# Hypothyroidism

Hypothyroidism is a common condition with various causes , but autoimmune disease (Hashimoto's thyroiditis) and thyroid failure following 131I or surgical treatment of thyrotoxicosis account for over 90% of cases, except in areas where iodine deficiency is endemic. Women are affected approximately **six times** more frequently than men.

18.11 Causes of hypothyroidism			
Causes	Anti-TPO antibodies <sup>1</sup>	Goitre <sup>2</sup>	
Autoimmune			
Hashimoto's thyroiditis	++	±	
Spontaneous atrophic hypothyroidism	-	-	
Graves' disease with TSH receptor- blocking antibodies	+	±	
latrogenic			
Radioactive iodine ablation	+	±	
Thyroidectomy Drugs:	+	- <	
Carbimazole, methimazole, propylthiouracil	+	±	
Amiodarone	+	±	
Lithium		±	
Transient thyroiditis			
Subacute (de Quervain's) thyroiditis	+	±	
Post-partum thyroiditis	4	±	
lodine deficiency			
e.g. In mountainous regions	-	++	
Congenital			
Dyshormonogenesis	_	++	
Thyroid aplasia	-	_	
Infiltrative			
Amyloidosis, Riedel's thyroiditis,	+	++ ~	
sarcoidosis etc.			
Secondary hypothyroidism TSH deficiency	-	-	
<sup>1</sup> As shown in Box 18.8, thyroid autoantibodies are common in the healthy population, so might be present in anyone. ++ high titre; + more likely to be detected than in the healthy population; - not especially likely. <sup>2</sup> Goitre: - absent; $\pm$ may be present; ++ characteristic. (TPO = thyroid peroxidase; TSH = thyroid-stimulating hormone)			

#### **Clinical assessment**

The clinical presentation depends on the duration and severity of the hypothyroidism. Those in whom complete thyroid failure has developed insidiously over months or years may present with many of the clinical features listed below. A consequence of prolonged hypothyroidism is the infiltration of many body tissues by the mucopolysaccharides hyaluronic acid and chondroitin sulphate, resulting in a low-pitched voice, poor hearing, slurred speech due to a large tongue, and compression of the median nerve at the wrist (carpal tunnel syndrome). Infiltration of the dermis gives rise to non-pitting oedema (myxoedema), which is most marked in the skin of the hands, feet and eyelids.

	Hypothyroidism		
	Symptoms	Signs	
Common	Weight gain Cold intolerance Fatigue, somnolence Dry skin Dry hair Menorrhagia	Weight gain	
Less common	Constipation Hoarseness Carpal tunnel syndrome Alopecia Aches and pains Muscle stiffness Deafness Depression Infertility	Hoarse voice Facial features: Purplish lips Malar flush Periorbital oedema Loss of lateral eyebrows Anaemia Carotenaemia Erythema ab igne Bradycardia hypertension Delayed relaxation of reflexes Dermal myxoedema	
Rare	Psychosis (myxoedema madness) Galactorrhoea Impotence	lleus, ascites Pericardial and pleural effusions Cerebellar ataxia Myotonia	

The resultant periorbital puffiness is often striking and may be combined with facial pallor due to vasoconstriction and anaemia, or a lemon-yellow tint to the skin caused by carotenaemia, along with purplish lips and malar flush. Most cases of hypothyroidism are not clinically obvious, however, and a <u>high index of suspicion</u> needs to be maintained so that the diagnosis is not overlooked in individuals complaining of non-specific symptoms such as tiredness, weight gain, depression or carpal tunnel syndrome.

Care must be taken to identify patients with transient hypothyroidism, in whom life-long levothyroxine therapy is inappropriate. This is often observed during the first 6 months after thyroidectomy or 131I treatment of Graves' disease, in the post-thyrotoxic phase of subacute thyroiditis and in post-partum thyroiditis

### Investigations

In the vast majority of cases, hypothyroidism results from an intrinsic disorder of the thyroid gland (primary hypothyroidism).

In this situation, serum T4 is low and TSH is elevated, usually in excess of 20 mIU/L. Measurements of serum T3 are unhelpful since they do not discriminate reliably between euthyroidism and hypothyroidism. Secondary hypothyroidism is rare and is caused by failure of TSH secretion in an individual with hypothalamic or anterior pituitary disease. In severe, prolonged hypothyroidism, the ECG classically demonstrates sinus bradycardia with low voltage complexes and ST-segment and T-wave abnormalities.

Measurement of thyroid peroxidase antibodies is helpful but further investigations are rarely required.

#### Management

Treatment is with levothyroxine replacement. It is customary to start with a low dose of 50  $\mu$ g per day for 3 weeks, increasing thereafter to 100  $\mu$ g per day for a further 3 weeks and finally to a maintenance dose of 100–150  $\mu$ g per day. In younger patients, it is safe to initiate levothyroxine at a higher dose (e.g. 100  $\mu$ g per day), to allow a more rapid normalisation of thyroid

hormone levels. Levothyroxine has a half-life of 7 days so it should always be taken as a single daily dose and at least 6 weeks should pass before repeating thyroid function tests (as TSH takes several weeks to reach a steady state) and adjusting the dose. Patients feel better within 2–3 weeks. Reduction in weight and periorbital puffiness occurs quickly but the restoration of skin and hair texture and resolution of any effusions may take 3–6 months.

The dose of levothyroxine should be adjusted to maintain serum TSH within the reference range. Some patients remain symptomatic despite normalisation of TSH and may wish to take extra levothyroxine, which suppresses TSH. However, suppressed TSH is a risk factor for osteoporosis and atrial fibrillation, so this approach cannot be recommended.

Some patients have a persistent elevation of serum TSH despite an ostensibly adequate replacement dose of levothyroxine; most commonly, this is a consequence of suboptimal adherence to therapy. In some poorly compliant patients, levothyroxine is taken diligently or even in excess for a few days prior to a clinic visit, resulting in the seemingly anomalous combination of a high serum T4 and high TSH.

#### Levothyroxine replacement in ischaemic heart disease:

Hypothyroidism and ischaemic heart disease are common conditions that often occur together. Although angina may remain unchanged in severity or paradoxically disappear with restoration of metabolic rate, exacerbation of myocardial ischaemia, infarction and sudden death are recognised complications of levothyroxine replacement, even using doses as low as 25 µg per day. In patients with known ischaemic heart disease, thyroid hormone replacement should be introduced at low dose and increased very slowly under specialist supervision.

Coronary intervention may be required if angina is exacerbated by levothyroxine replacement therapy.



## Hypothyroidism in pregnancy

Untreated hypothyroidism is associated with subfertility and so is uncommon in pregnancy. Subclinical hypothyroidism is more common, and is often due to poor adherence to levothyroxine in known primary hypothyroidism. Most pregnant women with primary hypothyroidism require an **increase** in the dose of levothyroxine of approximately  $25-50 \mu g$ daily to maintain normal TSH levels because there is an increased requirement for thyroxine during pregnancy. Furthermore, inadequately treated maternal hypothyroidism may be associated with *impaired brain development in the fetus*. Because of this, hypothyroid women should be monitored closely if planning a pregnancy; they should be advised to have their thyroid function checked as soon as possible after conception and increase their daily levothyroxine dose if necessary. During pregnancy, serum TSH and free T4 should be measured during each trimester and the dose of levothyroxine adjusted to maintain a normal TSH level.

Rarely, hypothyroidism may present during pregnancy with weight gain, constipation and lethargy. The diagnosis is easily missed since these symptoms are common in normal pregnancy. If suspected, the diagnosis can be confirmed by checking thyroid function tests, which show a raised TSH and low free T4.

#### Myxoedema coma

This is a very rare presentation of hypothyroidism in which there is a depressed level of consciousness, usually in an elderly patient who appears myxoedematous. Body temperature may be as low as 25°C, convulsions are not uncommon, and cerebrospinal fluid (CSF) pressure and protein content are raised. The mortality rate is 50% and survival depends on early recognition an treatment of hypothyroidism and other factors contributing to the altered consciousness level, such as *medication, cardiac failure, pneumonia, dilutional hyponatraemia and respiratory failure*.

Myxoedema coma is a medical emergency and treatment must begin before biochemical confirmation of the diagnosis. Suspected cases should be treated with an intravenous injection of 20  $\mu$ g liothyronine, followed by further injections of 20  $\mu$ g 3 times daily until there is sustained clinical improvement. In survivors, there is a rise in body temperature within 24 hours and, after 48–72 hours, it is usually possible to switch patients to oral levothyroxine in a dose of 50  $\mu$ g daily. Unless it is apparent that the patient has primary hypothyroidism, the thyroid failure should also be assumed to be secondary to hypothalamic or pituitary disease and treatment given with hydrocortisone 100 mg IM 3 times daily, pending the results of T4, TSH and cortisol measurement . Other measures include slow rewarming cautious use of intravenous fluids, broad-spectrum antibiotics and high-flow oxygen.

# Symptoms of hypothyroidism with normal thyroid function tests:

The classic symptoms of hypothyroidism are, by their very nature, nonspecific . There is a wide differential diagnosis for symptoms such as 'fatigue', 'weight gain' and 'low mood'. As has been noted, outside the context of pituitary and hypothalamic disease, serum TSH is an excellent measure of an individual's thyroid hormone status. However, some individuals believe that they have hypothyroidism despite normal serum TSH concentrations. There are a large number of websites that claim that serum TSH is not a good measure of thyroid hormone status and suggest that other factors, such as abnormalities of T4 to T3 conversion, may lead to low tissue levels of active thyroid hormones. Such websites often advocate a variety of tests of thyroid function of dubious scientific validity, including measurement of serum reverse T3, 24-hour urine T3, basal body temperature, skin iodine absorption, and levels of selenium in blood and urine. Individuals who believe they have hypothyroidism, despite normal conventional tests of thyroid function, can be difficult to manage. They require reassurance that their symptoms are being taken seriously and that organic disease has been carefully considered; if their symptoms persist, referral to a team specialising in medically unexplained symptoms should be considered.