Hyperthyroidism

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Hyperthyroidism (thyrotoxicosis)

- Hyperthyroidism causes sustained high plasma concentrations of T4 and T3. There is often generalized increase in the metabolic rate, evidenced clinically by, for example, heat intolerance, a fine tremor, tachycardia including atrial fibrillation, weight loss, tiredness, anxiety, sweating and diarrhea.
- The following biochemical features may be associated with hyperthyroidism:
- Hypercalcaemia is occasionally found in patients with severe thyrotoxicosis. There is an increased turnover of bone cells, probably due to a direct action of thyroid hormone.
- Hypocholesterolaemia can occur, due to increased LDL clearance.
- Hypokalaemia may also occur, associated with hyperthyrotoxic periodic paralysis.
- Plasma SHBG is increased.
- Plasma creatine kinase may be increased with thyrotoxic myopathy.

Causes of hyperthyroidism

- **Autonomous secretion**
- Graves' disease
- Toxic multinodular goitre (Plummer's disease) or a single functioning nodule (occasionally an adenoma)
- Subacute thyroiditis
- Some metastatic thyroid carcinomas
- **Excessive ingestion of thyroid hormones or iodine**
- Amiodarone
- Thyrotoxicosis factitia (self-administration of thyroid hormones)
- Administration of iodine to a subject with iodine deficiency goitre
- Jod–Basedow syndrome

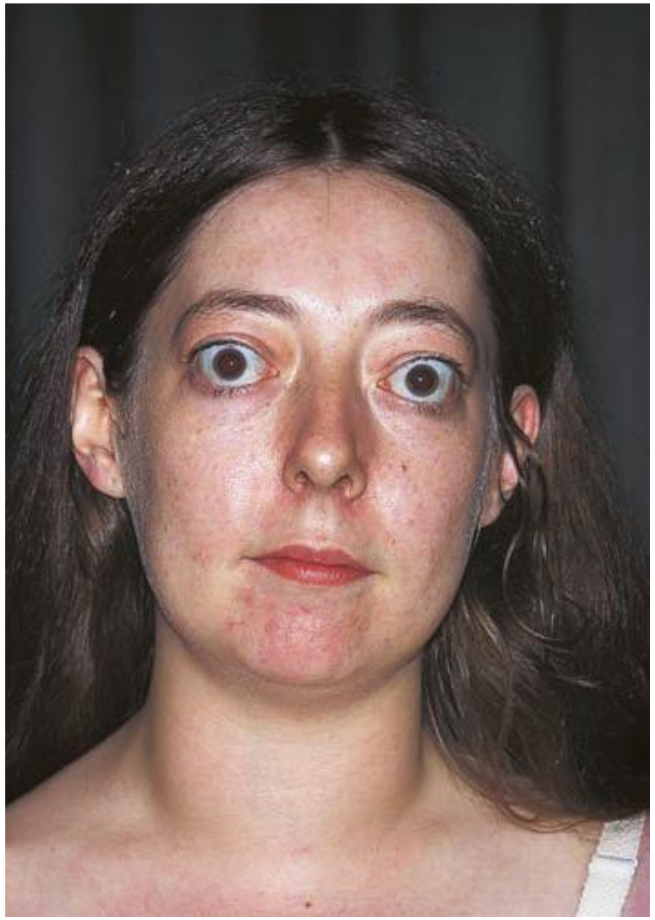
Rare causes

- Thyroid-stimulating hormone secretion by tumours, including pituitary tumours or those of trophoblastic origin.
- Struma ovarii (thyroid tissue in an ovarian teratoma).
- Excess human chorionic gonadotrophin, e.g. molar pregnancy or choriocarcinoma.
- Pituitary resistance to thyroid hormone.

Graves’ disease

- This is the most common form of thyrotoxicosis and occurs more often in females than in males. It may be caused by relatively autonomous secretion from a diffuse goitre and is characterized by:
- exophthalmos, due to lymphocytic infiltration and swelling of retro-orbital tissues of the eyes (Fig. 1.1),
- localized thickening of the subcutaneous tissue over the shin (pretibial myxoedema).

Figure 1.1 A patient with primary hyperthyroidism. Note exophthalmos and diffuse thyroid swelling.



Subacute thyroiditis

- This is a destructive thyroiditis resulting in the release of preformed thyroid hormones.
- There are three subtypes: granulomatous or painful, lymphocytic or silent and painless, and post-partum.
- This condition is associated with extremely elevated thyroid hormones and no radioactive iodine uptake by the thyroid gland.
- The clinical course progresses through 6–8 weeks of thyrotoxicosis, 2–4 months of hypothyroidism and a return to euthyroidism in about 90 per cent of patients.

Toxic nodules

- Toxic nodules, either single or multiple, in a nodular goitre may secrete thyroid hormones autonomously.
- The secretion of TSH is suppressed by negative feedback, as in Graves' disease.
- The nodules may be detected by their uptake of radioactive iodine or technetium, with suppression of uptake in the rest of the thyroid tissue ('hot nodules').
- Toxic nodules are found most commonly in older patients, who may present with only one of the features of hyperactivity, usually cardiovascular symptoms such as atrial fibrillation.
- Toxic multinodular goitre is also called Plummer's disease.

Pathophysiology of hyperthyroidism

- Plasma T_4 or fT_4 and T_3 and fT_3 concentrations are usually increased in hyperthyroidism.
- Much of the T_3 is secreted directly by the thyroid gland, and the increase in plasma T_3 concentrations is greater, and usually evident earlier, than that of T_4.
- Rarely, only plasma T_3 and fT_3 concentrations are elevated (T_3 toxicosis).
- In both situations, TSH secretion is suppressed by negative feedback, and plasma TSH concentrations are either very low or undetectable.

Treatment

- The aetiology of hyperthyroidism must be fully investigated and treatment started. Various forms of treatment are available, the selection of which depends on the cause, the clinical presentation and the age of the patient.
- b-blocker drugs such as propranolol, which inhibit the peripheral conversion of T4 to T3, may be used initially. Additional treatment includes the use of such drugs as carbimazole or propylthiouracil. Carbimazole inhibits the synthesis of T3 and T4; propylthiouracil additionally inhibits T4 to T3 conversion. Some clinicians use block-and-replace regimens:
- Carbimazole is used to ‘block’ thyroid secretion, and simultaneous exogenous T4 maintains and replaces T4 concentrations.
- It is important to remember that carbimazole can have the potentially lethal side effect of bone marrow suppression, and patients should be warned about infections such as sore throats and about the need to have their full blood count monitored.

- Radioactive iodine can be used in resistant or relapsing cases; surgery is rarely indicated, but may have a place if there is a large toxic goitre that is exerting pressure or if drug therapy fails but radioactive iodine is contraindicated.
- Thyroid function must be checked regularly, as some patients may become hypothyroid or may relapse after radioiodine or surgery.
- The progress of a patient being treated for hyperthyroidism is usually monitored by estimating plasma TSH, fT_4 and fT_3 concentrations, and trying to restore these to normal (although TSH concentration may be slow to normalize).

- Overtreatment may induce hypothyroidism, with a rise in plasma TSH concentrations and low plasma T4/fT4 and T3/fT3 concentrations. In some patients with severe prolonged hyperthyroidism, such a rise in plasma TSH may be delayed because of the effects of prolonged feedback suppression of T4 on the pituitary.
- Subclinical hyperthyroidism
- Subclinical hyperthyroidism may occur with a low or suppressed TSH concentration but normal (usually high-normal) plasma fT4 and fT3 concentrations.
- The condition may progress to full-blown hyperthyroidism with suppressed plasma TSH and raised plasma fT4 and fT3 concentrations.
- Subclinical hyperthyroidism may be associated with atrial fibrillation, decreased bone mineral density and other features of hyperthyroidism.
- Plasma TSI may be raised.

Laboratory investigation of suspected hyperthyroidism

- A careful history (including drugs) should be taken and examination performed, checking for a goitre.
- The plasma TSH, fT3 and fT4 concentrations should be measured.
- The plasma fT4 and fT3 concentrations are clearly high and the TSH concentration is suppressed in clinically thyrotoxic patients.
- In the face of suppressed plasma TSH, a clearly elevated plasma fT3 concentration confirms the diagnosis of hyperthyroidism.
- Remember that in T3 thyrotoxicosis the plasma fT4 may be normal.
- If the plasma fT4 concentration is raised and the TSH concentration is normal, this is suggestive of biochemical euthyroid hyperthyroxaemia (see below for causes).

- Measurement of thyroid antibodies is useful, particularly if the concentration of TSIs is raised, which supports a diagnosis of Graves' disease.
- The rare TSH-secreting pituitary tumours need pituitary assessment . a-subunit concentrations may be useful, as they are usually raised in such circumstances.
- In difficult cases, determination of plasma SHBG concentration can help decide whether the patient is hyperthyroid, as it is lowered in hypothyroidism and raised in hyperthyroidism.
- Radioiodine uptake studies of the thyroid can be useful to distinguish some of the causes of hyperthyroidism.
- The TRH test is sometimes useful in the diagnosis of unclear cases.

Thank you