Hyperthyroidism

Hyperthyroidism is most commonly caused by Graves disease. It may also be due to toxic nodular goitre, thyroiditis or rare conditions such as Jod-Basedow phenomenon (high iodine intake), TSH secreting pituitary tumour, ectopic thyroid tissue, trophoblastic tumour and factitious hyperthyroidism.

How may patients with hyperthyroidism present?

The patient may present with features of thyrotoxicosis or Graves disease (table). Elderly patients may not have these classical features but may complain of weight loss or depression (apathetic hyperthyroidism), or cardiovascular problems (eg. heart failure, atrial fibrillation).

Table. **Some clinical features of hyperthyroidism**

Symptoms	*Signs*
Weight loss	Fine tremor
Diarrhoea	Choreoathetosis
Increased appetite	Proximal myopathy
Irritability/hyperactivity	Pretibial myxoedema*
Palpitations	Thyroid acropathy*
Increased sweating/ heat intolerance	Onycholysis
Muscle weakness	Warm peripheries
Oligomenorrhoea/ ameonorrhoea	Eye signs
	• Lid lag/retraction
	• Exophthalmos*
	• Ophthalmoplegia*
	Tachycardia/bounding pulse/atrial fibrillation
	Goitre
	• Diffuse/nodular
	• Bruit

*Seen in Graves disease

Evaluation of a patient with suspected hyperthyroidism

The history may reveal features of thyrotoxicosis (table) or thyroiditis (pain over the thyroid, recent viral fever, pregnancy). Drug history should include details of iodine containing compounds and other drugs known to cause thyrotoxicosis (eg.amiodarone). Other autoimmune diseases should be sought in the patient and thyroid disorders should be looked for in the family.

The patient should be examined for evidence of thyrotoxicosis, Graves disease (table), cardiac failure and tachyarrhythmias.

Once hyperthyroidism is clinically suspected, biochemical investigations should be carried out to establish the diagnosis.

Serum thyroid-stimulating hormone (TSH) and free thyroxine (FT_4) should be checked. Characteristically, TSH is depressed and FT_4 elevated. The TSH assay should be sensitive enough to detect low levels found in hyperthyroidism. Low TSH and normal T_4 should warrant the testing of triiodothyronine (T_3) which is elevated in early hyperthyroidism or 'T_3 toxicosis'. If TSH is not suppressed with high T_4/T_3, the patient may have a rare TSH secreting pituitary tumour. However, low TSH may be seen in other conditions such as 'non-thyroidal illness' or amiodarone treatment.

If Graves disease is suspected, TSH receptor antibodies (TSHRAb) and thyroid peroxidase antibodies (TPOAb) would help in confirming the diagnosis. Radioisotope scanning with technicium (^{99}Tc) or iodine (^{125}I) would differentiate between Graves disease (diffuse uptake), toxic nodular goitre (hot nodule) and thyroiditis (low uptake).

Management

The aim of management is to make the patient euthyroid and asymptomatic as soon as possible.

Three options are available for the management of hyperthyroidism: antithyroid drugs (ATD), radioactive iodine (^{131}I) and surgery.

Antithyroid drugs (thionamides)

ATD (carbimazole/methimazole or propylthiouracil) are used as primary therapy or to render the patient euthyroid before radioiodine therapy or surgery. They are usually given for 6 months to 2 years when used as primary therapy. Graves disease may remit with ATD. The usual initial doses are 10-40mg/day for carbimazole and 100-600mg/ day for propylthiouracil. Once the patient is euthyroid, the dose could be reduced to maintain the euthyroid state. Some physicians prefer the 'block and replacement' regimen with thyroxine and ATD combined, where the thyroxine dose is maintained at 125 µg per day, and the ATD are adjusted according to the thyroid status.

The patient should be reviewed every 4-12 weeks with TSH and FT_4 levels, till euthyroid state is achieved. TSH may remain suppressed for weeks or months after initiation of ATD, thus the drug doses should be titrated against FT_4 (FT_3 in T_3-toxicois). Once ATD are discontinued, they should be seen at 4-6 week intervals in the first 3-4 months and then at less frequent intervals.

The most serious adverse effect of ATD is agranulocytosis, occurring in 0.3% of patients. Patients should be advised and given written instructions to stop treatment and see the physician if they develop fever, sore throat, rash, arthralgia or jaundice, and appropriate evaluation including a white cell count is required.

Radioactive iodine (RAI) treatment with ^{131}I

Most patients require treatment with RAI as there is a low remission rate with ATD in Graves disease (<50%, especially in severe biochemical disease, large goitre and in men), and the lack of curative effect in toxic nodular goitre. Radioiodine is contraindicated in pregnancy, up to 6 months before pregnancy and during lactation.

The patient should be made euthyroid with ATD before administrating RAI, to minimise the risk of ^{131}I induced thyrotoxicosis. To obtain the best results with treatment, ATD should be stopped at least 4 days before, and not restarted earlier than 3 days after RAI. Those on a 'block and replacement' regimen need to stop both thyroxine and ATD 4 weeks before RAI. Following successful treatment, the patient may become hypothyroid, requiring lifelong thyroxine replacement. They should initially be reviewed at 4-6 week intervals and then annually.

Thyroidectomy

Surgery is considered in patients allergic to ATD and do not wish to have RAI, those with very large goitres who may be relatively resistant to both ATD and RAI, or pregnant patients allergic to ATD. The patient has to be made euthyroid before surgery and counselled regarding the possibility of

hypothyroidism following surgery and other complications.

Adjunctive therapy

Beta blockers (eg. propranolol) are useful for the rapid relief of adrenergic symptoms (eg. tachycardia, tremor). This is usually the sole therapy required for the thyrotoxic phase of thyroiditis.

Additional treatment with salicylates or glucocorticoids may be required in patients with thyroiditis, for symptomatic relief.

Special situations: thyroid storm (thyrotoxic crisis)

This is a life-threatening condition with severe thyrotoxicosis, fever and altered mental state. It is usually seen with Graves disease and precipitated by concurrent illness or injury, following RAI treatment for hyperthyroidism, or withdrawal of ATD.

When it is suspected, the patient should receive ***immediate*** treatment with ATD, β blockers, potassium iodide to inhibit release of thyroid hormones, steroids and supportive care.

Piyusha Atapattu, MD (Colombo), MRCP (UK). *Senior Lecturer in Physiology, Faculty of Medicine, Colombo 8. e-mail: <piyushaatapattu@yahoo.com>. Competing interests: none declared.*