The thyroid gland regulates metabolism, therefore thyroid dysfunction has an impact throughout the body. In iodine-replete areas, autoimmune disease is the commonest cause of thyroid disorders. Thyroid function tests (especially TSH) accurately reflect thyroid function in the majority of cases. Subclinical thyroid dysfunction should be monitored regularly; if persistent, patients may require active treatment to prevent cardiovascular disease.

INTRODUCTION

The thyroid gland regulates a wide range of physiological functions in the body including growth, metabolism and energy homeostasis, via the secretion of thyroid hormone (TH).1,2 Clinical abnormalities in thyroid function are estimated to affect >5% of individuals during their lifetime.3 Subclinical abnormalities are more common and there is much debate over whether or not they should be actively treated.3 The prevalence of thyroid dysfunction increases with age and diagnosis may be complicated in the older age group due to concomitant disease or therapy. Early diagnosis and management of thyroid disease are crucial however, since it is associated with increased morbidity and mortality, especially in the elderly.4 In Ireland, levothyroxine (T4) is one of the most frequently prescribed medicines on the community drug schemes, reflecting a high level of treated hypothyroidism in clinical practice.5 This bulletin outlines the management of hypothyroidism and hyperthyroidism and reviews the current guidance on how to manage subclinical thyroid dysfunction.

PHYSIOLOGY OF THE THYROID GLAND

The thyroid gland produces TH (which includes levothyroxine (T4) and triiodothyronine (T3)), under the direct control of thyroid-stimulating hormone (TSH or thyrotropin), secreted from the pituitary gland.6 TSH is under the control of thyrotropin-releasing hormone (TRH), secreted by the hypothalamus. Regulation of thyroid function depends on normal functioning of the hypothalamic-pituitary-thyroid axis (via a negative feedback loop), whereby precise control of the axis is maintained by the inhibitory actions of T4 and T3 on both TRH and TSH secretion.8 Serum TSH is exquisitely sensitive to small changes in serum TH concentrations - a 50% reduction in free T4 produces a 90-fold increase in serum TSH.9,7 T3 is the active form of TH and has a shorter half-life (t1/2 = 1 day) in the circulation compared with T4 (t1/2 = 7 days); most of the T3 in the body results from deiodination of T4 in the peripheral tissues.10 More than 99% of circulating TH is bound to protein, primarily thyroid-binding globulin (TBG). The levels of free circulating TH remain normal irrespective of the concentration of binding proteins; this is important for interpretation of thyroid function tests.

PATHOGENESIS OF THYROID DISEASE

The thyroid is the main site of iodine uptake in the body, which is then incorporated into TH. The highest iodine content is found in fish, with smaller amounts in milk, eggs and meat.7 Iodine deficiency is typically due to the consumption of local produce in areas where the soil has low iodine content (such as high mountainous areas and lowlands situated far from the oceans).9 The recommended daily intake of iodine for adults is 150-300 micrograms (mcg). Reduced iodine intake is the principal cause of thyroid disease worldwide;6 intake of <50mcg/day is associated with reduced thyroid function (either hypothyroidism in adults or cretinism in the presence of inadequate intake from birth) or goitre (diffuse or nodular enlargement of the gland) whereby the gland size increases to compensate for the lower iodine in an effort to maintain normal TH levels.6,10 Over time, there is a risk that a goitre may develop "autonomy", resulting in production of TH, not under TSH control, potentially resulting in hyperthyroidism.10,11 In iodine-replete regions, the commonest cause of thyroid dysfunction is autoimmune thyroid disease (AITD). This has been shown to affect up to 2% of the population in some regions and can result in over- or under-activity of TH.1,9 AITD is known to have a genetic component, probably involving multiple genes; 40-50% of patients report another family member with a thyroid disorder and there is a 5-10 fold increased risk in women compared with men.8,9,10 The genetic predisposition is thought to be triggered by environmental factors such as infectious agents, pollutants, hormones (especially oestrogens), drugs (including lithium, interferon-α) and cytokines.11,12 Patients with AITD are at significantly increased risk of additional autoimmune diseases including pernicious anaemia, rheumatoid arthritis, Addison’s disease and coeliac disease.12 Therefore patients with AITD should be screened for other autoimmune diseases if clinically indicated.12,14 AITD may result in hyperthyroidism, hypothyroidism or subclinical dysfunction. In addition, thyroid-specific antibodies (anti-thyroid peroxidase (anti-TPO) antibodies), suggesting the presence of AITD have been reported in up to 12% of healthy populations.9 Follow-up studies on these individuals show a steady progression to development of subclinical or overt thyroid dysfunction over time.9

MEASUREMENT OF THYROID FUNCTION

TSH and T4 (either total or free) can be easily measured in most laboratories.15,16 Free T4 levels are preferable since they do not depend on serum protein levels. TSH gives an accurate reflection of thyroid function in the majority of patients who are not, or have not recently been, taking therapy for thyroid dysfunction; these include patients with a palpable goitre, patients with symptoms and signs suggestive of thyroid dysfunction, or those with non-specific symptoms and a family history of thyroid dysfunction.7 A typical reference range for TSH is 0.4-4.0mU/L (the range may vary according to assay and laboratory).15,16 It is important to note that free T4 (and sometimes free T3) levels may be needed if the diagnosis is uncertain.15,16 TSH levels may take up to 5 weeks to reflect the full impact of any change in TH level (because of T4’s long t1/2 of 7 days); monitoring of TSH either after the introduction or discontinuation of treatment for thyroid dysfunction should take this time lag into account.7 Metabolic changes during severe illness can make thyroid function testing difficult to interpret and it should be avoided during such periods.7 Certain medications can also interfere with the levels of either TSH (high-dose corticosteroids and dopamine infusions can suppress levels) or free T4 (the hormone is displaced from its protein binding sites by certain drugs e.g. phenytoin or carbamazepine), resulting in potentially false diagnoses of thyroid dysfunction.15,16 TSH and TH levels are also affected by pregnancy.16 Additional testing (e.g. TRH stimulation test, anti-thyroid antibodies) may be required in difficult-to-diagnose cases.7
HYPOTHYROIDISM

Hypothyroidism is the commonest clinical disorder of thyroid function.17 The majority of cases are caused by damage to, removal of, or inhibition of the function of the thyroid gland (known as primary hypothyroidism).18 Table 1 outlines the commonest causes, symptoms and signs of hypothyroidism.

Table 1: Causes, symptoms and signs of hypothyroidism4,17,18

| Causes | Primary: chronic autoimmune thyroiditis; prior radiation therapy (either13,14 or radiation to head and neck); subtotal / total thyroidectomy; defective TH production (due to iodine deficiency, use of drugs such as lithium, iodine, some contrast agents); infiltrative diseases of thyroid (amyloidosis, scleroderma); post-viral / postpartum thyroiditis*. |
|        | Secondary (central): pituitary or hypothalamic disease. |
| Symptoms | Fatigue, lethargy, sleepiness, weight gain, cognitive impairment, depression, dry skin, hair loss, decreased perspiration, cold intolerance, paraesthesia, carpal tunnel syndrome, constipation, menstrual disturbances. |
| Signs | Slow movements and slow speech, hoarseness, bradycardia, dry skin, delayed relaxation of reflexes, hyporeflexia, vitiligo, premature grey hair. |
| Laboratory findings | T4 ↓; TSH↑; presence of anti-thyroid specific antibodies***; (T3 not usually helpful / may be normal therefore not usually tested). Possible findings **: ↑ LDL; ↑ LFTs; ↑ myoglobin; anaemia. |

These are potentially reversible; these findings are usually seen with more severe / chronic untreated hypothyroidism; presence not required for diagnosis of autoimmune thyroiditis. TH=thyroid hormone; I=iodine; I31=radioactive iodine; T4=levothyroxine; TSH=thyroid stimulating hormone; T3=triiodothyronine; LDL=low density lipoprotein; LFTs= liver function tests.

Autoimmune thyroiditis is the commonest cause of hypothyroidism; it is known as Hashimoto’s disease when there is a non-tender goitre (due to lymphocytic infiltration) or atrophic thyroiditis when the size of the thyroid gland is diminished or normal.18 It frequently has an insidious onset, with an increased incidence with increasing age - studies have reported hypothyroidism in up to 6% of subjects >65 years - and an increased prevalence in women compared with men.19 Autoimmune thyroiditis may be accompanied by vitiligo and B12 deficiency (due to pernicious anaemia), therefore B12 levels should be checked regularly if clinically indicated.14,19 Other causes of primary hypothyroidism are listed in Table 1. Secondary hypothyroidism, due to hypothalamic and/ or pituitary disease is rare and usually is accompanied by dysfunction in other hormones (e.g. adrenocorticotropic (ACTH) / gonadotropin production).18

Clinical Presentation of Hypothyroidism

The symptoms and signs of hypothyroidism are due to the slowing of the body’s metabolic functions (Table 1); their severity depends on the extent and duration of TH reduction.20 Because of the insidious onset of the disease in many patients, and the fact that the symptoms are often non-specific, diagnosis may be difficult, especially as patients become passive about their symptoms as the dysfunction progresses.21 Hypothyroidism is usually diagnosed by an elevated TSH level and a low T4; the presence of specific anti-thyroid antibodies confirms autoimmune thyroiditis but they may not always be found.

Management of Hypothyroidism

T4 is the replacement therapy of choice because of its long half-life, allowing once daily administration, ease of administration and low cost.8,20 It has been estimated that the full replacement dose of T4 for an athyreotic person (i.e. with no endogenous TH) is 1.6mcg/kg/day (median dosage of 125mcg/day). The starting dosage depends on the age, clinical status and TSH level of the patient. For patients <50 years, with no evidence of cardiovascular disease (CVD), a starting dose of 50-100mcg/day of T4 is recommended; in older patients and/ or those with CVD the starting dose should not exceed 50mcg (this may be further reduced to 25mcg in the presence of severe CVD).22 Response to T4 therapy should be monitored by TSH levels (taking into account the time lag in TSH response) and the dosage increased at 25-50mcg increments, up to a maximum daily dose of 200mcg, until clinical evidence of normal function is present and TSH levels are restored to within the normal range.20 In general, T4 replacement therapy is for life (except in the case of post-viral or postpartum thyroiditis).4,19 T4 should be taken on an empty stomach in the morning and should not be taken at the same time as certain minerals or vitamins that interfere with its absorption (e.g. calcium).20,22 Metabolism is enhanced by microsomally-inducing enzymes such as rifampicin, and carbamazepine. Note of the dosage of concomitant medications (e.g. for CVD, diabetes mellitus, anticoagulation) may need to be readjusted when normal thyroid function is restored.22 Side effects are usually due to excessive dosage for the individual and include gastrointestinal disorders, palpitations and myalgia; these are reversible upon reduction of the dosage.8

Failure to respond to treatment: If a patient continues to have clinical symptoms despite treatment and restoration of TSH levels to within the normal range, the following factors should be considered:5,20 (1) sub-optimal compliance/ problems with absorption (2) subtle under-treatment (TH just below the upper level of normal, but patient still clinically hypothyroid) - it is recommended that these patients have their T4 dosage adjusted to achieve TSH levels at the lower level of normal (3) concomitant illness such as depression, which is often associated with Hashimoto’s thyroiditis and which needs to be treated independently or (4) the patient may (rarely) require both T4 and T3 replacement in order to restore physiological function.

HYPERTHYROIDISM

Hyperthyroidism (thyrotoxicosis) results from elevated secretion of TH, resulting in increased metabolism.6,11 It is accompanied by suppressed TSH (to undetectable levels).11,23 A UK epidemiological study reported hyperthyroidism in 2% of women and 0.2% of men in the cohort;24 over a 20-year follow-up period the mean incidence of hyperthyroidism was 0.8/1,000 female survivors (with negligible levels noted in males).23 Untreated hyperthyroidism may lead to CVD and severe thyrotoxicosis, known as thyroid storm (very rare, precipitated by e.g. infection) is associated with a mortality of 20-50%.26,27 The causes, symptoms and signs of hyperthyroidism are outlined in Table 2.

Table 2: Causes, symptoms and signs of hyperthyroidism11,23,27

| Causes | Common: Graves’ disease; toxic multinodular goitre; solitary toxic adenoma; thyroiditis (autoimmune / post-viral); exogenous TH (excess intake, either iatrogenic or factitious). |
|        | Uncommon: TSH-secreting pituitary adenoma; drug-induced (iodine, iodine-containing drugs such as amiodarone, contrast agents); inflammatory (excess release of TH due to damage to thyroid gland). |
| Symptoms | Fatigue, nervousness, anxiety, insomnia, palpitations, dyspnoea, diarrhoea, weight loss despite good appetite, heat intolerance, weakness, irregular menses, libido (males), ocular symptoms (gritty sensation, drooping eyelids). |
| Signs | Hyperactivity, hyperreflexia, heart rate, atrial arrhythmia, SBP. signs of high output cardiac failure, fine tremor, muscle weakness, goitre, perspiration, signs of weight loss, lid lag / lid retraction, osteoporosis, anaemia. |

Ocular symptoms diagnostic of Graves’ disease: soft tissue swelling, proptosis, extra-ocular muscle problems → diplopia, corneal problems due to lid closure failure, sight loss due to optic nerve compression (specialist referral).
Graves’ disease accounts for 80% of hyperthyroidism in iodine-replete areas; it is due to the production of anti-TSH receptor antibodies that stimulate the thyroid gland, resulting in overproduction of TH.11 The female: male ratio varies from 5:10:1 and the peak incidence is between 40 and 60 years of age although it can occur at any age.21 The next most frequently occurring cause is autonomous overproduction of TH by either a solitary thyroid adenoma or multinodular goitre (especially common in areas of low iodine intake).10,21 Other causes are listed in Table 2. Of note, iodine / iodine-containing medicines can induce thyrotoxicosis in certain patients, especially those with nodular goitres; regular assessment of thyroid function is recommended for patients on chronic therapy with medicines such as amiodarone.9,26 Over-treatment with TH can also result in the signs and symptoms of thyrotoxicosis.

Clinical Presentation of Hyperthyroidism

The signs and symptoms of hyperthyroidism, irrespective of the cause, relate primarily to over-stimulation of the cardiovascular, GI and nervous systems (see Table 2). Younger people with thyrotoxicosis may present with any of the symptoms but older patients are more likely to present with CVD such as atrial fibrillation and/or heart failure.27 A thyroid bruit over the thyroid gland only occurs with Graves’ disease.11,27 Similarly, although all patients can present with ocular symptoms (such as lid lag, grittiness), certain eye signs and symptoms are diagnostic of Graves’ disease (see Table 2). More than 80% of patients with Graves’ disease are noted to have eye involvement on orbital imaging, although this is clinically apparent in just 30-50% of patients; any history of interference with vision requires emergency referral to specialist services.25,26

Diagnosis of hyperthyroidism is based on serum TSH (which should be undetectable, due to the negative feedback loop); diagnostic accuracy is improved if free T4 is measured at the same time.1,11,23,29 Free T3 levels may be helpful to confirm the diagnosis, especially if T3 toxicity is suspected (with normal T4). The presence of anti-TSH receptor antibodies is diagnostic of Graves’ disease.16 The presence of other anti-thyroid antibodies may be helpful in diagnosing autoimmune thyroiditis.

Management of Hyperthyroidism

Treatment options for hyperthyroidism include pharmacotherapy, surgery and radioactive iodine (131I). Studies have shown similar outcomes between the various options (although pharmacotherapy may be associated with increased risk of relapse), therefore treatment is usually tailored to the individual patient, taking into account the likelihood of remission with medication alone, the potential (and timing) of future pregnancies, goitre size, presence of co-morbidities and patient preference.11,23,29 Patients with confirmed hyperthyroidism should be referred for specialist care in order to optimise their management plan.16 Table 3 outlines the typical uses, advantages and disadvantages of the three treatment options.

Table 3: Treatment options in hyperthyroidism11,23,30

<table>
<thead>
<tr>
<th>Treatment option</th>
<th>Indications for use</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antithyroid drugs</td>
<td>Newly diagnosed disease; short-term therapy before surgery or 131I; during pregnancy.</td>
<td>Non-invasive; low cost; outpatient therapy; ↓ risk of hypothyroidism. May have immune-suppressive properties (see text).</td>
<td>Low cure rate; ADRs in 1-5%; compliance important (therapy for up to 18 months); regular follow-up needed.</td>
</tr>
<tr>
<td>Surgery</td>
<td>Presence of large goitre; serious eye disease; serious ADR to antithyroid drugs (including during pregnancy).</td>
<td>Rapid control of thyroid function; rapid relief of compression symptoms; 100% “cure”.</td>
<td>Invasive and expensive (in-patient); produces permanent hypothyroidism; risk of hypoparathyroidism and recurrent laryngeal nerve damage; painful.</td>
</tr>
<tr>
<td>Radioactive I (131I)</td>
<td>Newly diagnosed disease; relapsed disease; toxic nodular hyperthyroidism.</td>
<td>Effective “cure” i.e. definitive treatment; outpatient therapy; easily administered; reduces goitre size.</td>
<td>Slow return to normal thyroid function; &gt;60% develop hypothyroidism; adherence to radioactive guidelines needed; pregnancy must be deferred for 6 months.</td>
</tr>
</tbody>
</table>

*not authorised in Ireland; ADR=adverse drug reaction

Antithyroid drugs, known as thionamides, inhibit the production of TH in the thyroid gland, by interfering with the iodination process.30 In addition, they may have immunosuppressive effects, which may be beneficial in promoting remission in autoimmune hyperthyroidism.25,28 Carbimazole, the antithyroid medicine authorised in Ireland, is usually started at a daily dose of 20-60mg, titrated against thyroid function (TH/TSH) until the patient is euthyroid (usually by 4 weeks).2,23,31 Maintenance therapy (usual range 5-15mg/day) is continued for up to 18 months according to TH/TSH response. There is conflicting evidence of additional benefit after 18 months’ treatment; patients may remain on the drug or be considered for 131I therapy if disease is still active.16 Common side effects include skin rash, pruritus, arthralgia, and GI upset which are usually self-limiting.31 Cholestatic jaundice has been reported rarely. Another rare but potentially life-threatening adverse drug reaction is agranulocytosis; full blood counts should be checked regularly, especially in the early months of treatment and patients should be warned to seek immediate help if they develop sore throat, fever or other evidence of infection.19,21

Symptomatic management of hyperthyroidism: patients may require a β-blocker to alleviate tremor, palpitations and sweating, while the above interventions take effect.29 Atrial fibrillation should revert to normal with restoration of normal thyroid function; if still present at 12 weeks, it is unlikely to reverse and the patient should be evaluated in terms of the need for anticoagulation.27

Patients with ophthalmic Graves’ disease should have specialist review.

SUBCLINICAL THYROID DYSFUNCTION

Subclinical thyroid disease refers to a biochemical finding of altered TSH levels (i.e. above or below the normal range), in the presence of normal TH levels.1 Subclinical thyroid dysfunction has been reported to increase the risk of developing organ damage (e.g. CVD or skeletal disease) in some patients.1,23

Subclinical Hypothyroidism

Subclinical (SC) hypothyroidism is identified as an elevated serum TSH (i.e. above the upper limit of normal range) in the presence of normal serum TH levels. Table 4 lists the main causes of SC hypothyroidism.

Table 4: Causes of subclinical hypothyroidism.18,32

<table>
<thead>
<tr>
<th>Classification</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent subclinical hypothyroidism</td>
<td>Chronic autoimmune thyroiditis; partial thyroidectomy or 131I therapy; drugs that interfere with thyroid function (lithium, iodine, some contrast agents); infiltrative diseases of thyroid (see Table 1). Inadequate replacement of T4 / poor compliance with T4 therapy.</td>
</tr>
<tr>
<td>Transient subclinical hypothyroidism</td>
<td>Recovering thyroiditis: (viral, post-partum). Recovery phase of severe non-thyroid illness.</td>
</tr>
</tbody>
</table>
Other conditions that cause elevated TSH levels (i.e. above the normal range) but which do not represent SC disease include renal failure, obesity or pituitary disease.

**SC Hyperthyroidism** is the commonest type of SC thyroid dysfunction and is most commonly due to chronic autoimmune thyroiditis.\(^{37}\) Prevalence estimates range from 6-15% in those aged >65 years, with an annual rate of up to 4% for the development of overt hyperthyroidism.\(^{1,4,32}\)

### Follow-up and Management:

Results from studies are inconclusive with respect to the level of risk for the development of CVD or cognitive decline with untreated SC hyperthyroidism or the benefit of T4 therapy, due to a lack of randomised controlled trial data.\(^{3,33,34}\) A Cochrane review reported some improvements in cardiac parameters and lipid profile with T4 therapy for SC hyperthyroidism but noted the quality of the studies was poor.\(^{35}\) Current guidance recommends to repeat an elevated TSH level after 2-3 months; if the abnormality persists, consideration should be given to treating the following groups: (1) younger people (<70 years) with TSH >10mU/L or with TSH 4-10mU/L plus symptoms and (2) older patients (>70 years) with TSH>10 mU/L and symptoms or high risk of CVD.\(^{3,32,36}\) Response to T4 therapy should be reviewed after 3-4 months and T4 stopped if no improvement. Older patients with TSH <10mU/L (especially those >80 years old) should be carefully followed with a wait-and-see strategy and T4 introduced only if deemed clinically necessary.\(^{36}\)

**Subclinical Hypothyroidism**

SC hypothyroidism is identified as a low serum TSH concentration (i.e. less than the lower limit of the normal range) and a normal serum TH, in the absence of hypothalamic or pituitary disease, non-thyroidal illness or ingestion of drugs that inhibit TSH.\(^{37}\) Table 5 lists the main causes of SC hyperthyroidism.

### Table 5: Causes of subclinical hyperthyroidism\(^{37,32}\)

<table>
<thead>
<tr>
<th>Classification</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent subclinical hyperthyroidism</td>
<td>Endogenous: toxic multinodular goitre; solitary toxic (autonomous) nodule; Graves’ disease. Exogenous: iatrogenic (either intentional or unintentional over-treatment with levothyroxine).</td>
</tr>
<tr>
<td>Transient subclinical hyperthyroidism</td>
<td>Treatment of clinical hyperthyroidism with antithyroid drugs or radioactive iodine therapy. Evolving thyroiditis: (viral, post-partum, silent autoimmune, amiodarone-induced thyroiditis).</td>
</tr>
</tbody>
</table>

Other conditions that cause low TSH levels (i.e. below the normal range) but which do not represent SC thyroid disease include early pregnancy, treatment with some drugs like high dose glucocorticoids or dopamine, or smoking.\(^{32}\) Normal TSH levels usually return with resolution of the underlying condition.

The true prevalence of SC hyperthyroidism is uncertain as the definition used is not consistent across studies.\(^{1,3}\) Studies suggest a prevalence of 3% (more common in women and elderly patients, many of whom are on T4 therapy). Follow-up studies are likewise limited but appear to confirm that those with exogenous causes were more likely to revert to normal over time, whereas the annual rate of development of overt hyperthyroidism is 5-8% in those with antithyroid antibodies or with a goitre.\(^{1}\)

**Follow-up and Management:** There is insufficient evidence from well-controlled studies to provide definitive guidelines on management. It is recommended that patients with SC hyperthyroidism should have their TSH and TH levels measured regularly as many may revert to normal (Table 5). There is some evidence that patients with persistent suppression of TSH, especially in the presence of antithyroid antibodies, may be at increased risk of developing CVD (especially arrhythmias and/ or cardiac failure) or osteoporosis.\(^{1,32}\) Consideration should be given to treating patients (especially those >65 years) with persistent suppression of TSH and evidence of either CVD or osteoporosis.\(^{3}\)

**THYROID DYSFUNCTION DURING PREGNANCY**

During pregnancy, high oestrogen levels cause TBG to rise, resulting in high levels of total T4 and T3.\(^{1,3,37}\) In addition, TSH levels may fall, due to the thyroid-stimulating effect of human chorionic gonadotropin (HCG). These are physiological events and resolve spontaneously during pregnancy.\(^{35}\) Sufficient intake of maternal iodine is required (WHO recommends ≥200mcg/day) as the foetal thyroid starts to trap iodine by 12 weeks.

**Hyperthyroidism** makes conception difficult; however, it should be suspected in pregnant women with vitiligo, premature grey hair or a positive family history.\(^{11}\) Pregnant women already on T4 replacement therapy will require increased dosage during pregnancy (to achieve normal TSH levels); studies have reported reduced IQ and increased foetal loss in untreated or inadequately treated hyperthyroidism during pregnancy.\(^{16}\) It is important to remind patients not to take T4 tablets at the same time as mineral or vitamin supplements.\(^{22}\)

**Hyperthyroidism** complicates 1 in 500 pregnancies and is associated with adverse outcomes if untreated.\(^{11}\) This may arise de novo or may represent a relapse of previously diagnosed Graves’ disease.\(^{37}\) If pharmacotherapy is required in the first trimester, specialists may recommend propylthiouracil (not authorised in Ireland) due to the potential increased risk of congenital anomalies with carbimazole.\(^{37}\) If propylthiouracil is used, carbimazole should be introduced from the second trimester, due to the potential risk of hepatotoxicity with long-term use of propylthiouracil.\(^{38}\) Regular review of T4, T3 and TSH are recommended to titrate the dosage (results are trimester-dependent).\(^{11,16}\) In severe / difficult to control cases, surgery may be required (from second trimester on) but 11\(^{1}\) is contraindicated, because of potential damage to the foetus.

**Post-partum thyroiditis** is the commonest thyroid condition associated with pregnancy, affecting up to 9% of women in iodine-replete areas.\(^{37}\) This frequently progresses from hyperthyroidism (up to 3 months) to hypothyroidism or euthyroidism for up to 2 years post-partum. Those with anti-thyroid antibodies are less likely to regain normal thyroid function.\(^{10,37}\) Management depends on the presentation and therapy is titrated to achieve normal TSH levels.

### PRACTICE POINTS

- Thyroid disorders are among the most prevalent of medical disorders, especially in women; therefore the possibility of thyroid disease should be included in the differential diagnosis of a patient especially in the presence of non-specific symptoms.
- Assessment of TSH and T4 should provide definitive evidence of overt / subclinical thyroid dysfunction.
- In subclinical hypothyroidism, the higher the level of TSH, the more likely the patient is to develop overt hyperthyroidism over time.
- Patients with evidence of subclinical hyperthyroidism require regular clinical and laboratory follow-up.

A useful guideline on the use of thyroid function tests for primary care physicians (developed by the British Thyroid Association, the British Thyroid Foundation and the Association for Clinical Biochemistry) is available online at:


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List of references available on request. Date of preparation: April 2014

Every effort has been made to ensure that this information is correct and is prepared from the best available resources at our disposal at the time of issue.

Prescribers are recommended to refer to the individual Summary of Product Characteristics (SmPC) for specific information on a drug.
30. Cooper d Antithyroid drugs. NEJM 2005; 352: 905-17
38. Antithyroid drugs in British National Formulary 64 (September 2012). Section 6.2.2. pps455-6