

Section Thyroid disease

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Symptoms, assessment and guidelines for primary care referral

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KEY POINTS

- Thyroid function disorders are common in the general population and can cause significant morbidity. Primary care physicians should therefore have a low threshold for checking thyroid-stimulating hormone (TSH) as a screening test for thyroid disease
- Hypothyroidism can be insidious and may be associated with other conditions. It should be screened for in this setting and in the whole population over the age of 65 years. Most patients with hypothyroidism can be diagnosed and managed within the primary care setting
- Hyperthyroidism is less common than hypothyroidism. It is associated with atrial fibrillation and osteoporosis, and should always be considered when these conditions are present. Patients should be referred to an endocrine specialist for diagnosis of the cause and continued management
- Thyroid goitre is common. Worldwide, it is often associated with insufficient iodine consumption
- Thyroid nodules are also common. Solitary or clinically obvious nodules should be investigated as they carry a small but significant malignant potential. Thyroid cancer is rare and, with appropriate early diagnosis and management, survival rates are generally very good.

INTRODUCTION

This chapter gives a brief overview of the salient features of hypothyroidism, hyperthyroidism and thyroid swellings, with particular emphasis on the primary care management of these conditions. Case studies have been used to highlight specific clinical scenarios which the primary healthcare physician may encounter when managing patients with thyroid disease. This introductory chapter serves to outline some of the pertinent features of thyroid disease which will be expanded in greater detail in subsequent chapters.

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HYPOTHYROIDISM

Hypothyroidism is a condition in which the body lacks sufficient thyroid hormone. Lack of thyroid hormone affects many organs or systems and results in a slow body metabolism. It is common in western populations. In the UK, primary hypothyroidism is found in 3.5 per 1000 women and in 0.6 per 1000 men. A brief outline is given below, and further details of this condition are described in Chapters 2 and 6.

Clinical diagnosis

Hypothyroidism is notoriously difficult to diagnose in its early stages due to its variable and gradual presentation. The presence of other conditions may detract the primary care clinician from appreciating that hypothyroidism is associated with, or indeed is the primary cause of, these symptoms. Initially, the diagnosis may be easily overlooked (see Case study 1). In view of this, it is important for the clinician to be familiar with its incidence and aetiology, particularly in the primary care setting.

Aetiology (Table 1.1)

Primary hypothyroidism occurs due to intrinsic failure of the thyroid gland which is characterized by a rise in thyroid-stimulating hormone (TSH). The most common cause of chronic hypothyroidism in the UK is autoimmune thyroiditis (Hashimoto's thyroiditis). Worldwide, iodine deficiency is common and in older individuals thyroid atrophy is a well-recognized cause. In the long term, autoimmune thyrotoxicosis is often associated with hypothyroidism. The latter arises following treatment with radioactive iodine or thyroidectomy, or eventually results from the natural history of the condition itself. Iatrogenic hypothyroidism occurs due to inappropriately monitored thionamide therapy and is also precipitated by amiodarone, lithium and other immune-modulating medications.

Table 1.1 Aetiology of hypothyroidism

Cause of hypothyroidism	Comments
Autoimmune (Hashimoto's disease)	Most common cause: The patient may present with a goitre
Atrophic (idiopathic)	Common in the elderly
Congenital	One in 4000 births either absence of the thyroid or absence of enzyme in thyroid hormone synthesis
Iodine deficiency	Common on a worldwide basis
Iatrogenic	Following inappropriately monitored thionamides, radioactive iodine, amiodarone, lithium, interferon α
Previous thyroid surgery or neck irradiation	
Secondary	Following pituitary tumour

Temporary hypothyroidism (which sometimes progresses to permanent deficiency) occurs with thyroiditis. Post-viral, subacute or De Quervain thyroiditis are usually temporary. Lymphocytic and post-partum thyroiditis account for the vast majority of cases, and the associated hypothyroidism is usually permanent.

Congenital hypothyroidism occurs due to the anatomical absence of the thyroid gland or absence of one of the enzymes required for thyroid hormone biosynthesis. Infants may also be born with the condition due to thyroid-suppressing drugs taken by the mother during pregnancy which cross the placenta. Hypothyroidism is screened for in all neonates in the UK by a heel-prick blood test which is usually performed 6 days after birth. By the age of 25, one-third of individuals with Down syndrome develop hypothyroidism¹. Annual TSH screening is therefore recommended in this group.

Secondary hypothyroidism is caused by pituitary failure leading to an absence of TSH secretion and resulting atrophy of the thyroid gland. Pan-hypopituitarism was first described by Simmonds (Simmond's syndrome) in 1914. When it rises in the peri-partum period, it is referred to as Sheehan's syndrome. Secondary hypothyroidism following a pituitary tumour (or its treatment) is usually one of the later hormone deficiencies from the anterior pituitary gland.

Presenting symptoms

In infants it is important to recognize the condition as early as possible because, when left untreated, it causes

**Fig. 1.1** Features of cretinism.

growth and mental retardation. Signs of hypothyroidism in the newborn include prolonged periods of sleep, puffy myxoedematous facies, protruding tongue, hoarse cry, hypothermia, prolonged neonatal jaundice, constipation, feeding difficulties and abdominal distension (see Fig. 1.1). In adults, there may be no symptoms at all in the early stages of hypothyroidism. Speed of onset is variable and symptoms may take many months to develop. Classically these include fatigue, generalized aches and pains, weight gain, constipation, heat sensitivity, dry skin and hair, fluid retention, mental slowing and depression. Patients with sleep apnoea and persistent hoarseness should always have their thyroid function checked.

Clinical signs and conditions associated with hypothyroidism

Clinical findings associated with hypothyroidism are outlined in Table 1.2.

Examination may reveal a thyroid swelling, oedema of the eyes, hands or lower limbs, dry skin and hair, hair loss and sluggish reflexes, particularly the ankle jerk (see Fig 1.2). Cardiovascular manifestations include hypertension, sinus bradycardia and hyperlipidaemia. Neuropsychiatric sequelae also occur.

Case study 1

A 54-year-old female patient underwent routine cholesterol screening which was elevated (>8.5 mmol/l). Following commencement of a statin by the primary healthcare physician, the cholesterol level dropped to 6.0 mmol/l. The following year, she reported

significant weight gain and became increasingly lethargic. Concentration and memory were noticeably impaired and her husband was unable to sleep in the same room due to her prolific snoring. She was subsequently referred to a respiratory specialist. A sleep study confirmed moderate sleep apnoea and, following commencement of continuous positive airways pressure (CPAP), symptoms improved. Twelve months later, she presented to her local A&E Department with chest pain. Blood pressure was persistently elevated and an abnormally raised cholesterol level was again noted. Six months later, she presented with a thyroid swelling to the primary care physician, who organized thyroid function tests, thyroid autoantibodies and a neck ultrasound scan. Serum TSH was greater than $100 \mu\text{U/l}$ (normal TSH $0.4\text{--}4.5 \mu\text{U/ml}$), indicative of hypothyroidism. The patient was referred to an endocrine specialist.

Comment. This case illustrates how the presence of other pathology can significantly delay diagnosis of hypothyroidism, which in turn may have a profound effect on the patient's quality of life. Hypercholesterolaemia, weight gain, lethargy, sleep apnoea and hypertension may all, individually, be indicators of hypothyroidism. The primary care physician should have a low threshold for organizing thyroid function tests in a patient with these symptoms.

Clinical investigations in primary care

TSH measurement is the most universally accepted standard for assessing thyroid function. The normal TSH range is $0.4\text{--}4.5 \mu\text{IU/ml}$. When the TSH is abnormal, the free hormones should be assessed. Usually free thyroxine (T4) is measured when the TSH is elevated to confirm hypothyroidism or investigate subclinical



Fig. 1.2 Patient exhibiting hypothyroid facies.

hypothyroidism. When the TSH is suppressed, the free tri-iodothyronine (T3) can be used to investigate thyrotoxicosis. Thyroid function tests should be requested to determine the thyroid status before further investigation to identify the cause of thyroid dysfunction³ (Level IV) (Table 1.3).

TSH levels will often be raised when thyroxine levels are normal and the patient is clinically euthyroid. This biochemical finding, termed 'subclinical hypothyroidism', may herald the development of hypothyroidism. If the clinician suspects that thyroxine supplementation has been prescribed inappropriately, it should be reduced or discontinued and thyroid function re-evaluated after an interval of 4–6 weeks.

Table 1.2 Symptoms and signs of hypothyroidism

General	Weight gain Intolerance of cold weather Goitre
Gastrointestinal	Constipation
Nervous system	Poor central nervous system development in children Loss of intellectual function Lethargy Slow relaxing reflexes
Dermatology	Dry skin Hair loss (in severe untreated hypothyroidism) Myxoedema (rare)
Cardiovascular	Reduced cardiac output Reduced exercise tolerance Angina pectoris (uncommon but may appear during treatment)
Reproductive	Menorrhagia in women Subfertility in men and women
Haematological	Macrocytosis and anaemia Hypercholesterolaemia (common and improves following thyroxine replacement)

Hypothyroidism can affect any system within the body, and a range of common symptoms are listed above. Although most patients with hypothyroidism in the UK are diagnosed before overt symptomatic presentation occurs, the clinical diagnosis is sometimes easily overlooked (see Case study 1).

Table 1.3 Differential diagnosis of abnormal thyroid function tests

TSH	T4	T4	T4
Increased >4.5 μ IU/ml	Normal Subclinical hypothyroidism	Decreased Hypothyroidism	Increased Hyperthyroidism (very rarely related either to TSH-producing adenoma or thyroid hormone resistance)
Decreased <0.4 μ IU/ml	Subclinical hyperthyroidism	Hypothyroidism (pituitary failure)	Hyperthyroidism

When thyroid function is abnormal, thyroid antibodies can be measured to investigate the possibility of autoimmune thyroiditis (Hashimoto's). Thyroid antibodies should not be measured in patients with normal thyroid function. Hashimoto's thyroiditis occurs due to an autoimmune inflammatory reaction resulting in an underactive thyroid. The condition is outlined in greater detail in Chapters 2 and 6. It is important to exclude Hashimoto's in pregnant women with abnormal thyroid function because thyroid antibodies cross the placenta, leading to congenital hypothyroidism.

Abnormal findings in screening tests for certain conditions should prompt the primary care clinician to check for thyroid disease. These include hypercholesterolaemia (manifest by a raised low-density lipoprotein), macrocytosis and anaemia.

Management of hypothyroidism in primary care

Diagnosis of thyroid dysfunction must be confirmed biochemically. There is no evidence base for the use of thyroxine in tired patients with normal thyroid function. The aim of treatment is to suppress the TSH to normal levels and render the patient symptom free, which can take several months. Treatment in affected patients is life-long. The ideal treatment range of TSH is 0.4–4.5 μ IU/ml. Thyroxine (in the form of levothyroxine) is prescribed, initially at a single dose of 50 μ g. The dose is increased by increments of 50 μ g every 4 weeks until the TSH level becomes normal and the T4 level is within or slightly above its reference range. In elderly patients or those with cardiac disease, the incremental dose increase should be halved to 25 μ g. Following an alteration in thyroxine dose it takes at least 2 months for thyroid function to stabilize. Therefore, repeat thyroid function tests should only be performed after this timeframe.

It may be desirable to obtain lower levels if the patient has no symptoms of hyperthyroidism. Undetectable TSH

levels may indicate overtreatment even if the serum thyroxine is normal. Even with appropriate thyroid hormone treatment, TSH suppression may be associated with osteoporosis, atrial fibrillation and possibly increased mortality.

Subclinical hypothyroidism

Subclinical hypothyroidism is not uncommon, affecting up to 10% of the adult population. The diagnosis is made in the asymptomatic patient who has a raised TSH level with normal free T4 and T3 levels. It is associated with potentially increased cardiovascular risk, hyperlipidaemia and neuropsychiatric effects. Up to 20% of patients progress to overt hypothyroidism. The management of subclinical hypothyroidism is somewhat controversial.^{4,5} The British Thyroid Association (BTA) recommends that thyroxine supplementation should be commenced if the serum T4 is normal and the TSH level is greater than 10 μ IU/ml.³ (Level IV) When thyroxine is prescribed, subsequent management is the same as for hypothyroid patients.

When the TSH is slightly raised but is less than 10 μ IU/ml, there is no evidence base for initiating thyroxine supplementation. A mild alteration in TSH levels is common in a wide range of acute and chronic illnesses, often referred to as 'sick euthyroid' syndrome (outlined in further detail in Chapter 6). As TSH suppression may be associated with atrial fibrillation and osteoporosis, repeating TSH measurement in 3–6 months, in addition to thyroid autoantibodies, is advocated in the first instance.

Screening for thyroid dysfunction

Screening for congenital hypothyroidism is appropriate, cost-effective and well established in the UK. However, evidence from community studies suggests that 'carte blanche' adult population screening only detects a few

cases of overt thyroid disease and is therefore unjustified except in the elderly and in patients with Down syndrome. In addition, patients treated with thyroid surgery or radioiodine have an increased risk of developing hypothyroidism and should also undergo routine surveillance. There is no consensus for screening women for post-partum thyroiditis, although those with type 1 diabetes mellitus have a higher risk and should therefore be followed-up after pregnancy. Patients treated with lithium or amiodarone are also at higher risk of thyroid dysfunction. TSH levels must be routinely screened before and after treatment. An abnormal result should prompt specialist referral, particularly as difficulties may arise in the interpretation of biochemical abnormalities in this group.

Follow-up

In the UK, the recommendation is that patients commenced on thyroxine in primary care should have their TSH monitored annually to ensure optimal dosage. TSH levels should be maintained between 0.4 and 4.5 μ IU/ml.

Specialist referral

Referral to an endocrinology specialist is not usually required unless there is an unusual presentation or associated feature. A patient presenting with hypothyroidism associated with a long-standing nodular goitre is unlikely to have thyroid cancer and can be referred routinely to an endocrinologist rather than the thyroid oncology multidisciplinary team (MDT). In contrast, a patient who presents with a thyroid lump which is new or enlarging should be referred to the thyroid MDT or to a clinician with a special interest in thyroid cancer⁶ (Level IV).

HYPERTHYROIDISM

Hyperthyroidism is a condition characterized by excess thyroid hormone which results in an overactive body metabolism. This is described in greater detail in subsequent chapters (Chapter 2 and 6), and a brief overview follows below.

Clinical diagnosis

In many cases the diagnosis is clear-cut, but sometimes the condition is difficult to recognize due to the insidious onset of symptoms. The primary care clinician should always be alert to the possibility of hyperthyroidism in

patients with certain symptoms which do not appear overtly endocrine, e.g. atrial fibrillation, dyslipidaemia, osteoporosis and subfertility.³ (Level IV).

Aetiology

Hyperthyroidism has an annual incidence of 0.5 cases per 1000 people and, as with hypothyroidism, there is a significant female preponderance (the female:male ratio is roughly 5:1). There may be a family history of thyroid disease, particularly Graves' disease, which is associated with a diffuse thyroid swelling and exophthalmos. Hyperthyroidism can be classified in terms of adenosine uptake (usually technetium is used). 'High uptake' thyrotoxicosis, in which the thyroid traps too much iodine and produces excessive thyroid hormone, accounts for 85% of thyrotoxic patients. This group includes autoimmune thyroid disease with thyrotoxicosis (known as Graves' disease in the UK or Jod Basedow in Europe), multinodular goitre with thyrotoxicosis, an autonomously functioning thyroid nodule or single toxic adenoma.

'Low uptake' thyrotoxicosis, in which the thyroid gland prematurely releases thyroid hormone following an insult, accounts for the minority. This group includes post-viral, post-partum and lymphocytic thyroiditis. In each of these conditions there is a thyrotoxic phase which typically lasts a few weeks, followed by a hypothyroid phase.

Fewer drugs cause hyperthyroidism compared with the hypothyroid patient. As with hypothyroidism, amiodarone causes thyroid dysfunction in 18–20% of patients. Therefore, TSH should be assessed before it is commenced and at a minimum of 6-monthly intervals. Excessive consumption of iodine preparations or thyroxine may also precipitate the condition. Other causes arise from excess TSH secretion either directly by the pituitary or from rare tumours which contain thyroid tissue, such as hydatidiform mole.

Presenting symptoms

As with hypothyroidism, hyperthyroidism may develop insidiously. Patients present with wide-ranging symptoms relevant to different specialties including cardiology, gastroenterology, gynaecology, ophthalmology and dermatology.

It is unusual for hyperthyroidism to occur before puberty. A thyroid disorder should be suspected in children with an enlarged thyroid, weight loss, behavioural disorders (including attention deficit disorder) and

premature growth or development. It is equally unusual for cardiac symptoms to occur at an early age so the presence of palpitations should alert the clinician to the possibility of hyperthyroidism.

In adults, symptoms include heat sensitivity, increased appetite and weight loss, mood change, palpitations and neck swelling. Eye symptoms include protrusion, pain, excessive lacrimation and blurred vision.

Clinical signs and clinical conditions associated with hyperthyroidism

Typical findings on clinical examination are outlined in Table 1.4. The clinician should check for a thyroid swelling, hand tremor, anorexia, tachycardia and hypertension. There may be excessive sweating, brisk reflexes and eye signs. The latter includes lid retraction, proptosis, peri-orbital or conjunctival oedema, papilloedema and reduced visual acuity (although these may all be absent in children and the elderly). Atrial fibrillation, infertility and osteoporosis can all arise secondary to thyrotoxicosis (Fig. 1.3).

Table 1.4 Symptoms and signs of hyperthyroidism

General
Heat intolerance/sweating
Weight loss (despite increased appetite)
Cardiac
Palpitations with resting tachycardia
Respiratory
Shortness of breath
Central nervous system
Agitation and low temper threshold
Reflexes. (fatigue and muscle weakness)
Gastrointestinal
Increased bowel frequency
Features of autoimmune thyroid disease
Diffuse goitre
Exophthalmos
Ophthalmoplegia (lid lag and retraction occur with thyrotoxicosis of any aetiology)
Pre-tibial myxoedema
Vitiligo

Thyrotoxic patients may have one or more of the symptoms and/or signs listed. Even in the absence of symptoms, it is important to treat patients with hyperthyroidism to reduce their risk of atrial fibrillation and osteoporosis.

Case study 2

A 55-year-old woman was found to be tachycardic during investigations for osteoporosis. Her thyroid function was subsequently requested. This revealed an undetectable TSH and an elevated free T3 at 9.4. Thyroid autoantibodies revealed mildly positive thyroid peroxidase antibodies. In view of this, she was referred to an endocrinology specialist who requested a technetium scan. This demonstrated an autonomously functioning thyroid nodule (AFTN or 'single hot nodule'). She was treated with carbimazole until she became euthyroid and was then given radioactive iodine treatment. Following this, she remained euthyroid and did not require thyroxine therapy.

Comment. This case illustrates the importance of assessing thyroid function in patients with osteopenia/osteoporosis. The rationale for treatment is to improve her thyrotoxic symptoms and reduce the future risk of osteoporosis, atrial fibrillation and stroke. Thyroid peroxidase and TSH receptor antibodies have a relatively poor sensitivity. A technetium scan is indicated (rather than an ultrasound scan) as this will detect even a small nodule and successfully illustrate the abnormal toxic adenoma. This guides further management as radioactive iodine is the ideal treatment in



Fig. 1.3 Patient with Graves' disease exhibiting signs of exophthalmos and vitiligo.

this scenario. Once the patient has been protected from thyrotoxicosis with thionamide, she can receive radioactive iodine, which only affects the functioning nodule. The rest of the thyroid gland returns to normal and the patient becomes euthyroid with no need for subsequent thyroxine therapy.

Clinical investigations in primary care

Hyperthyroidism is diagnosed by a suppressed TSH concentration and an elevated serum free T₄ and/or free T₃ level which may be due to exogenous or endogenous causes. The former is prevented by optimizing levothyroxine dosage. The treatment of endogenous subclinical thyrotoxicosis depends on the clinical situation and existing co-morbidity (see 'Subclinical hyperthyroidism' below).

An ultrasound scan is not indicated in most hyperthyroid patients. However, euthyroid patients with a thyroid swelling require referral to the thyroid MDT. The primary care physician should not organize imaging in these cases due to the delay that may arise⁶ (Level IV).

Management of hyperthyroidism in primary care

There are three treatments for hyperthyroidism: antithyroid drugs, radioiodine (¹³¹I) and surgery. All patients, particularly the young and old, should be considered for treatment with β -blockers (in the absence of asthma) to protect against the risk of atrial fibrillation. The Royal College of Physicians and other guidelines recommend that patients are referred to an endocrinologist for further management.⁷

Subclinical hyperthyroidism

This is uncommon, affecting less than 2% in the adult population. Patients are usually asymptomatic and diagnosed biochemically; the TSH level is less than 0.4 μ IU/ml, with normal T₄ and T₃ levels. It is of clinical significance because of the associated risks of atrial fibrillation and osteoporosis.⁸ Furthermore, it may progress to overt hyperthyroidism.

Treatment is decided on an individual basis and it is advisable to monitor thyroid function every 3–6 months.^{2,4,5} (Level IV). Patients with a persistently low TSH and normal T₄ levels should be referred for specialist endocrinology opinion.

Specialist referral

In view of the uncertain clinical course and variety of treatment options (see Chapters 6 and 8), patients should be referred to an endocrinologist rather than managed in the primary care setting. Other indications for specialist endocrinology input include patients with persistent subclinical hyperthyroidism and thyrotoxic patients with single or multiple thyroid nodules⁶ (Level IV).

THYROID TUMOURS

Clinical diagnosis

The term goitre means swelling in the neck and, although this is common, non-thyroid causes should always be entertained. A thyroid goitre may be diffuse, nodular or multinodular (Fig. 1.4) Once the clinical diagnosis has been made, further investigation is necessary to determine the nature of the lesion (see Chapters 2–5).

Aetiology

The most common causes are benign hypertrophy or degeneration. The thyroid can be diffusely enlarged in both hyperthyroid conditions (Graves' disease) and hypothyroid states (Hashimoto's disease). There may be a family history of thyroid goitre or it can arise during puberty and pregnancy. It can also arise in later years and is possibly associated with the ageing process. Deficient dietary iodine intake causes goitre formation, which may have a geographical association. This is particularly evident in hilly regions where the drinking water contains



Fig. 1.4 Patient with a multinodular goitre.

low levels of iodine (endemic goitre). Conversely, too much iodine can also produce a goitre in susceptible individuals. Iodine occurs in a variety of foods and medications, e.g. iodine-containing cough remedies and artificial colouring such as E127.

Solitary nodules are prevalent in 5% of the population, and this figure increases with age. Autopsy studies have detected nodules in up to 50% of the population. Benign nodules are four times more common in females compared with males. A toxic or 'hot' nodule is an uncommon cause of hyperthyroidism.

Malignant nodules are rare, with a prevalence of 25 per million, a male:female ratio of 3:1 and an incidence of 1–2 per 100 000 per annum. Thyroid cancer usually presents as a solitary nodule and is more prevalent in children and those over 50 years of age. The patient is usually clinically and biochemically euthyroid.

Thyroid nodules may be multiple, and it is unusual for these to be malignant. The incidence of thyroid cancer is higher in patients with a long-standing thyroid goitre or thyroiditis. Solitary thyroid nodules have a 10–30% risk of malignancy (this increases to 50% in children). Radiation is a well recognized risk factor, such as radiation exposure from atomic fallout and radiotherapy to the neck. There is a genetic predisposition to thyroid cancer in families with the *RET* gene. The presence of this gene may result in families suffering multiple endocrine neoplasia (MEN) syndrome (see Chapters 9, 12, 13 and 15).

Presenting symptoms

Features that raise suspicion of malignancy are listed in Table 1.5.

Table 1.5 Clinical features which suggest thyroid malignancy

- Sudden or rapid growth of a nodule over a period of weeks, particularly in a pre-existing goitre or in a patient on long-term thyroid suppression
- Hard, fixed or irregular thyroid swelling
- Pain
- Hoarseness, or voice change
- Haemoptysis
- Dysphagia/globus
- Stridor
- Cervical lymphadenopathy
- Thyroid nodule or a goitre in a child
- Cervical lymphadenopathy associated with a thyroid lump
- Horner's syndrome (see Fig. 1.5)

Clinical signs

There is usually no evidence of thyroid dysfunction, but pulse and blood pressure should be recorded. Neck examination may reveal a firm thyroid lump. Not all cases of thyroid malignancy fit the classical description of a hard fixed swelling; over-reliance on the consistency of a thyroid lesion can be misleading. The primary care clinician should also palpate the cervical lymph node chain for associated enlargement.

Clinical investigations in primary care

Thyroid function and thyroid autoantibodies (thyroid peroxidase antibodies) must be assessed, as the management of a hypo- or hyperthyroid goitre is entirely different to that of a euthyroid goitre. An abnormal result warrants an endocrinology referral. If the results are normal and the patient has a palpable firm thyroid nodule, consideration should be given to referring the patient to a thyroid lump clinic.

Management of thyroid cancer in primary care

Recognition and referral (see below) is the role of the primary care physician. Specialist endocrinology input following treatment is important to monitor subsequent thyroxine replacement. The aim in these cases is to maintain TSH suppression to a level less than $0.1 \mu\text{IU/ml}^6$ (Level IV) (see Chapters 5, 11 and 12 for further details).

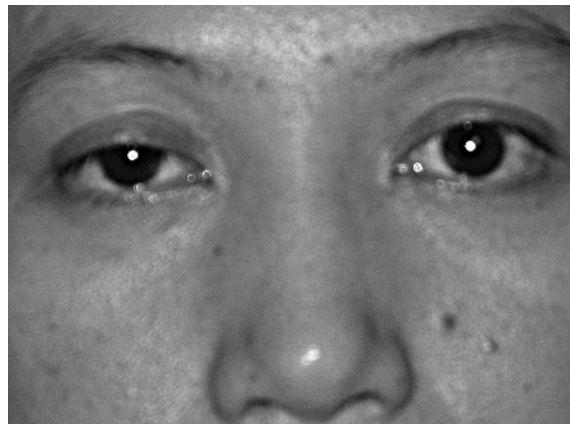


Fig. 1.5 Patient with thyroid cancer exhibiting clinical features of a right Horner's syndrome.

The overall 10-year survival for middle-aged adults is between 80 and 90%. Up to 20% of patients will develop locoregional recurrence, and 10–15% distant metastasis. Important poor prognostic factors include:

1. Age: <10 years or >40 years.
2. Male gender.
3. Grade: poorly differentiated tumours.
4. Histology: poorer prognosis is associated with particular papillary subtypes such as tall cell and columnar variants. Follicular variants associated with poorer prognosis include an insular pattern and Hurthle cell carcinoma.
5. Tumour extent: size of the primary tumour, extracapsular invasion, cervical lymph node metastases and distant metastases.
6. Completeness of resection.

Specialist referral

The updated BTA guidelines 2007 suggest that an urgent 'same day' referral to secondary care (A&E Department, Head and Neck or General Surgical emergency services) is warranted for any patient with stridor associated with a thyroid swelling.⁶ Urgent referral to a specialist in thyroid cancer or to a member of the thyroid MDT is indicated in the following circumstances.

- Unexplained hoarseness or voice change
- Thyroid nodule/goitre in a child
- Cervical lymphadenopathy associated with a thyroid lump (usually deep cervical or supraclavicular region)
- A rapidly enlarging painless thyroid mass over a period of weeks (a rare presentation of thyroid cancer and usually associated with anaplastic thyroid cancer or thyroid lymphoma).

Non-urgent referrals include patients who have abnormal thyroid function as cancer is very rare in these cases. Ideally, patients should be referred to an endocrinologist. Other indications include sudden onset of pain in a thyroid lump as this is likely to represent haemorrhage within a benign thyroid cyst. Non-urgent referral is also warranted when the thyroid lump has been increasing in size slowly over many months or years.

Case study 3

A 63-year-old male smoker with a previous history of neck irradiation presented to his primary care physician with non-productive cough, noisy breathing and hoarseness. He had run out of salbutamol and becotide inhalers several months earlier. On

examination, the patient was found to have biphasic transmitted breath sounds and an incidental firm thyroid swelling. Thyroid function was requested and the patient commenced on a course of oral antibiotics, steroid and salbutamol inhalers. The patient was reviewed 2 weeks later. His hoarseness persisted and it was now apparent that there was biphasic stridor at rest. The thyroid function test was normal. Immediate referral to the local Head and Neck Department was organized and the patient was admitted into hospital the same day. The patient was commenced on intravenous steroids and regular adrenaline nebulizers, and the stridor resolved over the next 24h. Flexible nasoendoscopy revealed a unilateral vocal cord palsy. Subsequent investigation was organized including cytology, ultrasound and non-contrast computed tomography (CT) scan head and neck.

Comment. This case illustrates that it is important for the primary care physician to be alert to the risk factors of thyroid cancer, i.e. previous history of irradiation. The 'patient factors' also suggest an increased likelihood of thyroid cancer. The presence of the chest infection may account for hoarseness but, in view of the other clinical information, thyroid malignancy should be suspected immediately. Stridor suggests advanced thyroid malignancy with recurrent laryngeal involvement. Same day referral, as previously outlined, is imperative.

Screening for thyroid cancer⁹ (Level IV)

Risk-directed screening, usually by a specialist secondary team, should be considered in patients with:

- Familial thyroid cancer, including medullary thyroid cancer (MTC)
- History of neck irradiation in childhood
- Family history of multiple endocrine neoplasia type 2 (MEN2).

The following carry a statistically increased risk of thyroid malignancy but screening is not recommended in the UK:

- Endemic goitre
- Hashimoto's thyroiditis (risk of lymphoma)
- Family or previous history of thyroid adenoma
- Cowden's syndrome (macrocephaly, mild learning difficulties, carpet-pile tongue, with benign or malignant breast disease)
- Familial adenomatous polyposis.

EVIDENCE APPRAISAL

Much of the evidence of this chapter has been taken from the most recent national guidelines. Where appropriate within the text, references have been classified into the definition of types of evidence based on Agency for Health Care Policy and Research (1992).

Level	Type of evidence
Ia	Evidence obtained from meta-analysis of randomized controlled trials
Ib	Evidence obtained from at least one randomized controlled trial
IIa	Evidence obtained from at least one well-designed controlled study without randomization
IIb	Evidence obtained from at least on other type of well-designed quasi-experimental study
III	Evidence obtained from well designed non-experimental descriptive studies
IV	Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

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MULTIPLE CHOICE QUESTIONS

Select the single most appropriate option.

- Thyroid hormone levels
 - Free T4 is the ideal screening test for thyroid function
 - TSH should be used to screen for thyroid disease and T3 or T4 used if the TSH is abnormal
 - In subclinical hypothyroidism TSH levels are within the normal range
 - A mild alteration in TSH levels is uncommon in acute and chronic illnesses
 - A TSH level greater than 4.5 $\mu\text{U/l}$ confirms clinical hypothyroidism
- Thyroid disease
 - Lethargy is a feature of both hyper- and hypothyroidism
 - Hyperthyroidism is obvious to diagnose clinically
 - Subclinical hyperthyroidism requires no treatment
 - Hypothyroidism is screened for in all neonates in the UK by a heel-prick blood test which is usually performed 6 weeks after birth
 - 'High uptake' thyrotoxicosis accounts for a minority of thyrotoxic patients.
- Thyroid swellings
 - The thyroid can be diffusely enlarged in both hyperthyroid conditions and hypothyroid states
 - Autopsy studies have detected nodules in up to 20% of the population
 - A toxic or 'hot' nodule is a common cause of hyperthyroidism.
 - Solitary thyroid nodules have a 5% risk of malignancy
 - The management of a hypo- or hyperthyroid goitre is the same to that of a euthyroid goitre
- Thyroid cancer
 - Patients with thyroid cancer usually show clinical signs of thyrotoxicosis
 - The overall 10-year survival for differentiated thyroid cancer is 80–90%
 - Multiple thyroid nodules have no significant malignant risk
 - Important poor prognostic factors include female gender and age >40 years

- E. The incidence of thyroid cancer is not significantly raised in patients with a long-standing thyroid goitre
5. In the UK, risk-directed screening:
- A. Is recommended in patients with Hashimoto's thyroiditis
 - B. Is recommended in patients with familial adenomatous polyposis
 - C. Is usually performed by the primary care physician
 - D. Recommendations are based on high level evidence
 - E. Should be considered in patients with a history of neck irradiation in childhood

Answers

- 1. B
- 2. A
- 3. A
- 4. B
- 5. E