

Thyroid Hormone Background

Synthesis: Iodide is actively transported into thyroid follicular cells. Thyroid peroxidase catalyses the iodination and coupling of tyrosine residues on thyroglobulin.

Release: Thyroglobulin → T4 (thyroxine, 80%) & T3 (triiodothyronine 20%). Both >99% plasma protein bound (mostly TBG). Free T3 more active form. Free T4 is peripherally converted to T3 (33%) and rT3 (45%). T3/T4 metabolised in kidney/liver. $T_{1/2}$ T3: 22h, $T_{1/2}$ T4: 6d.

Effects: Increases metabolism, sensitivity to catecholamines, betareceptors, GIT motility. Required for CNS neurone development, bone growth/epiphyseal closure, and lactation.

Primary hyperthyroidism is when the pathology is within the thyroid gland.

Secondary hyperthyroidism (rare) is when the thyroid gland is stimulated by excessive TSH.

Epidemiology

- Prevalence - In Caucasians, 2-3% in women and 0.2-0.3% in men.
- Risk Factors - Family history, high iodine intake, smoking, iodine-containing agents e.g. amiodarone, contrast agents.

Causes

- Graves' Disease:
 - Commonest (~85%). Autoimmune (TSI (IgG) antibody acts on TSH receptor).
 - Associated with other autoimmune conditions e.g. PA, T1DM
 - May also have antibodies to thyroglobulin, thyroid peroxidase (aka antimicrosomal antibodies), or sodium-iodide symporter
- Toxic nodular goitre: Presence of multi-nodular goitre without features of Graves'
- Solitary thyroid nodule: palpable, toxic adenoma.
- De Quervains Thyroiditis: transient viral disease with pyrexia and pain in the neck.
- Drugs: e.g. Amiodarone, lithium, exogenous iodine, exogenous thyroxine.
- Follicular Ca of thyroid gland. Ovarian teratomas
- Thyrotoxic hypokalaemic periodic paralysis esp in Asian Males

Presentation

Symptoms

- | | | |
|-------------------------|----------------------------|--------------------------------------|
| • Wt loss yet ↑appetite | • Weakness, fatigue | • Mental illness: anxiety, psychosis |
| • Heat intolerance | • Appetite changes | • Loss of libido |
| • Tremor, irritability | • Diarrhoea ± steatorrhoea | • Oligo-/amenorrhoea |
| • Sweating | | |

Signs

- | | | |
|----------------------|-------------------------|---------------------|
| • Palmar erythema | • Hair thin or alopecia | • Proximal myopathy |
| • Sweaty, warm palms | • Urticaria, pruritus | • Gynaecomastia |
| • Fine tremor | • Brisk reflexes | • Lid lag |
| • ↑HR- may be AF | • Goitre | |

Thyroid Storm: Uncommon (~1%) & usually have Graves' disease. Sev hyperthyroidism with:

- **Hyperpyrexia** (over 37.8°C but may reach 41°C)
- **Tachycardia** (often >145bpm) ± AF, hypotension, atrial dysrhythmias, CCF
- **Confusion**, agitation, delirium, psychosis, seizures or coma
- Nausea, jaundice, vomiting, diarrhoea, abdominal pain & dehydration may also occur.

- Thyroid storm precipitants:
 - Infection, other acute illness
 - MI, PE, DKA, hypoglycaemia
 - Recent trauma, surgery
 - Withdrawal of/non-compliance with Rx
 - Drugs: iodine, amiodarone, contrast

Extra signs in Graves' disease

- Eye changes >90% - exophthalmos, ophthalmoplegia, conjunctival oedema, papilloedema and keratopathy. May be severe enough to cause visual loss.
- Pretibial myxoedema <5% - swelling above the lateral malleoli due to accumulation of glycosaminoglycans (non-pitting plaques with pink/purple colour).
- Thyroid acropachy 10-20% - clubbing with painful swelling of digits.
- Diffuse enlargement of thyroid gland.
- Thyroid bruit.

Investigations (if thyroid storm looking for precip in addition to TFTs)

Bedside: Urine (urinalysis, M,C & S), ECG, VBG

Blood: TFTs, UEC (dehydration), Thyroid autoantibodies, UEC (K⁺), BSL (↑), LFTs (↑), Ca (↑), FBC (↓HB, ↑WCC, ↓Plt), culture

Imaging: Thyroid USS, thyroid uptake scans: to locate hot and cold spots. CXR

Management

Thyrototoxic Storm:

Supportive: IV Fluids, **Paracetamol**. Avoid aspirin (can increase T4). Active cooling if T>40°C

Beta blockers: **Propranolol** 1mg/min IV up to 10mg q4h, then 20-120mg q4-6h PO (CI: asthma - but not heart failure). Can use esmolol if concerned re CCF. **Diltiazem** can be used if BBs CI.

Antithyroid treatment: **PTU** or **carbimazole** -see below. Then give **Lugol's solution** after 1-4hrs.

Steroids: **Hydrocortisone** 100mg IV q6h - blocks T4 to T3 conversion & hormone release.

Treat precipitating cause.

Other: DC Cardioversion for arrhythmias. NGT, sedate with **chlorpromazine** if sev. Agitation.

Anticoagulation (**heparin**). If patient fails to improve within 1-2 days, consider exchange transfusion, peritoneal dialysis or haemodialysis. Involve ICU & endocrinologist.

Hyperthyroidism:

Antithyroid Rx: **Propylthiouracil (PTU)** 100-250mg q6h or **carbimazole (methimazole)** 10-20mg bd-tds. Inhibit the production of thyroid hormones. Onset ~1hr, full benefit may take 2-3 wks.

- Propylthiouracil also decreases peripheral T4 to T3 conversion
- "Dose titration" regime preferred to "block and replace" (thyroxine + antithyroid drug)
- Monthly TFTs. Remission is common 18-24 months and drugs can be weaned.
- **SE:** nausea, bitter taste, hypothyroidism, marrow suppression (FBC if sore throat)

Radioiodine: 200-600 MBq PO **CI:** pregnancy or pregnant within 4/12, lactation

- Taken up by thyroid gland leading to destruction. Preferred in toxic multi-nodular goitre
- **SE:** may ↑Graves' eye disease, urine excretion so avoid child contact, hypothyroid

Surgical:

- Sub-total or near total thyroidectomy achieves 98% cure rate. Indicated if suboptimal response to antithyroid medication or radioiodine and in children occasionally. **Cx:** haemorrhage, hypoparathyroidism and vocal cord paralysis.

Prognosis

- Hyperthyroidism is characterised by relapses and remittances.
- Thyroid storm mort >90% if untreated. Early Rx reduces mort to 10-15%.