may also be found. Thyroid function may on rare occasions be affected with initial mild hyperfunction and late hypofunction. Riedel<sup>2</sup> thyroiditis is a granulomatous reaction with marked fibrosis and is usually found in men.

The diagnosis may be made with aspiration cytology or when malignancy is feared, at surgery. In auto-immune thyroiditis and, occasionally, in other forms, certain antibodies (antimicrosomal antibody, antithyroglobulin antibody) may be elevated. There is no specific treatment of Hashimoto<sup>3</sup>, de Quervain or Riedel thyroiditis. Steroids and aspirin have been used with some success with the latter two forms.

### NEOPLASMS OF THE THYROID

The pathogenesis of most thyroid neoplasms is not clearly understood. There is no evidence that simple goitres predispose to malignancy. One rare form of medullary carcinoma may be inherited as an autosomal dominant; there are also extremely rare examples of previous irradiation to the area of the thyroid in childhood, which might have been carcinogenic. Exposure to nuclear fall-out (eg Chernobyl) frequently results in thyroid malignancy. Benign neoplasms are mainly follicular adenomas and further



descriptions relate to their histological appearances (embryonal, foetal, simple, colloid). A rarer variant is the Hurthle cell adenoma, which has large granular acidophilic cells. The malignant neoplasms are mainly carcinomas, but on rare occasions a lymphoma or a metastasis may be encountered. Thyroid carcinoma is uncommon, the incidence being less than 1/1000,000. The autopsy incidence is higher than the clinical incidence, indicating that many are indolent and do not come to clinical attention. Certain patients with thyroid carcinoma fare badly (adverse prognostic indices): older patients, males, undifferentiated lesions, capsular invasion, extraglandular spread and lymphadenopathy.

The TNM staging system is used: T1 (single nodule), T2 (multiple nodules or both lobes involved), T3 (extraglandular spread); N1 (nodal involvement), M1 (metastases).

Medullary carcinoma is thought to be derived from the APUD "C" cells, may secrete calcitonin, be familial and be associated with other components of the MEA (multiple endocrine abnormality) syndrome. These might include phaeochromocytoma hyperparathyroidism and neuro fibromatosis.

The presentation of thyroid malignancy may be with a single nodule in 50% of cases, multiple malignant nodules in 25% and the remaining 25% with cervical lymphadenopathy or other invasive complications. Conversely, of all apparent single nodules that present clinically, approximately 10% are malignant. The term 'lateral

aberrant thyroid' is regarded as a misnomer for a cervical metastasis from follicular carcinoma.

	age	5 yrs %	spread	comment
<b>Papillary</b>	Younger	80	Nodes	TSH dep
<b>Mixed</b>	Middle	80	Nodes	As papill'y
<b>Follicular</b>	Older	60	Mets	I <sup>131</sup>
<b>Medullary</b>	-	10	local	MEA2
<b>Undiff'ated</b>	old	10	local	-

The management involves making the diagnosis (see below), surgery and endocrine or radiotherapy. As papillary carcinoma may be TSH dependant, thyroxin is given to suppress TSH. Thyroxin is also given after total thyroidectomy for any malignancy. As follicular carcinoma may incorporate I 131, the isotope is initially given to scan for residual disease and then in a large ablative dose. Local radiotherapy may be given for invasive disease.

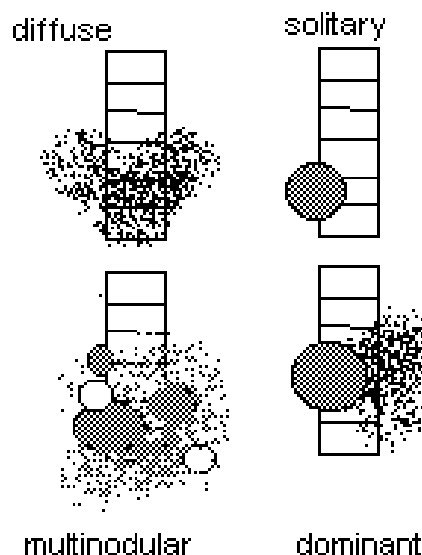
The prognosis depends on the histological type, the stage of the lesion and the age of the patient. Various acronyms [AGES, AMES, MACIS] relate to age, stage (size), metastases, extent), grade and completeness of resection.

### MANAGEMENT OF NODULAR THYROMEGALY

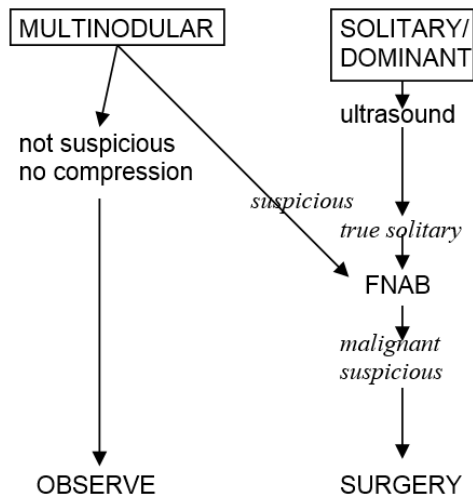
In broad terms there are three possibilities – a solitary nodule, a dominant nodule and a multinodular gland. The clinical distinction between these is important as referral, investigation and management differ considerably. In clinical usage, the term *solitary* implies that a single nodule (of any size) is palpable together with the trachea contralaterally; a *dominant nodule* implies that a single nodule is palpable together with the contralateral gland but not trachea; and a multinodular gland means that multiple nodules are palpable. Careful inspection and palpation with the patient swallowing, allow the clinician to make the diagnosis of one of these possibilities.

With both a *solitary* and *dominant* nodule, the main approach is to exclude malignancy by appropriate investigations. There is much wisdom in the saying that both must be regarded as carcinoma until otherwise proven. Such patients should be referred by general practitioners to specialists or centres for further investigation and management.

Ultrasonography indicates whether the lesion is solid (and likely to be an adenomatous nodule, an adenoma or carcinoma) or whether it is cystic (and probably benign). It can also detect whether the remaining gland is multinodular; in this event it is less likely that the nodule is malignant.



Aspiration cytology may indicate that the lesion is benign, indeterminate or malignant. Radio-isotope scanning relies on the premise that cysts never take up the isotope and carcinomas seldom do; both are therefore regarded as "cold". Hyperfunctioning nodules usually trap the isotope and are "hot". A normal scan in the presence of a nodule contributes no information for management.



*Surgery of solitary and dominant nodules.* This is undertaken when the diagnosis of carcinoma is made or when it is not possible to exclude this possibility. The usual circumstances are: a solid nodule as shown ultrasonographically, a cold area on isotope scanning, or cytology which is malignant. suspicious or indeterminate. In addition, a cyst which refills after aspiration should be removed surgically.

The suspicious nodule and the containing lobe are removed (hemilobectomy) for frozen section analysis. If the report is of benign disease (adenoma, adenomatous nodule) nothing further is required; if the report indicates malignancy, further action is determined by the type: in general a total thyroidectomy is performed for all types except papillary carcinoma. Papillary carcinoma may be managed more conservatively as many are young patients with localised disease - and have a good prognosis. The lesser surgery is undertaken in order to preserve parathyroid tissue.

Lymphadenectomy is controversial, the current view being that removal of apparently involved nodes (node picking) is appropriate for papillary carcinoma. Block dissection (radical lymphadenectomy) is no longer favoured.

*Surgery for multinodular goitre* is undertaken in selected instances. Most cases of multinodular goitre have no signs of malignancy, are uncomplicated and are of modest size, and reassurance of the patient is all that is required. The most common indication for surgery is *compression* (dysphagia, respiratory difficulty, retrosternal extension or even a superior mediastinal syndrome). In rare instances surgery may be undertaken for goitres that are very unsightly. A bilateral subtotal thyroidectomy (reducing the lobes to normal proportions) with preservation of the parathyroids is carried out. On certain occasions this operation is undertaken for malignancy. Features that suggest malignancy in a multinodular goitre are: the presence in children or males, rapid onset, pain, local invasion and lymph-adenopathy. Multinodular goitre disease may, on occasion, be unilateral

## THYROTOXICOSIS

The most common cause of hyperfunction is Graves<sup>4</sup> disease, which is believed to be an auto-immune response to the TSH receptor, which for unknown reasons becomes (non-self) antigenic. The body raises an antibody to the receptor (synonyms: LATS, long acting thyroid stimulator and HTSI, human thyroid stimulating immunoglobulin). These antibodies cause prolonged stimulation of the receptor and excessive thyroxin production. In addition to the features of thyroid excess, there may be ophthalmopathy and dermopathy.

### Causes of thyrotoxicosis

- *Graves disease*
- *Toxic nodular goitre*  
multinodular (Plummer  
uninodular (toxic adenoma)
- *Rarities*  
Excess TSH (pituitary,

paraneoplastic)  
 Excess T4 (iatrogenic,  
 paraneoplastic)  
 Excess iodine (Jod Basedow)  
 Transient during thyroiditis /  
 irradiation

The *diagnosis* of thyrotoxicosis is made from the clinical features and biochemical confirmation. TSH (0.4-4.0 micro-units) is the most commonly used screen: undetectable or subnormal levels suggest thyrotoxicosis. The free T4 (normal 6.3-22.8 pmol/L) may be used as confirmation. On occasion T3 (normal 3.3-8.1 pmol/L) may be measured, in order to diagnose "T3 toxicosis" where the predominant excretion is T3. This last possibility is usually suspected in elderly patients, patients with tachyarrhythmias or with solitary nodules.

The primary treatment is non-surgical. As the disease is transient in many, drugs are used for control until remission occurs. In some, remission does not occur or the disease is recurrent and partial thyroid ablation has to be considered: the options are either  $I^{131}$  or surgery. Most patients have propranolol and neomercazole and remission is awaited over 6-18 months; if this does not occur,  $I^{131}$  is given. Surgery is performed when specially indicated: this may be in pregnancy (during the second trimester), with a hot toxic nodule, after failed medical treatment, when  $I^{131}$  is contra-indicated (young women) or when there is a particularly large, usually multinodular, gland. All cases are assessed individually on merit. Both  $I^{131}$  and surgery have late hypothyroidism, which may occur over the ensuing 15 years.

### Complications of thyroidectomy

Thyroid surgery requires a meticulous technique as the structures in the neck are small and complex. The complications of this surgery include

endocrine problems and structural damage. Thyroid surgery should be performed by specialist surgeons.

	for	against	indications
<i>Neomercazole</i>	Most favoured	-Skin reactions -Agranulocytosis -high relapse -tedious	Most cases
<i>propranolol</i>	Rapid	Contra-indicated: asthma, cardiac	Most initially
$I^{131}$	Easy to give	-Delayed effect -irradiation -not pregnant	-Family complete -recurrent
<i>surgery</i>	Rapid effect compliance	-Complications	

### Complications of thyroid surgery

- Structural  
 laryngeal nerve damage  
 laryngeal oedema  
 tracheomalacia  
 haemorrhage
- Endocrine  
 hypoparathyroidism  
 hypothyroidism  
 thyroid crisis

Damage to one or both recurrent laryngeal nerves may cause hoarseness of the voice and respiratory difficulty. Serious airway obstruction may occur in the early post-operative period due to laryngeal oedema, tracheal collapse or haemorrhage. Early hypocalcaemia within 24 hours of surgery is usually due to metabolic bone disease in thyrotoxicosis; late hypocalcaemia is usually due to hypoparathyroidism.



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