THYROTOXICOSIS

★ Definitions :

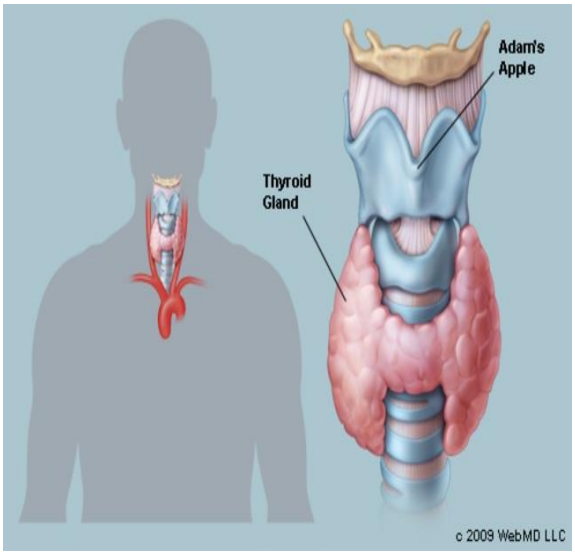
- ***Thyrotoxicosis*** is increase level of thyroid hormone in the circulation due to either **by thyroid source or extra-thyroid** source .Therefore **not all** manifestations of thyrotoxicosis are due to high level of thyroid hormone .
- ***Hyperthyroidism*** is increase level of thyroid hormone in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

★ Aetiology :

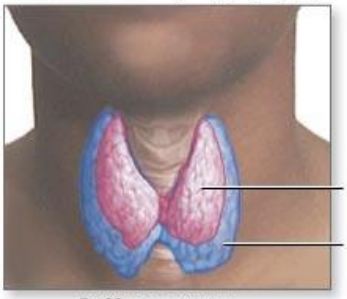
A) Toxic goiter :

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

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




Exophthalmos (bulging eyes)


Diffuse goiter

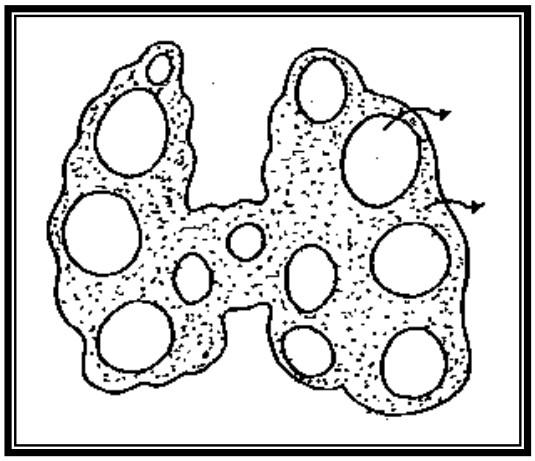
Graves' disease is a common cause of hyperthyroidism, an over-production of thyroid hormone, which causes enlargement of the thyroid and other symptoms such as exophthalmos, heat intolerance and anxiety

Normal thyroid

Enlarged thyroid

ADAM.

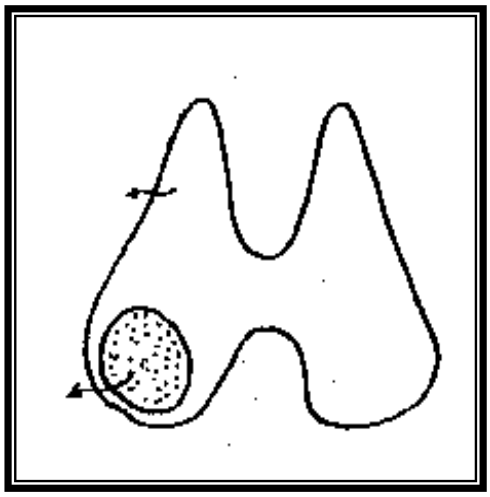
II) Secondary toxic goiter : (toxic nodular goiter = Plummer's disease) : 15%



- Thyrotoxicosis develops **on top** of simple nodular goiter.

III) Solitary toxic nodule : (5%)

- There is single active autonomous nodule .



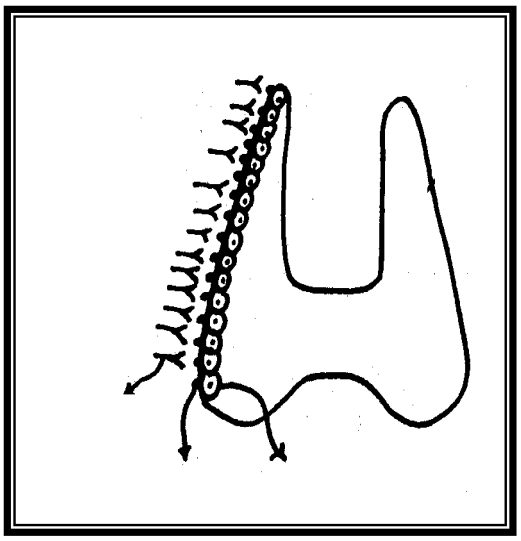
B) Rare causes of thyrotoxicosis : **5%**

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 goiter)
   - When large doses of iodine given to hyperplastic endemic goiter. 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 Goiter

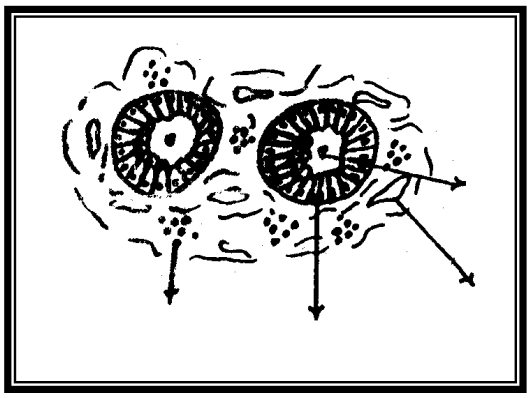
★ **Aetiology:**



- 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 diffuse ***smooth*** uniformly enlarged, ***small or large, , soft or firm***.

- There may be ***expansile*** pulsations, thrill & machinary 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 goiter)

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 goiter)

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, exertion 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.*** → diarrhea.

c) ***Renal*** → polyuria (increase renal blood flow and hyperglycemia & glucosuria).

d) ***Genital*** →

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

e) ***R.E.S*** → 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 .**

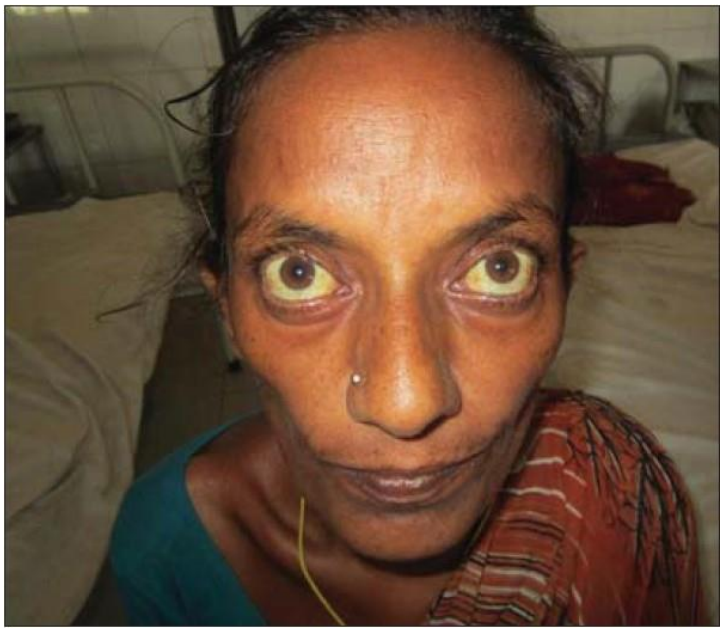
1. Graves' ophthalmopathy : (Eye manifestations)

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

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

VonGraefe's sign

Joffroy's sign



- Lack of **f**olds of the **f**orehead 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 paresis of **m**edial rectus **m**uscule ***(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 goiter 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:**

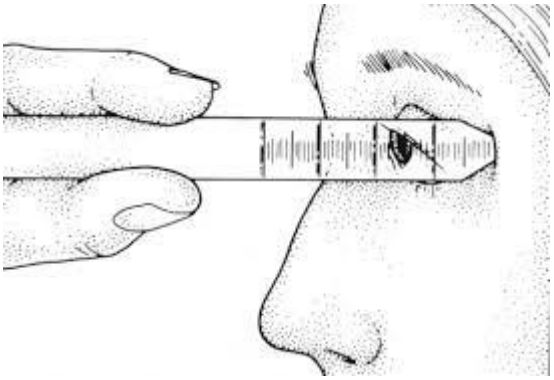
1. Presence of ***rim of sclera*** between cornea and lower eyelid .
2. ***Naffziger's test:*** **Stand behind** the seated patient *&* tilt his head backwards. Observe the eyeballs by looking from above. If the eyeballs protrude beyond the plane of the superciliary ridges → true exophthalmos.

Source: J.E. Tintinalli, J.S. Stapczynski, O.J. Ma, D.M. Yealy, G.D. Meckler, D.M. Cline: Tintinalli's Emergency Medicine: A Comprehensive Study Guide, 8th Edition
www.accessmedicine.com

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 surperior orbital & inferior orbital margin without touching the cornea . If the ruler touch the cornea without touching these 2 bony prominences , there is true exophthalmos .

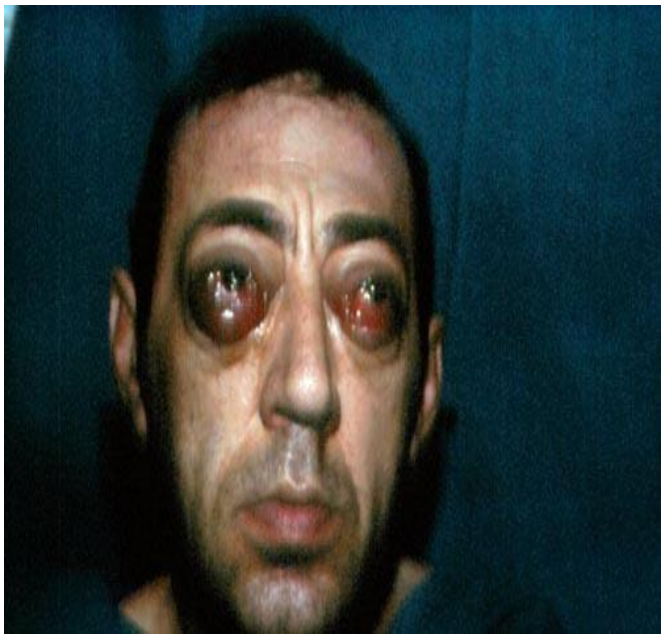
5. **Exophthalmometer** : measure the distance between the later orbital margin and the apex of cornea (normal less than 17 mm).

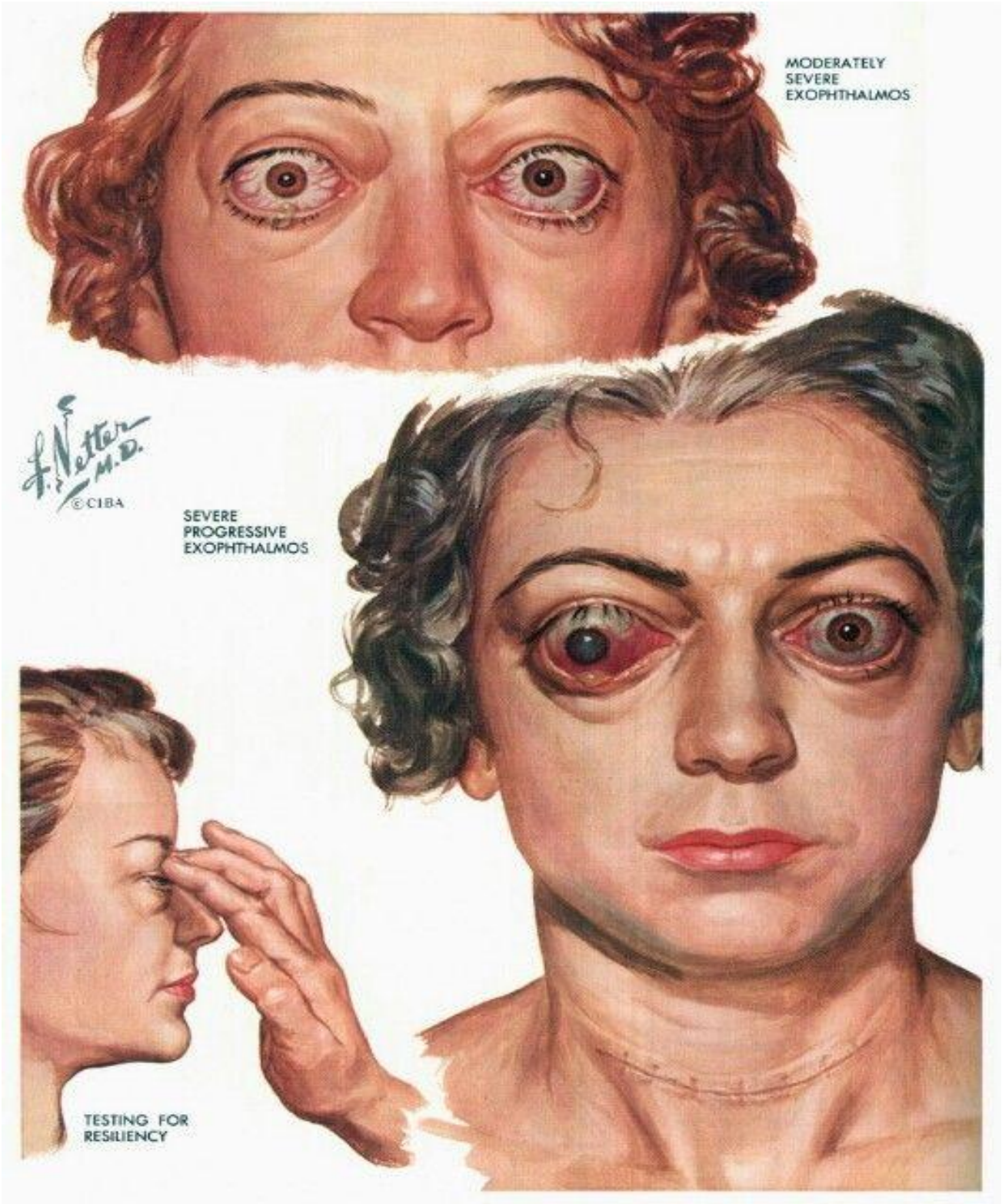


- **Degrees of true exophthalmos :**
  - **Moderate** : presence of rim of sclera between cornea & lower eyelis and upper eyelid retraction.
  - **Severe**: external ophthalmoplegia detected by Mobieus' sign ,

squint & diplopia .

- **Malignant** : rapid progressive exophthalmos , lagophthalmos , conjunctival congestion & edema , lacrimation, corneal ulceration , endophthalmitis , panophthalmitis , optic neuritis and loss of vision .




MODERATELY
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SEVERE
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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)

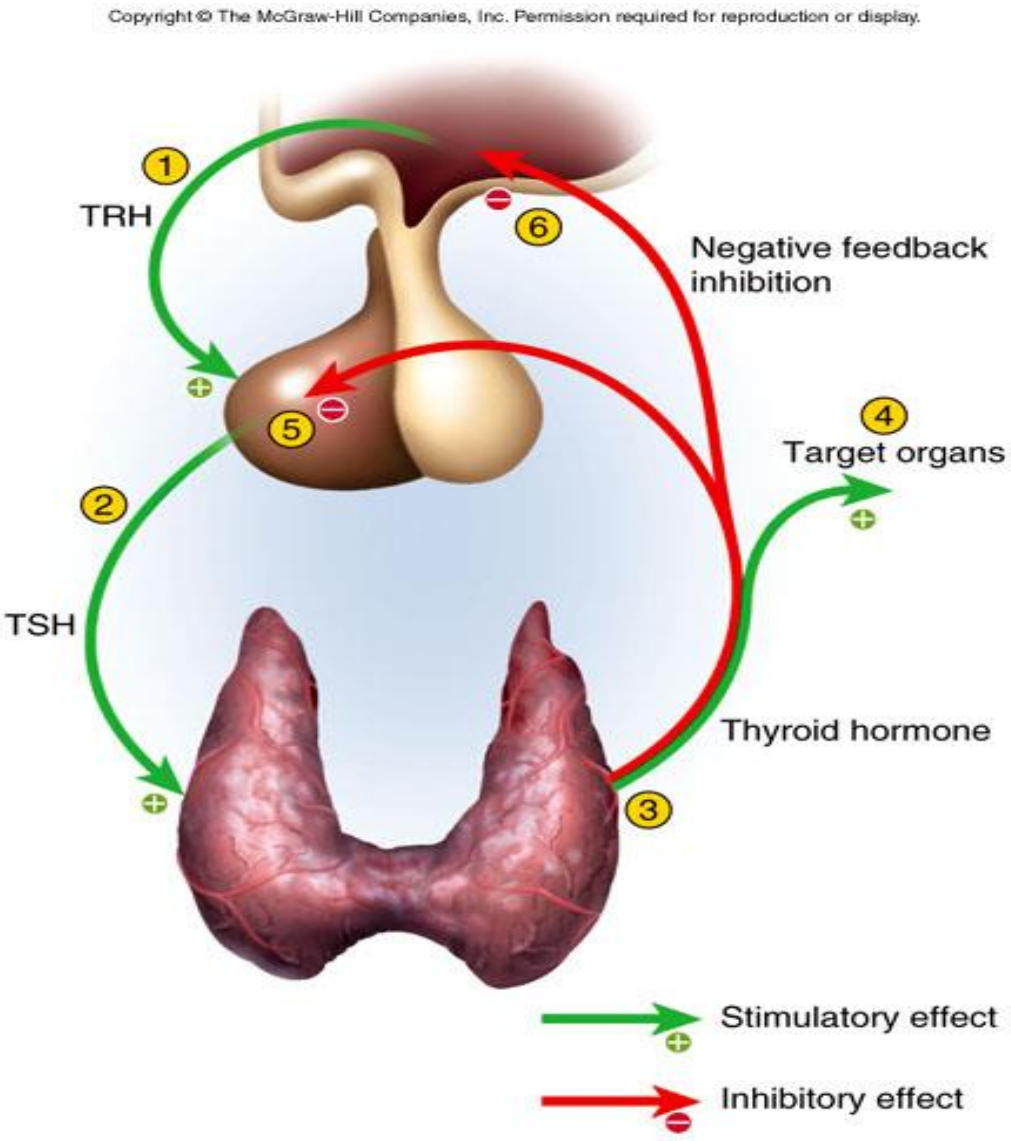
- Other causes of thyrotoxicosis especialy ***secondary thyrotoxicosis:***

	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 goiter & thyrotoxicosis .	♦ Usually **inciduous** *&* occurs on top of nodular goiter . ♦ Goiter 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 goiter.	♦ Nodular & irregular goiter.
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.

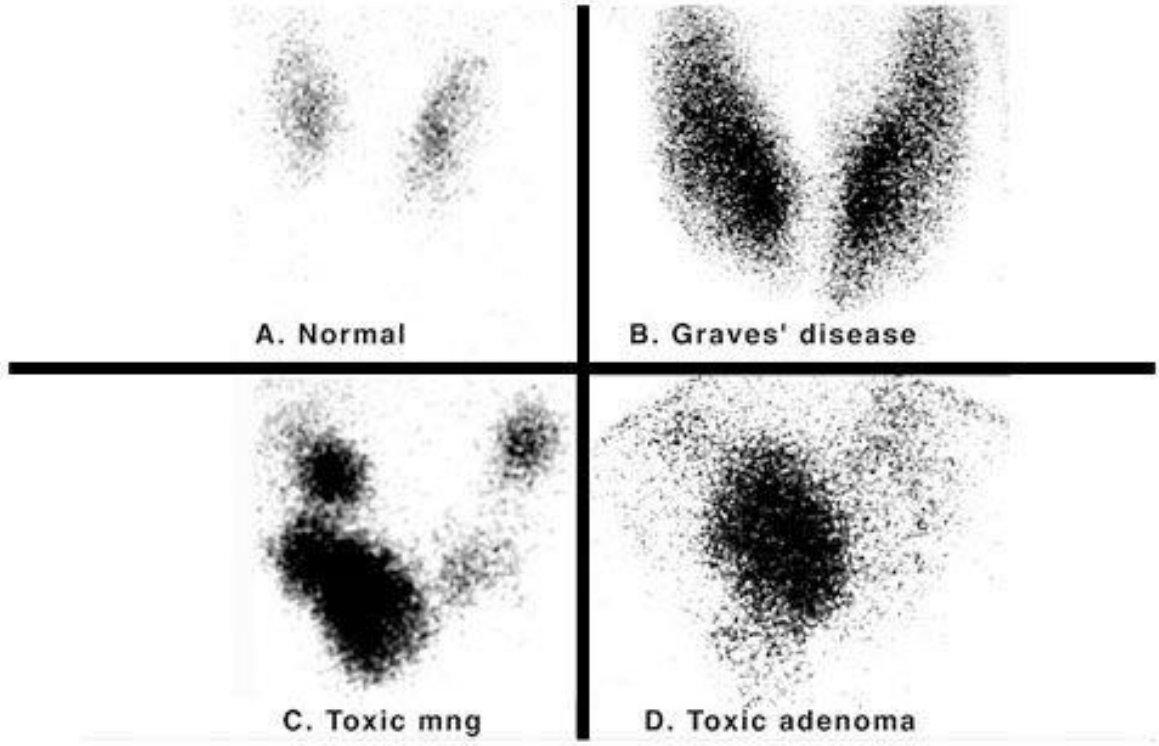
- **In thyroiditis** there is **decrease** iodine uptake by thyroid gland inspit of high level of thyroid normal hormones .

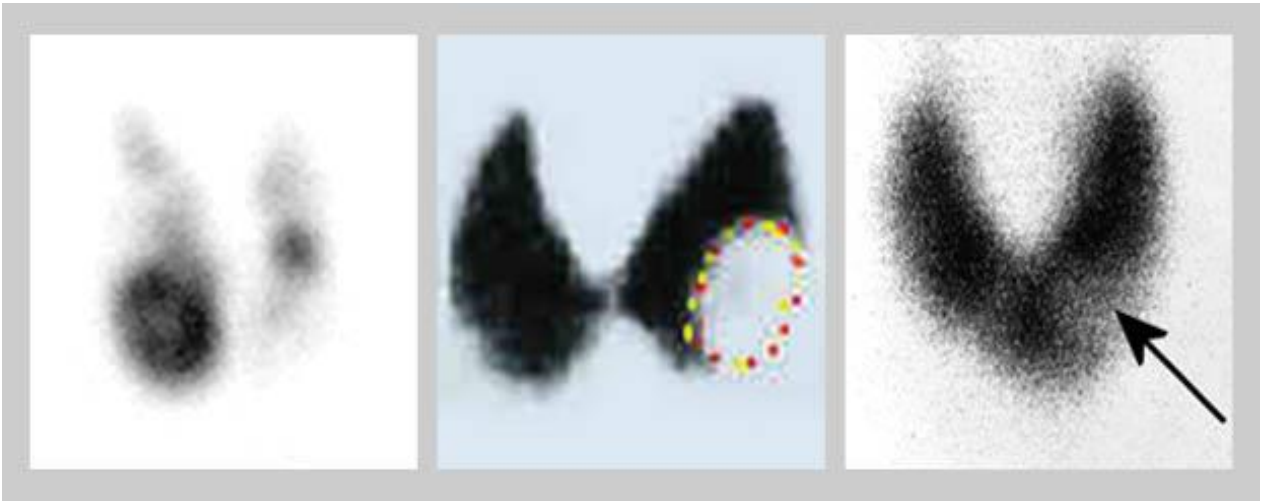
b) ***Scanning of the thyroid gland***: a dose of I^{123} (50 microcuries) or **nowadays technetium 99** is given orally then the gland is mapped using special scanner.

- ***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 goiter .
  - 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***).





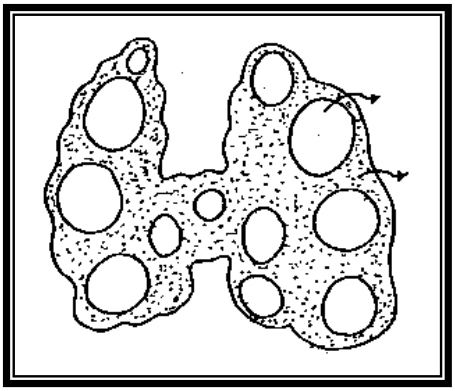
Solitary toxic nodule **Cold nodule** **Graves' disease**

★ 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 .

★ Treatment : (see the other files)

II) Secondary Toxic Goiter

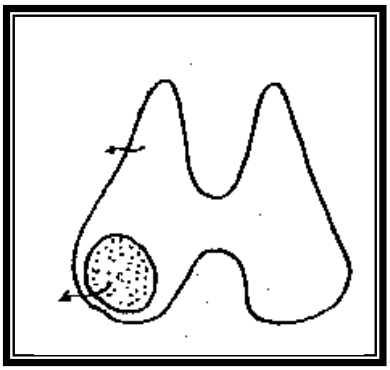


* Toxicity ***on the top*** of pre-existing simple nodular goiter.
* The *inter-nodular tissue is* the site of hyperactivity due to thyroid stimulating antibodies and rarely one or more hyperfunctioning autonomous nodules.

★ Treatment: Only *surgical*

- ♦ Subtotal thyroidectomy to remove the overactive tissues with the same considerations in primary thyrotoxicosis.
- ♦ Radioactive iodine is ineffective due to fibrosis.

III) Solitary Toxic Nodule



* Single autonomous active nodule with the surrounding tissues inactive (due to suppression of TSH).
* It is not due to thyroid simulating antibodies. It may be ***a functioning thyroid adenoma.***

★ Treatment:

1. ***Hemithyroidectomy*** to remove the overactive tissues **or.**
2. ***^{123}I with no risk of myxoedema*** as the surrounding thyroid tissue docs not take ^{123}I.

- ♦ ***Antithyroid drugs can not cure toxic nodule*** as the overactive tissues are autonomous and recurrence of hyperthyroidism is certain when the drug is discontinued.

Hypothyroid Goitre

(Hypothyroidism)

★ **Definitions :** ***Hypothyroidism*** is decrease level of thyroid hormone in the circulation due to hypofunction of thyroid gland .

★ **Aetiology :**

1- Failure of **development** of thyroid gland .

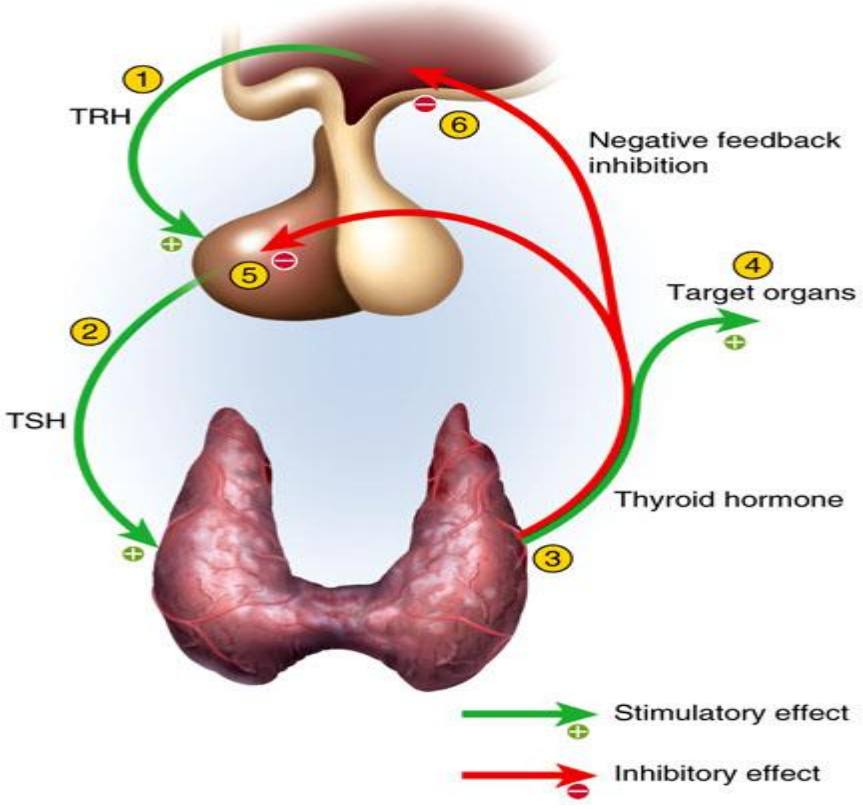
2- Congenital deficiency of **thyroid enzymes** eg. Peroxidase enzyme .

3- Failure of secretion of **TSH** by the anterior pituitary .

4- **Primary** hypothyroidism due to autoimmune disorder .

5- **Iatrogenic** hypothyroidism after subtotal or total thyroidectomy or radioactive iodine .

6- Late stages of **thyroiditis** .



★ **Complications :**

1- **Coronary thrombosis** due to hypercholesterolaemia .

2- **Coma** if the patient is subjected to stressful condition .

3- Carpal tunnel syndrome .

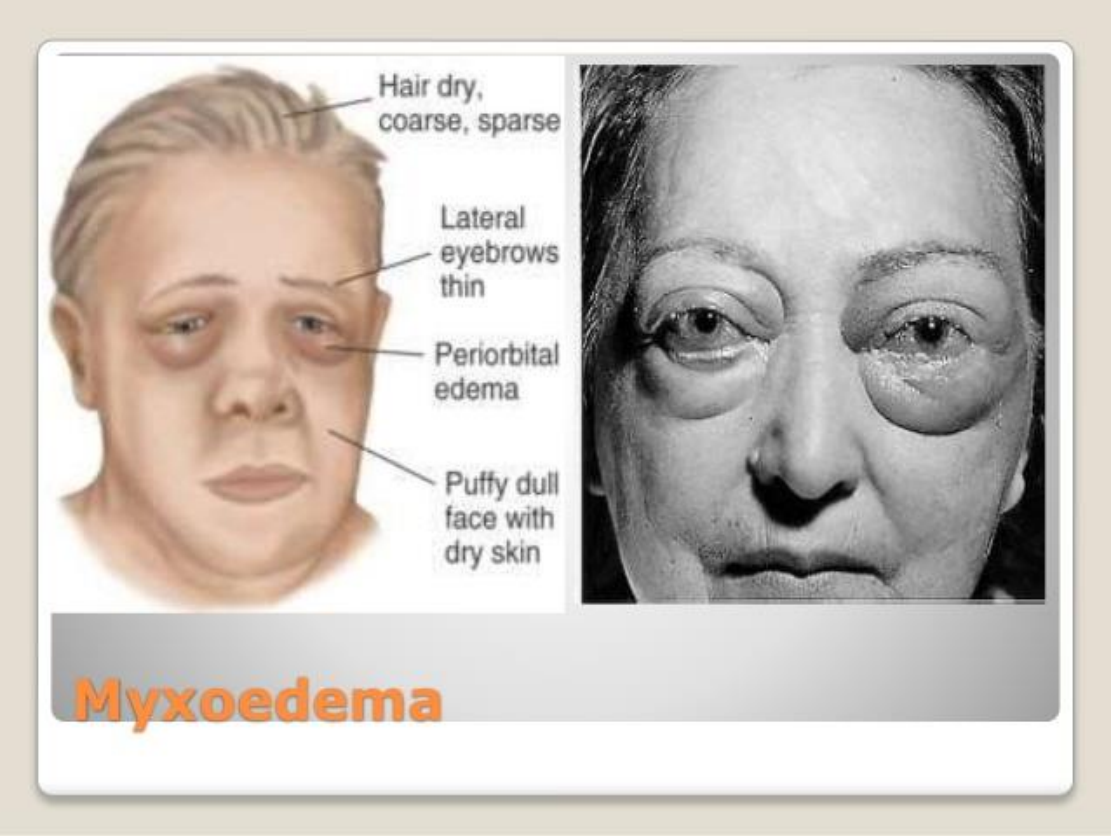
★ **Clinical picture :**

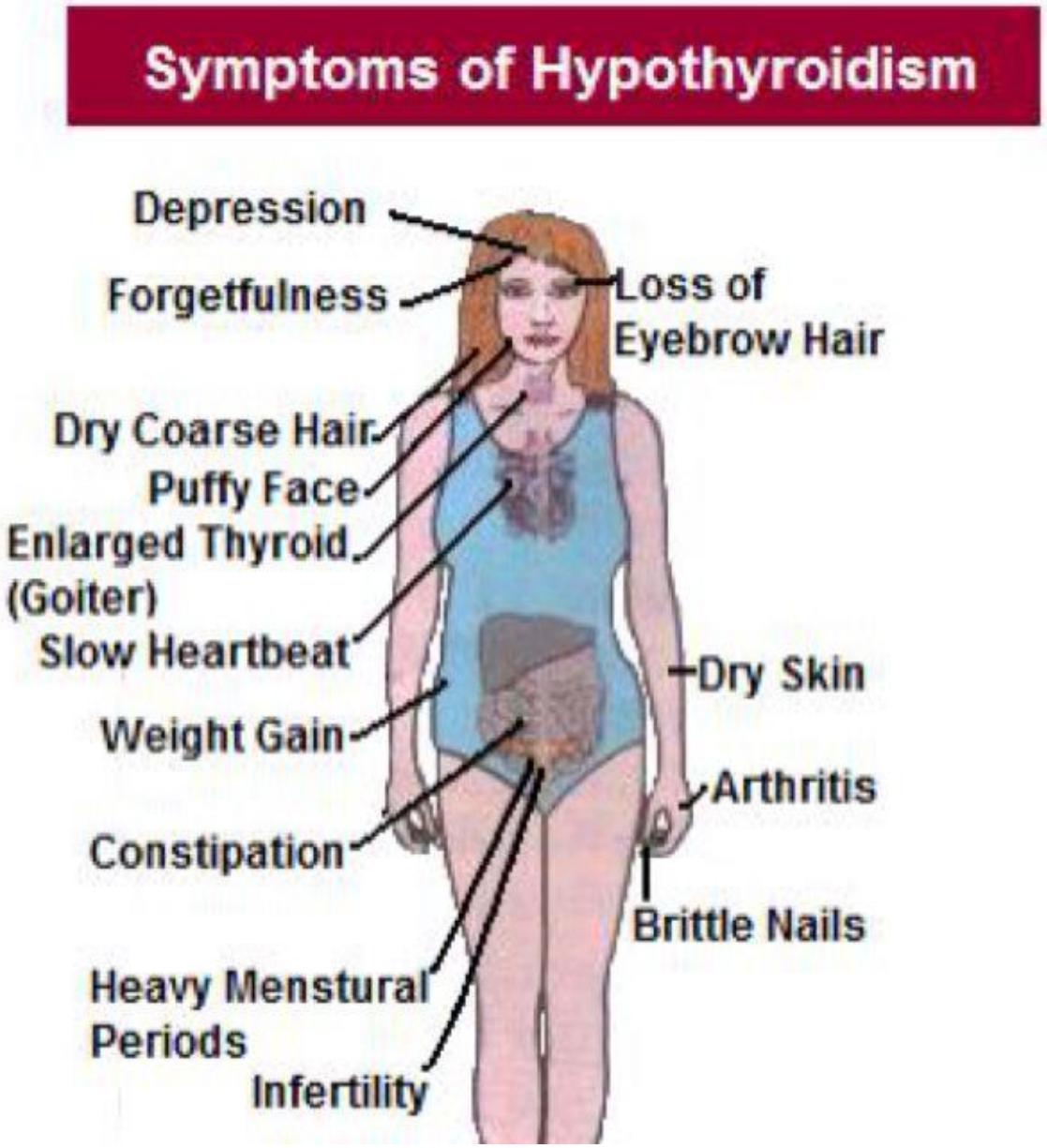
I)In infants and children → **cretinism .**

- **Impairment of development and growth** with delay development of teeth , delay of walking and the patient is stunted .
- **The child has** apathic look , with depressed nose , thick lips and thick protruded tongue .
- The abdomen is distended with umbilical hernia .

II) In adults → **myxoedema**

- Manifestations of myxoedema are nearly the reverse to those of hyperthyroidism .
- The patient complains of depression , lethargy , weakness , gaining weight in spite of poor appetite and intolerance to cold weather .
- The patient looks apathetic with sluggish reactions .
- The face is puffy with periorbital edema and supraclavicular pad of fat .
- Loss of lateral part of eyebrows .
- Bradycardia with low volume pulse and pericardial effusion .
- Dry , cold skin with coarse dry hair .
- Menstrual irregularity , infertility .
- Conistipations .





III) Goitre : smooth or nodular firm goitre .

★ **Investigations :** TSH is raised with low T3 & T4 .

★ **Treatment :**

- L-thyroxine , +0.2-0.3 mg/ day for adults .
- Early treatment of cretin infants may save the patient otherwise the changes are irreversible .

III. THYROID NEOPLASMS

★ **Classifications:**

A. Benign: Include follicular adenoma.

B. Malignant:

1. Well-differentiated carcinoma (85%).
2. Undifferentiated (Anaplastic) carcinoma **(**10%).
3. Other malignant tumours (5%) including lymphoma, sarcoma or metastatic tumours.

A. Benign Tumours

★ **Incidence:** Very rare.

★ **Pathology:**

- ***Origin:*** from thyroid follicles.
- ***Follicular adenoma****:* like follicular carcinoma but histologically there is no invasion of the local capsule, lymphatics or blood vessels.

★ **C/P:** It presents as **solitary thyroid nodule.** It should not be diagnosed clinically but **only after excision biopsy**, (no capsular or vascular invasion).

★ **Treatment:** Hemithyroidectomy and biopsy.

Carcinoma OF Thyroid

★ **Incidence:** More in females (except anaplastic carcinoma)

★ **Predisposing factors:**

1. ***Irradiation to the neck*** of a child which was previously used for treatment of haemangioma or thymic gland enlargement .
2. ***Radioactive iodine*** may be theoretically carcinogenic (rare) .
3. ***Precancerous thyroid lesions:***
   a) Thyroid adenoma.
   b) Simple nodular goiter (Possibly due to **TSH** stimulation).
4. ***Excess TSH & endemic goiter.***
5. ***Genetic:*** Hereditary factor is marked in **medullary** carcinoma.

★ **Pathology:**

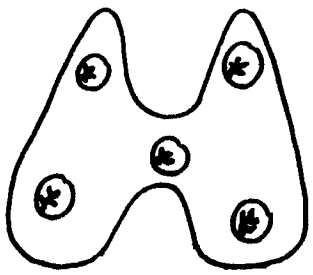
I. ***Types:*** **Adenocarcinoma** arising from **follicular** epithelium (**except medullary** type which arise from para-follicular **C cells**).

a) Differentiated carcinoma: 85%.

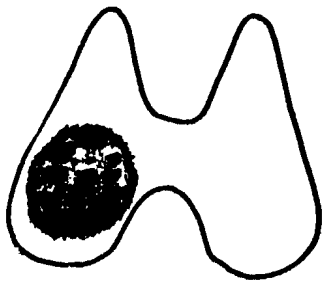
1. **Papillary** carcinoma: 60%.
2. **Follicular** carcinoma: 20%.

3. **Medullary** carcinoma***:*** 5%**.**
   - Arises from ***parafollicular C cell*** (producing **calcitonin**).
   - It is usually ***sporadic*** but may ***be familial.***
   - **Familial** occurrence of medullary carcinoma may be a part of ***multiple endocrinal neoplasia*** (MEN II).
   - ***Familial*** occurrence of medullary carcinoma usually occur in **children & young** adults .
   - Early ***diagnosis of familial*** predisposion by screening of the family by genetic testing (**RET proto-oncogene**).
   - If **familial** predisposion is diagnosed , ***prophylactic total thyroidectomy*** should be done .
   - Early ***lymphatic*** spread, massive ***direct & blood*** spread are also common.
   - The tumor marker of medullary carcinoma is ***calcitonine*****.**

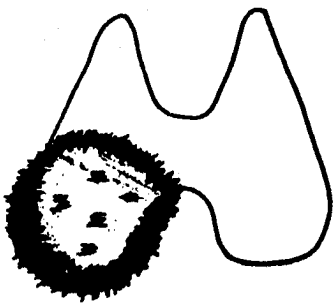
b) Undifferentiated carcinoma: Anaplastic carcinoma 10%.



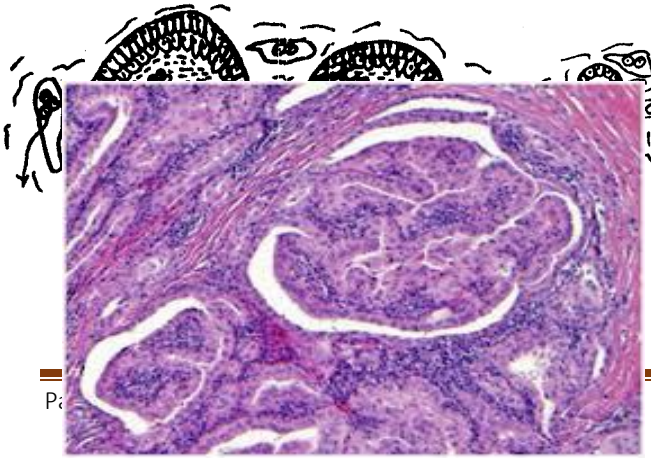
★ ***Papillary carcinoma***



★ ***Follicular carcinoma***



★ ***Anaplastic carcinoma***

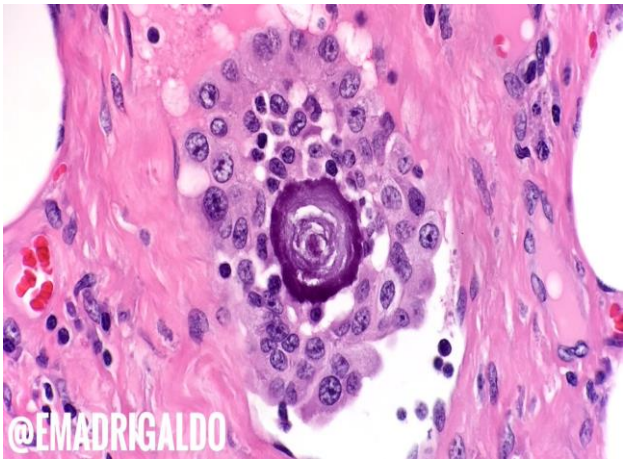


Papillary carcinoma

II. *Microscopic picture:*

1. Papillary	2. Follicular	3. Anaplastic
* ***Cystic areas*** lined by several layers of malignant cells with intracystic ***papillary projections*** which consist of a core of fibrous tissue covered by several layers of malignant cells * ***Lamminated calcification*** (Psamoma bodies) usually present in the stroma. * ***The lymphatics are invaded***	* Malignant cells are arranged in complete & incomplete ***irregular acini*** or in groups. * The ***local capsule & blood vessels*** are infiltrated. (D.D. from follicular adenoma in which local capsule & B.V. are not infiltrated).	* Masses of giant cells, spheroidal & spindle shape cells separated by variable amount of fibrous tissue.
* ***Mixed*** papillary & follicular carcinomas are classified as papillary carcinoma because they have similar behaviour.		

Psamoma bodies



III- Behaviors of the 3 commonest types of thyroid carcinoma:

	1. Papillary	2. Follicular	3. Anaplastic
***Incidence**	***60%**	***20%**	***10%**
***Age**	* Usually in children or young adults below 40 years	* 40 - 60 years	* Elderly above 60 years.
***Multifocal**	* ln 80% due to intraglan-dular lymphatic spread or multicentrically	* Rare	* Rare
* S**pread**	*Early & mainly **lymphatic** spread . * Blood & extensive direct spread occur in **extra-thyroid** tumors .	*Early& mainly **blood** spread .	***** ***Early & extensive spread by all means of spread.***
***Response to** ^{131}I	* Responds	* Responds	* Not Responds
***Response to irradation.**	* Not Responds	* Not Responds	* Temporary decrease in size.
***Dependency on T.S.H.**	* Marked	* Less marked	* No effect.
***10 years survival**	***97 %** in intra-thyroid tumor .	* 90% in tumors without capsular or vascular invasion	* Death occurs within a year in 90% of cases.

★ Staging : TNM system

- **T : Size of 1ry tumor**
  - **T0 :** no evidence of 1ry tumor .
  - **T1 :** 2 cm or less .
  - **T2 :** 2- 4 cm
  - **T3 :** more than 4 cm .
  - **T 4 :** tumor of any size with infiltration of the capsule i.e extra-thyroidal tumor
- **N : lymph node metastases .**
  - **N0 : no evidence of regional lymph node metastases .**
  - **N1 : regional lymph node metastases .**
- **M : Distal metastases**
  - **M0 : no evidence of distal metastases .**
  - **M1 : presence of distal metastases .**

★ **Prognosis : depends on**

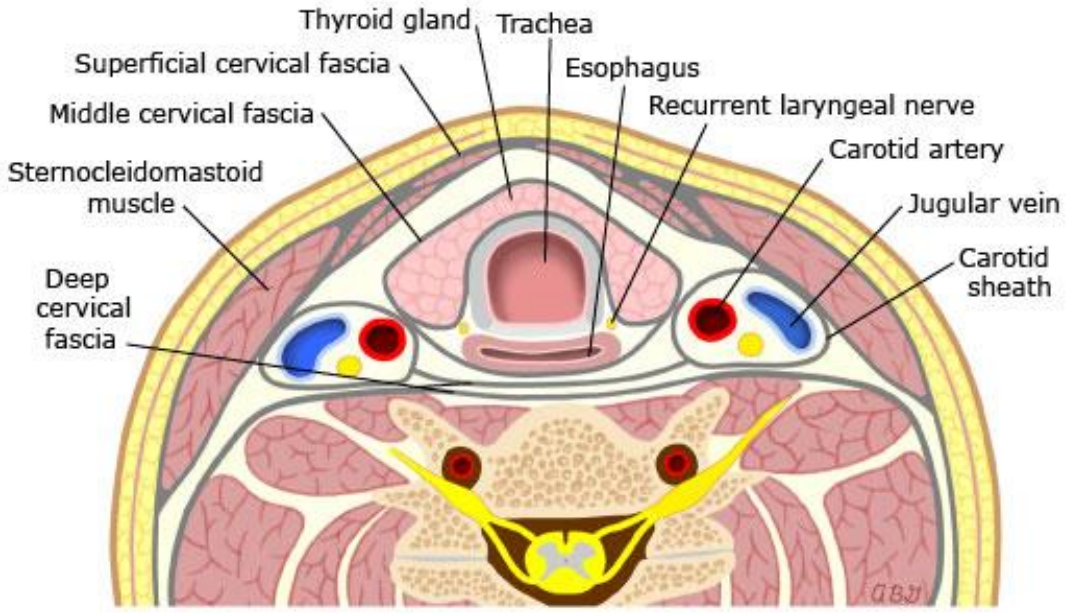
- **Low risk patient** include patient below 40 years , well differentiated tumor , primary tumour less than 4 cm & no extra-thyroid spread .
- **High risk patient** include the reverse of previous features .

★ **Complications :**

I) Spread :

1- Direct spread :

- Mainly & early **in anaplastic carcinoma** but late in other types .
- To the surrounding structures :
  - **Early** to trachea , RLN and para-thyroid glands**.**
  - **Later** on to esophagus , surround & compression of carotid sheath , sternomastoid & pretracheal muscles and skin .



2- Lymphatic spread :

- Mainly & early **in papillary carcinoma**.
- **Early to recurrent laryngeal** lymph nodes .
- **Then pre-laryngeal , pre-tracheal & paratracheal** lymph nodes .

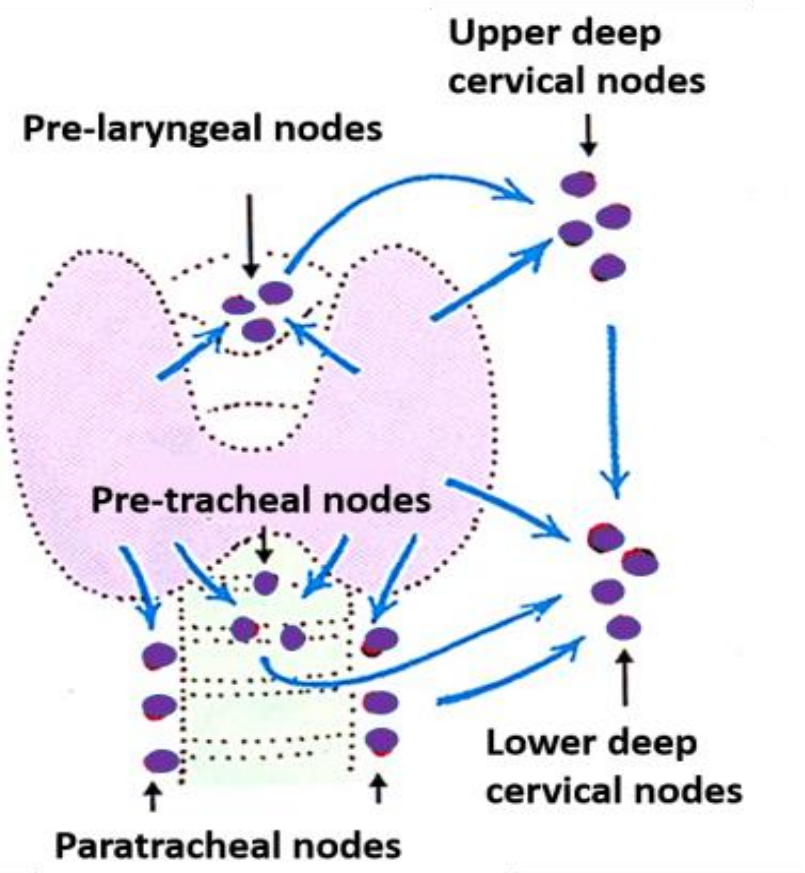
- Finally most lymph from thyroid pass **mainly to lower deep cervical** lymph nodes & to less extend to the upper deep cervical lymph nodes.

- **Mediastinal lymph nodes** may be affected in carcinoma of lower pole of lateral lobes .

3- Blood spread :

- Mainly & early **in follicular carcinoma**.
- Mainly to bones (cervical vertebrae , skull , clavicle & ribs) , lung & brain .

Lymphatic Drainage Of Thyroid Gland

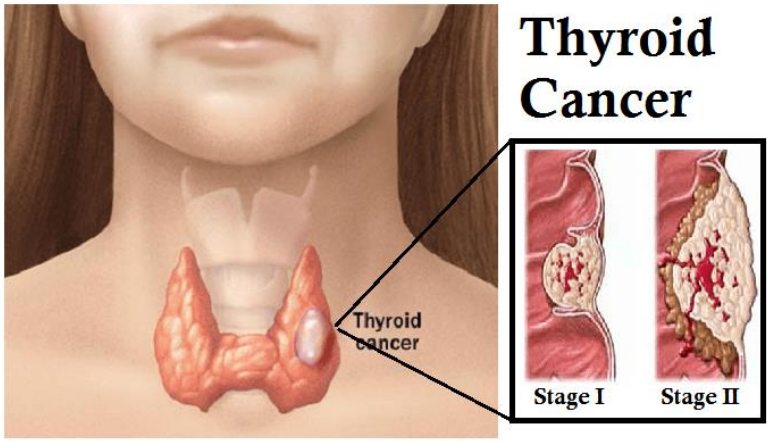


II) Fungation , ulceration , hemorrhage , anaemia , cachexia & death .

Fungation & ulceration of thyroid cancer

★ **Clinical Picture: (swelling + 3 nerves + 3 tubes + 3 spread+Diarrhea)**

1. ***Thyroid swelling*** **(usually solitary nodule) is the** ***commonest*** *&* early presentation which is hard, rapidly growing, irregular and ill-defined. Any solitary thyroid nodule is suspicious for malignancy.



2. Progressive persistant ***Pain*** which is felt in the goiter or radiate to the auricle along the Arnold's nerve which is the auricular branch of vagus ***(one of earliest symptoms of malignancy)***.
3. ***Hoarsness*** **or changes** ***of voice*** (infiltration of R.L.N is one of ***earliest symptoms of infiltration*** of surrounding structures).
4. ***Horner's syndrome*** in late cases (infilteration of sympathetic chain).
5. ***Dyspnea*** at rest , constant **cough** not related to cold weather and **haemoptysis** (infiltration of *trachea) with* ***loss of movement*** of the goiter over the trachea (one of ***earliest manifestation*** **of infilteration** of surrounding structures).

5. ***Dysphagia*** more marked to solids (infiltration of ***esophagus).***
6. ***Berry's sign****:* weak in normal position or absent carotid pulsations because the tumour compresses and surrounds the carotid artery.
7. ***Fixity*** to skin and sternomastoid.
8. ***L.Ns. metastasis****:* Enlarged, hard, painless, not tender, mobile & discrete cervical L.Ns. which later on become fixed, matted & painful.
9. ***Manifestations of distal metastases****.*
10. ***Diarrhoea*** in *30%* of cases with medullary carcinoma due to production of 5-hydroxytriptamine & prostaglandines.

★ **D.D :**

- **Causes of hard thyroid :** carcinoma , calcified nodule , Reidle's thyroiditis , tense cyst .
- **Other causes of goiter .**

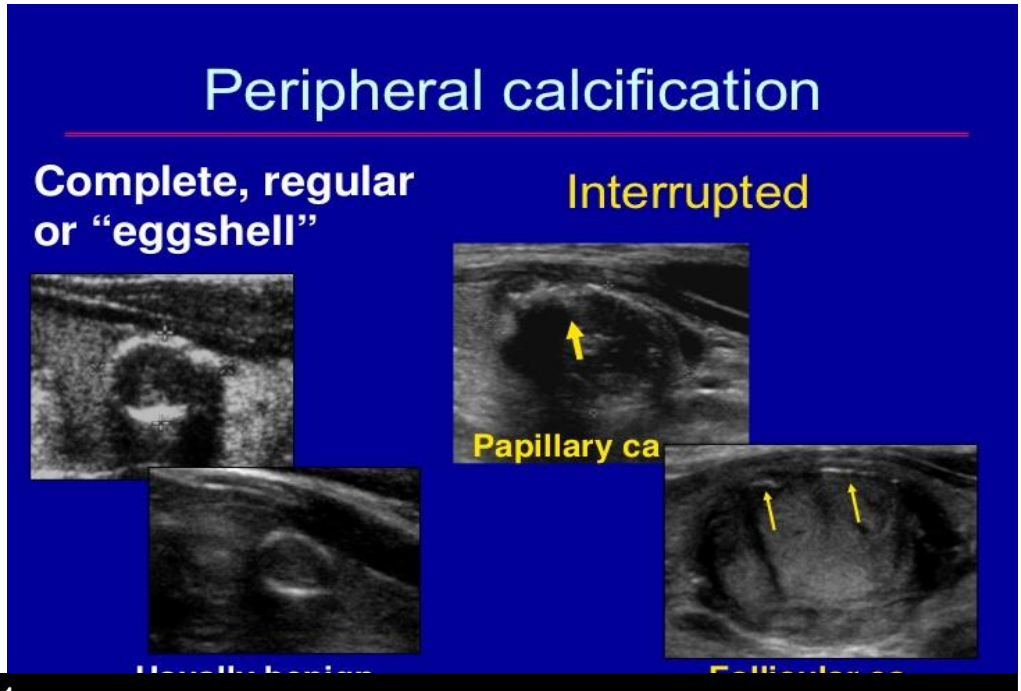
★ **Investigations :**

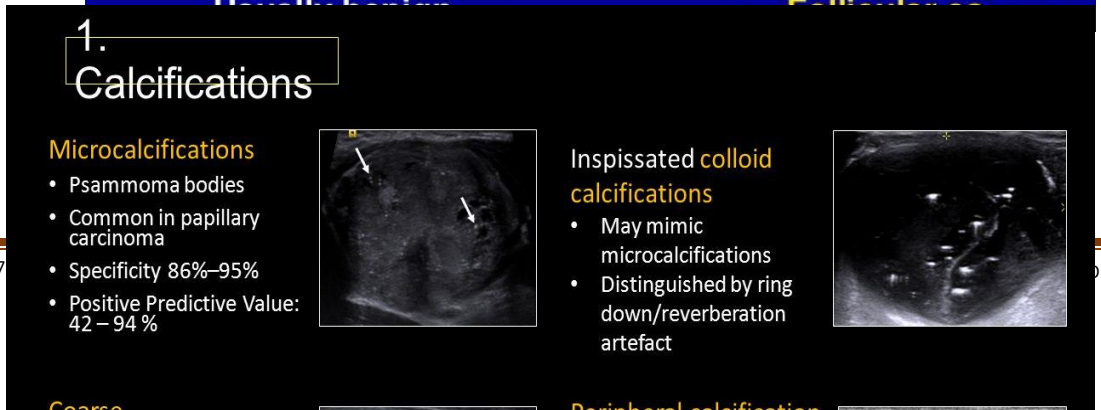
I) Investigations to diagnose the 1ry tumor :

1. ***I*** ^{123} ***Scanning:*** **A cold nodule** is suggestive and **a hot nodule is rarely malignant. Re-scanning** of the whole body after thyroidectomy to **detect metastases and it is** useful for **follow up** to detect early recurrence.
2. ***Ultrasonography*** can detect **non-palpable** nodules , differentiate **cyst from solid** nodule, shows **size** of the gland, may show **infiltration** of surrounding structures , thyroid **calcification** , assess **vascularity** of the swelling , detect any **lymph node** enlargement and guide the **biopsy** .

Thyroid ultrasound

- N.B : **Types thyroid calcifications** in U/S or plain x-ray :
  1- ***Microcalcification*** : 1mm or less (punctuate calcification) , usually in papillary carcinoma (psamoma bodies) .
  2- ***Peripheral rim calcification***, may be regular , complete (egg shell) in benign nodules or irregular , interrupted in malignant nodules .
  3- ***Coarse calcification*** in medullary carcinoma .





3. ***Biopsy:*** Diagnostic and ***most important*** investigation. It is better **ultrasonic guided** .It may be:

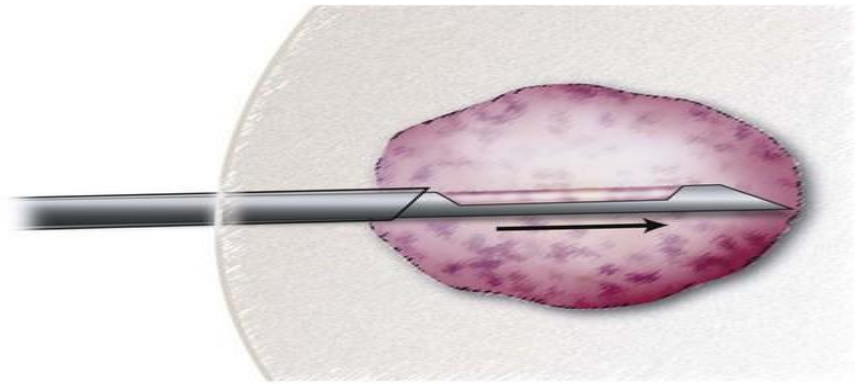
   a) **Fine Needle aspiration cytology**. (FNAC)

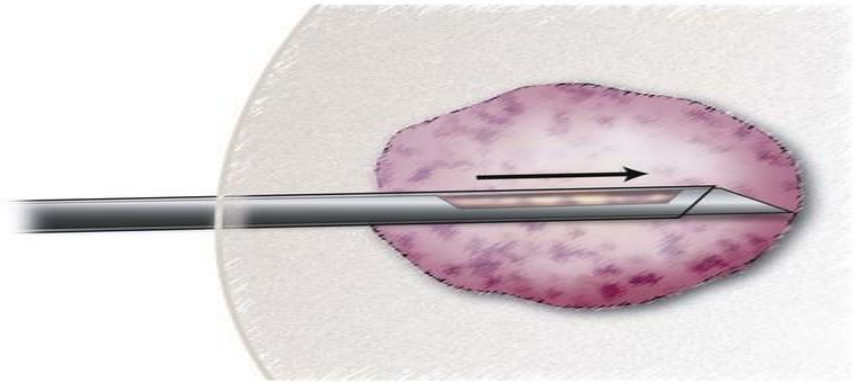
   - Simple, inexpensive & accurate is 90% in nodules more than 0.5 cm.
   - It can not differentiate follicular adenoma from carcinoma (depends on capsular or vascular invasion).

* Benign cyst	* Malignant cyst
• The aspirate ***is clear***	• The aspirate is ***haemorrhagic***.
• ***Disappears*** completely after aspiration	• Residual mass ***after aspiration***
• ***No reaccumulation*** of fluid	• Rapid ***reaccumulation*** of fluid .
• Cytology is ***negative***.	• Cytology is ***postive*** for malignancy.

b) **Tru-cut thick needle biopsy:** (**rarely** used in thyroid swelling)

- It obtains a core for pathological exam. of a nodule **more than 2 cm.**
- It may produce **haematoma**.





c) **Excision biopsy** (hemithyroidectomy) then perform one of the followings :

- **Frozen section** exam. during the operation and if malignancy is diagnosed definitive surgery is performed .
- **Paraffin section** exam. after the operation.

d) Pre-operative **L.N. biopsy** from an enlarged cervical L.Ns.

III) Investigations to detect spread : (metastatic work up)

1- PET scan (positron emission tomography scan) **:** show l**ocal** tumor , **nodal** & **distal** metastases for accurate staging.

2- A PET scan and CT scan may be done at the same time. This is called a **PET-CT** for **accurate** staging.

3. *Plain X-ray:*

a) **To the neck**: may show position of the **trachea**, **retrosternal** extension & to **differentiate** calcified nodule from carcinoma.

b) **To chest and bones:** To detect secondaries.

4. *Investigations to detect local spread*:

- **Laryngoscopy**: examine mobility of vocal cord to detect **RLN** infilteration.
- **Bronchoscopy**: to detect infilteration to **trachea**.
- **Barium swallow & esophagoscopy** to detect spread to **oesophagus**.

5. *Other investigations to detect distal metastasis*:

- **Liver functions** impaired in liver metastases .
- Serum **alkaline phosphatase** is elevated in early liver & bone metastases even before clinical evidences .
- X-ray **chest and bones** to detect bone and lung metastases .
- Liver , lung , bone & brain **scan** when metastases are suspected in

these sites .

♦ **CT scan and MRI** when metastases are suspected in any sites .

IV) Tumor markers : It is only useful for **following** patients after surgery to detect recurrence.

1. ***Serum levels of thyroglobulin****:* It is the tumor marker for **papillary and follicular** carcinoma.

2. Detection of ***serum calcitonin*** elevation in **medullary** carcinoma

V) Routine investigations before thyroidectomy .

VI) Investigations to detect multiple endocrinal neoplasia .

★ **Treatment:**

I. Operable cases:

♦ ***Features of operability:*** No infiltration to important vital surrounding structures , no distal metastasis, mobile L.Ns and the patient is fit for surgery .

♦ ***Method****:* Depends on pathological types.

A. ***Papillary & follicular carcinoma:***

I) Treatment of the primary tumor:

1. Total thyroidectomy:

- **Indications:** The most popular operation for treatment of all operable cases.
- **Advantages:**
  - To ensure removal of ***multifocal tumor*** within the gland.
  - Complete removal of all thyroid tissues competing for iodine → possible detection of metastases by post-operative I^{123}***scanning***

& serum thyroglobulin and ***treatment of these*** metastasis by I^{131}.

2. Total lobectomy & isthmusectomy: (**hemithyroidectomy**)

- **Indication**: It is recommended by some surgeons in early cases (tumor less than 1 cm) in low risk patient .
- **Advantages**: No difference in survival rate between hemithyroidectomy *&* total thyroidectomy (which have a risk of hypoparathyroidism or RLN injury) .

II) Management of lymphatic spread:

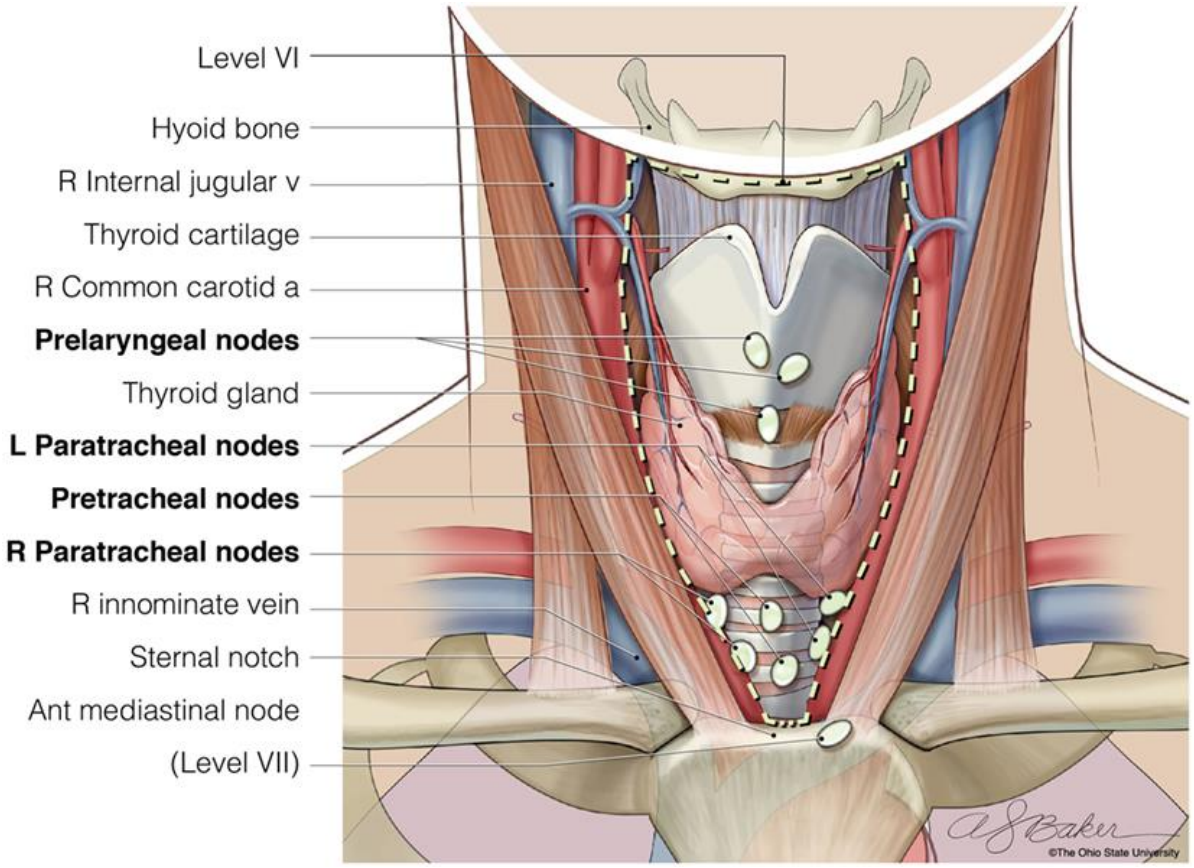
1) ***If lymph nodes are -ve*** (by frozen section) → routine resection of central lymph nodes .

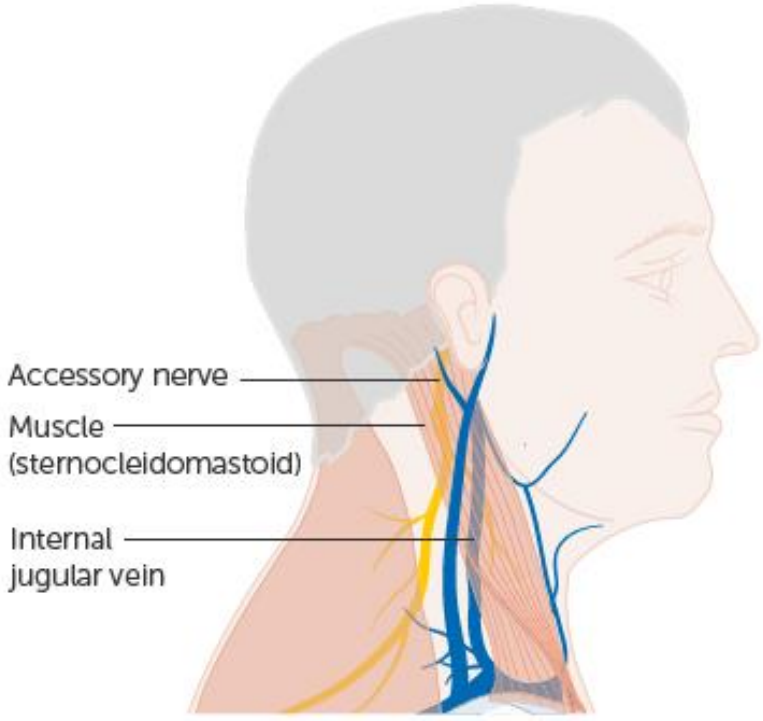
- N.B : **Resection of central cervical lymph nodes** include resection of all lymph nodes from hyoid bone superiorly , manubrium inferiorly , carotid sheath lateral and pre-vertebral fascia posteriorly .This include removal of prelaryngeal , pretracheal , paratracheal and recurrent laryngeal lymph nodes .

2) ***If few lymph nodes metastases*** → selective picking up of these L.Ns.

3) ***If L.Ns are extensive*** (by frozen section or grossly enlarged)

- **Modified block dissection** of cervical lymph nodes with preservation of internal jugular vein , spinal accessory nerve & sternomastoid muscle .





Cancer Research UK

III) Management of occult blood spread:

1. Full dose of ***thyroxine*** should be given for all cases to suppress TSH (reduce incidence of recurrence) and to prevent hypothyroidism.
2. ***Postoperative I^{123} scan*** of whole the body to detect any local residual tumor or distal metastases.
3. ***Postoperative I^{131} therapy*** is indicated in local recurrence, extensive tumor or distal metastasis. The dose is 100 - 200 millicuries.

B. In medullary carcinoma: Should be treated by ***total thyroidectomy*** with routine ***modified block dissection*** of cervical lymph nodes .

II- Inoperable cases:

- **Features of inoperability**: (The reverse of operable cases) + anaplastic carcinoma.
- **Methods:**
  1. ***Palliative total thyroidectomy****:* to relieve pressure, to diminish pain, to enhance I^{131} uptake by malignant cells by removing normal thyroid tissues competing for iodine uptake .
  2. ***Palliative isthmusectomy*** may be performed to relieve tracheal compression .
  3. ***External irradiation****:* Only for anaplastic carcinoma.
  4. ***Radioactive iodine.***
  5. ***Palliative chemotherapy*** for anaplastic carcinoma .

★ THE "APUD" CELLS ★

* These are cells which have the ability for **amine precursor uptake** & then their **decarboxylation** to produce hormones.
* These are endocrinal cells of ***ectodermal origin arising from the neural Crest & migrate*** during intrauterine life to different organs in the body.
* ***Apudomas*** are neoplasia affecting the APUD cells in one organ or may involve different APUD cells in different organs producing **m**ultiple **e**ndorine **n**eoplasia (**MEN**).
* 3 Types of ***multiple endocine neoplasia*** (MEN) have been identified:
  1. ***Type I: (Wermer's syndrome)*** involves hyperparathyroidism, pancreatic tumour in non-B cells & pituitary tumour.
  2. ***Type IIa: (sipple's syndrome)*** involves medullary carcinoma of thyroid, pheo-chromocytoma & hyperparathyroidism.
  3. ***Type IIb: (mucosal neuroma syndrome)*** involves medullary carcinoma of thyroid, pheochromocytoma & multiple neuromatous mucosal nodules.

JJ Medicine

Multiple Endocrine Neoplasia Type 1



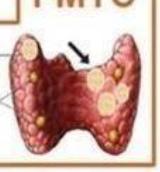
Multiple Endocrine Neoplasia type 2 (*RET*)

- All Medullary thyroid cancer should have *RET* analysis
  - 25% of all MTC are hereditary vs 75% sporadic, more often bilateral and multifocal

5% *de novo* mutation rate — Type 2A

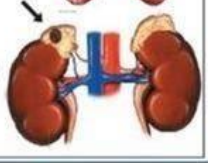
FMTC

Medullary Thyroid Carcinoma > 90%



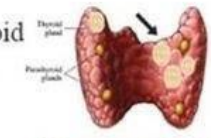
Parathyroid Hyperplasia 0-20%

Pheochromocytoma 0-50%



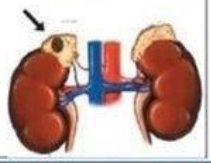
50-75% *de novo* mutation rate — Type 2B

Medullary Thyroid Carcinoma 100%



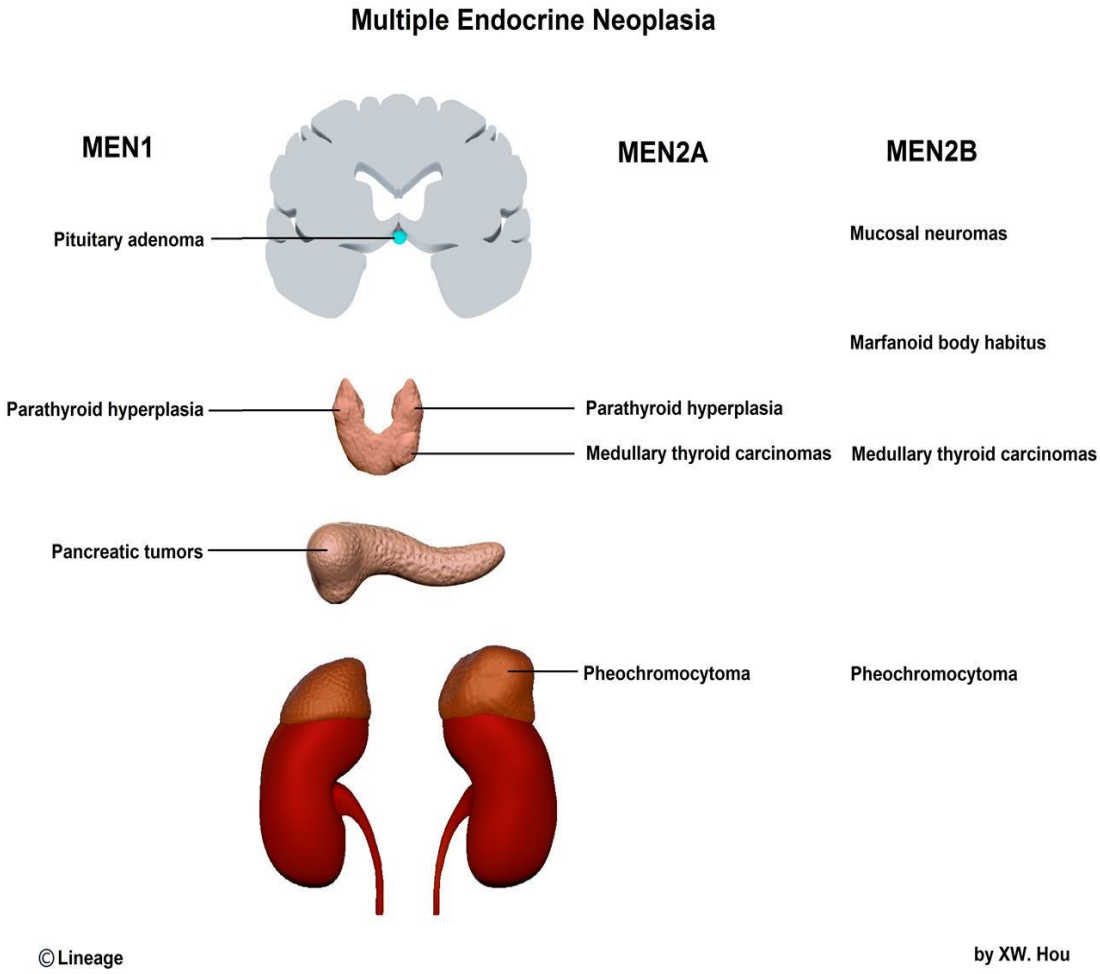
MEN2B Phenotype 100%

Pheochromocytoma ~50%



Cote, Gilbert

UHN Princess Margaret Cancer Centre


Multiple Endocrine Neoplasia
MEN1
MEN2A
MEN2B
Pituitary adenoma
Mucosal neuromas
Marfanoid body habitus
Parathyroid hyperplasia
Parathyroid hyperplasia
Medullary thyroid carcinomas
Medullary thyroid carcinomas
Pancreatic tumors
Pheochromocytoma
Pheochromocytoma
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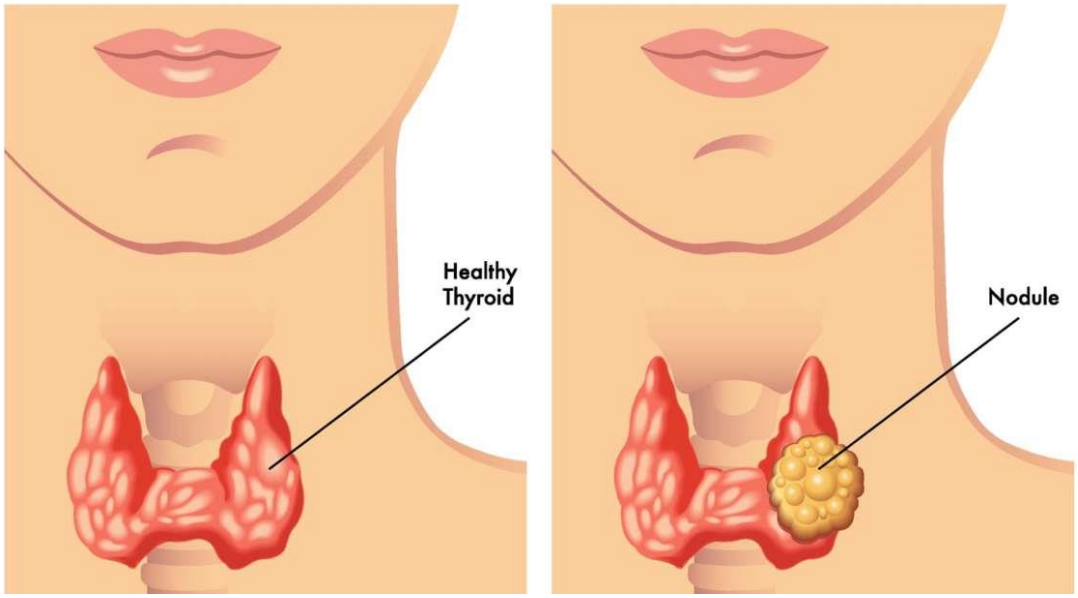
by XW. Hou

SOLITARY THYROID NODULE

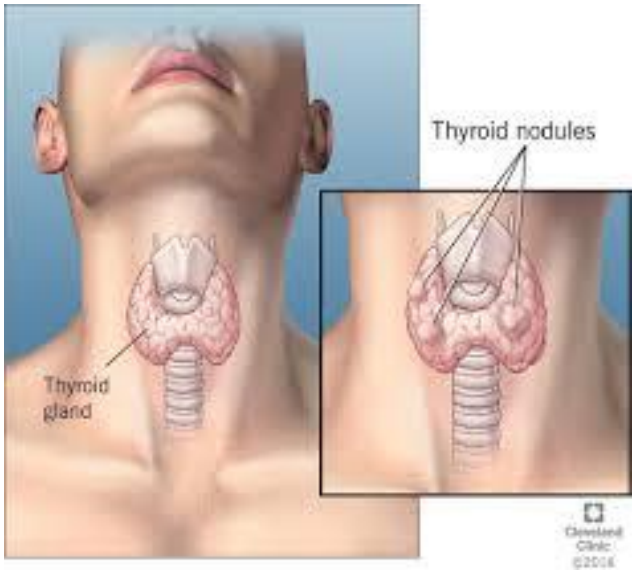
★ **Definition:** A single nodule in an otherwise normal thyroid gland.



★ **Incidence:** More common in females.

★ **Aetiology:**

1. ***The commonest is simple nodular goiter*** with one palpable nodule (dominant nodule) and the other nodules are not clinically palpable .



2. ***Toxic nodule.***
3. ***Malignant nodule.***
4. ***Inflammatory nodule*** (thyroiditis): very rare.
5. ***True benign tumor*** of thyroid: follicular adenoma.
6. ***Thyroid cyst*** which may be benign or malignant.

★ **Clinical picture:** The importance of solitary nodule lies in the risk of malignancy.

A. Malignant manifestations: The patient is euthyroid. Malignancy is suspected in the following conditions:

1. ***Recent onset & rapid growth especially in young or elderly patient*** .
2. **Pain** in the goiter or referred to the ear.
3. ***The nodule*** is hard, irregular with limited mobility.
4. Evidences of *infiltration* of surrounding structures (mention in short).

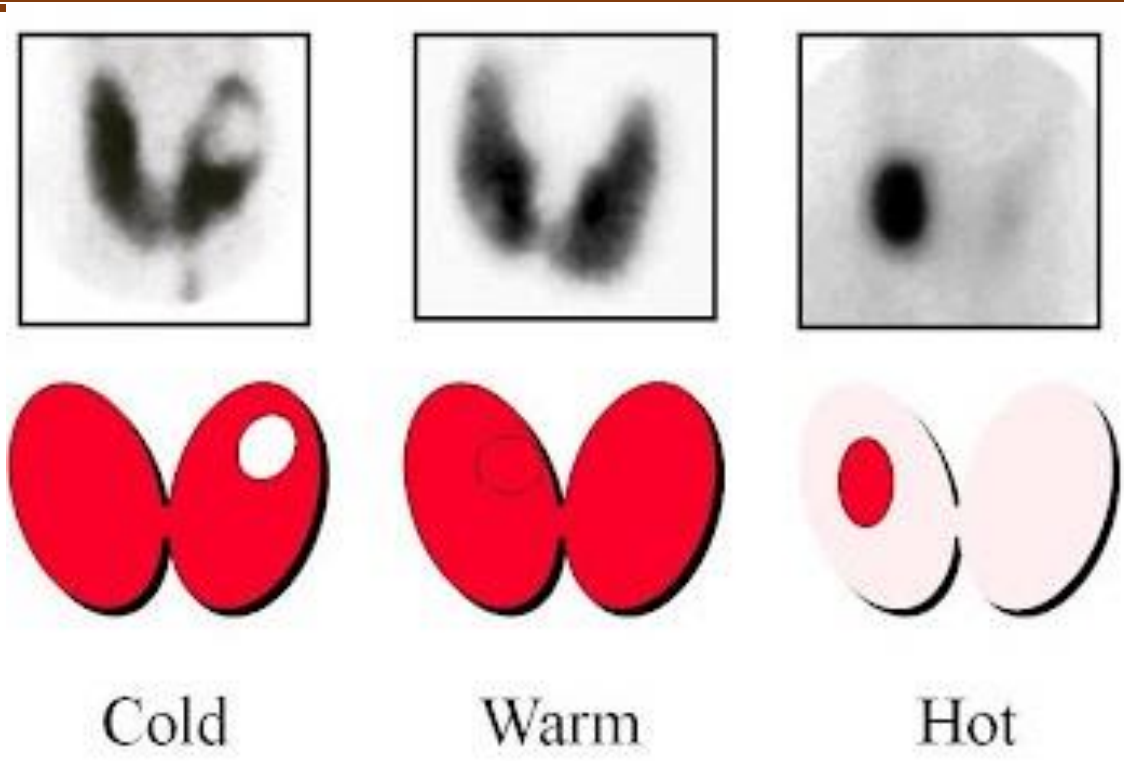
B. Toxic manifestations: (see thryrotoxicosis but ***no autoimmune manifestations as true exophthalmos or Graves' dermopathy***).

C. Cases which are not frankly malignant or toxic:

♦ In these cases, ***investigations are essential*** to diagnose the case.

★ Investigations:

1. ***Thyroid scanning*****:** One of the followings results may be obtained:
   a) **Hot nodule** (over active) and the patient is hyperthyroid → toxic nodule, rarely malignant or functioning adenoma.
   b) **Warm nodule** (active) and the patient is euthyroid → usually simple nodule , rarely functioning adenoma and possibility of malignancy is only 3%.
   c) **Cold nodule** (inactive) and the patient is euthyroid → malignant nodule 10-15 % but it may be degenerated, cystic or calcified simple nodule and rarely inflammatory.



2. **Level of TSH & *free T_3 & T_4*** ***e***especially for patient with toxic manifestation or hot nodule.
3. ***Ultrasonography:*** (look for U/S in carcinoma of thyroid) .
4. ***Biopsy is diagnostic*** & the most important investigation (Mention its types).
5. ***Estimation*** of thyroid antibodies may be needed to exclude thyroiditis.

★ Treatment:

1. ***Malignant nodule:*** (mention treatment of carcinoma in short).
2. ***Toxic nodule:*** Radioactive iodine or preoperative preparation followed by hemi-thyroidectomy.
3. ***Cases which are not frankly malignant or toxic:*** **Hemithyroidectomy** and histological examination, i.e excision biopsy & frozen section.
   - ♦ If not malignant → nothing more is needed.
   - ♦ If malignant → (mention treatment of carcinoma in short).

IV. Inflammatory Goiter

A- Acute Thyroiditis

★ **Aetiology**: Viral or pyogenic infection as a complication of infectious fever.

★ **C/P**: Acute onset of neck pain, dysphagia & fever.

★ **Treatment**: Antibiotics & drainage if pus is formed.

B. Subacute thyroiditis
(De Quervain Disease)

★ **Aetiology:** Most probably viral infection.

★ **C/P:**

- ♦ Rapid onset after upper respiratory tract infection with remission & exacerbation for few months but usually it is self limited .
- ♦ There are Pain in front of neck with fever & malaise .
- ♦ Firm , irregular & slightly tender thyroid .The goiter is variable is size .

★ **Investigations:**

- ♦ High ESR with normal or depressed leucocytic count .
- ♦ Decrease iodine uptake by the gland with slight elevation of serum T_4 is a feature.

★ **Treatment:** Rapid response to oral prednisone is diagnostic with anti-inflammatory drugs .

C. Chronic thyroiditts

I. T.B. & Syphilitic thyroiditis are very rare

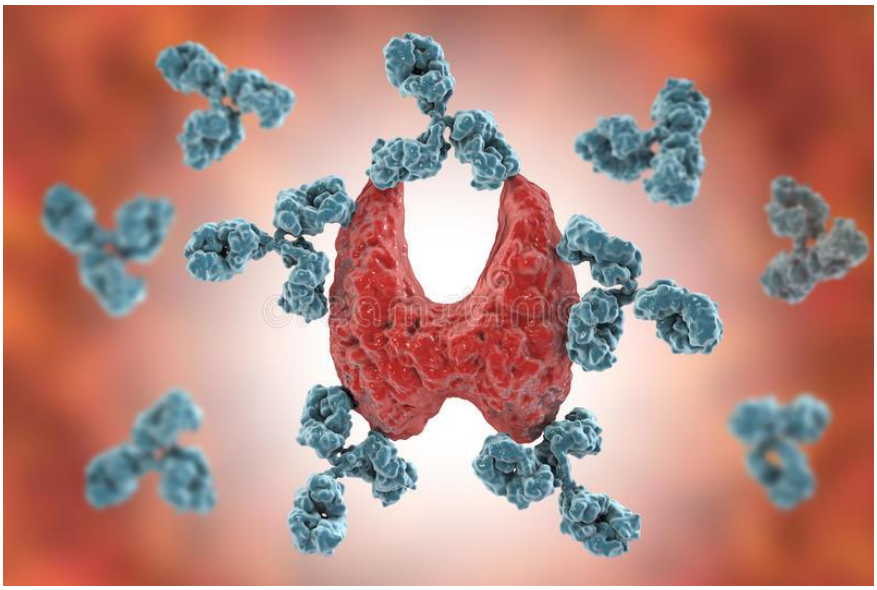
II. Hashimoto's thyroiditis*:*

★ **Incidence :** It is the ***commonest*** form of thyroiditis , usually affect females at menopause .

★ **Aetiology :** It is an ***autoimmune*** disease leading to formation of antibodies against thyroid antigen.

★ **Pathology** : The thyroid gland shows leucocytic & plasma cell infilteration gradually replacing the thyroid follicles .

★ **Complications** : Hypothyroidism and development of lymphoma .



★ Clinical Picture :

1. The onset is variable , it may be insidious asymptomatic or sudden painful .
2. ***The goiter*** may be diffuse or localized to one lobe, small or large, soft or firm.
3. Intially, there is mild hyperthyroidism but finally hypothyroidism is the role.

★ Investigations:

1. Detection of antimicrosomal and antithyroglobulin antibodies
2. Fine needle or true cut needle biopsy may be needed to exclude malignancy .

Hashimoto's thyroiditis

★ **Treatment:**

1. Full thyroxine replacement .
2. Thyroidectomy for large goiter or suspicious for malignancy.

III. Reidel's Thyroiditis:

★ It is probably ***a collagen disease***.

★ **Pathology:** The gland & surrounding structures are infiltrated by extensive dense fibrosis and may be associated with retroperitoneal fibrosis .

★ **C/P:**

- ♦ The gland is hard, irregular & fixed to the surrounding structures.
- ♦ Hypothyroidism & compression symptoms are common.

★ **D.D:** From anaplastic carcinoma by open biopsy.

★ **Treatment:** ***Resection of isthmus*** to relieve tracheal compression & biopsy to exclude malignancy .

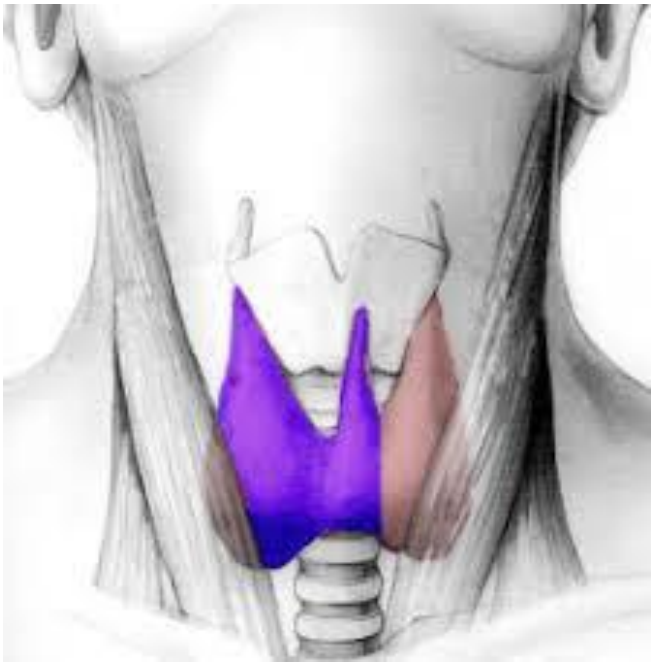
Reidel's Thyroiditis

Types of Thyroidectomy

★ Depending on the nature & extend of the pathology in the thyroid gland , thyroidectomy may be one of the followings :

1) Hemithyroidectomy :

- **Method :** total lobectomy + isthmusectomy
- **Indications :**
  - Excision biopsy of solitary thyroid nodule .
  - Solitary toxic thyroid nodule .
  - Thyroid adenoma .
  - Carcinoma of thyroid less than 1cm in low risk patient .



2) Subtotal thyroidectomy :

- **Method :**Removal of thyroid gland except postro-medial part each lobe (to preserve parathyroids and recurrent laryngeal nerves) to prevent post-operative hypothyroidism .

- In simple nodular goitre leave on each side a part ***equal to a normal lobe*** (8 – 10 gm = 2 x 1 x 1 inch). In the past this operation is called partial thyroidectomy ,
- In primary or secondary toxic goitre leave on each side a part ***equal to a ½ normal lobe*** (4 – 5 gm = 1 x 1/2 x 1/2 inch = strip equal to thickness of a finger).

➢ **Indications :**

- Large colloid & simple nodular goitre .
- 1ry & 2nd toxic goitre .

➢ **Disadvantage** : recurrence from the remaining thyroid tissues .

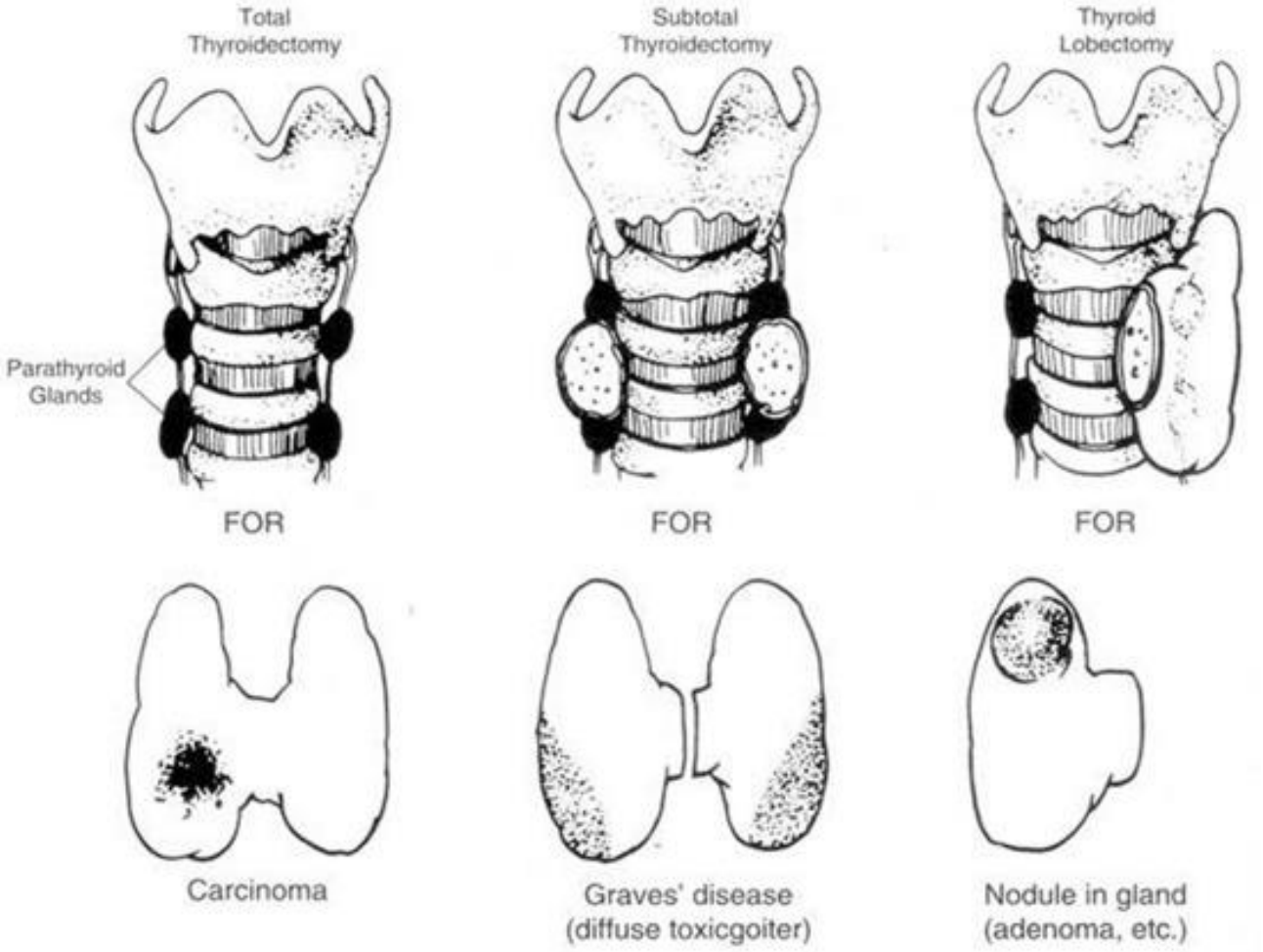
3) Near total thyroidectomy :

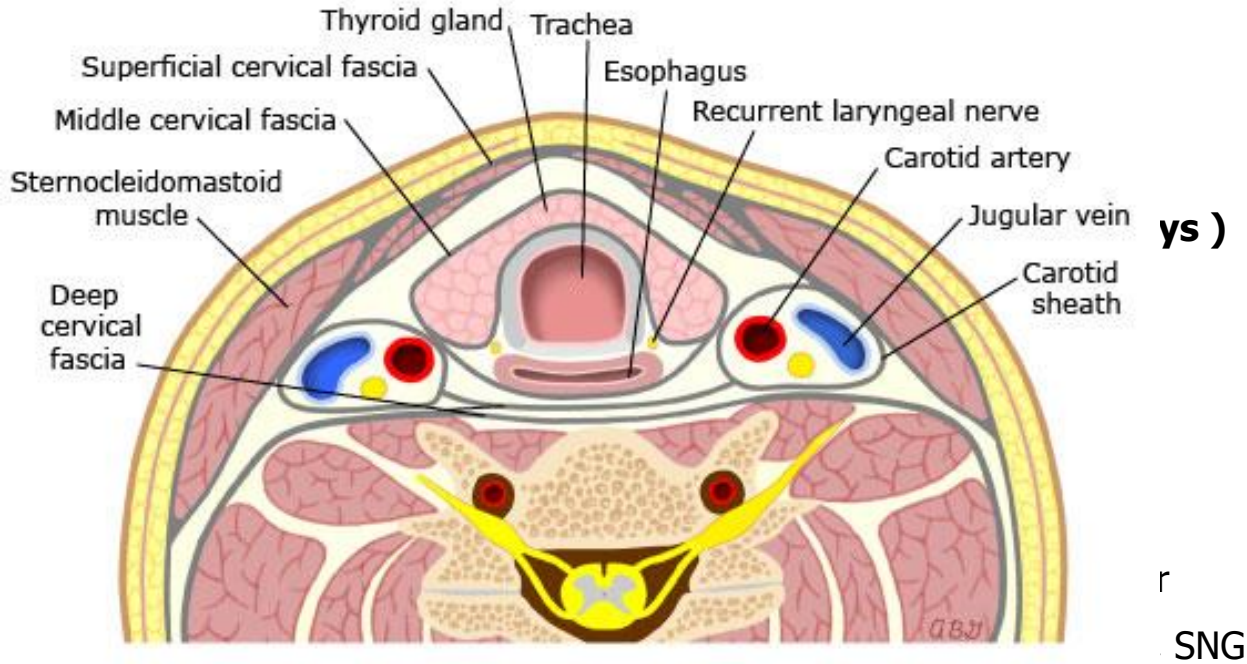
➢ **Method :**

- Total lobectomy on the same side of the pathology + isthmusectomy + leave only the posterior part of the capsule with a thin rim (2gm) of thyroid tissue on the contralateral side of the pathology .

➢ **Indications : (**Rarely performed nowadays)

- Unilateral operable carcinoma of thyroid less than 2 cm.
- To avoid recurrence , **many experienced surgeons** prefer nearly total thyroidectomy for simple nodular goitre especially if there is marked pathology on the postero-medial part of each lobe .


Total Thyroidectomy
Subtotal Thyroidectomy
Thyroid Lobectomy
Parathyroid Glands
FOR
FOR
FOR
Carcinoma
Graves' disease (diffuse toxicgoiter)
Nodule in gland (adenoma, etc.)


Thyroid gland
Trachea
Superficial cervical fascia
Esophagus
Middle cervical fascia
Recurrent laryngeal nerve
Carotid artery
Sternocleidomastoid muscle
Jugular vein
Carotid sheath
Deep cervical fascia

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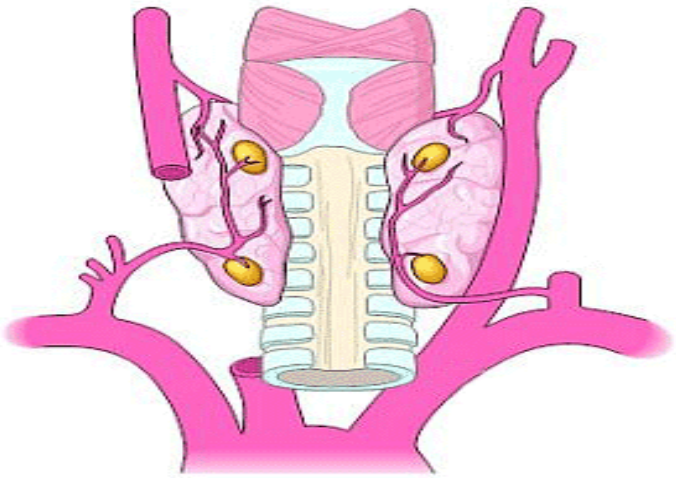
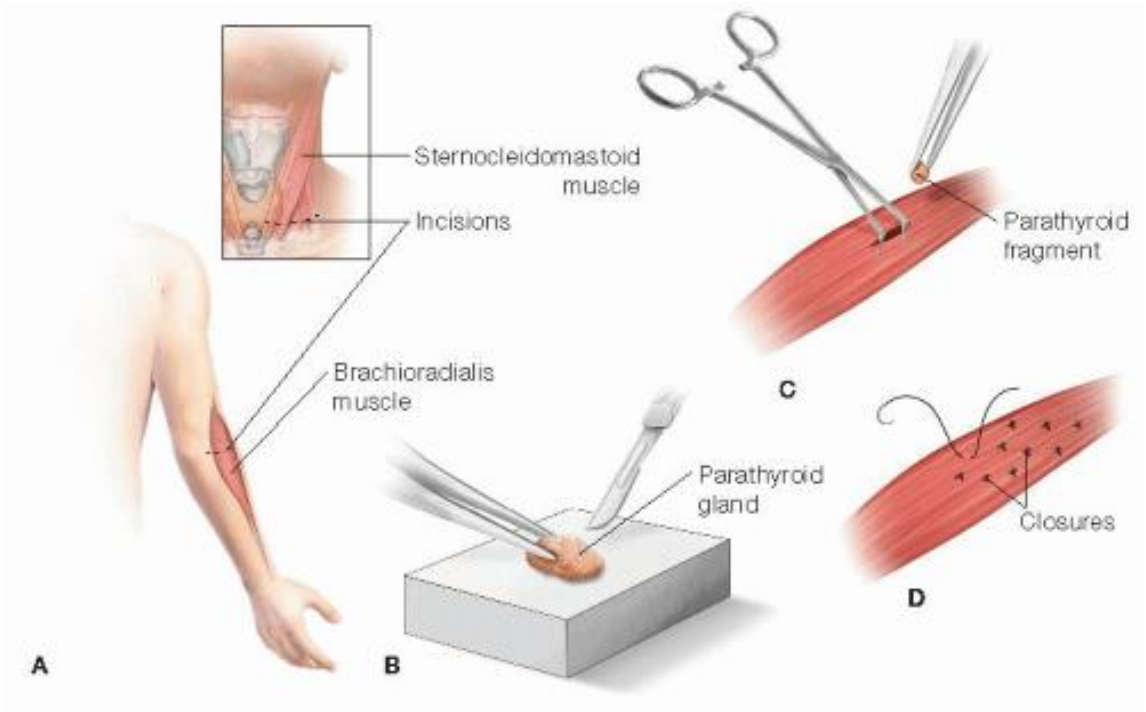
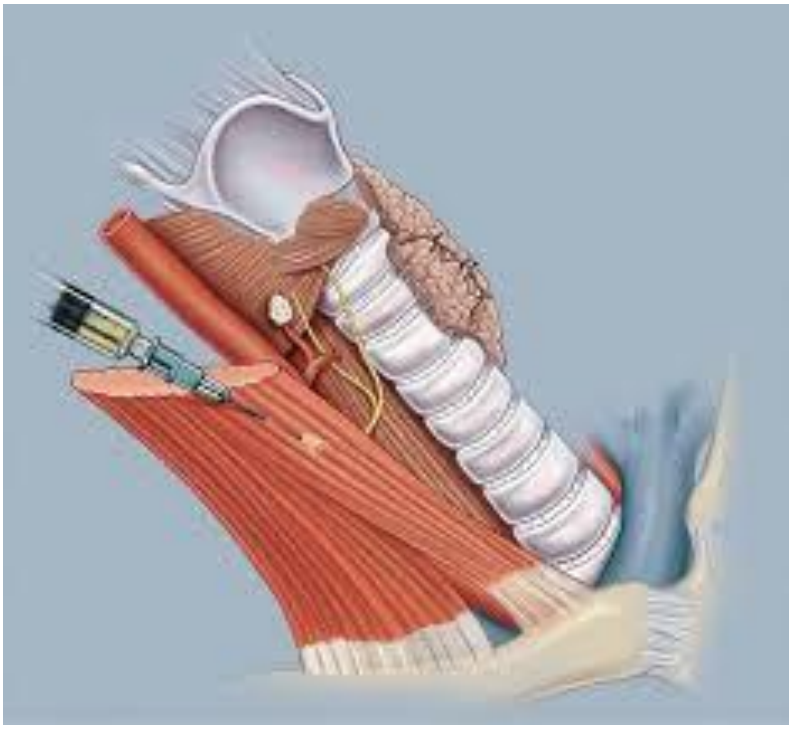
SNG

, 1ry & 2ry toxic goitre) especially if there is marked pathology on the postero-medial part of each lobe .

- **Complications :** It carries a risk of injury of parathyroid glands or recurrent laryngeal nerves .
- **Precautions :**
  - Parathyroid glands (with their blood supply) and recurrent laryngeal nerves should be exposed and preserved in situ (unless infilterated) .
  - The inferior thyroid artery should be ligated not truncally, but peripherally on the capsule of the thyroid gland to preserve the vascular supply to the parathyroid glands.
  - At least one parathyroid gland should be preserved .
  - If parathyroid glands are removedor devascularized , auto-graft (after frozen section confirmation of parathyroid gland) into the contralateral sternomastoid or recently in the muscles of forearm .







★ **N.B : You can live with ½ parathyroid gland .**

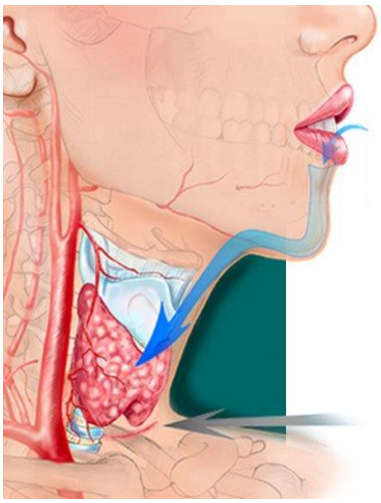
5) Isthmusectomy :

- **Indications :** Relief of tracheal compression and respiratory distress in Rediel's thyroiditis , lymphoma & anaplastic carcinoma .

★ **N.B : Subtotal lobectomy , total lobectomy and partial thyroidectomy are old terms not used nowadays and the least thyroid resection performed nowadays is hemi-thyroidectom .**

6) Trans-oral Endoscopic thyroidectomy :

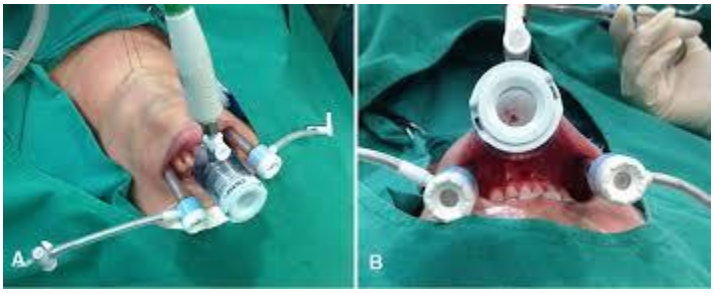
- It is a recent scarless thyroidectomy .
- Under general anesthesia with the patient supine & the neck hyper-extended .
- Through incisions in the lower lip , the instruments are introduced deep to the platysma .
- Divide the deep fascia in the middle line to separate the strap muscles on both sides to expose the thyroid gland .



NEW PIONEERING TECHNIQUE
MAY MONTHLY FOCUS

PerOral Endoscopic Thyroidectomy

based on the principles of natural orifice surgery, a completely scar-free surgery with minimal dissection.



Trans-oral Endoscopic thyroidectomy

ure 1 Cadaver with three robotic ports placed anterior to