Management of overt hypothyroidism involves replacement of thyroid hormones. For patients with hyperthyroidism, the aim is to treat the underlying condition and to relieve the associated symptoms.

Thyroid disorders management

By Jessica Lloyd, MRPharmS, Patricia Yerbury, DipClinPharm, MRPharmS, and Victoria Ruszala, DipClinPharm

Strategies for managing thyroid disorders aim to alleviate symptoms and restore normal levels of thyroid hormones and thyroid stimulating hormone (TSH). Treatment can involve drug therapy, radioactive treatments and surgery. The strategy will depend on the nature of the hormone imbalance — either hypo- or hyperthyroidism — and the severity of symptoms.

Hypothyroidism

All patients with overt hypothyroidism will require pharmacological replacement of thyroid hormone.1

Levothyroxine Levothyroxine, a synthetic form of thyroxine (T4), is the standard first-line treatment for hypothyroidism. Therapy is monitored by measuring thyroid stimulating hormone (TSH) and the aim is for levels to return to within normal range, which usually occurs after a few months of treatment.

Dosing depends on weight, age and sex. Men generally require 25–50µg more levothyroxine than women per day, and requirements fall during the seventh and eighth decades of life. Patients are usually started on 50–100µg of levothyroxine daily and most patients will require upward titration in steps of 25–50µg until a maintenance dose is reached.2 Doses are started low and gradually increased to raise the metabolic rate slowly.

Four to six weeks after starting treatment or changing dose, serum TSH levels should be assessed to monitor the need for further dose alteration. If the dose is too high the pituitary gland reduces TSH secretion and a low TSH level will be seen; conversely a dose that is too low will result in a high TSH level.

Patients should have their thyroid function monitored annually once their treatment is stabilised. It should be noted that pregnant women and patients with nephrotic syndrome or with diseases causing chronic malabsorption may require higher doses of levothyroxine.

Some medicines can reduce the absorption of levothyroxine (eg, cholestyramine, sucralfate, ferrous sulphate and calcium salts). Hepatic enzyme inducers, such as rifampicin and phenytoin, can increase levothyroxine metabolism. Oestrogen therapies (eg, oral contraceptives and hormone replacement) can increase thyroid binding globulin (TBG) levels.

Food can affect absorption of levothyroxine — taking a dose with food reduces absorption by 40–80% — and

SUMMARY

The management of thyroid disorders depends on whether there is a lack of thyroid hormones (hypothyroidism) or an overproduction of thyroid hormones (hyperthyroidism). The treatment strategy will also depend on the severity of a patient’s symptoms.

In overt hypothyroidism, thyroid hormone is replaced using levothyroxine, a synthetic version of thyroxine (T4). The aim of treatment is to achieve normal serum levels of thyroid stimulating hormone (TSH).

Generally the management of hyperthyroidism is more complex than that of hypothyroidism, and involves symptom management (eg, with beta-blockers) and treatment of the overactive thyroid (with antithyroid medicines, radioactive iodine or surgery).

Jessica Lloyd is a rotational pharmacist and Victoria Ruszala is a teacher practitioner pharmacist, both at North Bristol NHS Trust. Patricia Yerbury is cardiac lead pharmacist at King’s College Hospital NHS Foundation Trust.

E: victoria.ruszala@nbt.nhs.uk
intestinal absorption is highest when it is taken on an empty stomach. Therefore, patients should be counselled to take levothyroxine on an empty stomach, 30 minutes before food. In the past this has meant that most patients have been advised to take their levothyroxine before breakfast, but a recent study found that taking levothyroxine at night significantly improved thyroid hormone levels (see Box 1).

**Liothyronine**

Liothyronine sodium is the synthetic version of T3. It has a similar action to levothyroxine but is more rapidly metabolised, has a quicker onset of action and is more potent (liothyronine 20µg is equivalent to levothyroxine 100µg). The clinical effects of liothyronine occur a few hours after a dose and disappear within 24 to 48 hours of stopping treatment, so it can be used in severe hypothyroidism when a rapid response is desired.

Liothyronine should be used with caution in elderly patients and those with underlying cardiovascular conditions because it can increase pulse rate and cardiac workload.

**Combination treatment**

In the UK, most patients with hypothyroidism are treated exclusively with levothyroxine (T4), since the body converts T4 to active T3. However, there is debate about whether or not hypothyroidism should be treated with replacement using a combination of T4 and T3. A prospective study showed that, for patients who had undergone total thyroidectomy, normal T3 levels could be achieved with levothyroxine treatment alone.

In addition, a meta-analysis of 11 randomised controlled trials showed no obvious benefit from combined liothyronine and levothyroxine therapy.

A natural, porcine-derived thyroid hormone replacement containing both T4 and T3 is available in the US (Armour Thyroid). Although some patient groups have called for its use, the product is currently neither available nor recommended in the UK. In 2008, the Royal College of Physicians issued a statement advising that inclusion of T3 in treatment could not be supported until further validated research has been published.

**Hyperthyroidism**

Management of hyperthyroidism is more complex than that of hypothyroidism. The aim is to relieve symptoms and manage the underlying condition. (Treatment of exophthalmos is discussed in Box 2, p332.)

**Symptomatic treatment**

In the short term, treatment focuses on reducing the body’s response to excess thyroid hormones. Hyperthyroidism is associated with up-regulation of beta-adrenergic receptors and increased beta-adrenergic activity in many tissues — accounting for many of the symptoms of the condition (eg, tremor, sweating, tachycardia). Therefore, beta-blockers should be used for symptom control unless the patient has other comorbidities contraindicating their use.

Nadolol, metoprolol and propranolol are licensed as adjunct symptomatic treatments for hyperthyroidism.

**Antithyroid medicines**

Generally, treating the underlying cause of hyperthyroidism involves the use of an antithyroid drug, either carbimazole or propylthiouracil. These drugs — collectively known as thionamides — can be used for:

- Long-term treatment of hyperthyroidism
- Preparing patients with Graves’ disease for surgery or radioactive iodine treatment
- Treating hyperthyroidism associated with toxic multinodular goitre or toxic adenoma
- Treating women with hyperthyroidism during pregnancy

Thionamides can also be used to induce remission in Graves’ disease and 12–18 months’ treatment results in remission for 40–60% of patients.

Carbimazole and propylthiouracil impair binding of iodide to thyroglobulin (the polypeptide backbone for production and storage of thyroid hormones) and
Thionamides take around six to eight weeks to have an observable effect because they do not alter existing levels of T₃ and T₄. The optimal dose depends upon factors such as the size of goitre (if present) and the degree of hyperthyroidism. Higher doses are often prescribed early in treatment for people with large goitres and for those with severe hyperthyroidism.

Carbimazole tends to be the treatment of choice for most patients because, compared with propylthiouracil, it reverses hyperthyroidism more quickly, has fewer side effects and is more likely to result in successful radioactive iodine treatment. Usually propylthiouracil is reserved for patients who have a contraindication or intolerance to carbimazole. Carbimazole should not be used for patients with galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption.¹⁰

Thionamides carry a small risk of birth defects when given to pregnant women but the risk is lower with propylthiouracil, so this is the preferred drug for women who are pregnant. Each drug can cause temporary goitre and hypothyroidism in the fetus, so some women are given to pregnant women but the risk is lower with propylthiouracil, so this is the preferred drug for women who are pregnant. Each drug can cause temporary goitre and hypothyroidism in the fetus, so some women are treated with radioactive iodine before conception (for at least six months) to eliminate the need for antithyroid treatment during pregnancy.

Fatal cases of agranulocytosis and neutropenia have occurred with thionamide treatment (primarily with carbimazole). This adverse effect is most likely to occur within three months of starting treatment. A full blood count should be performed when treatment is started and if infection occurs, since early treatment of agranulocytosis is essential. Patients should be counselled about the symptoms of agranulocytosis (see Box 3, p335) and instructed to stop taking the medicine and seek medical attention immediately if they occur. A history of serious haematological disorder is a contraindication for thionamide treatment.

Thionamides have been associated with adverse hepatic effects (including hepatitis, hepatic failure, encephalopathy and hepatic necrosis). Patients should be counselled on the signs and symptoms of liver dysfunction, and liver function tests should be performed when the drug is started and if the patient exhibits any signs of hepatic injury. Treatment should be promptly withdrawn if this occurs.

Vasculitis has been reported with antithyroid treatment, although it is more common with propylthiouracil than carbimazole. Milder side effects of the thionamides include nausea, headaches, taste disturbance, mild skin rashes, itching or reddening of the skin, joint pain and fever.

**Regimens** There are two carbimazole treatment regimens. The “titration regimen” starts with a dose of 15–40mg daily, which is continued until the patient becomes euthyroid (this usually takes four to eight weeks). The dose is then gradually reduced to a maintenance dose of 5–15mg daily.² Carbimazole can then be taken once daily, despite the plasma half-life being only four to six hours, because the biological half-life is up to 40 hours. This regimen is usually continued for 18–24 months and achieves a remission rate of 40–50%.

An alternative approach is the “block and replace regimen”, in which carbimazole is started at a higher dose (40–60mg daily) and levothyroxine is usually added after six to eight weeks. The dose of carbimazole remains constant during treatment and levothyroxine dose is adjusted according to thyroid function test results, thereby maintaining a euthyroid state. This approach has the disadvantage of requiring the patient to take more tablets. However, some prescribers prefer this regimen because treatment aims can be achieved more quickly than with the titration method (in as little as six months). There are few data to suggest that this regimen is any more effective than titration.²³

Propylthiouracil is initially dosed at 200–400mg daily and this is maintained until the patient becomes euthyroid. The dose can then be reduced gradually to a maintenance dose of 50–150mg daily.² Because propylthiouracil must be taken two to three times daily, and since multiple tablets are usually required to make up the dose, adherence with treatment can be an issue.

**Radioactive iodine** Radioactive iodine is used to damage part of the thyroid gland and thereby reduce thyroid hormone release. Most patients with Graves' disease will respond well to radioactive iodine treatment and it is used first line for patients with toxic nodular goitre. It is given orally as either a capsule or liquid drink of iodine-131. Effects of thionamides can last for more than 24 hours, so these medicines should be ceased four days before radioactive iodine treatment and restarted three or more days after.

The goal of iodine-131 therapy is euthyroidism, without post-ablative hypothyroidism and the need for lifelong thyroid hormone replacement. However, it is well

---

**Box 2: Treatment of exophthalmos**

Exophthalmos — protrusion of the eyeballs in their sockets (see Figure, inset) — is a symptom of Graves' disease and requires specialist treatment. Treatment aims to reduce swelling, expand the orbital space and improve the range of movement and co-ordination of the eye muscles.

Many patients with exophthalmos can be treated with simple measures, such as artificial tears and smoking cessation (there is an association between smoking and exophthalmos). However, some patients will require systemic treatment with high-dose corticosteroids to reduce swelling and congestion in the eye area. Immunosuppressants have historically been used but are no longer widely accepted as being safe and effective. Rituximab might be a future treatment option, since it has been used experimentally to treat thyroid-associated eye disease.²⁴
accepted that there is no single dose or treatment method that can reliably accomplish this goal. There are three general approaches to dosing of iodine-131:

- Fixed dose regardless of co-existing factors
- Dose adjusted based on the size of the thyroid and its ability to accumulate iodine
- Dose calculated to deliver a specific radiation dose to the thyroid

About 50–70% of patients who undergo iodine-131 treatment achieve normal thyroid function and reduction of goitre within six to eight weeks of treatment.

**Surgery**

Surgical removal of the thyroid gland (thyroidectomy) is usually reserved for patients who have not responded to drug treatment or those who are unable to tolerate antithyroid medication. Surgery is also performed to remove a goitre that is causing hyperthyroidism, is putting pressure on other structures or looks unsightly. Usually, patients should be treated with carbimazole before surgery until they are euthyroid, to avoid the risk of thyroid storm.

**Thyroid emergencies**

**Myxoedema crisis**

Myxoedema crisis is a medical emergency (see accompanying article, p323). Early diagnosis, rapid administration of thyroid hormones and adequate supportive measures are essential if deterioration into myxoedema coma is to be avoided.

Because myxoedema crisis and coma are rare they are difficult to study. Therefore, it is not known whether monotherapy with levothyroxine or liothyronine, or a combination of the two, is the optimal treatment. Due to a lack of available intravenous levothyroxine in the UK, liothyronine is the mainstay of treatment. Management options for myxoedema crisis are outlined in Box 4 (p336).

Most patients begin to show increases in body temperature within the first 24 hours of treatment. The absence of an increase in body temperature within 48 hours should lead to consideration of more aggressive T3 therapy. Most patients regain consciousness within a few days after an increase in body temperature.

**Thyroid storm**

Thyroid storm, also known as thyrotoxic crisis, should be managed jointly by intensive care specialists and endocrinologists (pharmacist involvement is discussed in Box 5, p336). Therapy aims to produce rapid inhibition of thyroid hormone synthesis and release, as well as inhibit the excessive peripheral effects of thyroid hormone (using beta-blockers). Precipitating illnesses should be managed and supportive measures should also be in place.13,16

Initial stabilisation and management should involve:

- Immediate provision of supplemental oxygen and ventilatory support
- Cautious administration of IV fluids if needed
- Aggressive control of hyperthermia using ice packs, cooling blankets and paracetamol (aspirin should be avoided)
- Beta-blockers (eg, propranolol 80–120mg every six to eight hours) should be administered promptly; calcium channel blockers may be useful for patients in whom beta-blockers are contraindicated. High-output thyrotoxic cardiac failure can be treated by controlling the heart rate using beta-blockers. In general the response to digoxin and diuretics is poor.
- Propylthiouracil can be given by mouth, nasogastric tube or rectally at a dose of 250mg every four to six hours. Carbimazole is less useful since it does not inhibit the conversion of T4 to T3.
- Iodide can transiently inhibit the release of thyroid hormones (despite its role in their synthesis); eight drops of Lugol’s iodine can be given every six hours, orally or via a nasogastric tube. It is important that this is administered one hour after starting propylthiouracil. This delay allows the antithyroid drug to inhibit synthesis of thyroid hormone, which would otherwise be increased by the iodide treatment.
- Cholestyramine (4g every six to eight hours) can be used to bind thyroid hormones that are enterohepatically

---

**Box 3: Thionamide counselling points**

Patients taking thionamide medicines should be taught to recognise the signs and symptoms of agranulocytosis and hepatic dysfunction and advised to report these symptoms to their doctor immediately.

Agranulocytosis may be indicated by:

- Sore throat
- Bruising
- Mouth ulcers
- Bleeding
- Fever
- Malaise

Clinical features of hepatic dysfunction include:

- General pruritus
- Jaundice
- Dark urine
- Pain in upper abdomen
- Nausea or vomiting
- Anorexia
recycled in the gut, leading to a more rapid lowering of circulating thyroid hormones.

Patients with thyroid storm can have some degree of adrenal insufficiency. For this reason, and because glucocorticoids can be used to decrease T3 levels, patients can be prescribed oral prednisolone or IV hydrocortisone.

Patients with thyroid storm should have any underlying conditions treated and comorbidities, such as diabetic ketoacidosis, should be excluded. Infection should be treated with antibiotics. In addition the following actions should be considered if necessary:

- Correction of electrolyte abnormalities
- Treatment of cardiac arrhythmias, which if not controlled sufficiently using beta-blockers (or if beta-blockers are inappropriate) can be treated with IV digoxin, eg, 1mg over two hours.
- Peritoneal dialysis and plasmapheresis can remove circulating thyroid hormones and have been required in cases resistant to the pharmacological measures outlined above.

With adequate thyroid-suppressive therapy and sympathetic blockade, clinical improvement should occur within 24 hours. Adequate therapy should resolve the crisis within a week. After initial treatment and recovery patients will require a definitive treatment plan for their hyperthyroidism.

Medical treatment is an option but, in general, surgery or radioactive iodine is preferred after a patient has experienced thyroid storm. If patients are given iodine as part of their treatment for thyroid storm, then radioactive...
Thyroid disorders

Lifelong Learning questions are available to complete in an online module on the Clinical Pharmacist section of PJ Online — accessible via www.clinicalpharmacist.com.

To complete the module, you will need to log in to the site. If you are a new visitor, it is simple to register as a user (free to all Royal Pharmaceutical Society members).

Questions
This month’s Lifelong Learning questions are based on the CLINICAL FOCUS articles on thyroid disorders, which were commissioned from independent authors.

Answers from the September module

Cystic fibrosis

1  (a) F, (b) T, (c) F, (d) F, (e) T
2  (a) T, (b) F, (c) T, (d) T, (e) F
3  (a) T, (b) T, (c) F, (d) T, (e) F
4  (a) T, (b) T, (c) F, (d) F, (e) T
5  (a) T, (b) T, (c) T, (d) F, (e) F
6  (a) F, (b) T, (c) T, (d) F, (e) T
7  (a) T, (b) F, (c) T, (d) T, (e) F
8  (a) F, (b) T, (c) F, (d) T, (e) T
9  (a) F, (b) T, (c) T, (d) T, (e) F
10 (a) F, (b) T, (c) F, (d) F, (e) T

The information in the Box (below) is there to help you identify knowledge gaps and undertake continuing professional development. This online module will close on 10 January 2012.

Answers

When you have completed the online module, your answers will be submitted for marking and Clinical Pharmacist will send you a certificate and your results by email within two weeks of the module closing. Please do not hesitate to contact us if you have technical problems with the module. E: clinicalpharmacist@pharmj.org.uk

How to undertake continuing professional development

Our CLINICAL FOCUS articles and the online Lifelong Learning modules can help you plan your CPD and record the benefits of the activity at www.uptodate.org.uk.

Reflect on your gaps in knowledge
- What are the clinical features of hypothyroidism and hyperthyroidism?
- How is hypothyroidism treated?
- What regimens can be used to manage patients with hyperthyroidism?
- How do thyroid emergencies manifest and how are these managed?

Act to enhance your practice
- Read the CLINICAL FOCUS articles in this issue (pp323–37)
- Test your knowledge by completing the questions at www.clinicalpharmacist.com

Evaluate the activity
- What have you learnt?
- How has it added value to your practice?
- What will you do now and how will this be achieved?

The questions in this Lifelong Learning module have been appraised by an independent reviewer for quality assurance.

Consider making this activity one of your nine CPD entries this year

Write for CLINICAL FOCUS

Pharmacists with ideas for CLINICAL FOCUS and those who wish to write for the series are invited to contact the editor.
T: 020 7572 2425  E: clinicalpharmacist@pharmj.org.uk

References
7 Royal College of Physicians. The diagnosis and management of Primary hypothyroidism. www.rcplondon.ac.uk/press-releases/therapy-only-hypothyroidism (accessed 17 April 2011).

iodine usually cannot be given for several weeks or even months afterwards, and thyroidectomy may be a more suitable option.