BENIGN THYROID DISEASES

HYPERTHYROIDISM

- Primary – Due to defects of thyroid gland itself
- Secondary – Due to anterior pituitary disorders
- < TSH and > T3, T4

AETIOLOGY

- Graves' disease, an autoimmune condition caused by stimulation by antibodies directed against the TSH receptor, is the cause in most patients.
- The development of one or more autonomously functioning thyroid nodules that produce excessive amounts of thyroid hormones
- Thyroiditis or thyroidal inflammation

CLINICAL FEATURES

- Elderly patients might not present with any symptom known as Masked Thyrotoxicosis.
- Nervousness or Anxiety, Tremor, Weight loss, Palpitations and Heat sensitivity
- Decreased Menses, Infertility, Decreased Libido, painful Gyanecomastia
- Poor concentration, personality changes
- Clinical findings include tachycardia, warm moist skin, the presence of an enlarged thyroid and a slight tremor.
- Elderly present with Atrial fibrillation, and rarely Congestive cardiac failure.
- Other indicators of hyperthyroidism include osteoporosis, hypercalcaemia, congestive cardiac failure, shortness of breath, muscle weakness, anxiety or amenorrhea.
- Hyperthyroidism may also present as thyroid storm, a life-threatening situation with signs including tachycardia, AF, congestive cardiac failure, hyperpyrexia, agitation, psychosis or coma.
- Thyroid storm typically occurs after a precipitating event, such as trauma, childbirth, infection or surgery, in a known hyperthyroid subject.

DIAGNOSIS OF HYPERTHYROIDISM
LABORATORY DIAGNOSIS

- TSH most important.
- The exceptions to this rule are very rare pituitary causes of thyrotoxicosis such as TSHoma or syndromes of thyroid hormone resistance. In these cases, there may be a modest rise in TSH accompanied by a rise in fT3 and fT4.
- TSH should be measured with free T4 and in specific cases free T3 also
- In most cases of hyperthyroidism, the typical picture is of undetectable serum TSH with elevated serum concentrations of fT4 and fT3.
- A low TSH and normal fT4 should prompt fT3 measurement as 10 per cent of cases of thyrotoxicosis are so called ‘T3 toxicosis’, with a rise in fT3 alone.

<table>
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<th>Laboratory investigations in suspected thyrotoxicosis.</th>
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<td>Thyroid function tests</td>
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THYROID SCINTIGRAPHY

- The 24 h radioactive iodine uptake
- Non specific
- Non specific as values can be high in cases of normal thyroid, Iodine deficiency, Hashimoto etc
- Values can be low in cases of Destructive thyroiditis that cause hyperthyroidism like sub acute or post partum thyroiditis.
- This imaging modality can be used to differentiate between 'hot' and 'cold' areas.

GRAVES' DISEASE

- It is defined as a syndrome consisting of hyperthyroidism, moderate goitre, ophthalmopathy and dermopathy.
- F:M = 5:1
- Any age but mostly 20 to 30 yrs.
- Graves’ disease is more common in smokers

AETIOPATHOGENESIS

- Autoimmune disorder characterized by antibodies in the circulation that are directed against the TSH receptor which mimic the effects of pituitary TSH.
Cause of **OPHTHALMOPATHY & DERMOPATHY** (Pretibial myxedema) is cross-reactivity between thyroidal antigens and antigens in orbital and extra-orbital tissues (especially preadipocyte fibroblasts).

- So **ETIOLOGY** includes:
  - Autoimmune
  - Smoking
  - Interferon α
  - Stress
  - Sex steroids
  - Dietary iodine intake

**CLINICAL MANIFESTATIONS**

- Gradual, insidious in onset.
- Goitre is usually symmetrical.
- Overlying palpable thrill and bruit may be present.
- The thrill and bruit result from the increased blood flow to the thyroid.
- Graves' disease is usually treated with anti-thyroid mediation in the first instance. During the administration of adequate therapy, the disease may be quiescent but may return if compliance diminishes or dosage is inappropriately reduced.
- As with many autoimmune conditions, Graves' disease is sometimes self-limiting and around 30 per cent of patients experience lasting remission after treatment.

**EXTRA-THYROIDAL MANIFESTATIONS OF GRAVES’ DISEASE**

**OPHTHALMOPATHY**

- Enlarged extraocular muscles. Patients who smoke are more likely to suffer eye disease.
- A feeling of **grittiness** and discomfort in the eye
- Retro bulbar pressure or pain
- Periorbital oedema, chemosis, scleral injection
- Exophthalmos (proptosis)
- Extra-ocular muscle dysfunction
- Exposure keratitis
- Optic neuropathy

**SIGNS**

- Wide palpebral aperture (**Dalrymple's sign**)
- Lid lag (**Von Graefe's sign**)
- Staring or frightened expression
- Infrequent blinking (**Stellwag's sign**)
- Absence of forehead wrinkling on upward gaze (**Joffroy's sign**)
- Inability to keep the eyeballs converged (**Mobius' sign**)
- Limitation of movement of the eyeballs, especially upward (**Ballet’s sign**)
- Fine tremor of the eye lid (**Rosenbach’s sign**)
- Tangential view (from patients back) shows protruding eyeballs (Nafziger’s Sign)
- Difficulty in passively everting upper eye lid (Gifford Sign)
- Becker’s Sign – on fundoscopy, abnormal retinal pulsations
- Diplopia
- Blurred vision due to inadequate convergence and accommodation
- Swelling of orbital contents and puffiness of the lids.
- Chemosis, corneal injection, or ulceration
- Visible and palpable enlargement of the lacrimal glands.
- Visible swelling of lateral rectus muscles as they insert into the globe, and injection of the overlying vessels.
- Compression of the sympathetic cervical ganglion due to massive goiter can lead to a Claude-Bernard-Horner Syndrome (enophthalmus, ptosis and miosis)
- Clinicians can estimate the activity and severity of thyroid eye disease using an internationally accepted scoring system.
- EUGOGO = European Group On Grave's Orbitopathy.
- Decreasing visual acuity and a loss of colour vision are ominous signs and maybe caused by pressure on the optic nerve by the swollen extraocular rectus muscles
- Severe opthalmopathy treated using Glucocorticoids, orbital irradiation or both.
- Orbital decompression is effective in patients with optic neuropathy

**DERMOPATHY**:
- Almost always accompanied by severe eye disease
- Pre tibial Myxoedema = Non-pitting oedema over shins
- May also occur at other sites including areas of trauma
- Skin becomes raised oedematous with a pink or brownish tinge.

**ACROPACHY**
- Very rare
- Clubbing of the fingers with sub-periosteal new bone formation

**LABORATORY DIAGNOSIS**
- fT3 and fT4 raised with undetectable TSH.
- Three thyroid auto antibodies may be measured in clinical practice, those against Thyroid Peroxidase (TPO), Thyroglobulin And TSH-Receptor.
- TPO antibodies positive in 90 percent cases (thyroglobulin – 49, TSH –R – 45)

**TOXIC MULTINODULAR GOITRE**
- At least two autonomously functioning thyroid nodules that secrete excess thyroid hormone, producing typical signs and symptoms of hyperthyroidism.
- Younger age groups, because of iodine deficiency.
In patients with underlying non-toxic multinodular goitre, pharmacological doses of iodine (e.g. from iodinated contrast agents), can lead to hyperthyroidism (iodine-induced hyperthyroidism or Jod-Basedow effect).

TOXIC ADENOMA (PLUMMER'S DISEASE)

EPIDEMIOLOGY AND AETIOLOGY

- A single toxic adenoma is a benign tumour autonomously secreting thyroid hormone.
- A mutation in the TSH receptor gene occurs in 20-83 percent, leading to autonomous function not under pituitary control.

CLINICAL MANIFESTATIONS
- Patients with a toxic adenoma are often younger than those with a toxic MNG, and present in the fourth or fifth decade.
- The level of thyroid hyperfunction is again less than is seen in Graves' disease, so the symptoms and signs may not be so florid.

TREATMENT OF HYPERTHYROIDISM

- Three modalities of treatment exist: Drug Therapy, Radioiodine Treatment And Surgery.

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<tr>
<th>Treatment</th>
<th>Advantages</th>
<th>Disadvantages</th>
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<tbody>
<tr>
<td>Thionamides</td>
<td>Rapid symptom relief, Inexpensive, Chance of remission, No exposure to radioactivity</td>
<td>Risk of severe side effects, Frequent clinic visits, Common mild side effects, Long course of treatment, High chance of relapse</td>
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<tr>
<td>Radioiodine</td>
<td>Definitive treatment, Outpatient procedure</td>
<td>Risk of hypothyroidism, Radiation protection measures, Radiation thyroiditis</td>
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<tr>
<td>Surgery</td>
<td>Definitive treatment, Histological diagnosis</td>
<td>Inpatient procedure, Risk of surgery, Permanent hypothyroidism, Risk of hypocalcaemia</td>
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- All three are equally effective.

ANTI-THYROID DRUGS

- Carbimazole and propylthiouracil (THIOAMIDES) (carbamazole faster and given OD)
PTU used only if patient develops adverse reactions to carbimazole or is not responding OR FIRST TRIMESTER OF PREGNANCY.

- Carbimazole ➔ 20 mg / day OD. In severe cases 30 mg /day
- PTU ➔ 200mg/day BD i.e. 100mg per dose.
- Optimal duration of treatment is 12 – 18 months
- They disrupt the thyroid's incorporation of iodine and thus control thyroid hormone synthesis.
- fT4, TSH measured regularly, ideally every 4-6 weeks initially, then 8-12 weekly once control is achieved.
- Some prefer “BLOCK AND REPLACE THERAPY” i.e. uses thionamides to completely block endogenous thyroid hormone production which is then replaced with Thyroxine.
- Carbimazole is teratogenic. The most common side effects are pruritic eruptions, fever, gastrointestinal upset and Arthralgias, Agranulocytosis, Vasculitis and Liver damage
- Propranolol 40 mg twice daily useful adjuncts to thionamides in the treatment of, thyroid hormone excess

**RADIOIODINE I^{131} TREATMENT**

- Treatment of choice for relapsed Graves’ disease and toxic nodular hyperthyroidism
- Treatment of autonomous thyroid nodules and to induce shrinkage of benign goitres.
- Radioiodine is administered orally as sodium I^{131} in a single capsule in the outpatient setting
- It is incorporated in thyroid tissue and the β-emissions result in lasting thyroid tissue damage.
- There is a lag effect with max ablation at 6 weeks to 4 months.
- Fifteen to 20 per cent of patients require a second or (rarely) third dose, given 6-12 months after initial treatment.
- Most, centers will administer a fixed dose of 400-600 MBq.
- Permanent hypothyroidism may occur many years later.
- I^{131} treatment is given when biochemical euthyroidism is restored.
- Thionamides are often restarted temporarily following I^{131} therapy to avoid exacerbation of hyperthyroidism due to radiation-related thyroiditis.
- Drug must be discontinued 1 week before radioiodine administration to allow max uptake into the gland.
- Radioiodine may worsen ophthalmopathy, especially in smokers. Most physicians delay administration of radioiodine until moderate or severe eye disease has been stable for 12 months. Pregnancy, Lactation, Mentally ill is absolute contraindication.

**SURGERY**

**THYROIDITIS**

- Thyroiditis refers to any inflammatory condition of the thyroid.
The classification of thyroiditis is confusing but may be divided into those processes in which pain and tenderness develop, and those which do not have pain as a predominant feature.

**Box 21.6: Classification of Thyroiditis**

1. Associated with pain and tenderness
   a. Subacute granulomatous thyroiditis
      (De Quervain's or giant cell thyroiditis)
   b. Infectious thyroiditis
   c. Radioiodine-induced thyroiditis

2. Not associated with pain and tenderness
   a. Subacute lymphocytic thyroiditis (silent)
      i. Postpartum thyroiditis
      ii. Drug-induced thyroiditis (e.g. lithium)
   b. Chronic lymphocytic thyroiditis
      i. Hashimoto's thyroiditis
      ii. Postpartum thyroiditis
   c. Fibrous thyroiditis (Riedel's thyroiditis)
   d. Amiodarone-induced thyroiditis

- Raised inflammatory markers (ESR, CRP)
- Initial thyrotoxicosis but after 12 to 16 weeks there might be hypothyroidism

**SUBCLINICAL HYPERTHYROIDISM**

- This is essentially a biochemical diagnosis consisting of low or undetectable serum TSH concentration with a normal serum fT4 and fT3 concentration. Subclinical hyperthyroidism may be **exogenous** as a consequence of treatment with thyroxine, or **endogenous** as a result of nodular thyroid disease or undetected early Graves' disease.
- Increased risk of AF and cardiovascular disease and loss of bone mineral density
- Anti-thyroid treatment should be considered in those with persistent suppression of TSH and evidence for underlying thyroid disease.
HYPOTHYROIDISM

Epidemiology

- Primary or secondary like Hyperthyroidism

Clinical Features

- Fatigue, cold intolerance and weight gain, coarse dry skin, hair loss and doughy peripheral oedema

Iatrogenic Hypothyroidism

Iatrogenic hypothyroidism may result from surgery, treatment with radioactive iodine and external beam radiotherapy in patients who have undergone treatment for head and neck malignancy.

- Overtreatment with anti-thyroid medication
- Iodine Deficiency related Thyroid, Central Hypothyroidism

Treatment of Hypothyroidism

- Thyroxine is the drug of choice for the treatment of hypothyroidism, absorbed from the upper small bowel.
- Thyroxine is a pro-hormone which is de-iodinated in peripheral tissues to the active hormone T3.
- The majority of patients require **100-125 ug daily** to achieve euthyroidism but variation exists.
- In cardiac patients starting dose shouldn’t be more than **25µg with increment of 25µg every 4 to 6 weeks**