

Hyperthyroidism

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Red Flags

- Hyperthyroidism complicated by cardiac (rapid atrial fibrillation or heart failure), or respiratory compromise or other indications of severe illness (fever, vomiting, dehydration, labile blood pressure, altered mental state or psychosis)
- Neutropenic sepsis in patient taking carbimazole or propylthiouracil
- Hyperthyroidism with hypokalaemia or paralysis
- Significant and sight-threatening thyroid eye disease (TED), e.g., drop in visual acuity, altered colour perception, diplopia.

Background – About Hyperthyroidism

Hyperthyroidism is defined biochemically by a low TSH and raised FT4 and/or FT3. A nuclear scan is the most useful test to determine the underlying cause.

Common causes of hyperthyroidism:

- Graves' disease – normal or high homogeneous uptake on a nuclear medicine scan:
 - Autoimmune disease
 - Most common cause of hyperthyroidism (about 70%)
 - 10 times more common in women
 - Has diffuse goitre
 - May have associated thyroid eye disease (TED) also known as thyroid associated orbitopathy or Graves' ophthalmopathy (20 to 40%)
 - TSH receptor antibodies (TRAb) are present in 90% of patients with Graves' disease.
- Toxic adenoma or multinodular goitre with autonomy – focal areas of increased radionuclide uptake.
- **Thyroiditis**, thyroxine excess, or exogenous iodine load (kelp, radio contrast) – no radionuclide uptake.

Thyroiditis

- The most common cause of thyroiditis is sub-acute (**de Quervain's**) thyroiditis.
 - Subacute thyroiditis (also known as de Quervain's)**
Where there is a tender diffuse goitre with transient hyperthyroidism followed by hypothyroidism before the restoration of normal thyroid function. It is presumed to be caused by a viral infection or post-viral inflammatory process. Beta blockers and non-steroidal anti-inflammatory drugs may be used for symptom control.
 - May also be painless.
 - This is a destructive process.
 - Patients with subacute thyroiditis do not respond to carbimazole.
 - Other causes of thyroiditis include [postpartum thyroiditis](#) (painless), medications (amiodarone, lithium, interferon, immunomodulatory drugs in cancer), and external radiation.

Practice Point

Statewide Referral Criteria

Thyroid ultrasound is not appropriate for investigating hyperthyroidism.

1. Assess for:

- Clinical thyroid hormone status e.g., tachycardia, heart failure, goitre, weight loss despite increased appetite, palpitations, sweating, fine tremor, mood disturbance with increased agitation or anxiety.
- Pregnancy, breastfeeding, or considering pregnancy. See [Thyroid Disease in Pregnancy](#).
- Medication (e.g., lithium, amiodarone, interferon pembrolizumab), which may affect thyroid function. Consider over-replacement if on thyroxine.
- Abnormal thyroid gland. Palpate for size, nodules, and tenderness.

2. Arrange **thyroid function tests** and consider if **other investigations** are required.

Thyroid function tests (TFTs)

TSH is now accepted as the initial test for assessment of thyroid function.

Statewide Referral Criteria (SRC) recommend:

If TSH is low, arrange free triiodothyronine (T3), free thyroxine (T4), anti-thyroid peroxidase (TPO) antibodies, thyroid stimulating hormone receptor antibody (TRAb), and thyroid stimulating immunoglobulin (TSI).

The Royal College of Pathologists of Australasia (RCPA) note that [TSH receptor antibodies](#) have superseded the insensitive TSI (also known as LATS) test.

See:

- RCPA – [Hyperthyroidism](#)
- [Thyroid Function Tests](#)

Other investigations

Consider other investigations as determined by the clinical findings:

- *Ultrasound (US) examination:*
 - *thyroid ultrasound has no role in the diagnosis of thyroid disorders in the absence of known or palpable thyroid nodules.*
 - *conventional grey scale analysis and colour-flow or power Doppler examination may be recommended to support the diagnosis of Graves' hyperthyroidism.*
- *Radionuclide thyroid scan – Scintigraphy of the thyroid is suggested when thyroid nodularity coexists with hyperthyroidism, and prior to radioactive iodine (RAI) treatment*

3. Consider **thyroid eye disease (TED)**, which may follow a separate course to the thyroid disease.

Thyroid eye disease (TED)

TED is also known as thyroid associated orbitopathy or Graves' ophthalmopathy.

TED affects approximately 20 to 40% of those with Graves' disease.

- Main reversible risk factor is smoking which increases risk by 20-fold.
- Usually occurs alongside thyrotoxicosis, but may occur before or after diagnosis of thyrotoxicosis.
- Significant and sight threatening thyroid eye disease is rare:
 - It may occur in the absence of proptosis.
 - It can threaten vision by optic neuropathy caused by compression of the optic nerve at the apex of the orbit or by ulceration of the cornea.



Inferior scleral show and upper lid retraction give the "surprised" look.

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- Always check **visual acuity** and colour vision.

Visual acuity

1. Ask if the patient has distance glasses with them, and if either eye has had known poor vision i.e., a lazy eye.
 2. Test their distance vision in each eye, while wearing glasses, using a 3 or 4 m chart.
 3. Check each eye separately, with distance glasses if worn.
 4. If acuity is subnormal, check with a pinhole.
 5. If vision improves with a pinhole, and no cataract is present, then the patient requires a review of their glasses.
 6. If unable to read any letters on chart, assess the following in descending order:
 - Finger counting
 - Hand movements
 - Light perception
 7. Test near vision while patient is wearing reading glasses.
- Check for **common symptoms of thyroid eye disease:**
 - Mild:
 - Gritty, irritable eyes
 - Mild eyelid swelling
 - No visual disturbance
 - Moderate:
 - At times painful eyes
 - Moderate erythema and swelling of eyelids
 - Moderate proptosis and/or lid retraction
 - Mild double vision on extremes of gaze
 - Severe:
 - Painful, red eyes
 - Severe swelling of eyelids
 - Severe proptosis and/or lid retraction
 - Visual disturbance, diplopia with modest eye movements

Management

Management depends on clinical context:

1. If hyperthyroidism and **significantly unwell** arrange [immediate endocrinology referral or admission](#).

Significantly unwell

- *Hyperthyroidism complicated by cardiac (rapid atrial fibrillation or heart failure), respiratory compromise, or other indications of severe illness e.g., fever, dehydration, vomiting, labile blood pressure, altered mental state or psychosis*
- *Fever (a temperature > 38°C may indicate thyroid storm)*
- *Neutropenic sepsis in patient taking carbimazole or propylthiouracil*
- *Hyperthyroidism with hypokalaemia or paralysis*

2. If thyroid eye disease (TED), refer depending on severity. If:

- **significant and sight-threatening**, arrange [immediate ophthalmology referral or admission](#).

Significant and sight-threatening

- *Drop in visual acuity*
- *Altered colour perception*
- *New diplopia*
- severe TED, arrange [urgent ophthalmology referral](#). Discuss with [ophthalmologist](#) if required or if symptoms worsen.
- mild to moderate TED, arrange [urgent or routine endocrinology referral](#) and describe eye symptoms. Consider symptomatic measures such as lubricant eye drops. Elevating the top of the bed may help if there is periorbital oedema while waiting for review.

3. Seek [endocrinology advice](#) or refer for [urgent or routine endocrinology review](#):

- if the patient is generally unwell.
- if the patient is **breastfeeding**:
 - *Less than 1% of both propylthiouracil (PTU) and carbimazole are excreted into breast milk. Doses up to carbimazole 20 mg daily and PTU 300 mg daily appear safe.*
 - *Antithyroid drugs should be given in divided doses and taken immediately after breastfeeding.*
- if managing a recurrent episode (including Graves' disease) to discuss definitive treatment i.e., radioactive iodine or surgery.
- for the assessment of newly identified hyperthyroidism (including Graves' disease).
- for advice on, or review of, management plan for stable hyperthyroidism.

4. If the patient is pregnant, see [Thyroid Disease in Pregnancy](#) pathway.

5. If reduced TSH and normal FT4 and normal FT3, see [Subclinical Hyperthyroidism](#) for more information.

Management of all other stable patients

1. Arrange [routine endocrinology referral](#) for all patients with stable hyperthyroidism for advice on, or review of management plan.
2. Arrange radionuclide thyroid scan to assist with **diagnosis** if this cannot be made on clinical assessment and investigations above. Anti-thyroid drugs need to be stopped 5 to 7 days prior to the scan.

Diagnosis

- Normal or high homogeneous uptake on a nuclear medicine scan indicates de novo synthesis of hormone e.g., **Graves' disease**.
 - **Graves' disease**
 - An Autoimmune disease.
 - Most common cause of hyperthyroidism (about 70%).
 - 10 times more common in women.
 - Usually associated with diffuse goitre.
 - May have associated thyroid eye disease (TED) also known as Graves' ophthalmopathy or thyroid orbitopathy (20 to 40%).
 - TSH receptor antibodies (TRAb), are present in 90% of patients with Graves' disease.
 - Focal or heterogenous uptake is most likely due to toxic adenoma or toxic multinodular goitre.
 - Near absent radioiodine uptake indicates either inflammation or destruction of thyroid tissue (i.e., **thyroiditis**), iodine-induced hyperthyroidism or an extra-thyroidal source of thyroid hormone e.g., thyroxine or other thyroid supplements.
 - **Thyroiditis:**
 - The most common cause of thyroiditis is sub-acute ([de Quervain's](#)) thyroiditis. **Subacute thyroiditis (also known as de Quervain's):** Where there is a tender diffuse goitre with transient hyperthyroidism followed by hypothyroidism before the restoration of normal thyroid function. It is presumed to be caused by a viral infection or post-viral inflammatory process. Beta blockers and non-steroidal anti-inflammatory drugs may be used for symptom control.
 - May also be painless.
 - This is a destructive process.
 - Patients with subacute thyroiditis do not respond to carbimazole.
 - Other causes of thyroiditis include [postpartum thyroiditis](#) (painless), medications (amiodarone, lithium, interferon, immunomodulatory drugs in cancer), and external radiation.
 - Amiodarone can cause hyperthyroidism by mixed mechanisms (iodine induced or destructive thyroiditis) and the scan often shows low uptake.

3. Manage according to diagnosis:

- **Graves' disease:**

If normal or increased uptake, start **carbimazole** with or without a **beta blocker**. Note: Propylthiouracil (PTU) is not considered first-line therapy outside of first trimester of pregnancy due to increased risk of hepatotoxicity.

- **Beta blocker**

Consider adding a beta blocker for initial control of marked symptoms (tachycardia, palpitations, tremor, etc).

Traditional advice is to use [propranolol](#), 10 to 40 mg, 3 to 4 times a day.

- **Carbimazole dose**

- Subclinical (normal FT4 and FT3): 2.5 to 5 mg daily.
- Mild (FT4 or FT3 < twice the upper limit of normal): 5 to 10 mg daily.
- Moderate (FT4 or FT3 > twice the upper limit of normal): 10 mg twice a day.
- Severe (FT4 or FT3 > 3 times the upper limit of normal) or with marked symptoms (tachycardia, rapid weight loss): 15 mg twice a day plus a beta blocker.

Warnings about carbimazole

- Document informed consent and warn patient about the risks of treatment:
 - **Congenital abnormalities**
Antithyroid drugs increase the risk of congenital abnormalities.
 - If treatment is required during pregnancy, use propylthiouracil over carbimazole during the first trimester, as it is associated with less severe congenital abnormalities.
 - Switch existing carbimazole therapy to propylthiouracil before conception.
 - **Agranulocytosis risk** – sudden and serious complication
Advise patients to stop taking carbimazole and seek medical attention straight away if they develop symptoms of infection e.g., fever, flu-like symptoms, sore throat, mouth ulcers.
 - Arrange urgent FBE so that results are available on the same day. If neutrophil count is low, arrange [immediate endocrine surgery referral or admission](#).

The incidence of agranulocytosis resulting from carbimazole therapy or propylthiouracil (PTU) is reported to be between 0.2% (1 in 500) to 0.5% (1 in 200).

- Hepatotoxicity
 - Other less serious adverse effects are rashes, arthralgia, and gastritis
- Take baseline FBE and LFTs before starting carbimazole.

Baseline FBE and LFTs before starting carbimazole

Mild neutropenia or mild liver function derangement are often seen as a result of hyperthyroidism, and should normalise as thyroid hormone levels return to normal.

Consider adding a beta blocker for initial control of marked symptoms (tachycardia, palpitations, tremor, etc.).

- Hepatitis rarely occurs with carbimazole so routine monitoring of LFTs is not recommended.
 - Routine FBEs are not recommended.
- While waiting for endocrinology assessment, repeat thyroid function every 4 to 6 weeks and adjust carbimazole dose accordingly.

- For Graves' thyrotoxicosis, the aim is to treat most patients for 12 to 18 months with carbimazole. 50% will relapse despite this treatment.
- If any problems with carbimazole, discuss with an [endocrinologist](#) other options such as propylthiouracil or radioiodine.
- If long term treatment is needed, radioactive iodine or surgery is preferred.
- The TSH may stay suppressed for some months, so it is more appropriate initially to titrate treatment against FT4 and FT3 levels.
- Thyroiditis – if radionuclide scan shows low uptake, **treat as thyroiditis**.
 - **Management of subacute thyroiditis**
 - Stop carbimazole (if taking) and check CRP and ESR, which are usually raised.
 - Consider beta blocker while symptomatically hyperthyroid.
 - NSAID or even steroids may be required for thyroid pain in patients with subacute thyroiditis.
 - 80% of patients resolve spontaneously.
 - Some patients develop transient hypothyroidism, before spontaneously recovering.
 - Monitor TFTs every 4 to 6 weeks for 3 to 4 months or until 2 successive tests are normal.
 - For those who become symptomatically hypothyroid or TSH > 20, consider temporary treatment with thyroxine and [arrange urgent or routine endocrinology referral](#).

Referral

Include the results of thyroid function tests, and if available radionuclide imaging in all referrals.

- If hyperthyroidism and [significantly unwell](#) arrange [immediate endocrinology referral or admission](#).
- If thyroid eye disease, refer depending on severity. If:
 - significant and sight threatening thyroid eye disease (TED), arrange [immediate ophthalmology referral or admission](#).
 - severe TED, arrange [urgent ophthalmology referral](#). Discuss with [ophthalmologist](#) if required, or if symptoms worsen.
 - mild to moderate TED, arrange [urgent or routine endocrinology referral](#).
- Seek [endocrinology advice](#) or refer for [urgent or routine endocrinology review](#):
 - if generally unwell.
 - if breastfeeding.
 - if recurrent episode (including Graves' disease) to discuss definitive treatment i.e., radioactive iodine or surgery.
 - for the assessment of newly identified hyperthyroidism (including Graves' disease).
 - for advice on, or review of, management plan for stable hyperthyroidism.
 - for those who become symptomatically hypothyroid or TSH > 20.

Information

For health professionals

Further information

- Australian Family Physician – [Thyroid: August 2012](#)
- BMJ Learning – [Hyperthyroidism: Diagnosis and Treatment](#) [requires registration]

- bpacnz – [Management of Thyroid Dysfunction in Adults](#)
- NCBI – [2018 European Thyroid Association Guideline for the Management of Graves' Hyperthyroidism](#)
- Royal College of Pathologists of Australasia (RCPA) – [Common Sense Pathology \(CSP\): Investigation of Common Thyroid Problems](#)

For patients

- Better Health Channel:
 - [Thyroid: Hyperthyroidism](#)
 - [Thyroid Gland](#)
- Patient:
 - [Overactive Thyroid Gland: Hyperthyroidism](#)
 - [Thyroid Function Tests](#)
- Royal College of Pathologists of Australasia (RCPA) – [Common Sense Pathology \(CSP\): Investigation of Common Thyroid Problems](#)

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4. Saravanan P, Dayan CM. [Thyroid autoantibodies.](#) Endocrinol. Metab. Clin. North Am. 2001 Jun;30(2):315-37, viii.

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