Hyperthyroidism

Disclaimer

Contents

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 ophthalmopathy (20 to 40%)*
  - *10% do not have positive standard thyroid antibodies (TSH receptor antibodies)*
- *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 or painless 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.*

Red flags

- Significantly unwell, especially if fever
- Rapid atrial fibrillation or heart failure
- Severe dehydration
- Psychosis
- Significant and sight-threatening thyroid orbitopathy, e.g., drop in visual acuity, altered colour perception, new diplopia.

Assessment

Practice point

- *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.
    - Pregnancy or breastfeeding.
    - 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 TSH.
3. If TSH is low, arrange FT3, FT4, thyroid antibodies, and TRAb.
4. Consider ***thyroid eye disease*** (also known as thyroid associated or Graves' orbitopathy), which may follow a separate course to the thyroid disease.

Thyroid eye disease

Thyroid associated ophthalmopathy 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 the 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.

Measuring visual acuity

- *Ask if the patient has distance glasses with them, and if either eye has had known poor vision i.e., a lazy eye.*
- *Test their distance vision in each eye, while wearing glasses, using a 3 or 4 metre chart.*
- *Check each eye separately, with distance glasses if worn. If acuity is still subnormal, check with a pinhole.*
- *If vision improves with a pinhole, and no cataract is present, then the patient requires a review of their glasses.*
- *Near vision – test while patient is wearing reading glasses.*
  - *Visual fields to confrontation (count fingers in four quadrants for each eye)*
  - *Pupillary light reaction*

- Check for ***common symptoms.***

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*
  - *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

- *Fever (a temperature > 38°C may indicate thyroid storm)*
- *Rapid atrial fibrillation or heart failure*
- *Severe dehydration*
- *Psychosis*

2. If thyroid eye disease, refer depending on severity. If:
   - ***significant and sight-threatening thyroid orbitopathy***, arrange immediate ophthalmology referral.

Significant and sight-threatening thyroid orbitopathy

- *Drop in visual acuity*
- *Altered colour perception*
- *New diplopia*

- severe thyroid eye disease, arrange urgent ophthalmology referral. Discuss with ophthalmologist if required or if symptoms worsen.
- moderate thyroid eye disease, arrange urgent endocrinology referral and describe eye symptoms.
- mild thyroid eye disease, arrange routine endocrinology referral. 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. If generally unwell, discuss with an endocrinologist.

4. If the patient is pregnant, use best practice guidelines for thyroid disease in pregnancy.

5. If the patient is ***breastfeeding***, discuss with an endocrinologist.

Breastfeeding

- *During breastfeeding, propylthiouracil (PTU) is the preferred drug of choice. Less than 1% of both 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 right after nursing.*

6. If managing a recurrent episode, consider arranging routine endocrinology referral to discuss definitive treatment i.e., radioactive iodine or surgery.

7. If reduced TSH and normal FT4 and normal FT3, see Subclinical Hyperthyroidism pathway.

Management of all other stable patients

1. 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 ophthalmopathy (20 to 40%).*
  - *10% do not have positive standard thyroid antibodies (TSH receptor antibodies).*

- *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.*
- *Amiodarone can cause hyperthyroidism by mixed mechanisms (iodine induced or destructive thyroiditis) and the scan often shows low uptake.*

2. 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

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

- *Warn all patients about the sudden, serious complication of* **agranulocytosis**.

Agranulocytosis risk

- *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 is reported to be between 0.2% (1 in 500) to 0.5% (1 in 200).

- *Document informed consent about the risks of agranulocytosis and hepatotoxicity.*
- *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.*
- *Other less serious adverse effects are rashes, arthralgia, and gastritis.*
- *Routine FBEs are not recommended.*

3. Arrange routine endocrinology referral for all stable patients with hyperthyroidism.

4. While waiting for endocrinology assessment, repeat thyroid function every 4 to 6 weeks and adjust carbimazole dose accordingly.

5. If radionuclide scan shows low uptake, ***treat as thyroiditis.***

Management of subacute or painless thyroiditis

- *Stop carbimazole 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 mIU/L, consider temporary treatment with thyroxine and arrange endocrinology referral.*

6. The TSH may stay suppressed for some months, so it is more appropriate initially to titrate treatment against FT4 and FT3 levels.

7. For Graves' thyrotoxicosis, the aim is to treat most patients for 12 to 18 months with carbimazole. 50% will relapse despite this treatment.

8. If long term treatment is needed, radioactive iodine or surgery is preferred.

9. If any problems with carbimazole, discuss with an endocrinologist other options such as propylthiouracil or radioiodine.

Referral

If available, include the results of thyroid function tests, and radionuclide imaging in all referrals.

- If ***significantly unwell*** arrange immediate endocrinology referral or admission.

  Significantly unwell

  - *Fever (a temperature > 38°C may indicate thyroid storm)*
  - *Rapid atrial fibrillation or heart failure*
  - *Severe dehydration*
  - *Psychosis*

- If thyroid eye disease, refer depending on severity. If:
  - ***significant and sight threatening thyroid orbitopathy***, arrange immediate ophthalmology referral.

    Significant and sight-threatening thyroid orbitopathy

    - Drop in visual acuity
    - Altered colour perception
    - New diplopia
  - severe thyroid eye disease, arrange urgent ophthalmology referral. Discuss with ophthalmologist if required, or if symptoms worsen.
  - moderate thyroid eye disease, arrange urgent endocrinology referral and describe eye symptoms.
  - mild thyroid eye disease, arrange routine endocrinology referral.

- If generally unwell, discuss with an endocrinologist.
- If breastfeeding, discuss with an endocrinologist.
- If recurrent episode, consider routine endocrinology referral to discuss definitive treatment.
- If stable, arrange routine endocrinology referral.

Information

For health professionals

- BMJ Learning (requires registration) – Hyperthyroidism: Diagnosis and Treatment
- bpacnz – Management of Thyroid Dysfunction in Adults

For patients

- Better Health Channel:
  - Thyroid: Hyperthyroidism
  - Thyroid Gland
- Patient:
  - Overactive Thyroid Gland: Hyperthyroidism
  - Thyroid Function Tests

Sources

Select bibliography

Campbell K, Doogue M. Evaluating and managing patients with thyrotoxicosis. Australian Family Physician. 2012 [cited 2018 Jun 20];41(8):564-572.

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