Module 1764
Thyroid disorders

This module covers:

- How the thyroid gland functions and problems that may occur
- Symptoms of hypo- and hyperthyroidism and how each is diagnosed
- Complications that may occur if hypo- and hyperthyroidism are left untreated
- Management of thyroid disorders and counselling that should be provided to patients receiving drug treatment

October

Clinical: Endocrinology

Thyroid disorders	October 3*
Cushing's syndrome	October 10
Low testosterone	October 17
Growth disorders	October 31*

Practice:

Effective appraisal	October 24

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Hypothyroidism and hyperthyroidism cost the NHS in England more than £130 million last year, data from the Health and Social Care Information Centre shows. This means community pharmacists are all too familiar with dispensing levothyroxine – but less familiar with the conditions behind the prescriptions, which can include iodine deficiency and hypothalmic disease.

Located just in front of the trachea in the neck, the thyroid gland helps regulate the body's metabolism. It does this by producing several hormones, though the majority (around 80%) is thyroxine (T4).

This chemical is inactive in the body until it is converted, predominantly in the liver, into triiodothyronine (T3). T3 is found either free in the blood or bound to globulins in the blood; it is the free T3 that regulates metabolism.

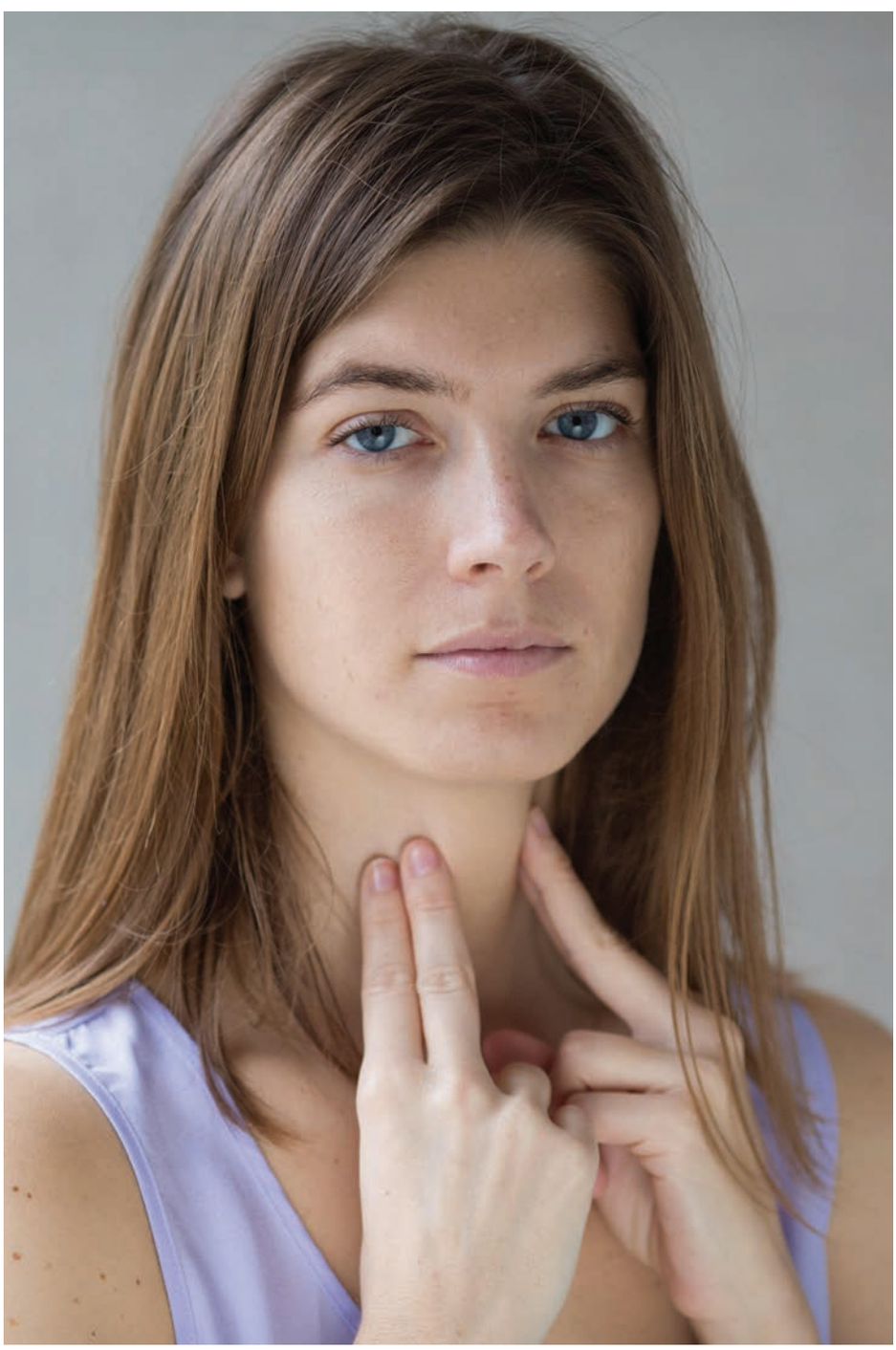
The pituitary gland in the brain is responsible for controlling the thyroid gland, which it does by secreting thyroid-stimulating hormone (TSH). If the levels of T3 and T4 fall, TSH is released, which prompts T4 production and subsequently T3. The relationship between the thyroid and the pituitary is sometimes likened to a central heating system: while the radiators (the thyroid) perform the function of warming up a house, they are at the will of the thermostat (the pituitary) to tell them that they need to work. There are a number of reasons why this system may become faulty, resulting in hypo- or hyperthyroidism.

Hypothyroidism

This occurs when the thyroid fails to produce enough T4.

Primary causes, which prompt dysfunction of the thyroid gland, include:

- an autoimmune reaction (most common)
- damage resulting from radiotherapy or surgery
- treatment for an overactive thyroid
- an adverse effect of drug treatment (culprits include amiodarone, lithium, interferon and tamoxifen)



The thyroid gland is located in front of the trachea and helps to regulate the body's metabolism

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- iodine deficiency
- inflammation
- infiltration of another condition such as sarcoidosis
- congenital predisposition

Secondary hypothyroidism may stem from pituitary underactivity, for example as the result of:

- a tumour or infarction
- hypothalamic disease
- TSH inactivity or deficiency.

Hyperthyroidism

Sometimes called thyrotoxicosis, this condition may also have a primary or secondary cause:

Primary causes include:

- Graves' disease, an autoimmune disorder in which TSH antibodies stimulate thyroid growth and function
- the development of thyroid nodules
- drug treatment, particularly with amiodarone or levothyroxine.

Secondary causes include:

- high levels of human chorionic gonadotrophin as a result of pregnancy or a tumour
- rarely, a pituitary adenoma or thyroid hormone resistance syndrome.

Diagnosis

Although symptoms *(see table, above right)* may point towards a specific thyroid condition, they can be non-specific and lead to a misdiagnosis. When the thyroid function is in question, a thyroid function test should be performed. In most underactive thyroid patients, TSH will be above and T4 below the reference ranges (>4.5mU/l and <9picomol/l respectively, though laboratories may differ). However, subclinical hypothyroidism often shows normal T4 and mildly elevated TSH levels.

In patients with an overactive thyroid, TSH levels will generally be lower than usual. T3 and T4 will be raised above the upper end of the reference range because the feedback mechanism in place to maintain regular T3 and T4 levels is not working.

Further tests are usually only carried out if the cause of the thyroid dysfunction is unclear, for example, an isotope iodine scan may be performed to identify whether hyperthyroidism is due to Graves' disease or an ultrasound scan may be undertaken to determine whether a previously identified nodule is cancerous or benign. If subclinical thyroid dysfunction is suspected, tests will be repeated at a later date to see if the results have changed over time.

Complications

While thyroid conditions can be slow to develop and therefore seem that they do not need sorting out in a hurry, the consequences of leaving them unmanaged can be serious.

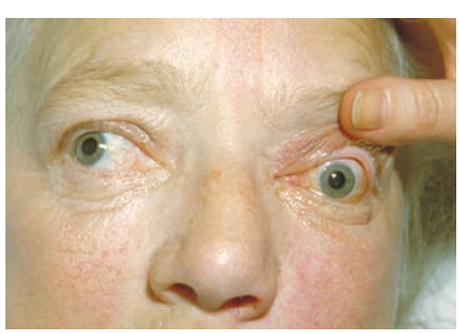
Hypothyroidism can lead to hypercholesterolaemia, which in turn increases the risk of cardiovascular disease. Other complications can include bradycardia, fertility problems, deafness and anaemia, and if the thyroid underactivity stems from an autoimmune problem, there is a risk of other immune conditions developing, such as kidney disease.

In rare cases, a severely underactive thyroid can cause a myxoedema crisis, which is considered a medical emergency. Myxoedema typically involves swelling of the skin and underlying tissues, giving a waxy consistency. The signs include hypotension, hypoglycaemia, hypothermia, shallow breathing and unresponsiveness and warrant urgent hospital treatment.

Hyperthyroidism, if left untreated, can lead to a sudden flare-up of symptoms known as a thyroid storm. The sufferer may experience symptoms such as:

- severe tachycardia
- fever
- jaundice
- chest pain
- dehydration due to vomiting and diarrhoea
- extreme agitation or confusion
- hallucinations or psychosis.

Again, this requires urgent hospital treatment. Graves' ophthalmology *(pictured below)* is a more common condition that can cause dry eyes, photophobia, double or reduced vision, increased tear production, and exophthalmia (bulging eyes), and warrants specialist treatment.



Symptoms of hypothyroidism and hyperthyroidism

Hypothyroidism	Hyperthyroidism
Hypothyroidism often develops very slowly and has non-specific symptoms, meaning sufferers may not realise they have a problem for several years. Common symptoms include fatigue, weight gain, being sensitive to the cold, constipation, enlarged goitre *(see below right)*, low mood and depression, difficulty concentrating, dry skin and hair, myalgia, loss of libido and menstrual irregularities. Older people may experience memory problems, which may be mistaken for the onset of dementia.	Hyperthyroidism symptoms develop more quickly than those of hypothyroidism but may also go undiagnosed because of their non-specific nature. These can include hyperactivity, mood swings, anxiety, insomnia, enlarged goitre *(see below)*, poor exercise tolerance, frequent bowel movements, heat intolerance, tremor, increased sweating, weight loss, increased appetite, menstrual disturbances, reduced libido, polyuria, thirst and generalised itching. Deterioration of existing conditions, particularly heart conditions and diabetic control, may also occur.

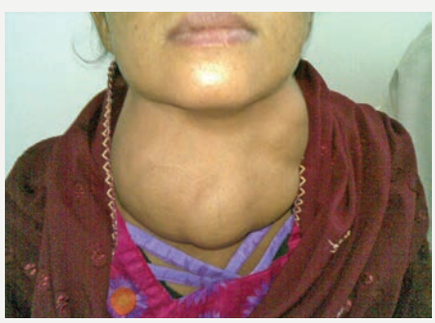
Management

The usual treatment for hypothyroidism is levothyroxine sodium, initially at a dose of 50-100mcg once daily. The maintenance doses are generally in the range of 100-200mcg each day and can be adjusted by 25-50mcg every three to four weeks, depending on response. These amounts are generally lower for the elderly and those with cardiac disease or a severely underactive thyroid. Regular blood tests are required during initiation of treatment, but they can be done annually once the patient is stable.

Side effects are rare unless the dosing has been miscalculated and the patient receives too much. In such cases, symptoms are similar to those of mild hyperthyroidism, for example, sweating, anxiety and gastrointestinal upsets.

An important counselling point about levothyroxine is that the dose should ideally be taken at least half an hour before breakfast.

Enlarged goitre



Any form of thyroid dysfunction can cause the gland to enlarge and form a goitre. Usually the swelling is relatively small and therefore unnoticeable, but in a small number of cases the goitre will grow to such a size that the patient may complain of hoarseness or a cough. Occasionally, it will get to the point where it is interfering with swallowing and even breathing.

This is because absorption of levothyroxine can be decreased when taken at the same time as calcium, iron, some foods and other drugs. Patients in England prescribed drugs for hypothyroidism are eligible for a medical exemption certificate, so do not have to pay prescription charges.

The drug liothyronine sodium is similar in action to levothyroxine, but is reserved for severe hypothyroidism when a rapid effect is needed. The drug is metabolised more rapidly, so dosing is much lower as a result, with 20-25mcg considered equivalent to 100mcg levothyroxine.

The most significant drug that thyroid hormones interact with is warfarin, due to a possible cumulative anticoagulant effect. Anyone on a coumarin who is prescribed a thyroid hormone should undergo frequent international normalisation ratio (INR) testing. This course of action should also be followed if the patient's clinical condition changes, particularly if any liver disease is detected or they make significant changes to their diet or alcohol intake.

Antithyroid drugs are used in the management of hyperthyroidism, most commonly carbimazole. Initially, a dose of 15-40mg daily is usually prescribed for around four to eight weeks until thyroid function tests fall within the normal range. At this point, the dose is gradually reduced to 5-15mg and treatment continued for another year or so.

The most common side effects of carbimazole are rash and pruritis, though these do not usually necessitate discontinuation of therapy and instead should be managed using antihistamines. The drug can also induce bone marrow suppression and patients should be counselled on the importance of reporting any signs of infection, such as sore throat, mouth ulcers, bruising or fever.

There is a slight risk of blood dyscrasias when carbimazole is used, meaning special care should be taken if more than one drug that has this potential side effect is given to the patient. The drug may also enhance the effect of anticoagulants, so additional INR testing is wise for patients on both agents. Serum levels of prednisolone, theophylline, erythromycin and cardiac glycosides may also be affected.

An alternative therapy for hyperthyroidism is propylthiouracil, although this is reserved for those intolerant or sensitive to carbimazole. Initially, around 200-400mg should be taken daily in divided doses. Once normal thyroid function is restored, it is appropriate to reduce to 50-150mg daily, again in divided doses. Hepatotoxicity can be a problem, and is the reason for the restrictions on this drug's use. Patients should be warned to seek medical help if they experience any signs of liver problems such as:

- nausea
- fatigue
- abdominal pain
- jaundice
- dark urine
- pruritis.

When prescribing carbimazole and propylthiouracil, care is needed if patients are also on theophylline, digoxin or beta-blockers due to the risk of interactions.

Both drugs are thionamide agents that reduce production of T3 and T4 by the thyroid gland. For this reason, it can take several weeks for an improvement to be felt and patients may suffer from some hyperthyroidism side effects. The patients may require a beta-blocker in order to combat symptoms such as tremor and tachycardia. Propranolol and nadolol are the agents most commonly employed for this purpose.

The patient should be monitored carefully because hyperthyroidism can increase beta-blocker clearance meaning that, as normal thyroid function is restored, a dose reduction may be required to reduce the risk of side effects.

Radioactive sodium iodide may be used in hyperthyroid patients who are non-adherent to other therapies or who have cardiac disease. While this form of treatment is very effective, it is more likely to cause rebound hypothyroidism and is also not suitable for those suffering from Graves' ophthalmology.

Total or partial thyroidectomy is sometimes performed for hyperthyroidism, most commonly because other treatments are unsuitable or inappropriate, the condition has recurred, the patient has a particularly large goitre or thyroid cancer. This does not remove the need for medication, rather it means lifelong levothyroxine is required.

For more information

- Clinical Knowledge Summaries pull together a range of resources to provide information on conditions and their management: cks.nice.org.uk/hypothyroidism and cks.nice.org.uk/hyperthyroidism.
- NHS Choices is a good source of information for patients and carers: www.nhs.uk/Conditions/Thyroid-under-active/Pages/Introduction.aspx and www.nhs.uk/Conditions/Thyroid-over-active/Pages/Introduction.aspx.
- LabTestsOnline UK provides information on tests that may be carried out in the diagnosis of thyroid disease: labtestsonline.org.uk/understanding/conditions/thyroid/start/2.
- Patient groups devoted to this clinical area include the British Thyroid Foundation and Thyroid UK. Their websites host a huge amount of useful information, including links to guideline documents, and can be found at www.btf-thyroid.org and www.thyroiduk.org.uk/tuk.
- The National Institute for Health and Care Excellence has issued guidance on the use of retrobulbar irradiation for thyroid eye disease, which can be accessed at www.nice.org.uk/guidance/IPG148.
- The *British National Formulary* (*BNF*) chapter 6.2 contains information on treatments for thyroid problems. This can be accessed online at https://www.medicinescomplete.com/about/ by registered users.
- Interaction information for thyroid hormones is listed in the *BNF*. For antithyroid drugs, the SPCs are the best source of data, and these can be accessed at the Electronic Medicines Compendium: www.medicines.org.uk/emc.

Tips for your CPD entry on thyroid disorders

Reflect **What are the primary causes of hypothyroidism? What complications can untreated thyroid disorders cause? Which drugs does carbimazole interact with?**

Plan **This article contains information about thyroid disorders including the function of the thyroid gland and the causes, symptoms and diagnosis of hypo- and hyperthyroidism. The management of thyroid disorders and the complications that can occur if they are left untreated is also discussed.**

Act **Read the Update article and the suggested reading (below), then take the 5 Minute Test (above). Update Plus subscribers can then access answers and a pre-filled CPD logsheet at chemistanddruggist.co.uk/mycpd.**

Read more about hypothyroidism on the Patient website
tinyurl.com/thyroid21

Read more about hyperthyroidism on the Thyroid UK website
tinyurl.com/thyroid22

Find out more about thyroid function tests on the Patient website
tinyurl.com/thyroid24

Identify any patients taking medication for thyroid disorders who may benefit from an MUR or counselling when they collect their prescriptions

Evaluate **Are you now confident in your knowledge of the causes, symptoms and diagnosis of hypo- and hyperthyroidism? Could you give advice to patients who have been prescribed drug treatment for these conditions?**

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5-Minute Test

1. The thyroid gland produces inactive triiodothyronine, which is converted into active thyroxine in the liver.
True/False

2. Primary causes of hypothyroidism include auto-immune reaction, damage resulting from radiotherapy or surgery and iodine deficiency.
True/False

3. Secondary hyperthyroidism may stem from pituitary underactivity due to hypothalamic disease or a tumour or infarction.
True/False

4. Common symptoms of hypothyroidism include fatigue, weight gain, sensitivity to the cold, constipation and depression.
True/False

5. Patients with an overactive thyroid will have high levels of thyroid-stimulating hormone.
True/False

6. Complications of hyperthyroidism include hypercholesterolaemia, fertility problems, deafness and anaemia.
True/False

7. Graves' ophthalmology is a common complication of hypothyroidism that can cause dry eyes, double or reduced vision and bulging eyes.
True/False

8. Levothyroxine should ideally be taken in the morning after breakfast.
True/False

9. A 20-25mcg dose of liothyronine sodium is equivalent to 50mcg levothyroxine.
True/False

10. Patients taking carbimazole and propylthiouracil may find it takes several weeks for an improvement to be felt.
True/False