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10-Minute Consultation

New diagnosis of hyperthyroidism in primary care

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This is part of a series of occasional articles on common problems in primary care. The BMJ welcomes contributions from GPs.

Box start

What you need to know

When hyperthyroidism is confirmed, offer referral for endocrinology assessment, after arranging initial investigations including thyroid auto-antibodies

While endocrine review is pending, offer beta blockers to manage adrenergic symptoms; if symptomatic and a non-transient cause is likely, start anti-thyroid drugs (ATDs) and recheck thyroid function tests 2-4 weeks later

Avoid pregnancy until normal thyroid function is restored

Box end

A 36 year old woman presents to her GP with a six week history of palpitations, agitation, and unintentional weight loss of 12 kg over four months. She initially attributed her symptoms to stress relating to work pressures and a recent house move. Blood tests are arranged, which show a fully suppressed thyroid stimulating hormone (TSH) of <0.01 mU/L and free thyroxine of 86.1 pmol/L.

Hyperthyroidism describes excess hormone production from the thyroid gland. Thyrotoxicosis arises from excess circulating thyroid hormones due to any cause, including hyperthyroidism (fig 1).

Hyperthyroidism is a biochemical diagnosis. Establishing the underlying aetiology is essential to determine the appropriate management.

Overall population prevalence is 0.3%-2% and annual incidence is 0.1-4 per 1000.^{1 2} Graves' disease accounts for up to 80% of cases, with peak incidence at age 30-50 (F:M 10:1). In older adults, toxic adenoma/multinodular goitre are responsible for a higher proportion of cases.

This article describes the first reasonable steps in diagnosing and managing hyperthyroidism for non-specialists in primary care.

Fig 1 **Causes of thyrotoxicosis**. Common causes are listed in bold, † non-nucleoside reverse transcriptase inhibitors ‡ protease inhibitors

What you should cover

- Establish the severity and duration of thyrotoxic symptoms. If patient has evidence of possible thyroid storm (box 1) this requires emergency referral.
- Explain that the condition is likely to be reversible with treatment. Box 2 covers useful key points for explanation to patients.
- Try to establish the likely cause. It is clinically relevant to distinguish between:
 - 1) Transient causes of thyrotoxicosis, such as thyroiditis, which typically require no specific treatment;
 - 2) Non-transient causes, principally Graves' disease and toxic adenoma/multinodular goitre; and
 - 3) Exogenous causes, due to the drugs listed in figure 1.

Fever and neck pain/tenderness suggest thyroiditis. Personal/family history of autoimmune disease increases the likelihood of Graves' disease. Smoking increases the risk of Graves' and thyroid eye disease. Exogenous causes of thyrotoxicosis include recent iodinated radiological contrast, intentional or unintentional thyroid hormone use (e.g. as a component of weight loss supplements), and over-the-counter supplements that contain iodine (e.g. kelp). Increasingly, new pharmacological agents, including antiretrovirals (non-nucleoside reverse-transcriptase inhibitors, protease inhibitors) and cancer immunotherapy drugs are seen to precipitate thyroiditis. Pregnancy within the last six months suggests postpartum thyroiditis, a common and self-limiting condition for which anti-thyroid drugs are not indicated. Risk of relapse of Graves' disease is also higher postpartum.

- Discuss plans for and risks associated with pregnancy in women of childbearing age. Active thyrotoxicosis confers a higher risk of miscarriage, pre-eclampsia, intrauterine growth restriction, preterm labour, and stillbirth. Pregnancy also influences treatment choice (see below).
- If concerns about thyroid cancer are raised, it is generally appropriate to reassure the patient that malignancy is exceedingly uncommon in functional thyroid nodules, i.e. those that release excess thyroid hormone to cause thyrotoxicosis.

Box start

Box 1 Complications of thyrotoxicosis

- Atrial fibrillation
- Cardiac failure

- Thyroid eye disease in Graves' disease
- Osteoporosis
- Psychiatric features: mood disorders, anxiety, rarely frank psychosis
- Thyrotoxic crisis (thyroid storm): tachycardia, fever, atrial fibrillation, vomiting, dehydration, jaundice, agitation, delirium, coma
- Adverse pregnancy outcomes: pre-eclampsia, intrauterine growth restriction, miscarriage, premature labour, stillbirth

Box end

Box start

Box 2 What to say to patients

What is hyperthyroidism?

The thyroid is a hormone-producing gland in the neck that regulates metabolism. Excess production or release of thyroid hormones, "hyperthyroidism," produces a state of overactive metabolism that can lead to symptoms including weight loss, tremor, sweating, insomnia, and restlessness. Symptoms vary considerably from person to person, and in some cases, there may be no symptoms at all. The diagnosis is made by blood tests to measure levels of circulating thyroid hormones.

What causes hyperthyroidism?

There are many possible causes of hyperthyroidism. The most common are:

- Graves' disease, an autoimmune condition which occurs when the immune system reacts inappropriately to produce antibodies that overstimulate the thyroid gland;
- Enlarged nodules within the thyroid gland, which overproduce thyroid hormones;
- Thyroiditis, or inflammation of the gland, which causes pre-formed hormones to leak into the blood; this doesn't cause hormone overproduction and is therefore generally temporary.

What is the recommended treatment?

Initial treatment with drugs known as "beta blockers" is given to relieve symptoms and to prevent excess thyroid hormones from affecting the heart. Medication to inhibit thyroid hormone production may also be started. Referral to an endocrinologist is required to determine the need for further tests to establish the cause, and to make an ongoing treatment plan.

Box end

What you should do

[QtoA: are there any guidelines/evidence references for these below?]

Assessment

Assess for complications of thyrotoxicosis (box 1). Assess and document pulse, blood pressure, and temperature. Assess for atrial fibrillation, signs of fluid overload or heart failure, goitre, clinically evident thyroid nodules, and stigmata of Graves' disease, including orbitopathy.

Repeat thyroid function tests (including fT4 and free triiodothyronine, fT3, if initial fT4 was normal) along with thyroid stimulating receptor antibodies (TRAbs).³ TRAbs are 98% sensitive and 99% specific for Graves' disease; other autoantibodies (anti-thyroid peroxidase (TPO), thyroglobulin) are non-specific and less helpful.⁴ Perform also baseline full blood count and liver function tests; these results will be useful if anti-thyroid drugs (ATDs) are commenced.

Thyroiditis—Inflammatory markers (C reactive protein/erythrocyte sedimentation rate) are useful if thyroiditis is suspected.

Goitre—Arrange thyroid ultrasound ahead of secondary care review if a large goitre is identified on examination. Further investigation of nodules does not need to be arranged before referring to secondary care *unless* there are specific features suspicious for malignancy (rapidly enlarging nodule, cervical lymphadenopathy, hoarseness/voice changes).⁵

Management

Offer referral to an endocrinologist for all patients with newly diagnosed hyperthyroidism for confirmation of the underlying cause, further investigation as necessary and to recommend a management plan.

For women of childbearing age, discuss and offer contraception until thyrotoxicosis is controlled.

Prescribe beta blockers for rate control in those with tachycardia.

Offer to prescribe anti-thyroid drugs (box 3) in patients who have a likely non-transient cause of hyperthyroidism and:

- Free thyroid hormones elevated above the upper limit of the local reference range; and
- Symptoms uncontrolled despite beta blockers.³

In elderly patients or those with underlying cardiac disease, there is a high risk of decompensation precipitated by thyrotoxicosis and initiation of treatment, and treatment can be considered even if symptoms are minimal or if the thyroid hormone levels are not markedly elevated.

Box start

Box 3 Starting anti-thyroid drugs (ATDs) in primary care

- Perform baseline full blood count and liver function tests before initiating ATDs.
- Explain that there is a risk of agranulocytosis (up to 5 per 1000 patients) and hepatotoxicity (up to 1 per 250 patients with carbimazole, up to 1 per 37 patients with propylthiouracil) associated with ATDs.^{6,7}
- Provide written information about the need to stop treatment and attend for urgent blood tests if fever, sore throat, mouth ulcers, or jaundice develop.
- ATDs usually reduce symptoms within days. Biochemical euthyroidism is typically achieved after 3-6 weeks.
- In Graves' disease, treatment aims to induce remission and is continued for 12-18 months before attempting withdrawal.
- In toxic adenoma/multinodular goitre, ATDs are used to induce a euthyroid state ahead of definitive intervention (radioiodine, thyroidectomy).
- Before initiation, seek guidance from a local endocrinologist on dosing, monitoring, or other aspects, if needed.

- **Pregnancy**—Propylthiouracil is the agent of choice for patients who are pregnant or planning to conceive. Initiation is not usually recommended in primary care. Seek specialist advice in such cases.

Box end

Reduce symptoms of thyrotoxicosis—Typically, high initial doses of carbimazole, e.g. 30-40 mg daily, are introduced where thyroid hormone levels are markedly elevated (fT4 >40 pmol/L), and down-titrated depending on biochemical and symptomatic response. Lower doses, e.g. 10-25 mg daily can be considered if the thyroid hormone levels are less markedly elevated (fT4 25-40 pmol/L).

Propylthiouracil is not typically the first line treatment in primary care because of a small risk of severe liver injury in 1 in 10,000 patients, but can be considered if there has been a previous history of adverse effects with carbimazole, or in women who are currently pregnant or considering pregnancy in the near future. Seek specialist advice in such cases.

Arrange review with repeat thyroid function tests in 2-4 weeks if ATDs have been initiated, or if the patient is at high risk of decompensation. Otherwise, monitor thyroid function 4-6 weekly while awaiting specialist review.³

Ongoing treatment (box 4)—If Graves' disease is confirmed, treatment is continued for 12-18 months, during which time the underlying autoimmune activity settles in about half of cases. Radioactive iodine or thyroidectomy constitute definitive treatment in toxic adenoma/multinodular goitre or persistent thyrotoxicosis in Graves' disease following withdrawal of ATDs. Thyroiditis generally requires no specific treatment, but thyroid function tests will be monitored until they normalise.

Eye symptoms—Discuss thyroid eye disease briefly in all patients in whom Graves' disease is suspected. If features of eye disease are present (grittiness, epiphora, proptosis, lid swelling, visual blurring), prescribe simple ocular lubricants (e.g. hypromellose) and arrange early ophthalmology referral, preferably to a specialist thyroid eye disease clinic. Graves' orbitopathy can occur in the context of hyper-, hypo-, or euthyroidism, and may precede onset of abnormal thyroid function. Various symptom severity scores may aid assessment of Graves' orbitopathy (e.g. DiaGO, CAS/EUGOGO—see box 7).^{8,9}

Refer urgently if sight threatening complications are suspected: corneal exposure (cornea/sclera visible with eyes closed), globe subluxation (restricted eye movements), or optic neuropathy (deterioration in visual acuity or colour discrimination). Strongly advise smoking cessation if applicable. Evidence supports the use of selenium 100 mcg twice daily, which can be purchased over the counter, to slow disease progression and improve quality of life in mild thyroid eye disease.¹⁰

Thyrotoxic crisis ('*thyroid storm*')—Though very rarely seen in primary care, this is a medical emergency. Consider the diagnosis if the patient appears acutely unwell, agitated, febrile, or has features of heart failure (box 1). The Burch-Wartofsky score (box 7) is a useful assessment tool. If suspected, arrange immediate admission for medical assessment.

Box start

Box 4 What happens in secondary care

- In the absence of thyroid stimulating hormone receptor antibodies, thyroid scintigraphy (radionuclide uptake scanning) and ultrasound ± colour-flow Doppler may provide useful information about aetiology, e.g. toxic adenoma or multinodular goitre.
- ATDs, radioactive iodine, and/or (sub)total thyroidectomy are the principal approaches to management. Choice of approach depends on the underlying aetiology, clinical factors and patient preference.
- Follow-up continues in secondary care until treatment is complete and the patient is stable, i.e. after resolution of thyroiditis, one year of remission in Graves' disease or once thyroid function is stable following radioactive iodine or surgery.
- At discharge, patients receive guidance about ongoing frequency of thyroid function monitoring in primary care.
- Lifelong monitoring in primary care is recommended for patients with Graves' disease due to the risk of future relapse.

Box end

Box start

Box 5 Education into practice

- How might this article encourage you to adapt your first consultations with patients with a new diagnosis of hyperthyroidism?
- How do you routinely discuss the risks of pregnancy in women of childbearing age who have thyrotoxicosis?
- How comfortable do you feel to start treatment with anti-thyroid drugs as a non-specialist?

Box end

Box start

Box 6 Patient resources

British Thyroid Foundation: <http://www.btf-thyroid.org>

American Thyroid Association: <https://www.thyroid.org>

Thyroid Eye Disease Charitable Trust: <http://tedct.org.uk>

Guide to anti-thyroid drug therapy, covering risks including agranulocytosis: <http://www.btf-thyroid.org/information/quick-guides/103-hyperthyroidism-antithyroid-drug-therapy>

Thyroid eye disease warning card: http://www.btf-thyroid.org/images/documents/teamed_warning_card.pdf

Box end

Box start

Box 7 Resources for clinicians

Thyroid eye disease assessment tools:

DiaGO: <http://www.btf-thyroid.org/images/documents/S4.pdf>

Modified CAS/EUGOGO: <http://www.btf-thyroid.org/images/documents/S3.pdf>

Thyroid storm assessment (Burch-Wartofsky) score: www.mdcalc.com/burch-wartofsky-point-scale-bwps-thyrotoxicosis

Box end

Box start

Box 8 Patient involvement

Janis Hickey, director of the British Thyroid Foundation, provided guidance regarding the scope and content of the article. She has extensive insight into the patient experience at diagnosis and beyond through her personal experience as a patient with Graves' and thyroid eye disease, and many years of patient advocacy. She contributed perspectives on important areas to highlight for a generalist audience, based on aspects of initial management that impact the patient experience.

Box end

Contributorship statement GB proposed authorship of the piece and developed the article overview, structure and content with a focus on the primary care setting. EK and BK provided guidance concerning treatment initiation and broader management considerations from a specialist secondary care perspective. Dr Anh Tran, GP with a special interest in endocrinology, provided valuable perspectives on the content of the article to reflect key priorities within the GP consultation based on her extensive experience of managing thyroid disease in primary care. AT contributed to an early draft of the article but has since left the authorship team.

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