Endocrine glands synthesise hormones that are released into the circulation and act at distant sites. Diseases may result from excessive or inadequate hormone production, or target organ hypersensitivity or resistance to the hormone. The main endocrine glands are the pituitary, thyroid, adrenals, gonads (testes and ovaries), parathyroids and the endocrine pancreas. With the notable exception of the pancreatic islet cells (which release insulin) and the parathyroids, most endocrine glands are themselves controlled by hormones released from the pituitary.

Since hormones circulate throughout the body, symptoms and signs of endocrine disease are frequently non-specific, affecting many body systems (Box 10.1). Often, endocrine disease is picked up incidentally during biochemical testing or radiological imaging. Careful history taking and examination are required to recognise characteristic patterns of disease. Thyroid disease and diabetes mellitus are common and frequently familial; establishing a detailed family history is therefore important. Some less common endocrine disorders (such as multiple endocrine neoplasia) show an autosomal dominant pattern of inheritance.

10.1 Common clinical features in endocrine disease

Symptom, sign or problem	Differential diagnoses
Tiredness	Hypothyroidism, hyperthyroidism, diabetes mellitus, hypopituitarism
Weight gain	Hypothyroidism, PCOS, Cushing's syndrome
Weight loss	Hyperthyroidism, diabetes mellitus, adrenal insufficiency
Diarrhoea	Hyperthyroidism, gastrin-producing tumour, carcinoid
Diffuse neck swelling	Simple goitre, Graves' disease, Hashimoto's thyroiditis
Polyuria (excessive thirst)	Diabetes mellitus, diabetes insipidus, hyperparathyroidism, Conn's syndrome
Hirsutism	Idiopathic, PCOS, congenital adrenal hyperplasia, Cushing's syndrome
'Funny turns' or spells	Hypoglycaemia, phaeochromocytoma, neuroendocrine tumour
Sweating	Hyperthyroidism, hypogonadism, acromegaly, phaeochromocytoma
Flushing	Hypogonadism (especially menopause), carcinoid syndrome
Resistant hypertension	Conn's syndrome, Cushing's syndrome, phaeochromocytoma, acromegaly
Amenorrhoea/oligomenorrhoea	PCOS, hyperprolactinaemia, thyroid dysfunction
Erectile dysfunction	Primary or secondary hypogonadism, diabetes mellitus, non-endocrine systemic disease, medication-induced (e.g. beta-blockers, opiates)
Muscle weakness	Cushing's syndrome, hyperthyroidism, hyperparathyroidism, osteomalacia
Bone fragility and fractures	Hypogonadism, hyperthyroidism, Cushing's syndrome, primary hyperparathyroidism

PCOS, *polycystic ovary syndrome.*

THE THYROID

Anatomy and physiology

The thyroid is a butterfly-shaped gland that lies inferior to the cricoid cartilage, approximately 4 cm below the superior notch of the thyroid cartilage (Fig. 10.1A). The normal thyroid has a volume of <20 mL and is palpable in about 50% of women and 25% of men. It is comprised of a central isthmus approximately 1.5 cm wide, covering the second to fourth tracheal rings, and two lateral lobes that are usually no larger than the distal phalanx of the patient's thumb. The gland may extend into the superior mediastinum and can be partly or entirely retrosternal. Rarely, it can be located higher in the neck along the line of the thyroglossal duct, an embryological remnant of the descent of the thyroid from the base of the tongue to its final position. Thyroglossal cysts can also arise from the thyroglossal duct; they often occur at the level of the hyoid bone (Fig. 10.1A) and characteristically move upwards on tongue protrusion. The thyroid is attached to the pretracheal fascia and thus moves superiorly on swallowing or neck extension.

Thyrotoxicosis is a clinical state of increased metabolism caused by elevated circulating levels of thyroid hormones. Graves' disease is the most common cause (Fig. 10.2 and Box 10.2). It is an autoimmune disease with a familial component and is 5–10 times more common in women, usually presenting between 30 and 50 years of age. Other causes include toxic multinodular goitre, solitary toxic nodule, thyroiditis and excessive thyroid hormone ingestion.

Hypothyroidism is caused by reduced levels of thyroid hormones, usually due to autoimmune Hashimoto's thyroiditis, and affects women approximately six times more commonly than men. Most other causes are iatrogenic and include previous radioiodine therapy or surgery for Graves' disease.

The history

Common presenting symptoms

Neck swelling

Goitre is enlargement of the thyroid gland (Fig. 10.3). It is not necessarily associated with thyroid dysfunction and most patients

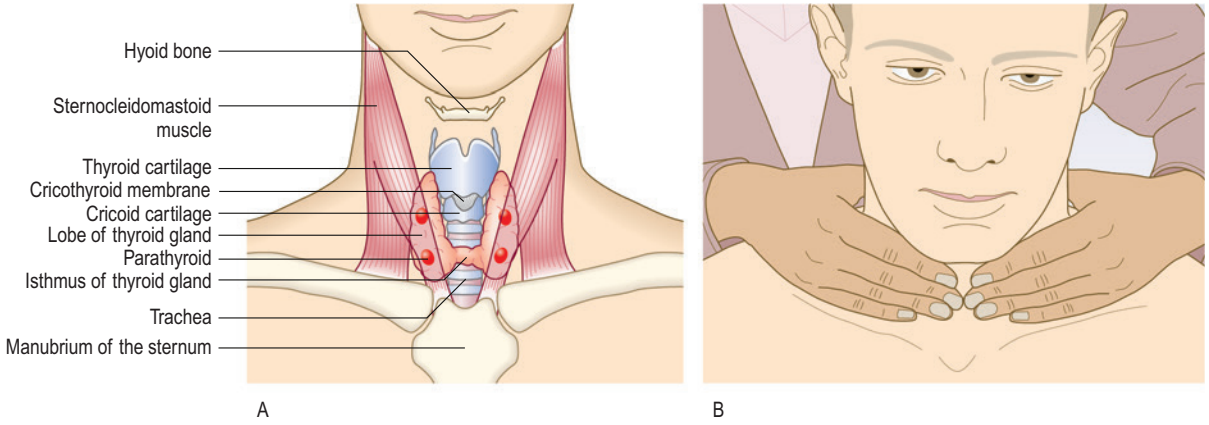

Fig. 10.1 The thyroid gland. A Anatomy of the gland and surrounding structures. B Palpating the thyroid gland from behind.

Fig. 10.2 Graves' hyperthyroidism. A Typical facies. B Severe inflammatory thyroid eye disease. C Thyroid acropachy. D Pretibial myxoedema.

with goitre are euthyroid. Large or retrosternal goitres may cause compressive symptoms, including stridor, breathlessness or dysphagia.

Thyroid nodules may be solitary (Fig. 10.3C) or may present as a dominant nodule within a multinodular gland. Palpable nodules (usually >2 cm in diameter) occur in up to 5% of women and less commonly in men, although up to 50% of patients have occult nodules; thus many are found incidentally on neck or chest imaging.

Neck pain

Neck pain is uncommon in thyroid disease and, if sudden in onset and associated with thyroid enlargement, may represent

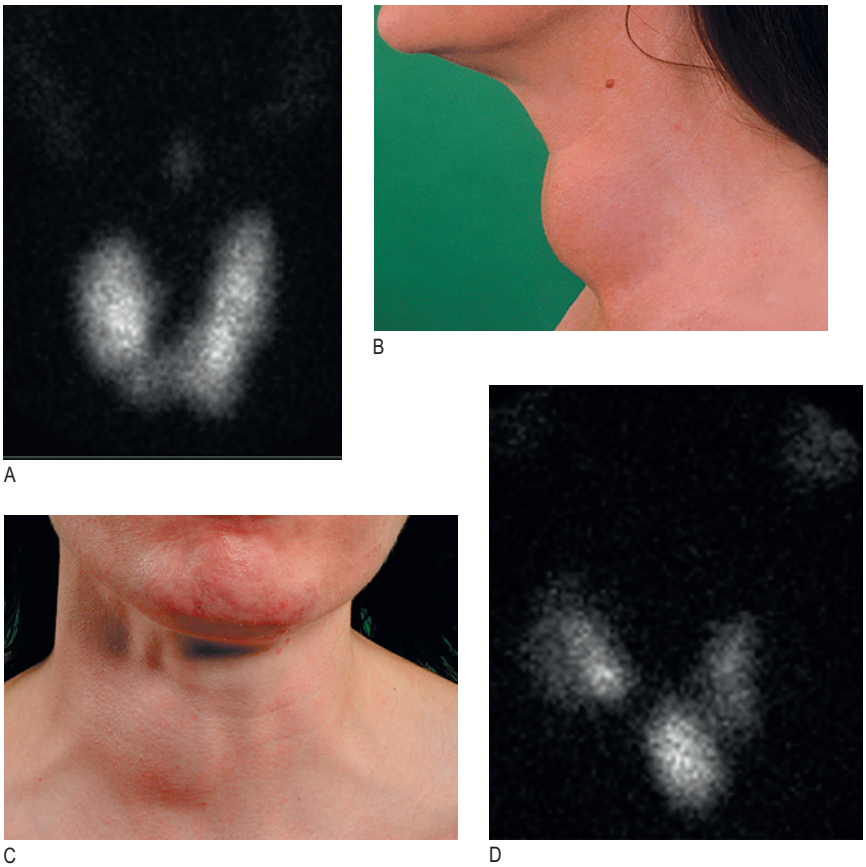

Fig. 10.3 Thyroid enlargement. A ^{99m}Technetium radionuclide scan demonstrating diffuse goitre due to Graves' disease. B Diffuse goitre due to Graves' disease. C Solitary toxic nodule. D ^{99m}Technetium radionuclide scan confirming multinodular goitre. *(A and D) Courtesy of Dr Dilip Patel.*

bleeding into an existing thyroid nodule. Pain can also occur in viral subacute (de Quervain's) thyroiditis.

History suggesting hyperthyroidism

Ask about:

- fatigue, poor sleep
- tremor, heat intolerance, excessive sweating (hyperhidrosis)
- pruritus (itch), onycholysis (loosening of the nails from the nail bed), hair loss
- irritability, anxiety, emotional lability
- dyspnoea, palpitations, ankle swelling
- weight loss, hyperphagia, faecal frequency, diarrhoea
- proximal muscle weakness (difficulty rising from sitting or bathing)
- oligomenorrhoea or amenorrhoea (infrequent or ceased menses, respectively)
- eye symptoms: 'grittiness', excessive tearing, retro-orbital pain, eyelid swelling or erythema, blurred vision or diplopia (these symptoms of ophthalmopathy occur in the setting of autoimmune thyroid disease).

History suggesting hypothyroidism

Ask about:

- fatigue, mental slowing, depression
- cold intolerance
- weight gain, constipation
- symptoms of carpal tunnel syndrome
- dry skin or hair.

10.2 Features suggestive of Graves' hyperthyroidism

History

- Female sex
- Prior episode of hyperthyroidism requiring treatment
- Family history of thyroid or other autoimmune disease
- Ocular symptoms ('grittiness', redness, pain, periorbital swelling)

Physical examination

- Vitiligo
- Thyroid acropachy
- Diffuse thyroid enlargement (can be nodular)
- Thyroid bruit
- Pretibial myxoedema
- Signs of Graves' ophthalmopathy (proptosis, redness, oedema)

Past medical, drug, family and social history

Ask about:

- prior neck irradiation (risk factor for thyroid malignancy)
- recent pregnancy (postpartum thyroiditis usually occurs in the first 12 months)
- drug therapy: antithyroid drugs or radioiodine therapy; amiodarone and lithium can cause thyroid dysfunction
- family history of thyroid or other autoimmune disease
- residence in an area of iodine deficiency, such as the Andes, Himalayas, Central Africa: can cause goitre and, rarely, hypothyroidism
- smoking (increases the risk of Graves' ophthalmopathy).

The physical examination

General examination

Look for signs of weight loss or gain (calculate the body mass index), and assess the patient's behaviour for signs of agitation, restlessness, apathy or slowed movements. Patients may have abnormal speech (pressure of speech suggests hyperthyroidism, while speech is often slow and deep in hypothyroidism). Hoarseness is suggestive of vocal cord paralysis and should raise suspicion of thyroid malignancy.

Features of hyperthyroidism and hypothyroidism on examination are summarised in Fig. 10.4.

Features of thyrotoxicosis include warm, moist skin, proximal muscle weakness (due to a catabolic energy state), tremor and brisk deep tendon reflexes. Hyperthyroidism may also be associated with tachycardia or atrial fibrillation, and a midsystolic cardiac flow murmur due to increased cardiac output.

Thyroid acropachy is an extrathyroidal manifestation of autoimmune thyroid disease. It is characterised by soft-tissue swelling and periosteal hypertrophy of the distal phalanges, and mimics finger clubbing (see Fig. 10.2C). It is often associated with dermopathy and ophthalmopathy. Pretibial myxoedema is a raised, discoloured (usually pink or brown), indurated appearance over the anterior shins; despite its name, it is specifically associated with Graves' disease and not hypothyroidism (see Fig. 10.2D).

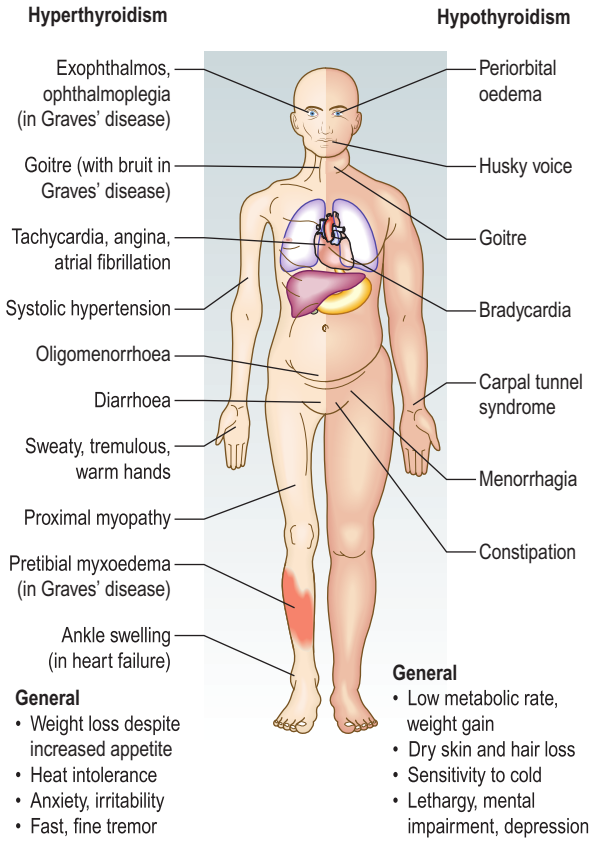

Fig. 10.4 Features of hyper- and hypothyroidism.

Many clinical features of hypothyroidism are produced by myxoedema (non-pitting oedema caused by tissue infiltration by mucopolysaccharides, chondroitin and hyaluronic acid; Figs 10.4 and 10.5). Other common findings in hypothyroidism include goitre, cool, dry or coarse skin, bradycardia, delayed ankle reflexes and a slowing of movement.

Examination sequence

- Observe the facial appearance, noting signs of dry or coarse hair and periorbital puffiness (Fig. 10.5).
- Inspect the hands for vitiligo, thyroid acropachy, onycholysis and palmar erythema.
- Assess the pulse (tachycardia, atrial fibrillation, bradycardia) and blood pressure.
- Auscultate the heart for a midsystolic flow murmur (hyperthyroidism).
- Inspect the limbs for coarse, dry skin and pretibial myxoedema.
- Assess proximal muscle power and deep tendon (ankle) reflexes (p. 139).

Thyroid gland

Examination sequence

- Inspect the neck from the front, noting any asymmetry or scars. Inspect the thyroid from the side with the patient's neck slightly extended. Extending the neck will cause the thyroid (and trachea) to rise by a few centimetres and may make the gland more apparent. Give the patient a glass of water and ask them to take a sip and then swallow. The thyroid rises (with the trachea) on swallowing.
- Palpate the thyroid by placing your hands gently on the front of the neck with your index fingers just touching, while standing behind the patient (see Fig. 10.1B). The patient's neck should be slightly flexed to relax the

Fig. 10.5 Typical facies in hypothyroidism.

sternocleidomastoid muscles. Ask the patient to swallow again and feel the gland as it moves upwards.
- Note the size, shape and consistency of any goitre and feel for any thrill.
- Palpate for cervical lymphadenopathy (see Fig. 3.27).
- Percuss the manubrium to assess for dullness due to retrosternal extension of goitre.
- Auscultate with your stethoscope for a thyroid bruit. A thyroid bruit (sometimes associated with a palpable thrill) indicates abnormally high blood flow and is most commonly associated with Graves' disease. It may be confused with other sounds: bruits from the carotid artery or those transmitted from the aorta are louder along the line of the artery.

Early simple goitres are relatively symmetrical but may become nodular with time. In Graves' disease the surface of the thyroid is usually smooth and diffuse; in uninodular or multinodular goitre it is irregular (see Fig. 10.3). Diffuse tenderness is typical of viral thyroiditis. Localised tenderness may follow bleeding into a thyroid cyst. Fixation of the thyroid to surrounding structures (such that it does not move on swallowing) and associated cervical lymphadenopathy increase the likelihood of thyroid malignancy. Further investigation of thyroid disorders is summarised in Box 10.3.

10.3 Investigations in thyroid disease

Investigation	Indication/comment
Biochemistry	
Thyroid function tests	To assess thyroid status
Immunology	
Antithyroid peroxidase antibodies	Non-specific, high in autoimmune thyroid disease
Antithyroid stimulating hormone receptor antibodies	Specific for Graves' disease
Imaging	
Ultrasound	Goitre, nodule
Thyroid scintigraphy (^{123}I, ^{99m}Tc)	To assess areas of hyper-/hypoactivity
Computed tomography	To assess goitre size and aid surgical planning
Invasive/other	
Fine-needle aspiration cytology	Thyroid nodule
Respiratory flow-volume loops	To assess tracheal compression from a large goitre

Eyes

Examination sequence

- Look for periorbital puffiness or oedema, and lid retraction (this is present if the white sclera is visible above the iris in the primary position of gaze; see Fig. 10.2A).
- Examine for features of Graves' ophthalmopathy, including exophthalmos (look down from above and behind the patient), lid swelling or erythema, and conjunctival redness or swelling (chemosis).
- Assess for lid lag: ask the patient to follow your index finger as you move it from the upper to the lower part of the visual field. Lid lag means delay between the movement of the eyeball and descent of the upper eyelid, exposing the sclera above the iris.
- Assess eye movements (see Fig. 8.11). Graves' ophthalmopathy is characteristically associated with restriction of upgaze.

Lid retraction (a staring appearance due to widening of the palpebral fissure) and lid lag (see earlier) are common eye signs associated with hyperthyroidism. Both are thought to be due to contraction of the levator muscles as a result of sympathetic hyperactivity. Periorbital puffiness (myxoedema) is sometimes seen in hypothyroidism.

Graves' ophthalmopathy occurs in around 20% of patients and is caused by an inflammatory infiltration of the soft tissues and extraocular muscles (see Fig. 10.2A,B). Features suggestive of active inflammation include spontaneous or gaze-evoked eye pain, and redness or swelling of the lids or conjunctiva. Proptosis (protrusion of the globe with respect to the orbit) may occur in both active and inactive Graves' ophthalmopathy and is often referred to as exophthalmos. Inflammation of the orbital soft tissues may lead to other more severe features, including corneal ulceration, diplopia, ophthalmoplegia and compressive optic neuropathy (see Fig. 8.8D).

THE PARATHYROIDS

Anatomy and physiology

There are usually four parathyroid glands situated posterior to the thyroid (see Fig. 10.1A). Each is about the size of a pea and produces parathyroid hormone, a peptide that increases circulating calcium levels.

The history

Common presenting symptoms

Parathyroid disease is commonly asymptomatic. In hyperparathyroidism the most common symptoms relate to hypercalcaemia: polyuria, polydipsia, renal stones, peptic ulceration, tender areas of bone fracture or deformity ('Brown tumours': Fig. 10.6A), and delirium or psychiatric symptoms. In hypoparathyroidism, hypocalcaemia may cause hyper-reflexia or tetany (involuntary muscle contraction), most commonly in the hands or feet. Paraesthesiae of the hands and feet or around the mouth may occur. Hypoparathyroidism is most often caused by inadvertent damage to the glands during thyroid surgery but may also be caused by autoimmune disease. Patients with the rare autosomal dominant condition pseudohypoparathyroidism have end-organ resistance to parathyroid hormone and typically have short stature, a round face and shortening of the fourth and fifth metacarpal bones (Fig. 10.6B,C).