Endocrinology
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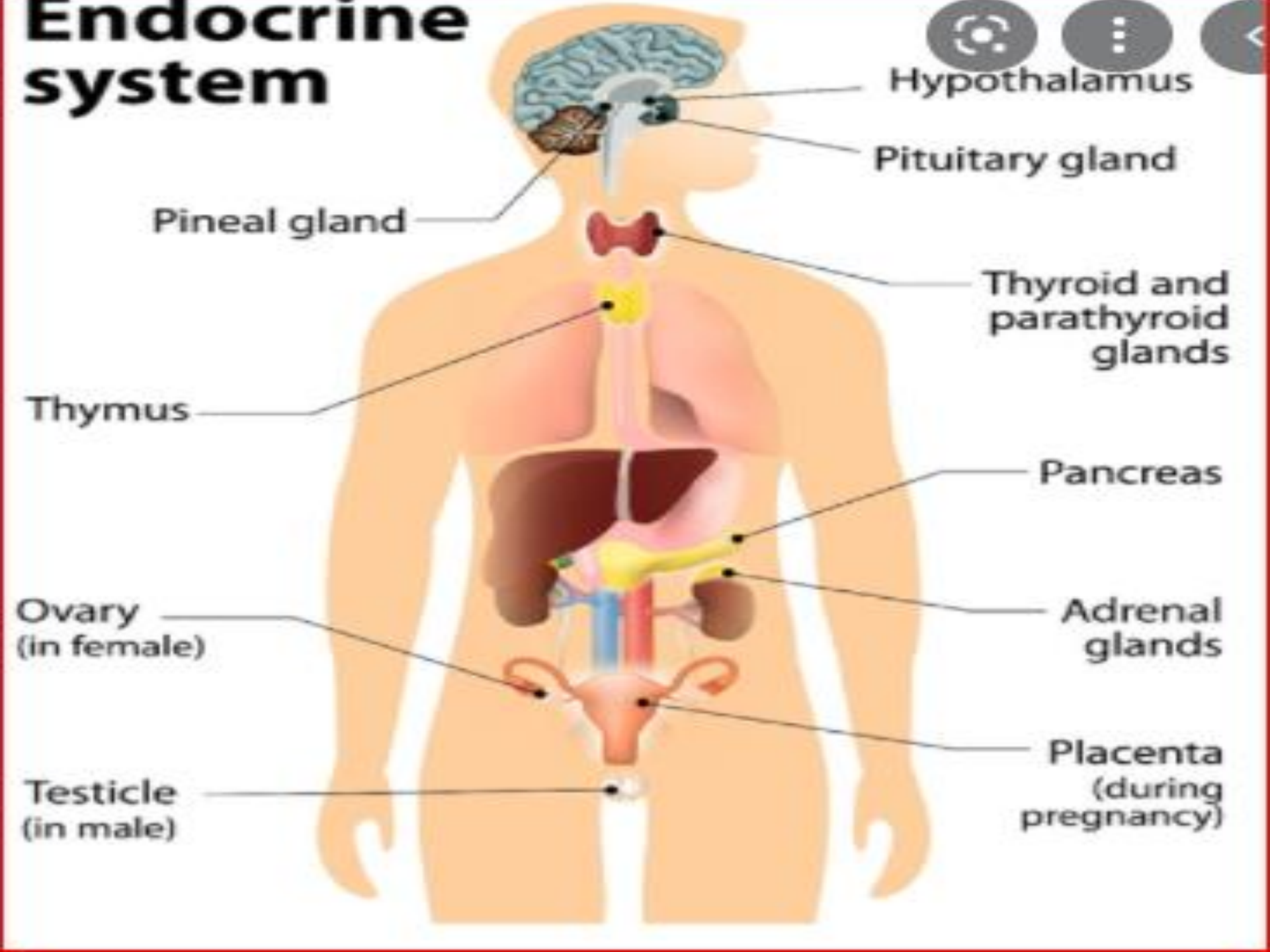
Endocrine system



Endocrinology

Endocrinology concerns the synthesis, secretion and action of hormones.

These are chemical messengers released from endocrine glands that coordinate the activities of many different cells.

hormones' function

- **Metabolism (break down food and get energy from nutrients).**
- **Growth and development.**
- **Emotions and mood.**
- **Fertility and sexual function.**
- **Sleep.**
- **Blood pressure.**
- **Body defense (immunity)**
- **Hemostasis and electrolyte distributions**

Endocrine diseases can therefore affect multiple organs and systems.

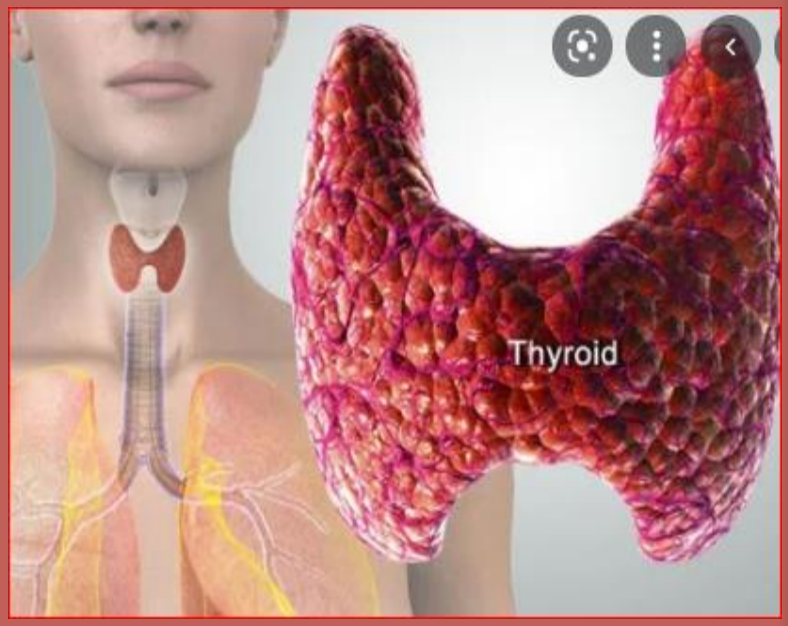
The classical model of endocrine function involves hormones which are synthesised in endocrine glands, are released into the circulation, and act at sites distant from those of secretion .

Many other organs secrete hormones or contribute to the peripheral metabolism and activation of prohormones.

Some hormones such as neurotransmitters act in a paracrine fashion to affect adjacent cells,or act in an autocrine way to affect behavior of the cell that produces the hormone.

- e.g.: **the cytokine interleukin-1 in monocytes**

THE THYROID GLAND



-Diseases of the thyroid predominantly affect females and are common, occurring in about 5% of the population.

-The thyroid axis is involved in the regulation of cellular differentiation and metabolism in all nucleated cells, so that disorders of thyroid function have diverse manifestations. .

FUNCTIONAL ANATOMY

- The follicular epithelial cells synthesise thyroid hormones by incorporating iodine into the amino acid tyrosine on the surface of thyroglobulin (Tg),
- Iodide is a key substrate for thyroid hormone synthesis;
- A dietary intake in excess of 150 µg/day-
- The thyroid secretes predominantly thyroxine (T4), and only a small amount of triiodothyronine (T3); approximately 85% of T3 in blood is produced from T4 by monodeiodinase enzymes which are active in many tissues including liver, muscle, heart and kidney.
- T4 can be regarded as a pro-hormone, since it has a longer half-life in blood than T3 (1 week compared with 18 hours) and binds and activates thyroid hormone receptors less effectively than T3.
- T4 can also be converted to the inactive metabolite, reverse T3

- The parafollicular C cells secrete calcitonin.

- -T3 and T4 circulate in plasma (> 99%) bound to transport proteins, mainly thyroxine-binding globulin (TBG).
- Unbound or free hormones(<1%) spread into tissues and have a variety of metabolic effects.
- it is possible to measure the concentration of total or free T3 and T4 in plasma,
- - The benefit of free hormone measures is that they are unaffected by changes in binding protein concentrations; for example, TBG levels rise during pregnancy.

- Production of T3 and T4 in the thyroid is stimulated by thyrotrophin (thyroid-stimulating hormone, TSH), a glycoprotein released from the thyrotroph cells of the anterior pituitary in response to the hypothalamic tripeptide, thyrotrophin-releasing hormone (TRH,).
- There is a negative feedback of thyroid hormones on the hypothalamus and pituitary such that in thyrotoxicosis, when plasma concentrations of T3 and T4 are raised, TSH secretion is suppressed. Conversely, in hypothyroidism due to disease of the thyroid gland, low T3 and T4 are associated with high circulating TSH levels.
- The anterior pituitary is very sensitive to minor changes in thyroid hormone levels within the normal range.
- For this reason, TSH is usually regarded as the most useful investigation of thyroid function.

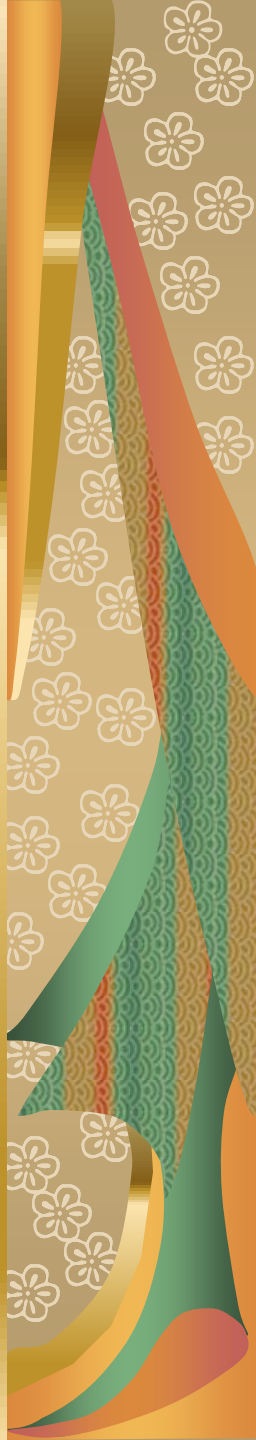
PRESENTING PROBLEMS IN THYROID DISEASE

- The most common presentations of thyroid disease are
- Thyrotoxicosis (i.e. hyperthyroidism), Hypothyroidism and Goitre (i.e. enlargement of the thyroid).
- -Asymptomatic
- -Non-specific complaints such as tiredness and weight gain

THYROTOXICOSIS

Aetiology

- In most patients, the thyrotoxicosis is due to
- Graves' disease,
- Multinodular goitre
- Autonomously functioning thyroid nodule (toxic adenoma).
- The prevalence of thyroiditis varies around the world according to likelihood of viral infections and therapy with amiodarone or iodine



THYROTOXICOSIS:Clinical assessment

- The most common symptoms are weight loss with a normal or increased appetite, heat intolerance, Warm, moist, smooth skin
- palpitations, tremor and irritability. Tachycardia, Systolic hypertension with wide pulse pressure,palmar erythema and lid lag are common signs. . Reduction in menstrual flow in female
- All causes of thyrotoxicosis can cause lid retraction and lid lag due to potentiation of sympathetic innervation of the levator palpebrae muscles,
- Only Graves' disease causes other features of ophthalmopathy, including periorbital oedema, conjunctival irritation, exophthalmos , diplopia and Pretibial myxoedema

THYROTOXICOSIS:Clinical assessment

- Thyrotoxicosis leads to increase in sympathetic nervous system symptoms. Younger patients tend to exhibit symptoms of sympathetic activation, such as anxiety, hyperactivity, and tremor, while older patients have more cardiovascular symptoms, including dyspnea and atrial fibrillation with unexplained weight loss. The clinical manifestations of thyrotoxicosis do not always correlate with the extent of the biochemical abnormality.

Thyrotoxicosis: investigations

It is important to confirm the presence of thyrotoxicosis biochemically by more than one test of thyroid function.

- - Serum T3 and T4 are elevated in the majority,
- -T4 is in the upper part of the normal range and T3 raised (T3 toxicosis) in 5% of patients.
- In primary thyrotoxicosis, serum TSH is undetectable at less than 0.05 mU/l.
- Further tests, which may be required to establish the etiology of thyrotoxicosis, include
- Measurement of TSH receptor antibodies (TRAb, elevated in Graves' disease.
- The most specific autoantibody test for autoimmune thyroiditis is anti–thyroid peroxidase (anti-TPO) antibody. significantly elevated in the most common type of hyperthyroidism, Graves thyrotoxicosis and 'Hashimoto's thyroiditis.
- Other non-specific abnormalities are common. An ECG may demonstrate tachycardia or atrial fibrillation

Thyrotoxicosis: investigations2

- -Radio-iodine uptake tests measure the proportion of isotope which is trapped in the whole gland,

In low-uptake thyrotoxicosis, the cause is usually a transient thyroiditis or Occasionally, patients induce 'factitious thyrotoxicosis.

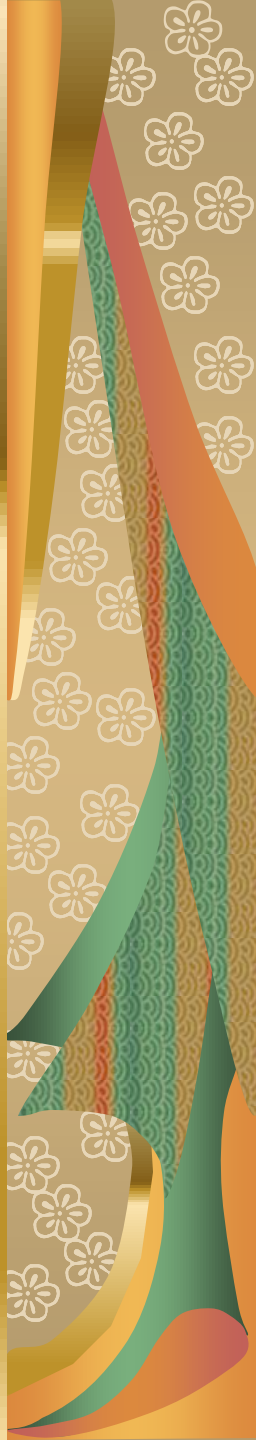
In **factitious thyrotoxicosis**: The exogenous thyroxine suppresses pituitary TSH secretion and hence iodine uptake, suppresses serum thyroglobulin and endogenous thyroid hormones.

The T4:T3 ratio (typically 30:1) while in **factitious thyrotoxicosis**) is increased to above 70:1

-The combination of negligible iodine uptake, high T4:T3 ratio and a low or undetectable thyroglobulin is diagnostic for 'factitious thyrotoxicosis

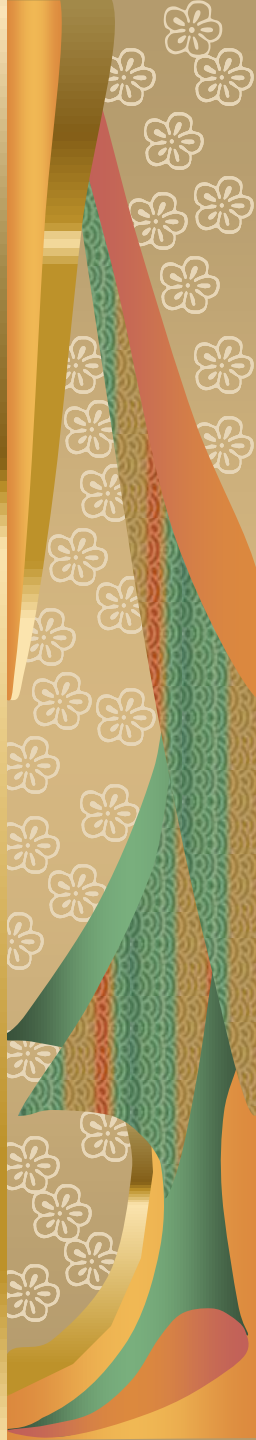
Thyrotoxicosis :management

- Definitive treatment of thyrotoxicosis depends on the underlying cause, and may include
- Antithyroid drugs
- Radioactive iodine
- Surgery.
- In all patients with thyrotoxicosis a non-selective β-adrenoceptor antagonist **(β-blocker**), such as propranolol (160 mg daily) or nadolol (40-80 mg daily) is affective



Atrial fibrillation in thyrotoxicosis

- -Thyrotoxicosis is an important cause of atrial fibrillation. -atrial fibrillation is present in about 10% of all patients.
- - The incidence increases with age so that almost half of all males with thyrotoxicosis over the age of 60 are affected,
- -the ventricular rate is little influenced by digoxin, but responds to the addition of a β-blocker.
- Once thyroid hormone and TSH concentrations have been returned to normal, atrial fibrillation will spontaneously revert to sinus rhythm in ~50% of patients. In the remainder, cardioversion will restore sinus rhythm in up to 50%



Thyrotoxic crisis ('thyroid storm)

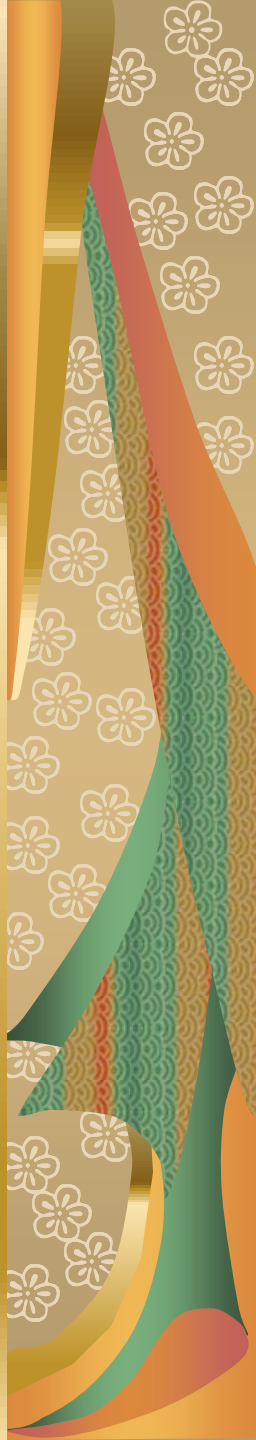
- This is a rare and life-threatening increase in the severity of the clinical features of thyrotoxicosis.
- The most prominent signs are fever, agitation, confusion, tachycardia or atrial fibrillation and, in the older patient, cardiac failure.
- It is a medical emergency and, despite early recognition and treatment, the mortality rate is 10%.
- Thyrotoxic crisis is most commonly precipitated by
- Infection in a patient with previously unrecognised or inadequately treated thyrotoxicosis.
- Shortly after subtotal thyroidectomy in an ill-prepared patient

within a few days of 131I therapy

- Fever > 38.5ºc
- Tachycardia
- Confusion and agitation
- Nausea and vomiting
- Hypertension
- Heart failure
- Abnormal liver function test

Thyroid storm: treatment

- Patients should be
- Rehydrated
- Ggiven a broad-spectrum antibiotic.
- Propranolol is rapidly effective orally (80 mg 6-hourly) or intravenously (1-5 mg 6-hourly).
- Sodium ipodate (500 mg per day orally) will restore serum T3 levels to normal in 48-72 hours. This is a radiographic contrast medium which not only inhibits the release of thyroid hormones, but also reduces the conversion of T4 to T3 and is, therefore, more effective than potassium iodide or Lugol's solution.
- -Dexamethasone (2 mg 6-hourly) and amiodarone have similar effects.
- Oral carbimazole 40-60 mg daily.
- If the patient is unconscious or uncooperative, carbimazole can be administered rectally with good effect, but no preparation is available for parenteral use. After 10-14 days the patient can usually be maintained on carbimazole alone



AUTOIMMUNE THYROID DISEASE

- Thyroid diseases are amongst the most prevalent antibody-mediated autoimmune diseases and are associated with other organ-specific autoimmunity Autoantibodies may produce;
- Inflammation and destruction of thyroid tissue resulting in hypothyroidism, goitre (in Hashimoto's thyroiditis) or sometimes even transient thyrotoxicosis ('Hashitoxicosis'),
- or they may stimulate the TSH receptor to cause thyrotoxicosis (in Graves' disease).
- There is overlap between these conditions, since some patients have multiple autoantibodies

Thyroid antibodies:

- **Thyroid peroxidase antibodies (TPOAb) :** Hashimoto's thyroiditis
- **Thyrotropin receptor antibodies (TRAb):** Graves' disease
- **Thyroglobulin antibodies (TgAb) and thyroglobulin.** Thyroid cancer

GRAVES' DISEASE

- The most common manifestation is thyrotoxicosis with or without a diffuse goitre.
- Graves' disease also causes ophthalmopathy and rarely pretibial myxoedema
- Graves' disease can occur at any age but is unusual before puberty and most commonly affects women aged 30-50 years

Pathophysiology

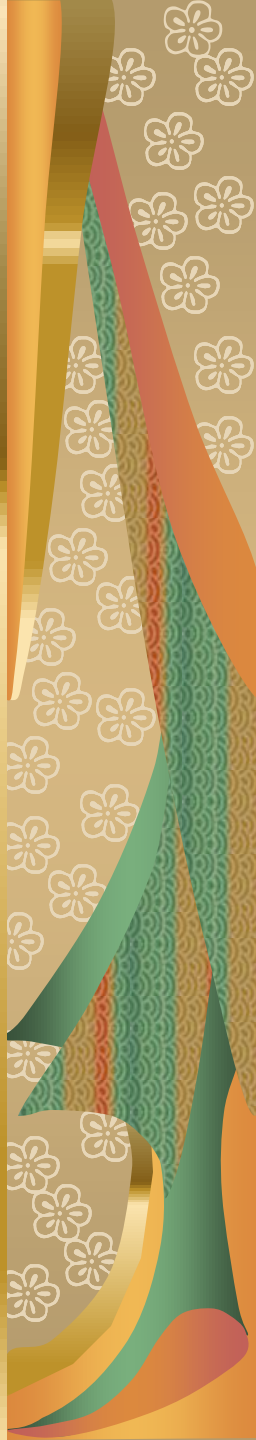
- **IgG** antibodies directed against the TSH receptor on the thyroid follicular cell
- These antibodies are termed thyroid-stimulating immunoglobulins or TSH receptor antibodies (TRAb) and can be detected in the serum of 80-95% of patients with Graves' disease.
- The concentration of TRAb in the serum is presumed to fluctuate.
- The ultimate thyroid failure seen in some patients is thought to result from the presence of blocking antibodies against the TSH receptor, and from tissue destruction by cytotoxic antibodies and cell-mediated immunity .

GRAVES' DISEASE cont.

- The trigger for the development of thyrotoxicosis in genetically susceptible individuals may be - infection with viruses or bacteria, Certain strains of the gut organisms Escherichia coli and Yersinia enterocolitica.
- In regions of iodine deficiency, iodine supplementation may result in the development of thyrotoxicosis, but only in those with pre-existing subclinical Graves' disease.
- Smoking is weakly associated with

Graves' thyrotoxicosis, but strongly linked with the development of ophthalmopathy .

- Patients with Graves disease often have more marked symptoms than patients with thyrotoxicosis from other causes



GRAVES' DISEASE: management

-Symptoms of thyrotoxicosis respond to β-blockade

-it would be appropriate to give an antithyroid drug for 12-18 months in whom a single episode was anticipated,

-destructive therapy with 131I or surgery for those likely to experience recurrent disease.

-persistent thyrotoxicosis is more likely in patients who are male, have large goitres, severe thyrotoxicosis and persistently high TRAb titres.

-For patients under 40 years of age many centres adopt the empirical approach of prescribing a course of carbimazole and recommending surgery if relapse occurs,

while 131I is employed as first or second-line treatment in those aged over 40.;

-younger people are more sensitive to radiation-induced thyroid cancer.

Antithyroid drugs

The most commonly used are carbimazole and its active metabolite, (methimazole) ,and Propylthiouracil

Reduce the synthesis of new thyroid hormones by inhibiting the iodination of tyrosine.

-Carbimazole also has an immunosuppressive action

-Antithyroid drugs are introduced at high doses, e.g. carbimazole 40-60 mg daily or prophylthiouracil 400-600 mg daily.

-subjective improvement within 10-14 days

-clinically and biochemically euthyroid at 3-4 weeks, when the dose can be reduced.

-The maintenance dose is determined by measurement of T4 and TSH, attempting to keep both hormones within their respective reference ranges.

-In most patients carbimazole taken daily dose and is continued for 12-18 months in the hope that during this period permanent remission will occur

.

-thyrotoxicosis recurs in at least 50%, usually within 2 years.

-Rarely, despite good drug compliance, T4 and TSH levels fluctuate between thyrotoxicosis and hypothyroidism

-The adverse effects of antithyroid drugs develop within 7-28 days of starting treatment.

-Allergic reactions(Rash) is common. Agranulocytosis is rare but fortunately is reversible. aplastic anemia, hepatitis, polyarthritis, and a lupuslike vasculitis

propylthiouracil are used for long-term control of hyperthyroidism in children, adolescents, and pregnant women

Methimazole is more potent than propylthiouracil and has a longer duration of action. In addition, methimazole is taken once daily,

Methimazole is not recommended for use in the first trimester of pregnancy.

whereas propylthiouracil is taken two to three times daily; consequently, patient compliance is often better with methimazole than with propylthiouracil.

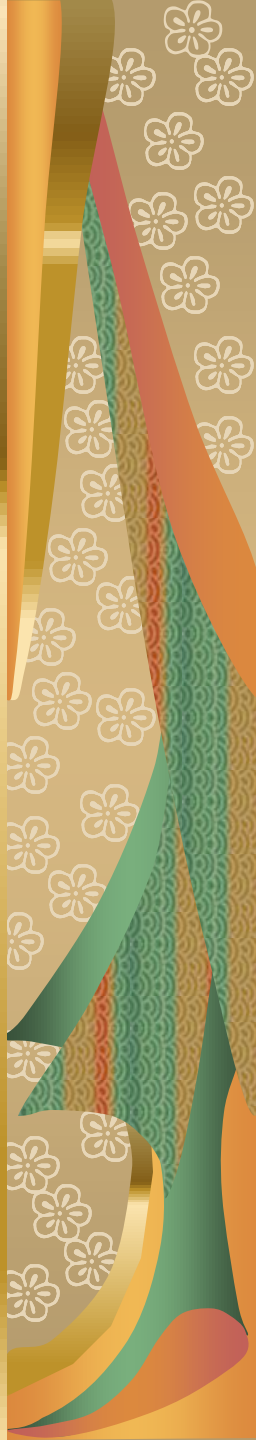
The antithyroid drug dose should be titrated every 4 weeks until thyroid functions normalize.

Radioactive iodine

- Administered orally as a single dose and is trapped and organified in the thyroid.
- Although it will decay within the thyroid in a few weeks, the effects of its radiation are long-lasting, with cumulative effects on follicular cell survival and replication.
- This regimen is effective in 75% of patients within 4-12 weeks.
- During the lag period, symptoms can be controlled by a β-blocker or, in more severe cases, by carbimazole(should be avoided until 48 hours after radio-iodine administration).
- If thyrotoxicosis persists after 12-24 weeks, a further dose of 131I should be employed.
- -The disadvantage of 131I treatment is that the majority of patients eventually develop hypothyroidism and long-term follow-up is, therefore, necessary

Subtotal thyroidectomy

- Patients must be rendered euthyroid with antithyroid drugs before operation.
- Potassium iodide, 60 mg 8-hourly orally, is often added for 2 weeks before surgery to inhibit thyroid hormone release and reduce the size and vascularity of the gland,
- Complications of surgery are rare. One year after surgery, 80% of patients are euthyroid, 15% are permanently hypothyroid and 5% remain thyrotoxic. Thyroid failure within 6 months of operation may be temporary.
- Long-term follow-up of patients treated surgically is necessary, as the late development of hypothyroidism



Graves ' ophthalmopathy

This condition is immunologically mediated

There is cytokine-mediated proliferation of fibroblasts which secrete hydrophilic glycosaminoglycans.

The eye is displaced forwards (proptosis, exophthalmos) and in more severe cases there is optic nerve compression Ophthalmopathy,

Eye disease is detectable in ~50% of patients when first seen with thyrotoxicosis,

It is more common in cigarette smokers and is exacerbated by poor control of thyroid function, especially hypothyroidism.

The most frequent presenting symptoms are related to increased exposure of the cornea, There may be excessive lacrimation made worse by wind and bright light,

- a 'gritty' sensation in the eye, and pain due to conjunctivitis or .corneal ulceration

Graves ' ophthalmopathy

There may be reduction of visual acuity and/or visual fields as a consequence of corneal edema or optic nerve compression.

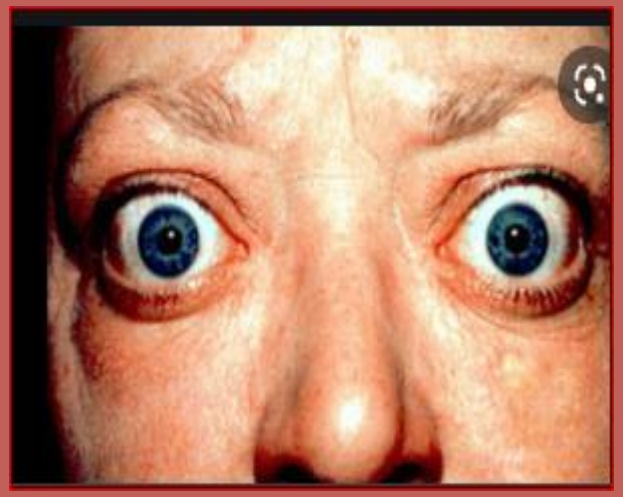
If the extraocular muscles are involved and do not act in concert, diplopia results .

The majority of patients require no treatment other than reassurance.

Methylcellulose eye drops and gel counter the gritty discomfort of dry eyes,

Severe inflammatory episodes are treated with oral glucocorticoids (e.g. prednisolone 60 mg daily) and sometimes orbital irradiation.

Loss of visual acuity is an indication for urgent surgical decompression of the orbit.



Gravie's ophthalmopathy is **inflammatory process of the eyes** cause soft tissue involvement(periorbital edema, congestion, and swelling of the conjunctiva), proptosis (anterior deplacement of the eye), extraocular muscle involvement leading to double-vision (diplopia), corneal lesions

Pretibial myxedema

- This infiltrative dermopathy(glycosaminoglycans) occurs in fewer than 10% of patients with Graves' disease
- It takes the form of raised pink-coloured or purplish plaques on the anterior aspect of the leg, extending on to the dorsum of the foot.
- The lesions nonpitting edema may be itchy and the skin may have a 'peau d'orange' appearance with growth of coarse hair
- Less commonly, the face and arms may be affected.
- Treatment is rarely required, but in severe cases topical glucocorticoids may be helpful

Thyrotoxicosis in pregnancy

- Gestational transient thyrotoxicosis (GTT), which occurs from the stimulatory action of human chorionic gonadotropin (HCG) on the TSH receptor.< 1%
- The coexistence of pregnancy and thyrotoxicosis is unusual
- Thyroid function tests must be interpreted in the knowledge that thyroid-binding globulin, and hence total T4 and T3 levels, are increased in pregnancy and that TSH normal ranges may be lower.
- A fully suppressed TSH with elevated free thyroid hormone levels indicates thyrotoxicosis.
- The thyrotoxicosis is almost always caused by Graves' disease.
- Both mother and fetus must be considered, TRAb and antithyroid drugs can all cross the placenta to some degree, exposing the fetus to risks of thyrotoxicosis, iatrogenic hypothyroidism and goiter.

Thyrotoxicosis in pregnancy

- Thyrotoxicosis is treated with antithyroid drugs which cross the placenta and also treat the fetus,
- Propylthiouracil may be preferable to carbimazole since the latter has been associated with a skin defect in the child known as aplasia cutis.
- It is important to use the smallest dose of antithyroid drug (optimally less than 150 mg propylthiouracil per day).
- TRAb levels can be measured in the third trimester. When TRAb levels are not elevated, the antithyroid drug can be discontinued 4 weeks before the expected date of delivery to avoid any possibility of fetal hypothyroidism at the time of maximum brain development.
- After delivery, propylthiouracil is the drug of choice
- If subtotal thyroidectomy is necessary, it is most safely performed in the second trimester.
- Radioactive iodine is absolutely contraindicated as it invariably induces fetal hypothyroidism

aplasia cutis

HASHIMOTO'S THYROIDITIS

- Hashimoto thyroiditis is part of the spectrum of autoimmune thyroid diseases (AITDs) and is characterized by the destruction of thyroid cells by various cell- and antibody-mediated immune processes. This condition is the most common cause of hypothyroidism.

- The term 'Hashimoto's thyroiditis' for patients with positive thyroid peroxidase autoantibodies and a firm goitre who may or may not be hypothyroid,
- Spontaneous atrophic hypothyroidism' for hypothyroid patients without a goitre in whom TSH receptor-blocking antibodies positive is specific for 'Hashimoto's thyroiditis.These syndromes can both be considered as variants of Hashimoto's thyroiditis since both are characterized by destructive lymphoid infiltration of the thyroid, ultimately leading to a varying degree of fibrosis which accounts for the varying degree of thyroid enlargement.

- Hashimoto's thyroiditis increases in incidence with age and affects 3.5 per 1000 women and 0.8 per 1000 men each year.
- Many present with a small or moderately sized diffuse goitre, which is firm or rubbery in consistency. The goitre may be soft.

HASHIMOTO'S THYROIDITIS cont.

- Around 25% of patients are hypothyroid at presentation. In the remainder, serum T4 is normal and TSH normal or raised, but these patients are at risk of developing overt hypothyroidism in future years.

- Thyroid peroxidase antibodies (anti-TPO)
- are present in the serum in > 90% of patients with Hashimoto's thyroiditis. It is the most specific autoantibody test for autoimmune thyroiditis.
- In those under the age of 20 years, antinuclear factor (ANF) may also be positive.
- Anti-Tg (anti-thyroglobulin) antibodies delineates the cause of hypothyroidism as Hashimoto thyroiditis or its variant;
- 10-15% of patients with Hashimoto thyroiditis may be antibody negative
- Hashimoto thyroiditis is a histologic diagnosis fine-needle aspiration of thyroid nodules to exclude malignancy or the presence of a thyroid lymphoma in fast-growing goiters.

Rx

- Thyroxine therapy is indicated not only for hypothyroidism, but also sometimes for goitre shrinkage., the dose of thyroxine should be sufficient to suppress serum TSH to low but detectable levels

TRANSIENT THYROIDITIS SUBACUTE (DE QUERVAIN'S) THYROIDITIS

Classical painful form, subacute thyroiditis is a virus-induced (e.g. Coxsackie, mumps or adenovirus) transient inflammation of the thyroid gland.

There is pain in the region of the thyroid that may radiate to the angle of the jaw and the ears, and is made worse by swallowing, coughing and movement of the neck. The thyroid is usually palpably enlarged and tender.

Systemic upset is common. Affected patients are usually females aged 20-40 years .

Painless transient thyroiditis also occurs, sometimes after viral infection and sometimes in patients with underlying autoimmune disease.

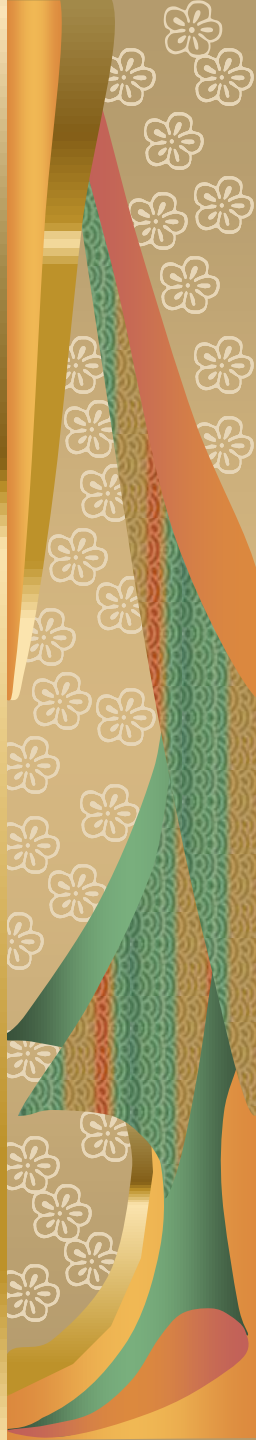
In both painless and painful varieties, inflammation in the thyroid gland is associated with release of colloid and stored thyroid hormones, but also with damage to follicular cells and impaired synthesis of new thyroid hormones.

As a result, T4 and T3 levels are raised for 4-6 weeks until the pre-formed colloid is depleted. Thereafter, there is usually a period of hypothyroidism of variable severity before the follicular cells recover and normal thyroid function is restored within 4-6 months

-In the thyrotoxic phase, the iodine uptake is low because the damaged follicular cells are unable to trap iodine and because endogenous TSH secretion is suppressed.

-Low-titre thyroid autoantibodies appear transiently in the serum, and the erythrocyte sedimentation rate (ESR) is usually raised.

-High titre autoantibodies suggest an underlying autoimmune pathology and risk of recurrence and ultimate progression to hypothyroidism



DE QUERVAIN'S THYROIDITIS Management

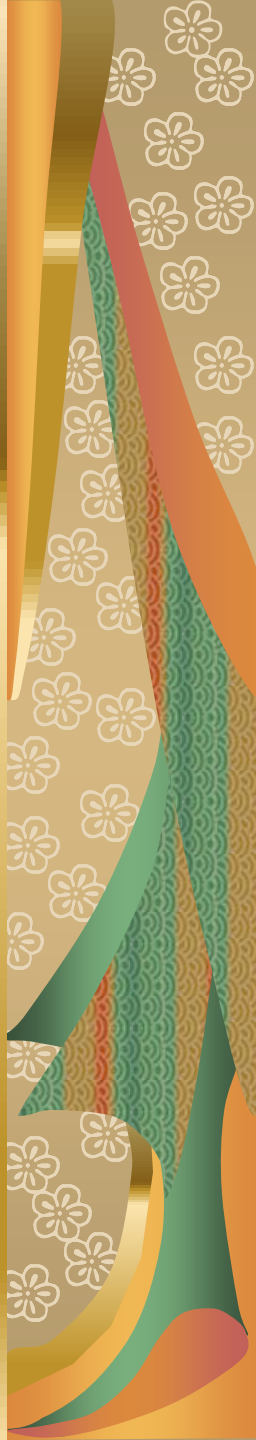
The pain and systemic upset usually respond to simple measures such as non-steroidal anti-inflammatory drugs (NSAIDs).

it may be necessary to prescribe prednisolone 40 mg daily for 3-4 weeks.

The thyrotoxicosis is mild and treatment with propranolol or nadolol is usually adequate.

Antithyroid drugs are of no benefit because thyroid hormone synthesis is impaired rather than enhanced. Careful monitoring of thyroid function and symptoms is required so that thyroxine can be prescribed temporarily in the hypothyroid phase.

Care must be taken to identify patients presenting with hypothyroidism who are in the later stages of a transient thyroiditis, since they are unlikely to require life-long thyroxine therapy.



POST-PARTUM THYROIDITIS

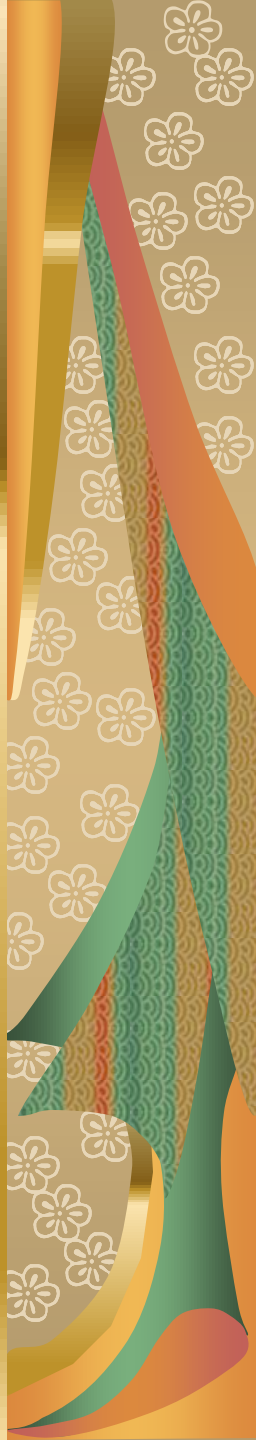
The maternal immune response, which is modified during pregnancy to allow survival of the fetus, is enhanced after delivery and may unmask previously unrecognised subclinical autoimmune thyroid disease.

occur in 5-10% of women within 6 months of delivery. Those affected are likely to have antithyroid peroxidase antibodies in the serum in early pregnancy.

- symptomatic thyrotoxicosis presenting for the first time within 6 months of childbirth is likely to be due to post-partum thyroiditis and the diagnosis is confirmed by radio-isotope uptake.
- The clinical course and treatment are similar to painless subacute thyroiditis.
- Post-partum thyroiditis tends to recur after subsequent pregnancies and eventually patients progress over a period of years to permanent hypothyroidism

IODINE-ASSOCIATED THYROID DISEASE

- In certain mountainous parts of the world, such as, the Himalayas and central Africa, where there is dietary iodine deficiency, thyroid enlargement is common (more than 10% of the population) and is known as endemic goitre.
- Most patients are euthyroid and have normal or raised TSH levels. In general, the more severe the iodine deficiency, the greater the incidence of hypothyroidism.
- Iodine supplementation programmes have abolished this condition in most developed regions.



IODINE-INDUCED THYROID DYSFUNCTION

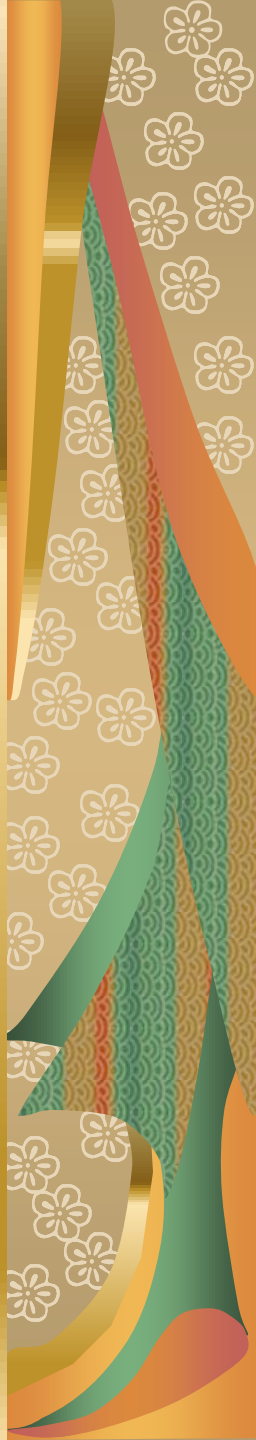
iodine administration can initially enhance, and subsequently inhibit, iodination of tyrosine and hence thyroid hormone synthesis.

In iodine-deficient parts of the world, transient thyrotoxicosis may be precipitated by prophylactic iodinisation programmes.

In iodine-sufficient areas, thyrotoxicosis can be precipitated by radiographic contrast medium or expectorants in individuals who have underlying thyroid disease predisposing to thyrotoxicosis, such as multinodular goitre or Graves' disease in remission.

Chronic excess iodine administration can, however, result in hypothyroidism. Increased iodine within the thyroid gland down-regulates iodine trapping so that uptake is low in all circumstances.

Iodine can act as an immune stimulator, precipitating autoimmune thyroid disease and acting as a substrate for additional thyroid hormone synthesis

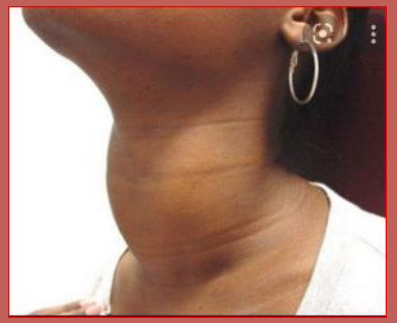


AMIODARONE

- The anti-arrhythmic agent amiodarone has a structure that is analogous to thyroxine
- Contains huge amounts of iodine; a 200 mg dose contains 75 mg iodine, compared with a daily dietary requirement of just 150 µg.
- Amiodarone has a cytotoxic effect on thyroid follicular cells and
- inhibits conversion of T4 to T3.
- Most patients receiving amiodarone have normal thyroid function, but up to 20% develop hypothyroidism or thyrotoxicosis.
- The ratio of T4:T3 is elevated and TSH provides the best indicator of thyroid function.

SIMPLE DIFFUSE GOITRE

- This form of goitre usually presents between the ages of 15 and 25 years, often during pregnancy, and tends to be noticed, not by the patient, but by friends and relatives.
- There is a tight sensation in the neck, particularly when swallowing. The goitre is soft and symmetrical and the thyroid is enlarged to two or three times its normal size- There is no tenderness, lymphadenopathy or overlying bruit. -T3, T4 and TSH are normal and no thyroid autoantibodies detected in the serum.
- No treatment is necessary and in most cases the goitre regresses.



MULTINODULAR GOITRE

- In Patients with 'simple goitre the unknown stimulus to thyroid enlargement persists and, as a result of recurrent episodes of hyperplasia and involution during the following 10-20 years, the gland becomes multinodular with areas of autonomous function
- Complete suppression of TSH occurs in about 25% of cases, with T4 and T3 levels often within the normal range (subclinical thyrotoxicosis, but sometimes elevated (toxic multinodular goitre,.
- The nodules represent multiple adenomas or focal hyperplasia.
- The prevalence of foci of thyroid cancer is increased in multinodular goitres, but for practical purposes patients can be reassured that it is a benign condition and malignancy need only be considered in patients with a large 'dominant' nodule that is 'cold' (i.e. does not take up radioisotope

Multinodular Goiter Clinical features &investigations

- Multinodular goiter is usually diagnosed in patients presenting with thyrotoxicosis, a large goiter with or without tracheal compression, or sudden painful swelling caused by haemorrhage into a nodule or cyst.
- The goiter is nodular or lobulated on palpation and may extend retrosternally.
- Very large goiters may cause mediastinal compression with stridor, dysphagia and obstruction of the superior vena cava. -Hoarseness due to recurrent laryngeal nerve palsy can occur, but is more suggestive of thyroid carcinoma
- The diagnosis is confirmed by a radioisotope thyroid scan

and/or ultrasonography., but CT or MRI of the thoracic inlet is optimal to quantify the degree of tracheal displacement or compression and the extent of retrosternal extension.

- In those with a 'dominant', 'cold' nodule, fine needle aspiration is indicated to exclude thyroid cancer

Goiter Management

- If the goiter is small, no treatment is necessary but annual review should be arranged as the natural history is progression to a toxic multinodular goiter. Partial thyroidectomy is indicated for large goiters which cause mediastinal compression or which are cosmetically unattractive.
- 131I can result in a significant reduction in thyroid size and may be of value in elderly patients.. Thyroxine is of no benefit in shrinking multinodular goiters .
- In toxic multinodular goiter treatment is usually with 131I. The iodine uptake is lower than in Graves' disease so a higher dose is employed and hypothyroidism is less common.
- In thyrotoxic patients with a large goiter, partial thyroidectomy may be indicated. Long-term treatment with antithyroid drugs is not usually appropriate as relapse is invariable after drug withdrawal .

Asymptomatic patients with subclinical thyrotoxicosis-

being treated with 131I on the grounds that a suppressed TSH is a risk factor for atrial fibrillation particularly in post-menopausal women,