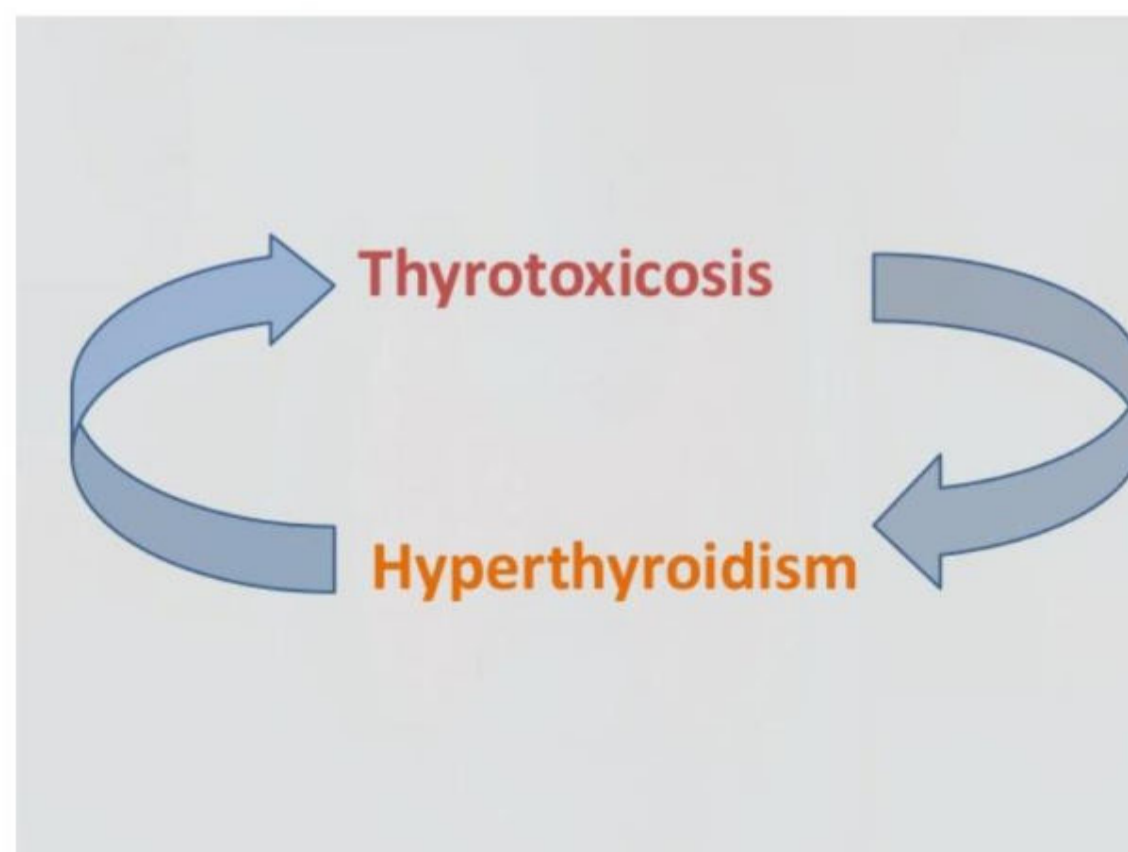


# THYROTOXICOSIS

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## Thyrotoxicosis Vs Hyperthyroidism

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# Thyrotoxicosis Vs Hyperthyroidism

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## .Thyrotoxicosis

Biochemical and physiological manifestation of Excessive thyroid hormone (irrespective of source).

Thyrotoxicosis need not be due to hyperthyroidism.

But hyperthyroidism mostly produce thyrotoxicosis.

## .Hyperthyroidism

Disorder that result in over production of hormone by the thyroid gland.

In short, hyperthyroidism the pathology is in the thyroid gland itself.

# Thyrotoxicosis Vs Hyperthyroidism

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## HYPERTHYROIDISM

- Grave's disease
- Multi-nodular toxic goitre
- Toxic adenoma
- Jod – Basedow's disease

## TOXICOSIS WITHOUT HYPERTHYROIDISM

- Subacute thyroiditis
- Ectopic functioning thyroid
- Silent thyroiditis
- Struma ovarii
- Metastatic follicular carcinoma
- Trophoblastic tumours
- Postpartum thyroiditis
- Thyrotoxicosis factitia

# Diffuse toxic goitre....

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- .Also known as Graves' disease after Robert Graves, an Irish physician who described three patients in 1835.
- .An autoimmune disease with a strong familial predisposition.
- .Female preponderance (5:1).
- .Peak incidence between the ages of 40 to 60 years.
- .Characterized by:
  - Thyrotoxicosis
  - Diffuse goitre
  - Extrathyroidal conditions - Ophthalmopathy/ Dermopathy (Pretibial Myxoedema)/ Thyroid Acropachy/ Gynecomastia.

# Diffuse toxic goitre....

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## .Etiology:

Exact etiology of the initiation of the autoimmune process is not known.

Possible triggering events:

- Postpartum state
- Iodine excess
- lithium therapy
- and bacterial and viral infections.

Genetic factors also play a role-*HLA-B8*, *HLA-DR3* and *HLADQA1\*0501*.

# Diffuse toxic goitre....

## Pathogenesis:

Stimulate B lymphocytes, which produce antibodies directed against the TSH-receptor.

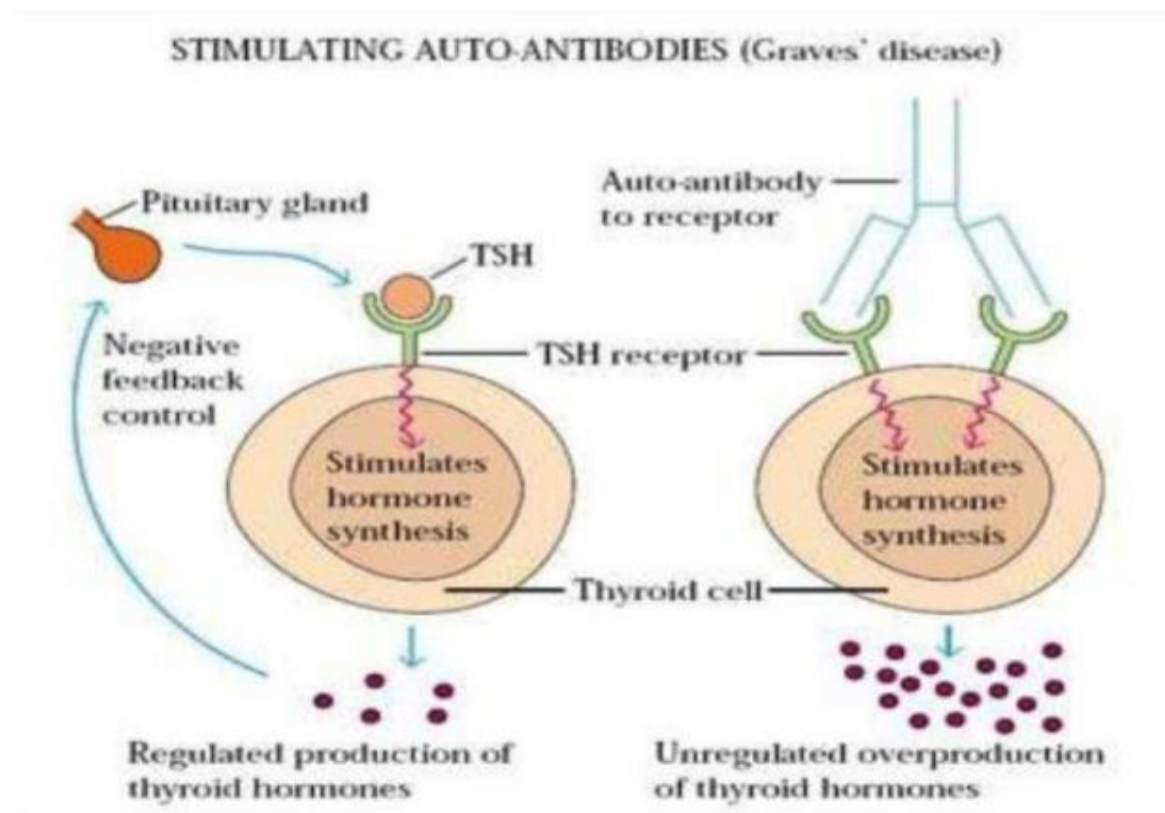
Thyroid stimulating Igs (TSIs) or antibodies that stimulate the TSH-R, as well as TSH-binding inhibiting immunoglobulins or antibodies have been described.

Thyroid-stimulating antibodies stimulate the thyrocytes to grow and synthesize excess thyroid hormone (hallmark of Graves' disease).

Graves' disease also is associated with other autoimmune conditions such as-

- type I diabetes mellitus, Addison's disease, pernicious anaemia, and myasthenia gravis.

# Diffuse toxic goitre....



# Diffuse toxic goitre

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## .Pathology:

### Macroscopically:-

- Thyroid gland is diffusely and smoothly enlarged
- With a concomitant increase in vascularity.

### Microscopically:-

- Gland is hyperplastic
- Epithelium is columnar with minimal colloid present.
- Nuclei exhibit mitosis
- And papillary projections of hyperplastic epithelium are common.

# Diffuse toxic goitre....

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## .Clinical manifestation: Divided into-

Related to hyperthyroidism.

And specific to Graves' disease.

# Diffuse toxic goitre....

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## Hyperthyroid symptoms:

Heat intolerance.

Increased sweating and thirst.

Weight loss despite adequate caloric intake.

Symptoms of increased adrenergic stimulation- palpitations, nervousness, fatigue, emotional lability, hyperkinesia, and tremors.

Most common GI symptoms include increased frequency of bowel movements and diarrhea.

Female patients- amenorrhea, decreased fertility, and an increased incidence of miscarriages.

Children- experience rapid growth with early bone maturation.

Older patients -cardiovascular complications such as atrial fibrillation and congestive heart failure.

# Diffuse toxic goitre....

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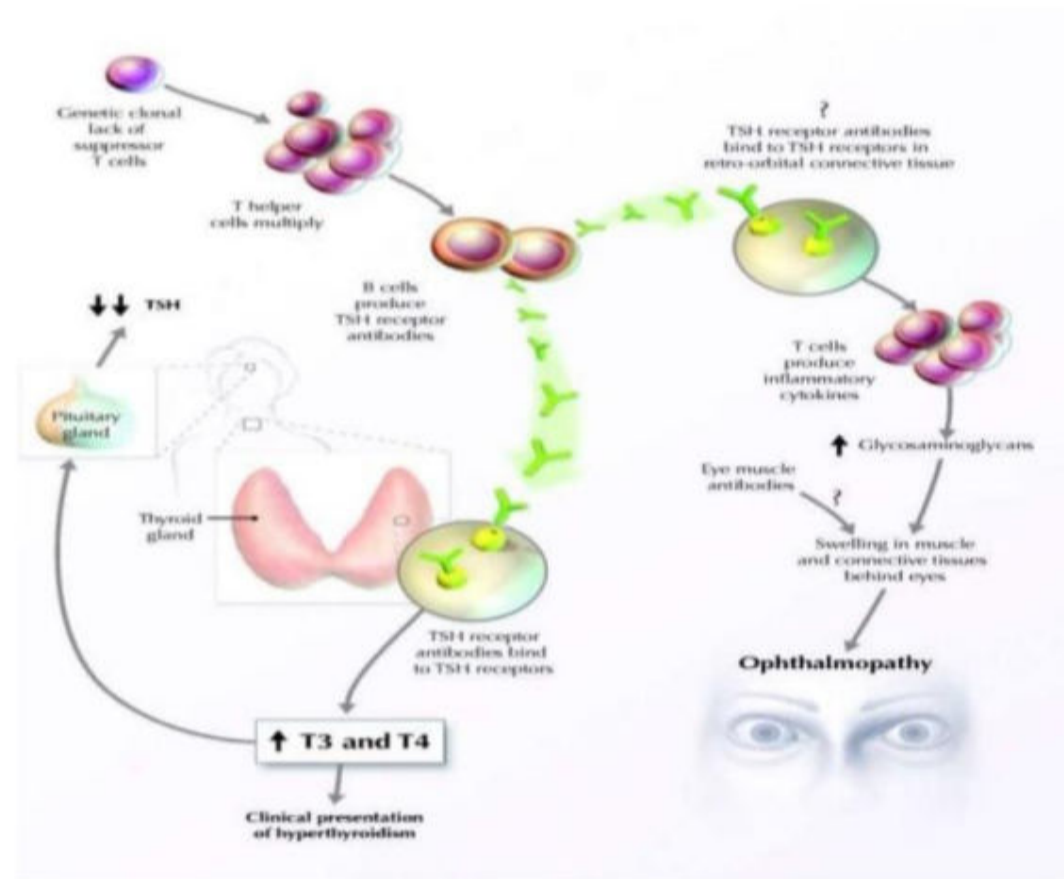
## Other manifestation of Grave's:

Approximately 50% of patients also develop clinically evident ophthalmopathy.

Eye signs:(due to catecholamine excess)

- Lid lag (von Graefe's sign)
- Spasm of the upper eyelid revealing the sclera above the corneo-scleral limbus (Dalrymple's sign)
- And prominent stare.

# Diffuse toxic goitre....



# Diffuse toxic goitre

• True infiltrative eye disease results in:

Periorbital edema.

Conjunctival swelling and congestion (chemosis).

Proptosis.

Limitation of upward and lateral gaze (from involvement of the inferior and medial rectus muscles, respectively).

Keratitis.

And even blindness due to optic nerve involvement.



# Diffuse toxic goitre....

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## Other manifestation of Grave's:

Dermopathy occurs in 1 to 2% of patients.

Rare bony involvement leads to subperiosteal bone formation and swelling in the metacarpals (Thyroid Acropachy).

Onycholysis, or separation of fingernails from their beds.



# Diffuse toxic goitre

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## Clinical signs:

Weight loss and facial flushing may be evident.

Skin- warm and moist and darkening of skin.

### Cardiovascular:

- Tachycardia or atrial fibrillation.
- Cutaneous vasodilation leading to a widening of the pulse pressure and a rapid falloff in the transmitted pulse wave (collapsing pulse).



# Diffuse toxic goitre

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## Clinical signs:

### Musculoskeletal:

- Fine tremor, muscle wasting.
- and proximal muscle group weakness with hyperactive tendon reflexes often are present.

### Thyroid:

- Diffusely and symmetrically enlarged, as evidenced by an enlarged pyramidal lobe.
- Overlying bruit or thrill and loud venous hum in the supraclavicular space.

# Diffuse toxic goitre....

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## Diagnostic Tests:

Suppressed TSH with elevated free T4 or T3 level.

If eye signs are present- other tests are generally not needed.

In the absence of eye findings- an I-131 uptake and scan should be performed.

- An elevated uptake, with a diffusely enlarged gland- confirms the diagnosis.
- It helps to differentiate it from other causes of hyperthyroidism.

Anti-Tg and anti-TPO antibodies are elevated in up to 75% of patients.

Elevated TSH-R or thyroid-stimulating antibodies (TSAb) are diagnostic of Graves' disease (about 90% of patients).

# Diffuse toxic goitre....

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## Management:

Treated by any of three treatment modalities-

- Anti-thyroid drugs.
- Thyroid ablation with radioactive I-131.
- Thyroidectomy.

# Diffuse toxic goitre....

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## Anti Thyroid Drugs:

Generally are administered in preparation for RAI ablation or surgery.

Drugs commonly used are-

- Propylthiouracil (PTU, 100 to 300 mg three times daily)
- and methimazole (10 to 30 mg three times daily, then once daily).

Both drugs reduce thyroid hormone production by **inhibiting** the organic binding of iodine and the coupling of iodo-tyrosines (mediated by TPO).

PTU also **inhibits** the peripheral conversion of T4 to T3, so useful for the treatment of thyroid storm.

PTU has a lower risk of transplacental transfer.

# Diffuse toxic goitre

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## Anti Thyroid Drugs:

Side effects of treatment include-

- Reversible granulocytopenia.
- Skin rashes, fever.
- Peripheral neuritis, polyarteritis, vasculitis.
- Rarely, agranulocytosis and aplastic anemia.

Catecholamine response of thyrotoxicosis can be alleviated by administering beta- blocking agents.

- **Propranolol** is the most commonly prescribed medication in doses of about 20 to 40 mg four times daily.

# Diffuse toxic goitre....

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## Radioactive Iodine Therapy (I-131):

RAI forms the mainstay of Graves' disease treatment in North America.

Major advantages- avoidance of a surgical procedure and its risks.

Dose - usually consists of 8 to 12 mCi administered orally.

Most patients become euthyroid within 2 months.

About 50% of patients treated with RAI are euthyroid 6 months after treatment.

And remaining are still hyperthyroid or already hypothyroid.

# Diffuse toxic goitre....

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## Radioactive Iodine Therapy (I-131):

RAI therapy is most often used in-

- Older patients with small or moderate-sized goiters
- Those who have relapsed after medical or surgical therapy.

Contraindication:

- Absolute : Women who are pregnant or breastfeeding.
- Relative : Young patients (i.e., especially children and adolescents), those with thyroid nodules, and those with ophthalmopathy.

# Diffuse toxic goitre....

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## Surgical Treatment:

Recommended when RAI is contraindicated:

- Have confirmed cancer or suspicious thyroid nodules.
- Young and Pregnant or desire to conceive soon after treatment.
- Severe reactions to anti-thyroid medications
- Large goitres causing compressive symptoms.
- Reluctant to undergo RAI therapy.

What surgical Procedure ?-(Solely based on discretion of surgeon and their experience.)

- Near total thyroidectomy
- Subtotal thyroidectomy
- Total thyroidectomy

## Toxic MNG....

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- . Usually occur in older individuals, who often have a prior history of a nontoxic multinodular goitre.
- . Over several years, thyroid nodules become autonomous to cause hyperthyroidism.
- . Hyperthyroidism also can be precipitated by iodide-containing drugs such as contrast media and the anti-arrhythmic agent amiodarone (jod-basedow hyperthyroidism).
- . Symptoms and signs of hyperthyroidism are similar to Graves' disease, but extra-thyroidal manifestations are absent.

## Toxic MNG....

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- . Blood tests- similar to Graves' disease with a suppressed TSH level and elevated free T4 or T3 levels.
- . RAI uptake also is increased, showing multiple nodules with increased uptake and suppression of the remaining gland.
- . Treatment – After adequately controlling hyperthyroid state Total Thyroidectomy is treatment of choice.

# Toxic Adenoma (Plummer's Disease)

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- .Hyperthyroidism from a single hyper-functioning nodule.
- .Typically occurs in younger patients who note recent growth of a long-standing nodule along with the symptoms of hyperthyroidism.
- .Most hyper-functioning or autonomous thyroid nodules have attained a size of at least 3 cm before hyperthyroidism occurs.

# Toxic Adenoma (Plummer's Disease)

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- .Physical examination- usually reveals a solitary thyroid nodule without palpable thyroid tissue on the contralateral side.
- .RAI scanning shows a "hot" nodule with suppression the rest of the thyroid gland.
- .Surgery (lobectomy and isthmusectomy) is preferred.

# Thyroid Storm

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- .A condition of hyperthyroidism accompanied by-  
Fever, central nervous system agitation or depression, cardiovascular dysfunction.
- .May be precipitated by infection, surgery or trauma.

# Thyroid Storm

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## .Management:

**Beta blockers**- given to reduce peripheral T4 to T3 conversion and decrease the hyperthyroid symptoms.

**Oxygen supplementation** and hemodynamic support should be instituted.

Non-aspirin compounds can be used to treat pyrexia.

**Lugol's iodine** or sodium ipodate (intravenously) should be administered to decrease iodine uptake and thyroid hormone secretion.

**PTU therapy** blocks the formation of new thyroid hormone and reduces peripheral conversion of T4 to T3.

Corticosteroids often are helpful to prevent adrenal exhaustion and block hepatic thyroid hormone conversion.