

INTRODUCTION

Thyroid disorders are common. Patients will either present with a neck swelling caused by an enlargement of the thyroid gland, or with symptoms and signs of thyroid dysfunction (either hypo- or hyper- thyroidism). It is important for a practitioner to be able to differentiate a thyroid swelling from the other causes of neck masses, and to recognize and manage patients with thyroid dysfunction accordingly.

ANATOMY

The thyroid gland consists of two lateral lobes joined anteriorly by the isthmus, which typically overlies the 2nd and 3rd tracheal rings (Figure 1). A superior extension near the midline is known as the pyramidal lobe, and may be present in up to 70% of cases (Figure 1).

Each thyroid lobe is cone shaped and measures approximately 5cm in length and is 2-3 cms wide in its transverse and anteroposterior dimensions. The thyroid gland weighs 15-25g. These dimensions and weights may be significantly affected by thyroid pathology.

A normal thyroid gland is not palpable. A visible or palpable thyroid almost always implies some degree of enlargement and pathology.

The intimate relationship between the thyroid gland and the recurrent laryngeal nerve (supplying innervation to the vocal cords), and the parathyroid glands explains the risk of voice change inherent to thyroid surgery, and postoperative hypocalcaemia respectively, and is critical knowledge for the thyroid surgeon.

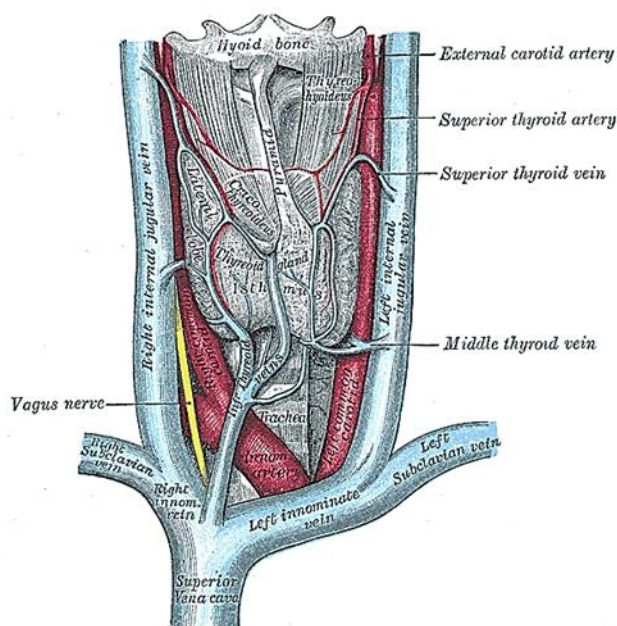


Figure 1: Anatomy of thyroid gland, pyramidal lobe and relations to carotid sheath and vasculature

PHYSIOLOGY

The thyroid gland produces thyroid hormones, the principal ones being *triiodothyronine* (T3) and *thyroxine*, also referred to as *tetraiodothyronine* (T4). These are critical in the regulation of the growth and rate of function of many organ systems in the body. T3 and T4 are synthesized from iodine and tyrosine. The thyroid also produces *calcitonin*, which plays a role in calcium homeostasis.

Hormonal output from the thyroid is regulated by thyroid-stimulating hormone (TSH) produced by the anterior pituitary, which itself is regulated by thyrotropin-releasing hormone (TRH) produced by the hypothalamus.

THYROID ENLARGEMENT

The thyroid may be symmetrically enlarged (i.e. the pathological process involves the entire gland); this is commonly called a “*goitre*”, an old

fashioned term still in routine clinical use.

Alternatively it may be asymmetrically enlarged because of focal pathology in either lobe, in an otherwise normal gland- clinically this is described as a “*solitary nodule*”.

A thyroid enlargement can be differentiated from other causes of a cervical mass by the fact that it occurs in the lower midline of the neck, and moves readily on swallowing.

Midline	
Thyroid enlargement	common
Submental lymphadenopathy	common
Thyroglossal cyst	rare
Lateral	
Cervical lymphadenopathy	very common
Salivary gland enlargement	occasional
Branchial cyst	rare
Cystic hygroma	rare
Pharyngeal pouch	v rare
Carotid body tumour	very rare

Table 1- Cause of neck swellings

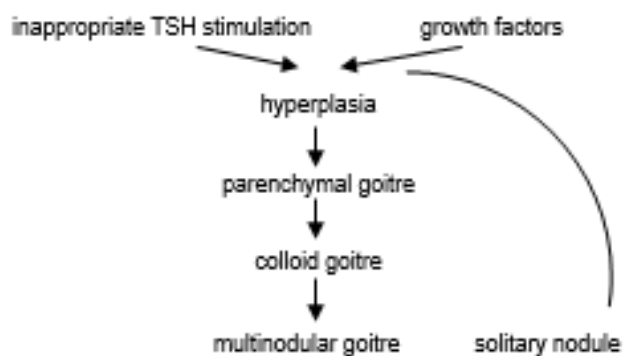
CAUSES OF GOITRE

Physiological goitre. The thyroid gland may be enlarged as part of a normal physiological process. This can occur in both sexes during puberty, and in women is common during pregnancy and lactation. The gland is soft, diffusely enlarged, and both visible and palpable. Reassurance is all that is required and medication is unnecessary and may be harmful.

Simple/ non nodular goitre. This is common in areas where iodine is in low concentration in drinking water and iodination of table salt not compulsory. This type of goitre is also referred to as *endemic goitre*. The widespread iodination of salt has made this type of disease a rarity. When simple goitre is encountered in

non-endemic areas it is referred to as a *sporadic goitre*.

Multinodular goitre. This is the commonest type of goitre encountered in clinical practice. The thyroid gland enlarges due to multiple adenomatous and colloid nodules, with occasional cystic degeneration. In fact subclinical nodularity off the thyroid is quite common, but occasionally it can reach massive size, and cause symptoms of local discomfort and airway compression. The pathophysiology is poorly understood, but 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.



Figure 2- large Multinodular Goitre

Thyroiditis. Inflammatory processes may, on rare occasions, involve the thyroid. Most present with diffuse thyromegaly, which may be firm or even multinodular. The commonest type encountered in practice is the autoimmune *Hashimoto's* thyroiditis. Pain and tenderness is a common feature with *de Quervain* 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 thyroiditis* is a granulomatous reaction with marked fibrosis and is usually found in men. It is very uncommon.

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, de Quervain or Riedel thyroiditis. Steroids and aspirin have been used with some success with the latter two forms.

<i>Multinodular</i>	very common
<i>Physiological</i>	occasional
<i>Thyroiditis</i>	occasional
<i>Thyroid carcinoma</i>	Uncommon* (<2%)

Table 2- Causes of a goitre. Thyroid carcinoma presents more commonly with an asymmetrical thyroid swelling*but on occasion can involve the entire gland

SOLITARY NODULE OF THE THYROID

In clinical usage, the term *solitary* implies that a single nodule (of any size) is palpable together with the trachea contra-laterally. The remainder of the gland is impalpable, and thus the thyroid mass is asymmetrical and can be ascribed to either the left or right lobe. The key focus is to exclude malignancy by appropriate investigations. There is much wisdom in the saying that a solitary nodule 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

<i>Hyperplastic/adenomatous nodule</i>	60%
<i>Simple cyst</i>	10%
<i>Follicular adenoma</i>	20%
<i>Thyroid carcinoma</i>	5-15%

Table 3- Causes of a solitary nodule. Thyroid carcinoma is not the commonest cause, but has to be excluded actively.

INVESTIGATION AND MANAGEMENT OF NODULAR THYROMEGALY

Ultrasonography is the imaging modality of choice. It helps to confirm whether the clinical differentiation of solitary nodule vs MNG is correct, it 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 identify features associated with malignancy, such as hypoechogenicity of the nodule, marked increase in vascularity, local lymphadenopathy, microcalcifications.

Aspiration cytology may indicate that the lesion is benign, indeterminate or malignant. The report should indicate the risk of malignancy according to the Bethesda Classification and help to guide management. Cytology of the thyroid is notoriously complex, and pathologists struggle particularly to differentiate a follicular carcinoma from a follicular adenoma. It is not unusual for the report to be in category 3 or 4, which leave significant uncertainty about the presence of malignancy.

Report	Risk of malignancy
1-non diagnostic	-
2- benign	0-3%
3-indeterminate	5-15%
4-suspicious for follicular neoplasm	15-30%
5- Suspicious for malignancy	60-75%
6- malignant	97-99%

Table 4- Bethesda Classification of reporting thyroid cytopathology, and associated risk of carcinoma.

Radio-isotope scanning relies on the premise that carcinomas hardly ever take up the isotope; and are therefore regarded as “cold”. Hyperfunctioning nodules usually trap the isotope and are “hot”, and are considered benign. A normal scan in the presence of a

nodule contributes no information for management.

CT scans are helpful in the evaluation of retrosternal goitre extension, and airway compression.

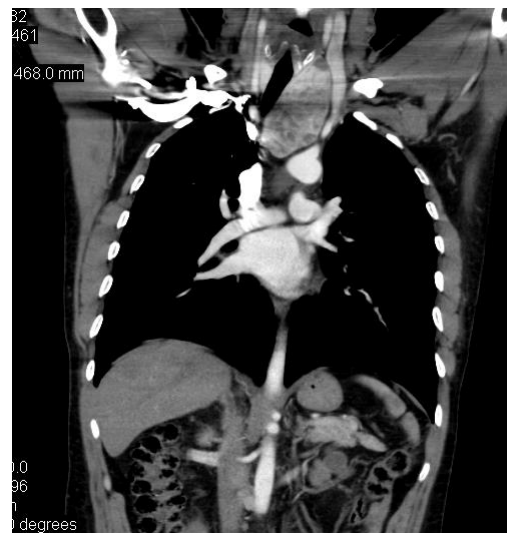


Figure 3- CT scan showing a thyroid mass displacing the trachea, with intra-thoracic extension

All patients must have recent **blood tests** to evaluate thyroid function. Tumour markers (calcitonin) are specific in the diagnosis of the rare medullary carcinoma, and serum thyroid antibodies are helpful in the diagnosis of autoimmune thyroiditis.

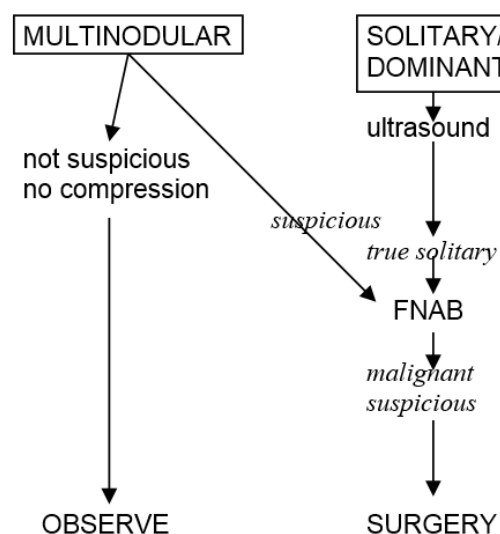


Figure 4- work up of nodular thyroid disease

Surgery of solitary nodules. This is undertaken when the diagnosis of carcinoma is made or when it is not possible to exclude this possibility. The usual indications are: a solid nodule as shown on US, 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 (thyroid lobectomy) for histological analysis. If the report is of benign disease (adenoma, or 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 of thyroid cancer except small (<1cm), unifocal papillary carcinoma. Papillary carcinoma may be managed more conservatively as many are young patients with localised disease - and have a good prognosis.

Surgery for multinodular goitre is undertaken in selected instances. Most cases of MNG 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*. On certain occasions this operation is undertaken for *concern of malignancy within a MNG*.

Surgery for MNG usually requires a total thyroidectomy with careful preservation of the parathyroid glands. Multinodular goitre disease may, on occasion, be unilateral, and in such cases a lobectomy only may be sufficient.

<i>asymmetrical goiter or solitary nodule in children or men</i> <i>rapid onset</i> <i>progressive increase in size</i> <i>pain</i> <i>local invasion</i> <i>lymphadenopathy</i> <i>hoarseness</i>
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Table 5- *Features of suggestive of malignancy in a thyroid mass.*

NEOPLASMS OF THE THYROID

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.

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 (e.g. Chernobyl) frequently results in thyroid malignancy.

Benign neoplasms are almost all follicular adenomas. A rarer variant is the Hurthle cell adenoma, which has large granular acidophilic cells.

Thyroid malignancy usually presents with an asymmetrical thyroid enlargement such as a single nodule in 50% of cases, multiple malignant nodules in 25% and the remaining 25% with cervical lymphadenopathy, distant metastases or other invasive complications. Conversely, of all apparent single nodules that present clinically, approximately 10% are malignant.

The malignant neoplasms are mainly carcinomas, but on rare occasions a lymphoma or a metastasis to the thyroid may be encountered.

<i>Well differentiated</i>	85%	Indolent Expect long term survival Surgery/ I^{131} / endocrine therapy used
<i>Medullary</i>	5%	Aggressive Cure can be achieved by surgery
<i>Anaplastic</i>	5%	Fatal Non responsive to treatment
<i>Lymphoma</i>	3%	Usually irresectable Will respond to chemo/radiotherapy
<i>other</i>	2%	

Table 6- types of thyroid carcinoma

Most are **well differentiated thyroid carcinomas (WDTC)** and may be classified histologically as *papillary*, *follicular* or *mixed*. In general these have an excellent prognosis, and most patients will have a normal life expectancy if managed correctly.

The management of WDTC is *surgical*, complemented by *radioactive iodine* doses and *endocrine therapy*. The usual operation is a total thyroidectomy, although a lobectomy may be sufficient in a subgroup of patients. This decision is best discussed in a multi-disciplinary team meeting. Lymphadenectomy is indicated in cases with lymph node involvement, typically in the papillary carcinomas. Since WDTC may iodine, I^{131} isotope is initially given to scan for residual disease and then in a large ablative dose. Most WDTC are TSH dependant, thus thyroxine is given in monitored doses to suppress TSH, and inhibit recurrence. External beam radiotherapy is very seldom used, and there is no established role for systemic chemotherapy agents.

The prognosis depends on the histological type, the stage of the

lesion and the age of the patient. Adverse prognostic indices are: older patients, males, undifferentiated lesions, spread to lymph nodes or distant metastases

<i>papillary</i>	40%	Small nodule may be multifocal LN spread common
<i>follicular</i>	30%	Larger single nodule Haematogenous spread, to bones and lung Specifically I^{131} sensitive
<i>Mixed</i>	30%	

Table 7- types of well differentiated thyroid carcinoma

Medullary carcinoma is thought to be derived from the calcitonin producing "C" cells. Approximately 30% are familial and may be associated with other components of the MEN 2 syndrome. These include pheochromocytoma, hyperparathyroidism, and neurofibromatosis. They are much more aggressive cancers than WDTC, and are treated by total thyroidectomy with nodal dissection to eradicate all disease at presentation. They do not respond to I^{131} therapy.

Anaplastic/ undifferentiated thyroid carcinoma is the most uncommon variant. It typically presents in older patients with a rapidly enlarging neck mass and symptoms of local invasion. They are very nasty, aggressive tumours that are frequently irresectable and incurable at presentation.

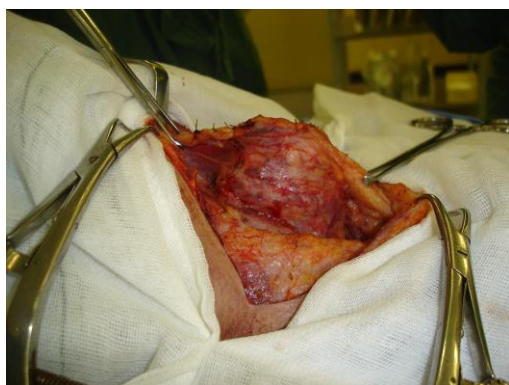


Figure 5- surgical exposure of anaplastic thyroid cancer

THYROTOXICOSIS

The most common cause of hyperthyroidism is **Graves' 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 thyroxine production. In addition to the features of thyroid excess, there may be ophthalmopathy and dermopathy.

Common

Graves' disease

Toxic multinodular goitre (Plummer's disease)

Toxic solitary nodule (toxic adenoma)

Rarities

Excess TSH (pituitary, paraneoplastic)

Excess T4 (iatrogenic, paraneoplastic)

Excess iodine (Jod Basedow)

Transient during thyroiditis / irradiation

Struma Ovarii

16.4 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 tachyarrhythmia 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 are started on 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.

Table 8- Causes of thyrotoxicosis.

The *diagnosis* of thyrotoxicosis is made from the clinical features and biochemical confirmation. TSH (ref 0.37 - 3.50 mIU/L) is the most commonly used screen: undetectable or subnormal levels suggest thyrotoxicosis. The free T4 (ref 7.2 -

	Pro's	Con's
<i>Neomercazole</i>	Most used	Skin reactions Agranulocytosis High relapse tedious
<i>Propranolol</i>	rapid	Asthma cardiac
<i>I¹³¹</i>	Once off Rx	Delayed effect Irradiation Not in pregnancy
<i>surgery</i>	Immediate effect compliant	Cost Complications

Table 9- Options in the management of thyrotoxicosis

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.

Complications of thyroid surgery

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

Damage to one or both recurrent laryngeal nerves may cause hoarseness of the voice and respiratory difficulty. Unilateral RLN paralysis presents as a breathy voice and hoarseness, and less commonly as dysphagia and aspiration. It may not be immediately apparent depending on the resting position of the vocal fold. Bilateral RLN paralysis usually manifests early following extubation with some stridor and airway obstruction. Should the patient be unable to maintain an adequate

airway then an emergency tracheostomy is indicated

Serious *airway obstruction* may occur in the early post-operative period due to a haematoma, and airway oedema; more uncommonly due to bilateral RLN injury or tracheomalacia, or later due to hypocalcaemia

Haematoma: A large haematoma is a surgical emergency as it may cause upper airway obstruction.

Tracheomalacia: This is characterized by flaccidity of the tracheal support cartilage, which in turn leads to tracheal collapse. It is thought that a longstanding goitre can act as an external support structure for the trachea and predispose to secondary tracheomalacia. Removal of the goitre therefore unmasks the tracheomalacia resulting in respiratory obstruction. In clinical practice this is a most uncommon cause of airway obstruction after thyroidectomy.

Hypocalcaemia: this may occur after a total thyroidectomy if the parathyroid glands have been inadvertently removed or rendered ischaemic.



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