



Meagan Brennan

BMed, FRACGP, DFM, FASBP, is a general practitioner and breast physician, NSW Breast Cancer Institute, Westmead Hospital, New South Wales. meaganb@bci.org.au

James French

MBBS, FRACS, is a breast and endocrine surgeon, NSW Breast Cancer Institute, Westmead Hospital, and Clinical Lecturer, University of Sydney, New South Wales.

Thyroid lumps and bumps

BACKGROUND

Thyroid nodules are extremely common, with 7% of adults having palpable nodules and up to 50% having nodules visible on ultrasound. About 5% of thyroid nodules are malignant. Thyroid nodules may occur as isolated, often incidental findings, or may be associated with systemic features of thyrotoxicosis or hypothyroidism. They may be solitary or may present as a dominant nodule in a multinodular goitre.

OBJECTIVE

This article presents an outline of the common causes of lumps in the thyroid (solitary and multiple) and provides a simple approach to diagnosis and management in the general practice setting. The focus is on the patient presenting with a lump in the thyroid rather than the patient presenting with hyper- or hypo-thyroidism.

DISCUSSION

The challenge for the general practitioner is to assess the nodule and determine which patients require referral for further investigation and management. Referral may be required to exclude or confirm malignancy and is also indicated for patients who are symptomatic from benign thyroid nodules.

A thyroid nodule is a 'discrete lesion within the thyroid gland that is palpably and/or ultrasonographically distinct from the surrounding thyroid parenchyma'.¹ Thyroid nodules are extremely common, with 7% of adults having palpable nodules² and up to 50% of adults having nodules visible on ultrasound.³ Around 5% of thyroid nodules are malignant.⁴ Thyroid nodules may occur as isolated, often incidental findings, or they may be associated with systemic features of thyrotoxicosis or hypothyroidism. They may be solitary or may present as a dominant nodule in a multinodular goitre. Solitary nodules have a higher likelihood of being malignant although overall the prevalence of cancer is similar between patients with a solitary nodule and patients with multiple nodules.⁵ The challenge for the general practitioner is to assess the nodule and determine which patients require referral to a surgeon or endocrinologist for further investigation and management. Referral may be required to exclude or confirm malignancy and is also indicated for patients who are symptomatic from benign thyroid nodules.

Classification of thyroid nodules

The classification of thyroid nodules is shown in *Table 1*.⁶ While the majority of thyroid nodules are benign, clinical assessment and investigation is essential and is aimed at excluding malignancy as a cause.

Important features in the history

Thyroid nodules are more common in women, the elderly, those with iodine deficiency, and in those with a prior history of exposure to radiation. Most patients with thyroid nodules do not have any significant symptoms. The absence of symptoms however, does not exclude malignancy. Symptoms that are significant if present include:

- obstruction such as difficulty swallowing (may indicate impingement of the oesophagus)
- shortness of breath (may indicate impingement of the trachea), and
- (uncommonly) hoarseness of the voice which suggests recurrent laryngeal nerve compression and therefore the possibility of malignancy.

History of duration of symptoms along with rapidity of change in symptoms, the presence of systemic features of hyper- or hypo-thyroidism, and family history of malignancy should all be explored.

The following features of the history increase the suspicion of the nodule being malignant:

- extremes of age (<20 or >70 years)
- male gender
- size >4 cm
- rapid growth (may suggest anaplastic carcinoma or lymphoma)
- family history of: thyroid malignancy or genetic disorders such as syndrome of multiple endocrine

Table 1. Classification of thyroid nodules⁶**Benign**

- multinodular goitre
- Hashimoto thyroiditis
- simple or haemorrhagic cysts
- follicular adenomas
- subacute thyroiditis
- colloid nodule

Malignant

- papillary carcinoma
- follicular carcinoma
- hurthle cell carcinoma
- medullary carcinoma
- anaplastic carcinoma
- primary thyroid lymphoma
- metastatic malignant lesion

neoplasia type 2 (MEN2), familial polyposis coli and Cowden syndrome

- prior exposure to radiation, including radiotherapy to the head and neck (eg. previous treatment of Hodgkin disease affecting the neck).

Most thyroid nodules are not painful, however the presence of pain may give a clue as to the aetiology of the nodule. Subacute thyroiditis may present as painful thyroid nodule (single or multiple). Haemorrhage into a colloid nodule or cyst can also be very painful. A malignant thyroid nodule that is painful may be an anaplastic lesion.

Clinical examination of the thyroid gland

Clinical examination must first distinguish a thyroid nodule from other causes of a neck

lump such as a lymph node, salivary gland, thyroglossal cyst and skin/subcutaneous lesion (eg. lipoma, sebaceous cyst). The technique for clinical examination of the thyroid is described in *Table 2*.⁷

Enlargement of the thyroid gland may be visible as well as palpable (*Figure 1a, b*). Clinical examination often underestimates the number of nodules compared with ultrasound. It is important to determine whether a goitre is present and if it is, to assess whether the gland is generally enlarged or if there is localised swelling. If a nodule is palpable, it should be determined if it is a solitary nodule or a dominant nodule of a multinodular goitre and an attempt should be made to characterise the lump. The most important aspect of clinical examination however, is the detection of the nodule(s) rather than the determination of its benign or malignant status. Signs that may suggest malignancy are:

- firm/hard or fixed nodule, ill defined nodule margins on palpation
- hoarseness/loss of voice
- presence of palpable cervical lymph nodes.

Clinical examination of a patient with a thyroid abnormality should include a generalised examination looking for signs of hyper- or hypo-thyroidism. This includes assessment for thyroid eye signs. While it is uncommon for autoimmune thyroiditis to present as a nodule, if eye signs are present this would alert the assessing clinician to the likely benign nature of the nodule.

In addition, assessment for Pemberton sign (described in *Table 2, Figure 1c*) should be included in the clinical examination. The patient is asked to lift both arms as high as possible. Pemberton sign is positive when signs of congestion (plethora), respiratory distress, inspiratory stridor and distension of the neck veins develop. When present, a positive Pemberton sign implies thoracic inlet obstruction, which may occur when there is retrosternal extension of the thyroid gland.

Investigations

All patients with clinical abnormalities in the thyroid should be investigated with thyroid function tests. Most should also have thyroid ultrasound and fine needle aspiration biopsy

Table 2. Clinical examination of the thyroid gland⁷**Inspection – look for:**

- scars – signs of previous surgery or injury
- goitre – swelling – look from front and side of neck; localised or diffuse
- movement with swallowing – ask the patient to swallow a mouthful of water and observe the neck – a goitre or thyroglossal cyst will rise during swallowing
- prominent veins – may be a sign of retrosternal extension of goitre (thoracic inlet obstruction)

Palpation

- position the patient
 - examine from behind the patient
 - neck slightly flexed to relax sternomastoid muscles
- feel each lobe and the isthmus of the gland
- determine clinical characteristics of goitre or nodule(s)
 - size, shape, consistency, tenderness, mobility
- examine cervical lymph nodes
- re-examine from the front
 - characteristics of nodules
 - position of trachea (may be displaced)

Percussion

- percussion over the manubrium
 - dullness may indicate retrosternal goitre – this procedure has been superseded by CT scan

Auscultation

- bruit may occur in Graves disease

Pemberton sign

- ask the patient to raise arms up as high as possible; wait a few moments
- signs of congestion occur from retrosternal extension of the thyroid gland

Generalised clinical examination

- signs of hyper- or hypo-thyroidism

(FNAB). Computerised tomography (CT) and magnetic resonance tomography (MRI) scans, as well as thyroid scintigraphy (nuclear medicine scanning) are generally used more selectively. Algorithms for investigation and management are shown (Figure 2, 3).

Thyroid function tests

Serum thyroid stimulating hormone (TSH) levels should be measured in every patient presenting with a clinical abnormality in the thyroid.

- If TSH is normal, further analysis of thyroid function tests (TFTs) is often not required. Some endocrinologists recommend also checking T4 levels on every patient presenting with a clinical abnormality in the thyroid
- If TSH is high, free T4 and thyroid peroxidase antibody (TPOAb) should be tested. High levels of this antibody suggest Hashimoto disease, which may occasionally present with a palpable nodule

- If TSH is low, then serum T4 and T3 should be measured to further investigate hyperthyroidism. Thyroid stimulating hormone receptor antibody (TRAb) is useful to distinguish Graves disease from toxic multinodular goitre.

The situation of a nodule that is associated with hyperthyroidism ('toxic' nodule) plays an important role in determining how the clinical lump is managed. In these cases nuclear medicine scan should be performed and FNAB may not be necessary.

Ultrasound of the thyroid

The role of ultrasound in the investigation of the clinically abnormal thyroid gland is increasing and it is now recommended as part of the routine investigation of a palpable thyroid nodule.^{1,6} Ultrasound allows correlation of the clinical features with the ultrasound appearance, allows the nodule to be characterised further, and may

detect other significant nodules that are not palpable.⁸ The risk of malignancy is the same for nodules found as incidental impalpable lesions as for nodules of the same size that are palpable.⁹ Therefore it is important to assess each nodule individually on ultrasound, looking for features suspicious of malignancy. While there is no single ultrasound feature that reliably predicts malignancy, ultrasound features that increase the risk of a nodule being malignant include:

- irregular margins
- presence of microcalcification
- hypoechogenicity
- absence of a halo
- predominantly solid composition
- intranodule vascularity.¹⁰

As ultrasound alone is limited in its ability to distinguish benign from malignant nodules, further investigation of palpable nodules with FNAB is usually required even when the lesion has a benign appearance on ultrasound.

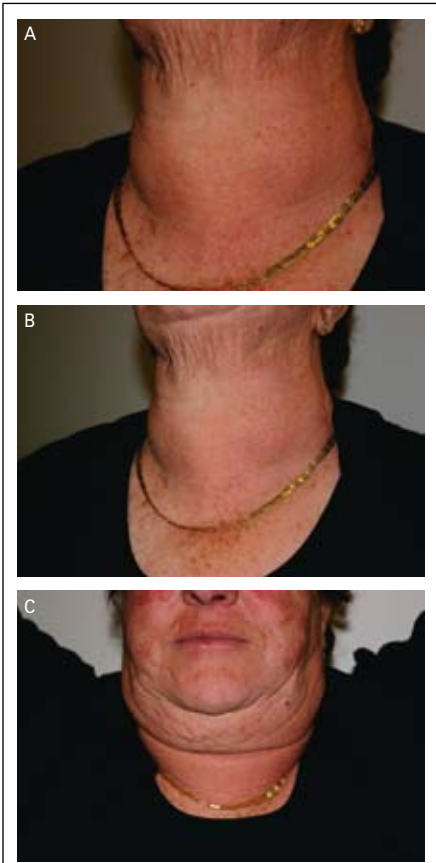


Figure 1a, b. Patient with a large multinodular goitre causing visible swelling in the neck
Figure 1c. Patient has a positive Pemberton sign with congestion developing when she raises her arms above her head

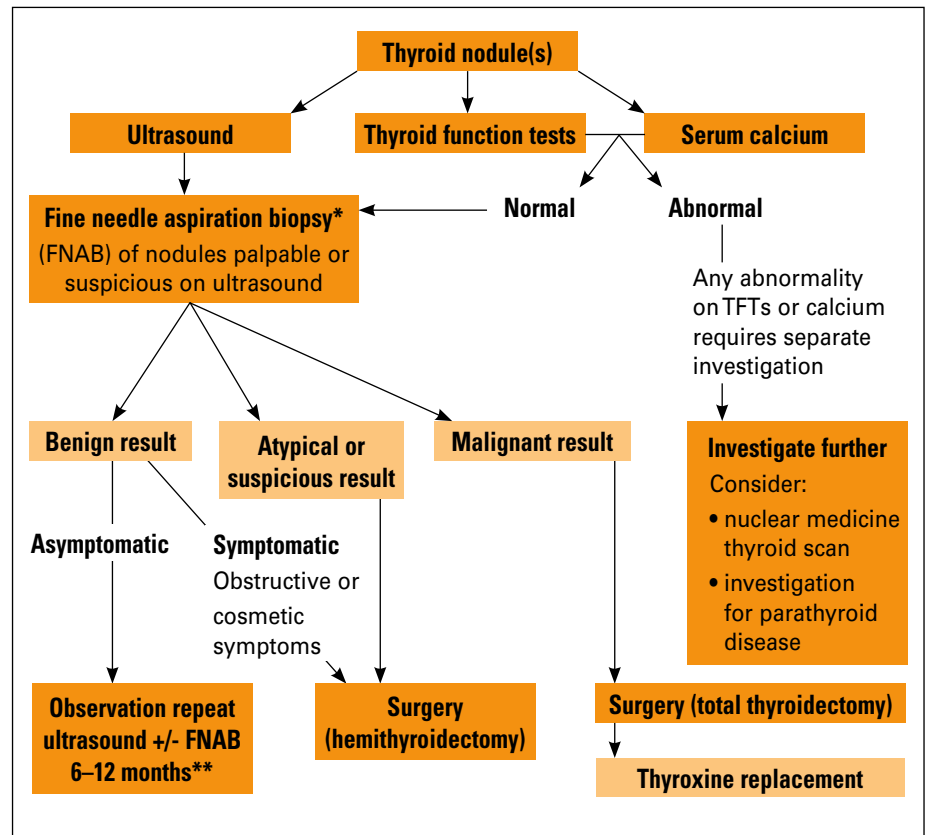


Figure 2. Initial investigation and management of a thyroid nodule

* FNAB may not be required if the TSH is suppressed. These nodules should be investigated with thyroid scintigraphy and if a 'hot' nodule is seen the risk of malignancy is minimal and management (radioactive iodine or surgery) may proceed without the need for FNAB

** There is no evidence on which to base recommendations for the interval and method of follow up. This interval is given as a guide only

Fine needle aspiration biopsy

Fine needle aspiration biopsy is indicated for nearly all palpable and symptomatic nodules and should be considered in other nodules >1 cm. Fine needle aspiration biopsy should also be performed for smaller nodules (<1 cm) that have suspicious clinical or ultrasound features.^{11,12}

The management of multiple incidental thyroid nodules seen on ultrasound is controversial. Biopsy of all these nodules is neither practical nor necessary. Focus should be on nodules that show concerning features on ultrasound and other nodules should probably be monitored with ultrasound. There is no consensus however, on the optimal follow up

interval for incidental asymptomatic lesions.

Nodules that do not routinely require FNAB are solitary nodules associated with a suppressed TSH (toxic nodules.) These nodules should be assessed with thyroid scintigraphy. If the nodule is hot, the risk of malignancy is minimal and FNAB is therefore usually not required. These nodules can then be managed with radioactive iodine or surgery.⁶

Fine needle aspiration biopsy is a simple and useful test but its usefulness is dependent on obtaining an adequate specimen and having it examined by an experienced cytopathologist. There is no consensus on the classification of thyroid cytology. In general, FNAB can be

reported as:

- insufficient (technically unsatisfactory)
- benign
- atypical, or
- malignant.

The main difficulty is in cases of follicular neoplasm. It can be impossible to distinguish a follicular adenoma (a benign lesion) from a follicular carcinoma on cytological assessment. Follicular lesions therefore often require excision and full examination of the lesion and its capsule before a definitive diagnosis can be made.

Rates of insufficiency vary from 4–20%.^{6,13} In more than half of these cases a sufficient sample will be achieved if the test is repeated.⁴ Fine needle aspiration biopsy has a sensitivity of 65–98%, specificity 72–100%, positive predictive value 50–96%, false-negative rate 1–11%, and false-positive rate of 0–7%.⁶ With an overall accuracy of 95%,⁶ it is a quick, safe, cost effective and reliable investigation in the detection of thyroid malignancy. It will give an atypical result in up to 20% of specimens. Surgical excision of these nodules for full histopathological assessment is recommended, as 30% may be malignant.⁴ The accuracy of FNAB increases when it is performed under ultrasound rather than manual guidance.^{14,15}

Fine needle aspiration biopsy may be seen as an accurate test to determine which nodules should be managed surgically and which may safely be observed.¹⁶ Nodules that are benign on FNAB and show no suspicious features on clinical and ultrasound assessment may be observed. Those showing atypical or malignant cytology should be surgically removed. Nodules returning a nondiagnostic result may be assessed with repeat FNAB or observed if there are no suspicious features on clinical and ultrasound assessment (Figure 2).

CT and MRI scan

Computerised tomography and MRI scans are not routinely indicated in the assessment of thyroid nodules. They cannot reliably distinguish benign from malignant lesions. The main indication for these scans is to determine the presence and extent of retrosternal extension and the presence and degree of tracheal compression when obstructive symptoms are present (Figure 4, 5). Computerised tomography

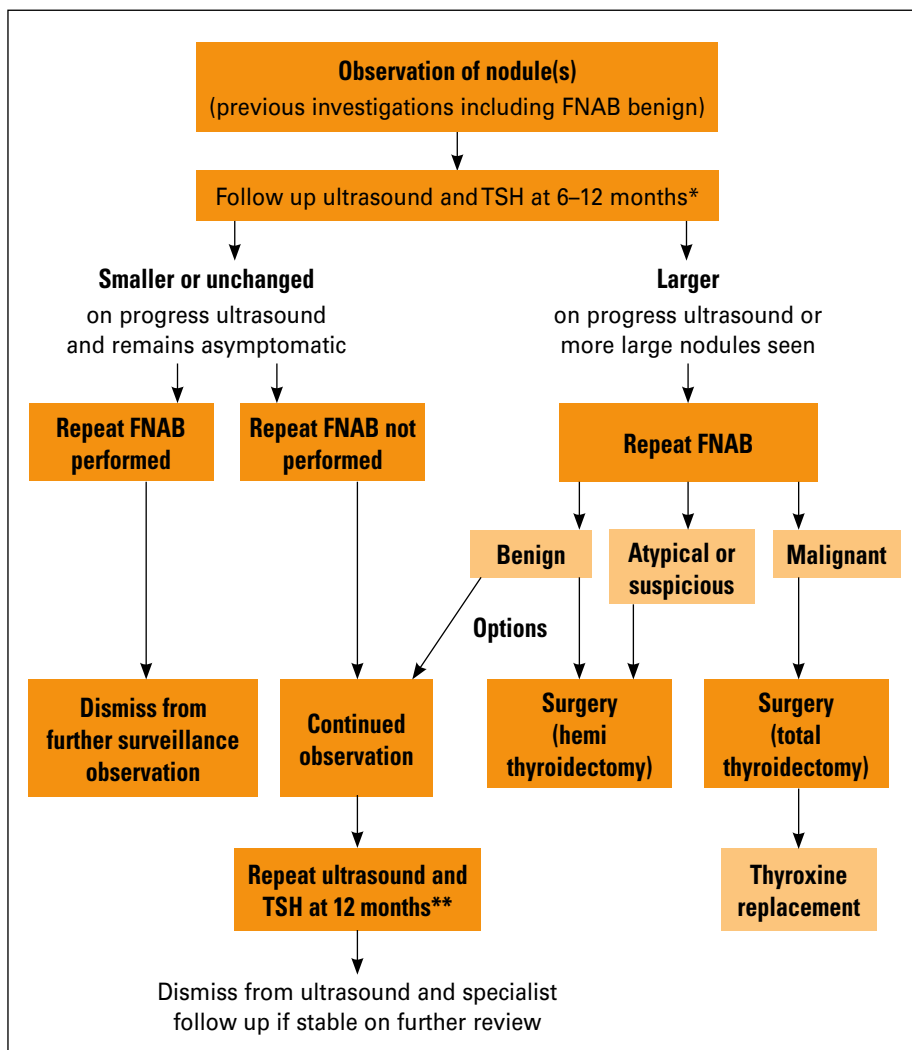


Figure 3. Follow up of a thyroid nodule

* There is no evidence on the optimal interval and method of follow up. Surveillance generally includes repeat assessment with clinical examination, ultrasound and TSH after a period of time. Some specialists do this review at 6–12 months and others recommend review 2–3 years later

** There is no evidence on which to base recommendations for the interval and method of follow up. This interval is given as a guide

and MRI scans are also useful when malignancy is likely and further information on the extent of disease, such as involvement of regional lymph nodes, is required.

Serum calcium

Measurement of serum calcium is important

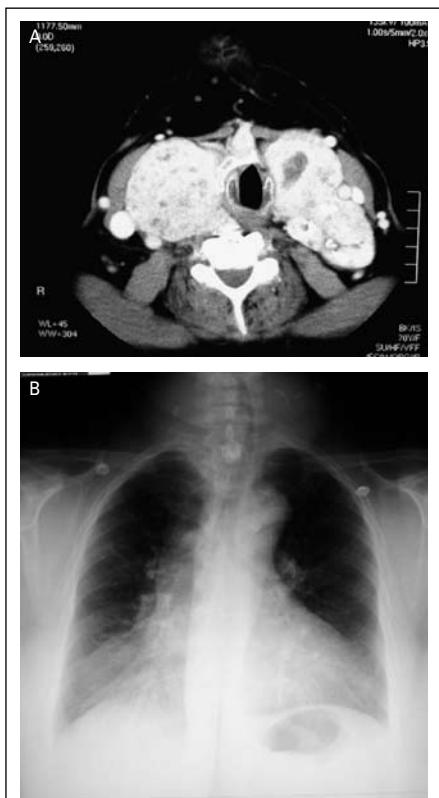


Figure 4a, b. CT scan and chest X-ray showing narrowing and deviation of the trachea due to a massively enlarged right lobe of the thyroid gland. These images are of the patient shown in Figure 1

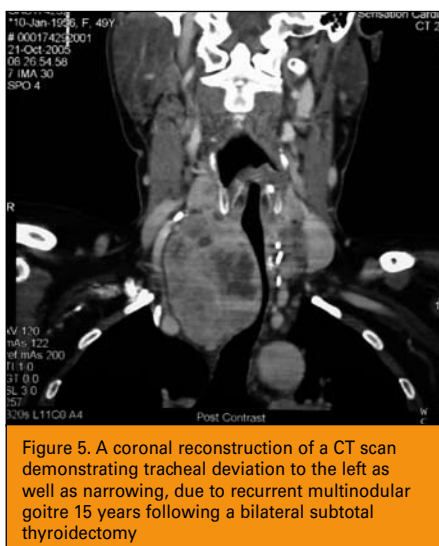


Figure 5. A coronal reconstruction of a CT scan demonstrating tracheal deviation to the left as well as narrowing, due to recurrent multinodular goitre 15 years following a bilateral subtotal thyroidectomy

in the routine assessment of patients with thyroid abnormalities to exclude the presence of coexisting hyperparathyroidism. If this is present, there may be an option of treating it surgically at the same time as thyroidectomy if the thyroid nodule requires surgical management.

Thyroid scintigraphy

A nuclear medicine scan may not always be necessary in the initial assessment of a thyroid nodule. There are some clinicians however, who recommend it routinely. Scintigraphy alone is unable to reliably distinguish malignant from benign nodules. The main clinical indication for thyroid scintigraphy is when hyperthyroidism (suppressed TSH) is present. The management of such a nodule differs to the management of a thyroid nodule that is not hyperfunctioning. A toxic nodule may be treated with radioactive iodine or may be treated surgically (usually with hemithyroidectomy). Thyroid scintigraphy is also useful to identify ectopic thyroid tissue or occult hyperfunctioning tissue and may have a role in the work up of some neoplasms.

Management of nodules

Thyroid nodules with a benign appearance on ultrasound and a benign cytology result on FNAB are usually observed (Figure 3). There is no evidence on the optimal interval and method of follow up. Surveillance generally includes repeat assessment with clinical examination and ultrasound after a period of time. Some specialists do this review at 6–12 months and others recommend review 2–3 years later. If the lesion has increased in size on review, repeat FNAB is recommended. Increase in size, however, is not always a sinister sign as many (89% in one study)¹⁷ cytologically benign nodules increase in size slowly over time. There is an increasing trend to repeat the FNAB at follow up examination even for lesions that are stable on review. Nodules that are benign again on repeat FNAB may be dismissed from further specific follow up and specialist review unless they become symptomatic. Lesions that are stable on follow up ultrasound but are not assessed with repeat FNAB are usually observed for longer before being dismissed from follow up.

Surgery

Surgery is indicated when there is/are:

- malignancy proven on FNAB
- possible malignancy (atypical, suspicious findings on FNAB)
- symptoms of compression from the nodule (dysphagia or tracheal compression. A sensation of choking alone without imaging evidence of tracheal compression is a 'soft' indication for surgery)
- hyperthyroidism (this may be treated with surgery or with radioactive iodine or medications)
- patient choice (usually for cosmetic reasons when nodules are >3 cm)
- other indications (eg. when an adequate sample cannot be obtained by FNAB on several attempts or when a nodule that has shown benign features on ultrasound and FNAB has grown during a period of observation).

Surgical procedures most commonly performed are:

- hemithyroidectomy – this is indicated for:
 - a solitary nodule that is 'hot' or atypical on FNAB
 - a dominant nodule in the context of a multinodular goitre where only one lobe is significantly affected
 - differentiated thyroid cancer <1 cm
- total thyroidectomy (Figure 6, 7) – this is indicated for:
 - thyroid malignancy, except small well differentiated cancers
 - hyperthyroidism due to Graves disease when thyroid eye signs are present or medical management is unsuccessful or contraindicated
 - symptoms or signs of compression of the trachea or oesophagus (Figure 5, 6)
 - multinodular goitre where both lobes are significantly affected
 - patient choice for cosmetic reasons related to a large goitre.

Other surgical options including removal of the nodule only and the operation of subtotal thyroidectomy are performed less often as they generally have no advantages over the operations listed above and rates of complications are similar. These procedures also have additional disadvantages over total



Figure 6. An intra-operative picture showing a large multinodular goitre. This patient had significant tracheal narrowing on chest X-ray and CT examinations (Figure 4)



Figure 7. A large multinodular goitre after excision

thyroidectomy or hemithyroidectomy, such as recurrence of symptoms or development of cancer in the remaining tissue. These problems may require re-operation. Re-do thyroid surgery is associated with a higher risk of complications such as recurrent laryngeal nerve injury and permanent hypocalcaemia compared to initial surgery.¹⁸

Thyroid surgery requires meticulous care to avoid damage to surrounding structures but is now a low risk procedure in experienced hands. Complications include:

- haemorrhage (an uncommon but potentially fatal complication – occurs in <1% of cases)
- voice disturbance or hoarseness due to injury to the recurrent laryngeal nerve (may be temporary or permanent – permanent damage occurs in <1% of cases). Injury to the external branch of the superior laryngeal nerve can cause less obvious voice changes. Patients may complain of an inability to project their voice and easy fatigability of their voice
- hypocalcaemia due to damage to the parathyroid glands or their blood supply (requires calcium supplementation; may be

temporary or permanent [2–3%])

- hypothyroidism is expected and is permanent following total thyroidectomy. It may also occur temporarily or permanently following hemithyroidectomy.

Other treatments

Radioactive iodine is indicated for toxic (hyper functioning) nodules and toxic nodular goitre. It is not recommended if symptoms of compression are present as surgery is usually the best treatment in this situation.

Percutaneous ethanol injection is available but is not routinely offered. It tends to be painful. This procedure can be performed under ultrasound guidance for cystic lesions. It has been shown to reduce the recurrence rate of cysts following aspiration. It is recommended only for nodules proven to be benign on FNAB and is not recommended for treating nodules that are solid or toxic.

Summary of important points

- Thyroid nodules are common and most do not cause significant symptoms. The absence of symptoms however does not reliably exclude malignancy so careful assessment of nodules is required.
- Nodules that are palpable should be assessed with ultrasound.
- FNAB is the single most useful test in the assessment of a thyroid nodule. It is indicated for most nodules that are palpable or show suspicious features on ultrasound and should be considered for nodules >1 cm. The main exception is a nodule in the context of hyperthyroidism, which should be assessed with thyroid scintigraphy and may go on to definitive management without the need for FNAB.
- A nodule that is not symptomatic and has benign features on ultrasound and FNAB may be safely monitored with clinical and ultrasound review. If FNAB is repeated and is again benign, then the nodule can be dismissed from further review unless symptoms develop.
- A nodule that is causing compressive symptoms or yields an atypical, suspicious or malignant result on FNAB should be managed surgically.

Conflict of interest: none declared.

Acknowledgments

Thanks to A/Prof Owen Ung (NSW BCI) who provided input on the algorithms, and Dr Greg Heard (NSW BCI) who provided editorial input. Thanks also to A/Prof Katherine Samaras (St Vincent's Hospital) who provided clinical comments on specific topics in the article. The NSW Breast Cancer Institute receives funding from NSW Health.

References

1. Cooper DS, Doherty GM, Haugen BR, et al. Management guidelines for patients with thyroid nodules and differentiated thyroid cancer. *Thyroid* 2006;16:1–33.
2. Mazzatelli EL. Management of a solitary thyroid nodule. *N Engl J Med* 1993;328:553–9.
3. Ezzat S, Sarti DA, Cain DR, Braunstein GD. Thyroid incidentalomas. Prevalence by palpation and ultrasonography. *Arch Intern Med* 1994;154:1838–40.
4. Mackenzie EJ, Mortimer RH. Thyroid nodules and thyroid cancer. *Med J Aust* 2004;180:242–7.
5. Frates MC, Benson CB, Doubilet PM, et al. Prevalence and distribution of carcinoma in patients with solitary and multiple thyroid nodules on sonography. *J Clin Endocrinol Metab* 2006;91:3411–7.
6. American Association of Clinical Endocrinologists and Associazione Medici Endocrinologi medical guidelines for clinical practice for the diagnosis and management of thyroid nodules. *Endocr Pract* 2006;12:65–102.
7. Talley NJ, O'Connor S. The endocrine system. In: Talley NJ, O'Connor S, editors. *Clinical examination: a guide to physical diagnosis*. Sydney: Williams & Wilkins and Associates 1988;243–52.
8. Marqusee E, Benson CB, Frates MC, et al. Usefulness of ultrasonography in the management of nodular thyroid disease. *Ann Intern Med* 2000;133:696–700.
9. Hagag P, Strauss S, Weiss M. Role of ultrasound guided fine needle aspiration biopsy in evaluation of non-palpable thyroid nodules. *Thyroid* 1999;8:989–95.
10. Frates MC, Benson CB, Charboneau JW, et al. Management of thyroid nodules detected at US: Society of Radiologists in Ultrasound Consensus Conference Statement. *Radiology* 2005;237:794–800.
11. Woeber KA. The year in review: the thyroid. *Ann Intern Med* 1999;131:959–62.
12. Utiger RD. The multiplicity of thyroid nodules and carcinomas. *N Engl J Med* 2005;352:2376–8.
13. Sangalli G, Serio G, Zampatti C, et al. Fine needle aspiration cytology of the thyroid: a comparison of 5469 cytological and final histological diagnoses. *Cytopathology* 2006;17:245–50.
14. Danese D, Sciacchitano S, Fasseti A, et al. Diagnostic accuracy of conventional versus sonography guided fine needle aspiration biopsy of thyroid nodules. *Thyroid* 1998;8:15–21.
15. Hatada T, Okada K, Ishii H, et al. Evaluation of ultrasound guided fine needle aspiration biopsy for thyroid nodules. *Am J Surg* 1998;175:133–6.
16. Udelsman R. The thyroid nodule. *Ann Surg Oncol* 2001;8:89–90.
17. Alexander EK, Hurwitz S, Heering JP, et al. Natural history of benign solid and cystic thyroid nodules. *Ann Intern Med* 2003;138:315–8.
18. Ozbas S, Kocak S, Aydinguz S. Comparison of the complications of subtotal, near total and total thyroidectomy in the surgical management of multinodular goitre. *Endocr J* 2005;52:199–205.

afp CORRESPONDENCE email: afp@racgp.org.au