THYROTOXICOSIS

★ **Definitions :**

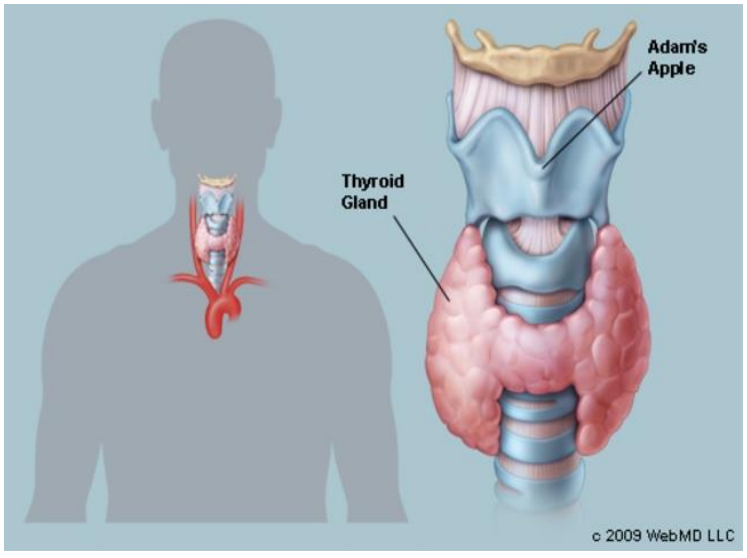
- ***Thyrotoxicosis*** is increase level of thyroid hormone in the circulation due to either by thyroid source or extra-thyroid source .Therefore not all manifestations of thyrotoxicosis are due to high level of thyroid hormone .
- ***Hyperthyroidism*** is increase level of thyroid hormone in the circulation due to hyperfunction of thyroid gland . Therefore all manifestations of hyperthyroidism are only due to high level of thyroid hormone with goitre .

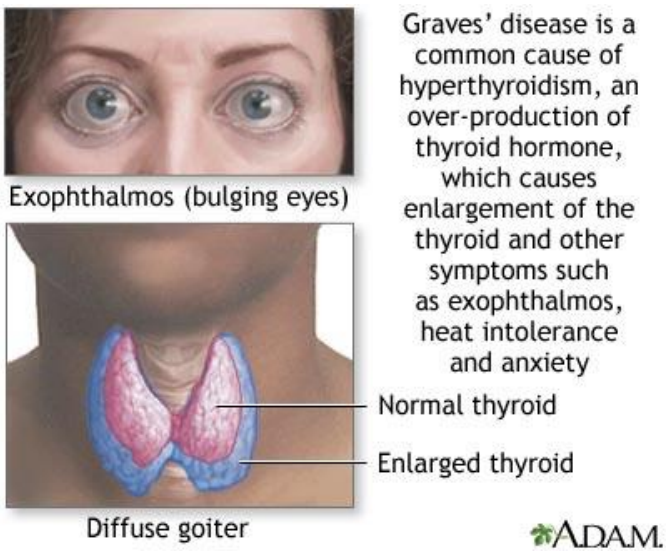
★ **Aetiology :**

A) **Toxic goitre :**

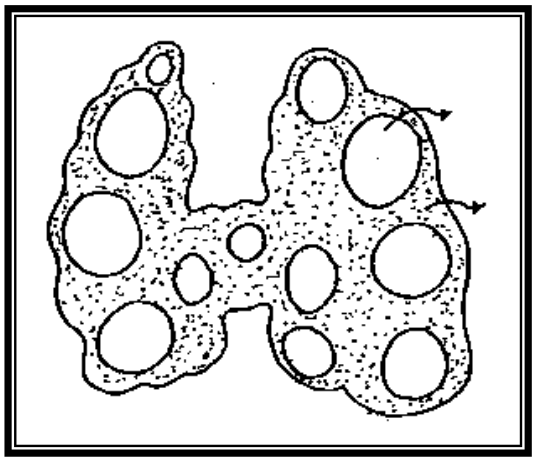
I) Iry toxic goitre : (the commonest , 75%)

- It is also called Diffuse toxic goitre , exophthalmic goitre or Graves' disease .
- There is diffuse over activity of the gland.





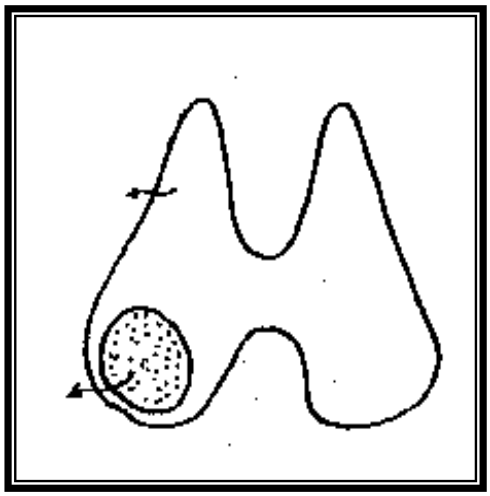
II) Secondary toxic goitre : (toxic nodular goitre = Plummer's disease) : 15%



- Thyrotoxicosis develops on top of simple nodular goitre.

III) Solitary toxic nodule : (5%)

- There is single active autonomous nodule .



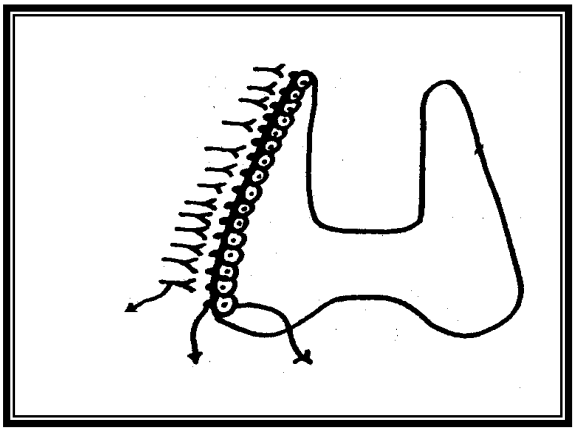
B) Rare causes of thyrotoxicosis : **5%**

1. Early stages of subacute **thyroiditis** & Hashimoto's disease.
2. **Thyrotoxicosis factitia** due to excessive exogenous intake of L-thyroxine.

3. **Neonatal thyrotoxicosis**:
   - It occurs in babies born to a 1ry toxic mother due to transmission of thyroid stimulating antibodies across the placenta.
   - The condition subside spontaneously within 3-4 weeks .
4. **Jod-Basedow thyrotoxicosis**: (iodine induced toxic goitre)
   - When large doses of iodine given to hyperplastic endemic goitre. It is usually temporary(-ve feed back mechanism).
5. Functioning thyroid **carcinoma**.
6. Functioning **metastases** of thyroid carcinoma.
7. T.S.H. secreting **pituitary tumour**.(all causes of thyrotoxicosis are associated with low TSH level except this cause)
8. **Rarely ovarian or placental tumours** (ectopic hormone production)

I) Primary Toxic Goitre

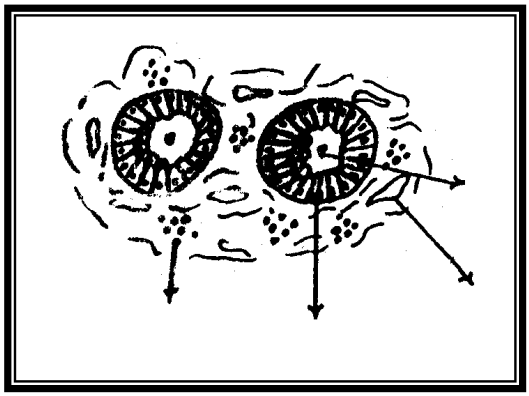
★ **Aetiology:**



- It is an autoimmune disease → formation of abnormal thyroid stimulating antibodies combines with TSH receptors in the follicular cells of the thyroid gland → prolonged severe stimulation of these cells to secret T3 & T4 .

★ **Incidence :** More in females , 20 - 40 years with stressful life.

★ **Pathology:**



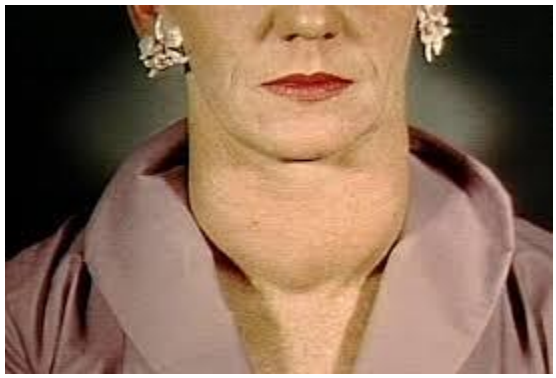
a) The follicles: Lined by many layers of cells with hyperplasia and hypertrophy with no or little stored colloid.

b) The stroma: There is increased vascularity with arterio-venous shunts & dense lymphocytic infiltration (evidence of autoimmunity).

★ **Clinical picture:**

I) Thyroid gland:

- It is uniformly enlarged, ***small or large, smooth, soft or firm***.
- There may be ***expansile*** pulsations, thrill & bruit especially over the upper pole of each lobe (most vascular where superior thyroid vessels enter the gland).



II) Manifestations of hyperthyroidism :

- **All the following manifestation are due to hyper-function of thyroid gland with high level of thyroid hormones in the circulation leading to hyper-metabolism .**

1. Metabolic manifestations:

a) Recent rapid ***loss of weight*** inspite of increase appetite.

b) Recent intolerance to warm or hot weather with preference for cold.

2. Nervous manifestations: (main symptoms in 1ry toxic goitre)

a) ***Insomnia*** , anxiety, nervousness, irritability & bad dreams.

b) ***Fine tremors*** in the hand, tongue & eyelids.

c) ***Reflexes*** are exaggerated due to hyperexcitability of neurons .

3.Cardiovascular: (main symptoms in 2nd toxic goitre)

a) ***Sleeping pulse****:* (in hospitalized patient)

- Mild toxicity : 80 - 90/min.
- Moderate toxicity : 90-110 /min.
- Severe toxicity : more than 110 /min.

b) ***Water hummer pluse:*** Due to high systolic B.P (increase C.O)

and low diastolic B.P (arteriovenous shunt in the thyroid & peripheral vasodiltation).

c) Palpitation, exertional dyspnea, anginal pain and H.F.

d) ***Any arryhthmia*** may occur , especially A.F. but never heart block.

4. Other Manifestations:

a) ***The skin*** is warm, flushed, with generalized excessive sweating.

b) ***G.I.T.*** $\rightarrow$ diarrhea.

c) ***Renal*** $\rightarrow$ polyuria (increase renal blood flow and hyperglycemia & glucosuria.

d) ***Genital*** $\rightarrow$

- In females : menstrual irregularities & infertility .
- In males : decrease lipido , impotence & infertility .

e) ***R.E.S*** $\rightarrow$ just palpable spleen and generalized lymphadenopathy.

f) ***Musculo-skeletal:*** Progressive proximal muscle weakness and bony pains.

5. Thyro-toxic crises:

- Rare nowadays. Usually occurs as a ***postoperative complication*** after thyroidectomy due to ***rough manipulation*** of the thyroid in an ***incompletely prepared*** patient.
- The patient is irritable and may pass into hallucination and coma ***(C.N.S),*** severe tachycardia which may lead to H.F and there is severe rise in systolic B.P with drop of diastolic pressure ***(C.V.S.),*** severe sweating **,** vomiting and diarrhea dehydration and collapse, **hyperthermia.**

III) Manifestations of autoimmunity :

> ➢ **All the following manifestation are due to autoimmunity because the high level of thyroid stimulating antibodies in the circulation attack extra-thyroid tissues → true exophthalmos (related signs) , Graves' dermopathy & thyroid acropachy .**

1. Graves' ophthalmopathy : (Eye manifestations)

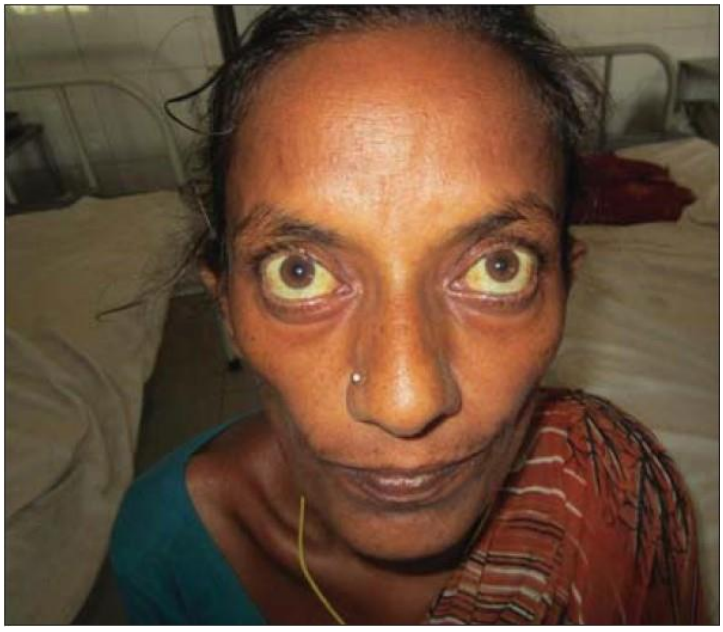
- ***Fine tremors*** in eye lids on light closure of the palpebral fissure (**Rosenbach's sign**) .
- Upper eyelid retraction with a rim of sclera between the upper eyelid and the upper border of cornea ***(Dalrymple's sign) .***
  - ***It is due to spasm of Mutter's muscle*** (part of levator palpabrae superioris muscle) due to sympathetic over tone & thyroid hormones sensitizes the muscle to circulating catecholamines or protrusion of eyeball .
- Infrequent blinking with a staring look ***(Stellwag's sign),*** due to lid retraction and limitation of lid movements by the protruded eye (normal blinking is 5-8/ minute) .

> ➢ The previous eye manifestations are due to hyperthyroidism .
> ➢ **Only true exophthalmos** and related signs are related to **autoimmunity** .

- The upper lid la**g**s behind the eyeball as the patient ***looks down*** without moving the head ***(lid lag or Von Graefe's sign)***.

VonGraefe's sign

Joffroy's sign



- Lack of corrugation of the forehead on **looking upwards** without moving the head, due to true exophthalmos ***(Joffroy's sign)***.
- Lack of proper **convergence** on looking at a near object due to **m**uscular paresis ***(Mobieus' sign)***.
- ***Exophthalmos:***
  - It may be unilateral or bilateral unequal.
  - It is divided into:

1. False (apparent) exophthalmos*:*

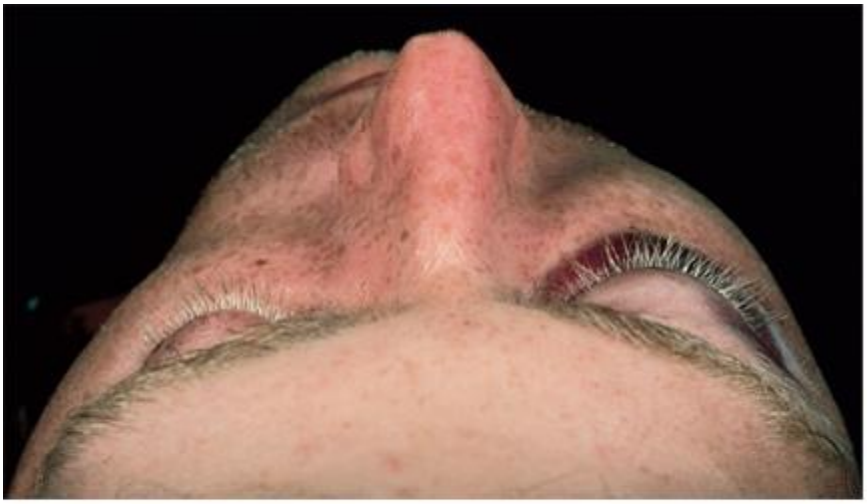
- It is due to ***widening*** of palpabral fissure due to ***retraction*** of upper eyelid without actual protrusion of the eyeball.
- It occurs ***in any toxic goitre or thyrotoxicosis*** .
- ***It disappears by treatment***.

Apparent exophthalmos

2. True exophthalmos:

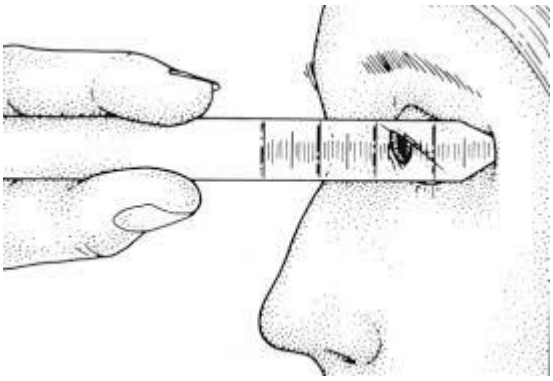
- It is ***an autoimmune*** disease affecting tissues surrounding the eye .

- It is due to ***actual protrusion*** of eyeball caused by ***deposition*** of retrobulbar mucoprotein, mucopolysaccharides, oedema and lymphocytic infiltration, external ophthalmoplegia & compression of ophthalmic veins.
- It is characteristic to ***Graves' disease***.
- It is usually self-limiting & ***may regress***.
- Hypothyroidism ***increases*** the condition.
- **Diagnosis of true exophthalmos:**
  1. Presence of ***rim of sclera*** between cornea and lower eyelid .
  2. ***Naffziger's test****:* Stand behind the seated patient *&* tilt his head backwards. Observe the eyeballs by looking from above. If the eyeballs protrude beyond the plane of the superciliary ridges → true exophthalmos.

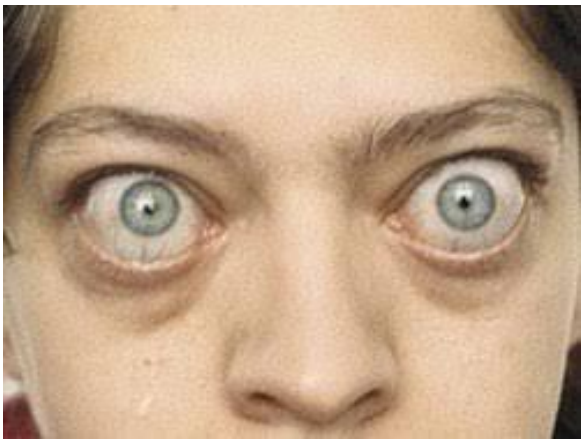


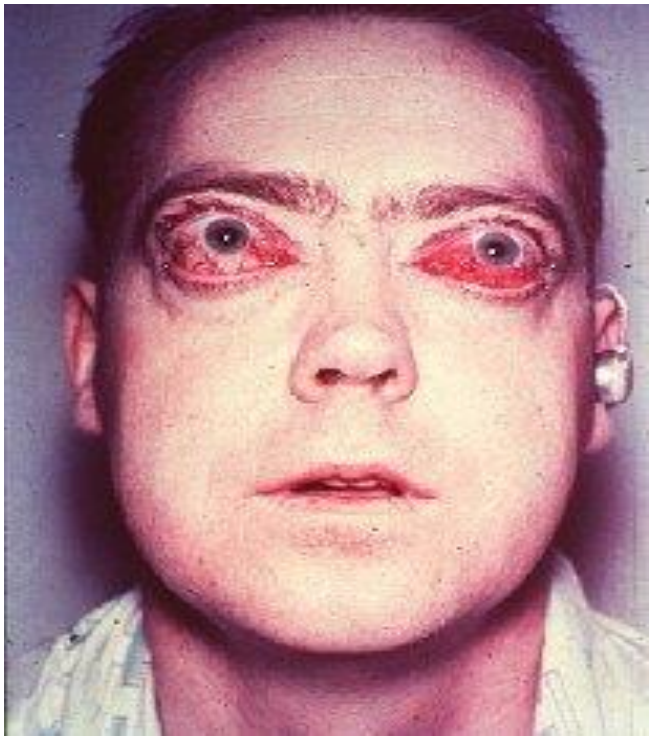
3. ***Russell Frazer's method:*** Examine the patient from the side with the eyes closed. If the sulcus between the superior orbital margin & the covered globe is shallow , obliterates or bulges → true exophthalmos.
4. **Ruler test :** Normally , a ruler can touch the surpra-orbital & infra-orbital margin without touching the cornea . If the ruler touch the cornea without touching these 2 bony prominences , there is true exophthalmos .

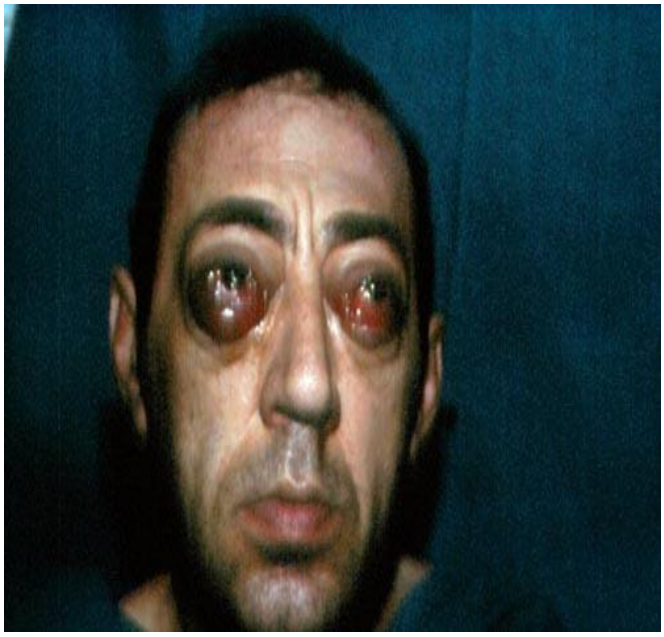
5. **Exophthalmometer** : measure the distance between the outer orbital margin and the apex of cornea (normal less than 17 mm).

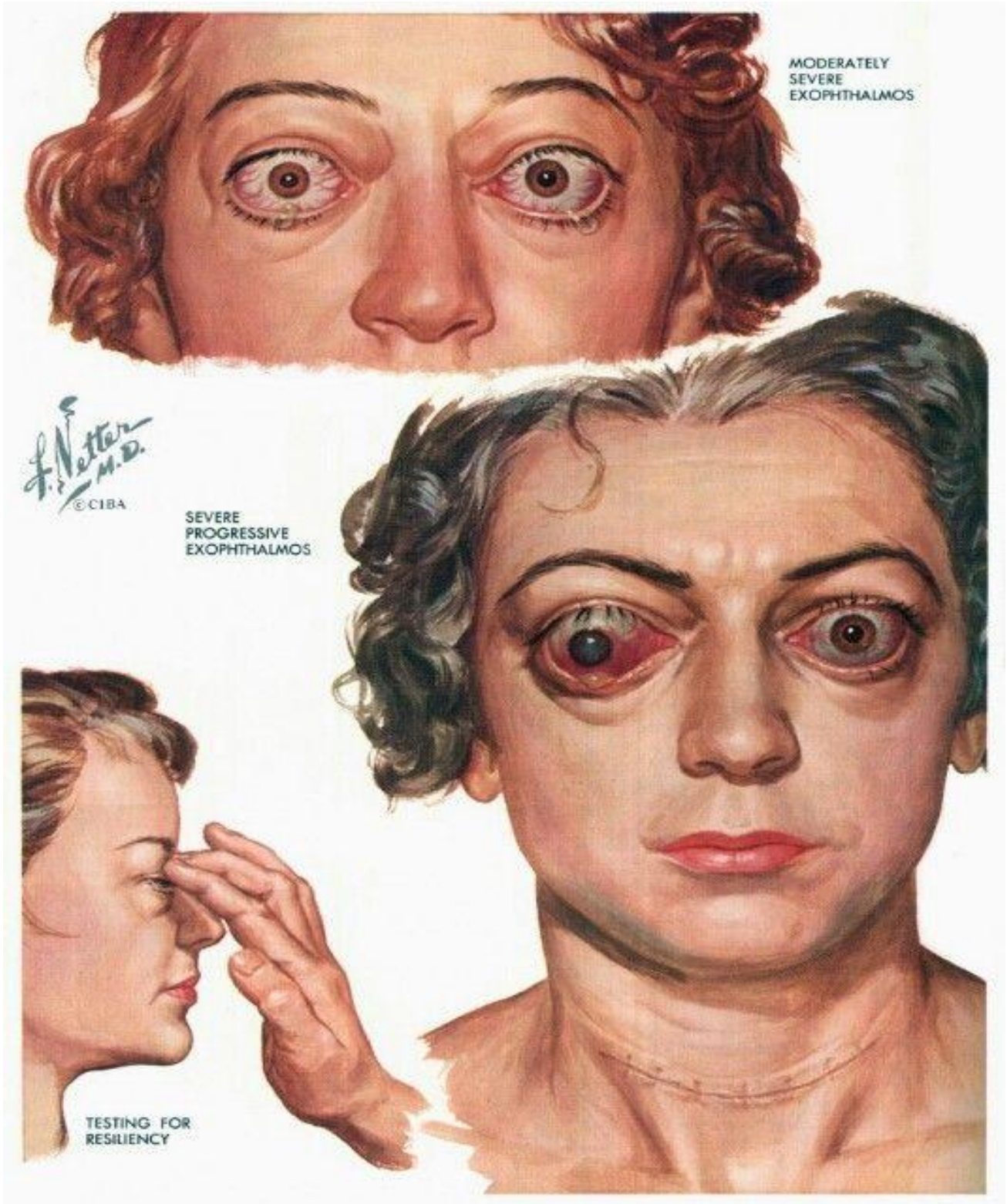


- **Degrees of true exophthalmos :**
  - **Moderate** : presence of rim of sclera below cornea & upper eyelid retraction.
  - **Severe**: external ophthalmoplegia detected by Mobieus' sign , squint & diplopia .
  - **Malignant** : rapid progressive exophthalmos , lagophthalmos , conjunctival congestion & edema , lacrimation, corneal ulceration , endophthalmitis , panophthalmitis , optic neuritis and loss of vision .





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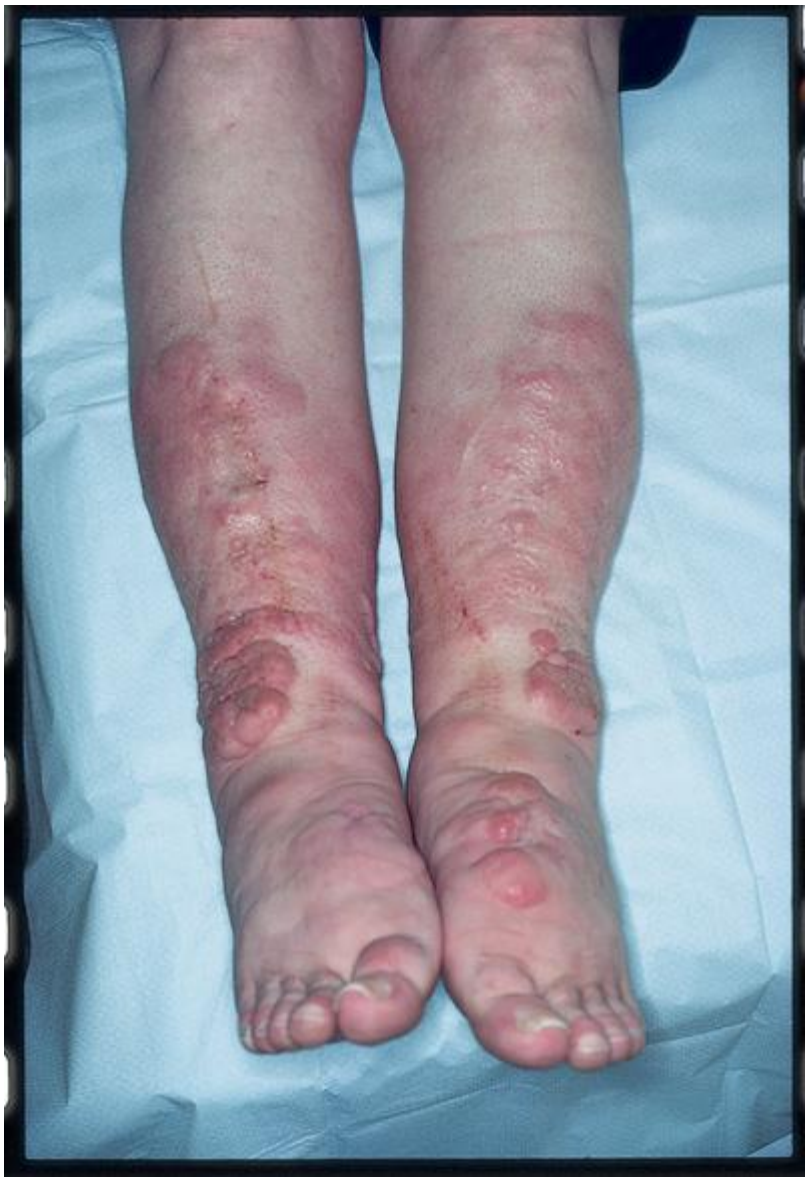
2. **Graves' dermopathy** : (*Pretibial myxoedema)*

- Irregular, tender, red or pigmented , itchy thickened skin over the of the tibia and dorsum of foot due to mucin deposition (manifestation of autoimmunity).

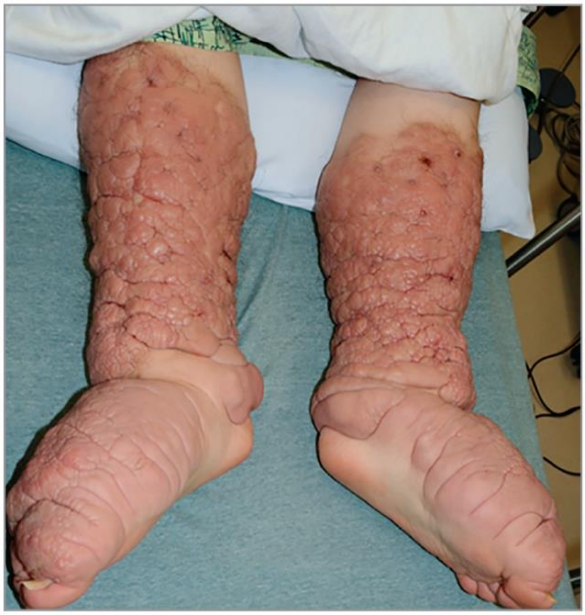


Graves' dermopathy

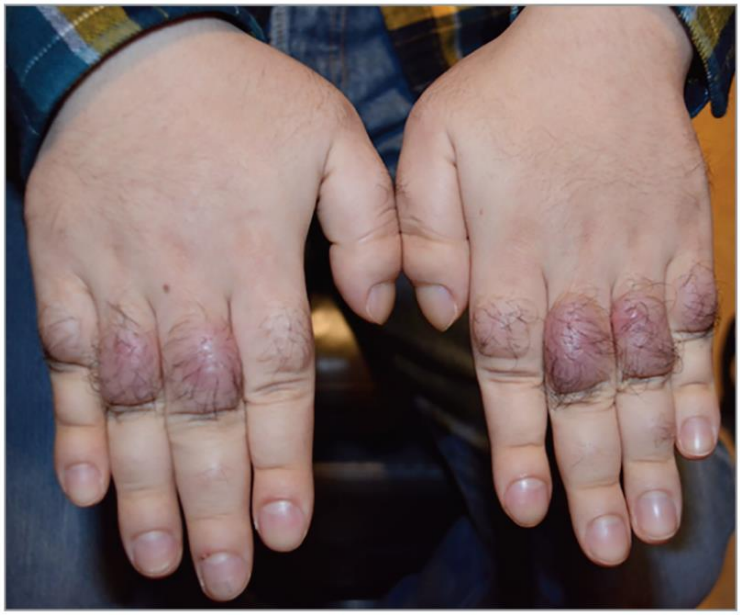
3.Thyroid acropachy :

- Painless clubbing of fingers and toes with pigmented soft tissue swellings in the hands & feet .
- Subperiosteal new bone formation in the metacarpal , metatarsal & phalanges .

A Severe dermopathy



B Bilateral acropachy



★**N.B.:** ***The most significant presentations are:*** True exophthalmos and presence of goiter, tachycardia, palpitations, or arrhythmia & loss of weight inspite of increase appetite.

★**D.D.:**

- Other causes of ***polyphagia with loss of weight*** : thyrotoxicosis , DM , parasitic infestations & malabsorption syndrome .
- ***Anxiety neurosis*** (investigations are essential)

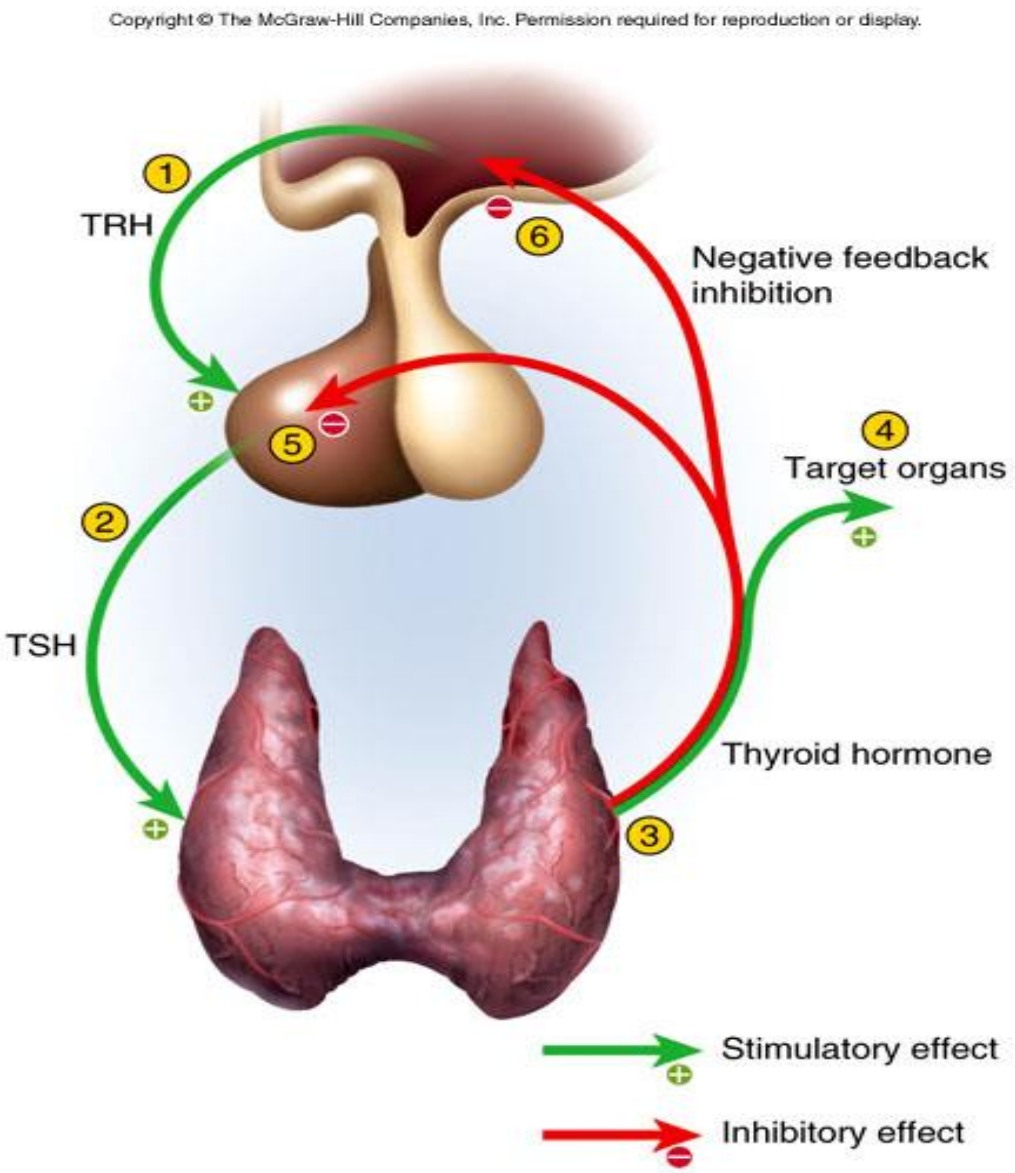
- Other causes of thyrotoxicosis especialy ***secondary thyrotoxicosis:***

	Primary thyrotoxicosis	**Secondary thyrotoxicosis**
1. Age	♦ Usually in young below 40 years .	♦ Usually above 40 years.
2. Onset	♦ Usually rapid *&* occurs on top of normal gland. ♦ Simultaneous appearance of goitre & thyrotoxicosis .	♦ Usually inciduous *&* occurs on top of nodular goitre . ♦ Goitre appears many years before thyrotoxicosis .
3. Course	♦ Remissions *&* excerbations	♦ No remissions.
4. Severity	♦ Usually severe	♦ Usually mild or moderate.
5. Metabolic & C.N.S.	♦ More Marked & usually main presentations.	♦ Less marked.
7. C.V.S.	♦ Less marked(young age)	♦ More marked (old age)
8. Eye signs	♦ Common, all eye signs are present & exophthalmos is true.	♦ Rare , limited eye signs & exophthalmos is apparent.
9. Thyroid	♦ smooth and diffuse goitre.	♦ Nodular & irregular goitre.
10.Autoimmunity	♦ Severe	♦ Mild or moderate .
11.Thyroid dermopathy & achropachy	♦ Occur only in Graves' disease .	♦ Not occur .

★ **Investigations:** (Normal values may vary with the lab.)

1. **Serum TSH :**

- **Normal value** *:* 0.5 – 5 milliunite/liter
- **Ultrasensetive T.S.H test** is the most sensitive test for assessment of thyroid function .
- It is low in all cases of thyrotoxicosis except high in pituitary tumors secreting TSH.



2. Free T_3 & T_4 in the serum*:*

- **Normal values*:***

  a) ***Free serum* T_4** = 8- 26 pico moles /Liter

  b) ***Free serum* T_3** = 3-9 pico moles /Liter

  - Essential if T_3 thyrotoxicosis is suspected .
  - It is more important than level of T4 because T3 is functionally more active .

3. T.R.H. test*:* *I.V. Thyrotropine releasing hormone:*

- ***Normal**:* rise of T.S.H. level in the serum.
- ***In thyrotoxicosis**:* no rise in T.S.H. level in the serum.
- This test is rarely used to assess ***border line cases .***

4.Thyroid antibodies are raised in Graves' disease and Hashimoto's thyroiditis (anti-microsomal , anti-thyroglobulin or anti-TSH receptor antibodies).

5. Radioactive Iodine studies*:*

a) ***I^{123} uptake by thyroid gland***:

- 5 microcuries of I^{123} is given orally $\rightarrow$ the uptake by the thyroid gland is measured after 4 hours $\rightarrow$ radioactive thyroid hormones are measured in the serum at 24 & 48 hours.
- **Normal thyroid uptake** of I^{123} after 4 hours is 10 - 55% of the given dose.
- **In thyrotoxicosis*:*** Very high dose of I^{123} is taken rapidly by the thyroid gland $\rightarrow$ high serum radioactive thyroid hormones at 24

and 48 hours.

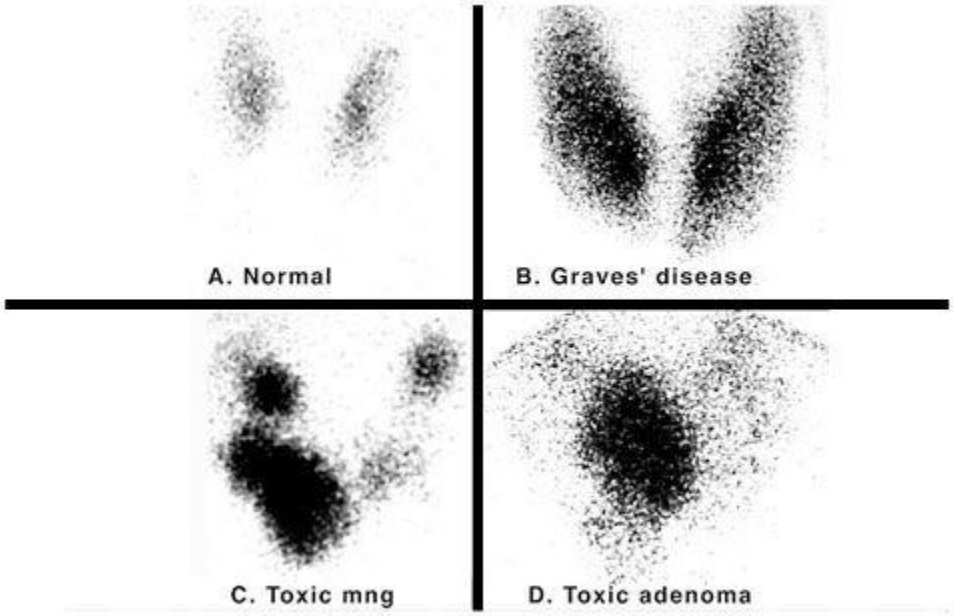
- **In thyroiditis** there is **decrease** iodine uptake by thyroid gland inspit of high level of thyroid normal hormones .

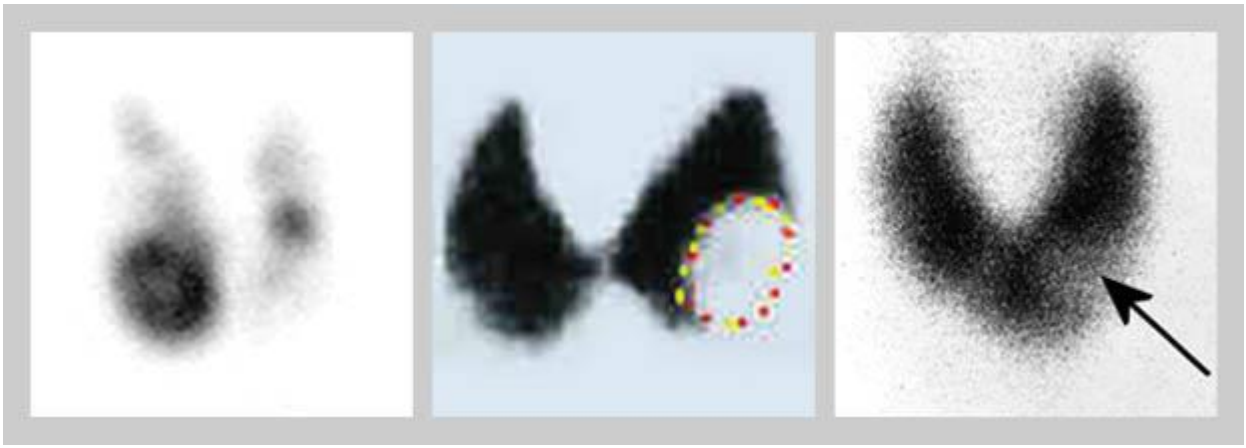
b) ***Scanning of the thyroid gland***: a dose of I^{123} (50 microcuries) or **nowadays technetium 99** is given orally then the gland is mapped using special scanner.

- ***Values:***
  - It gives an idea about the **size and the shape** of the gland.
  - Evaluation of **functional activity** of different parts of thyroid gland .
  - Differentiate **warm nodule** i.e normal activity or **hot nodule** i.e. increased activity (toxic) from a **cold nodule** ie. decreased activity (malignant nodule in 20 % , cyst , calcification , fibrosis , degenerative nodule or thyroiditis).
  - The main value is to identification of **autonomous toxic nodule** whether solitary or a part of toxic nodular goitre .
  - Detect functioning **thyroid metastasis**.
  - It detects **retrosternal** extension.
  - Detect **ectopic thyroid** tissues eg. Thoracic or lingual .

6.Routine investigations before thyroidectomy .

★ ***Practically*** TSH and free T4 & T3 in the serum are the most important . (***Thyroid profile***).





Solitary toxic nodule **Cold nodule** **Graves' disease**

★ NB :

- Non radioactive iodine is I^{127} .
- Radioactive iodine I^{123} have short half life (12 hours) and used in investigations .
- Radioactive iodine I^{131} have long half life (8 days) and used in treatment .