Thyroid Disorders

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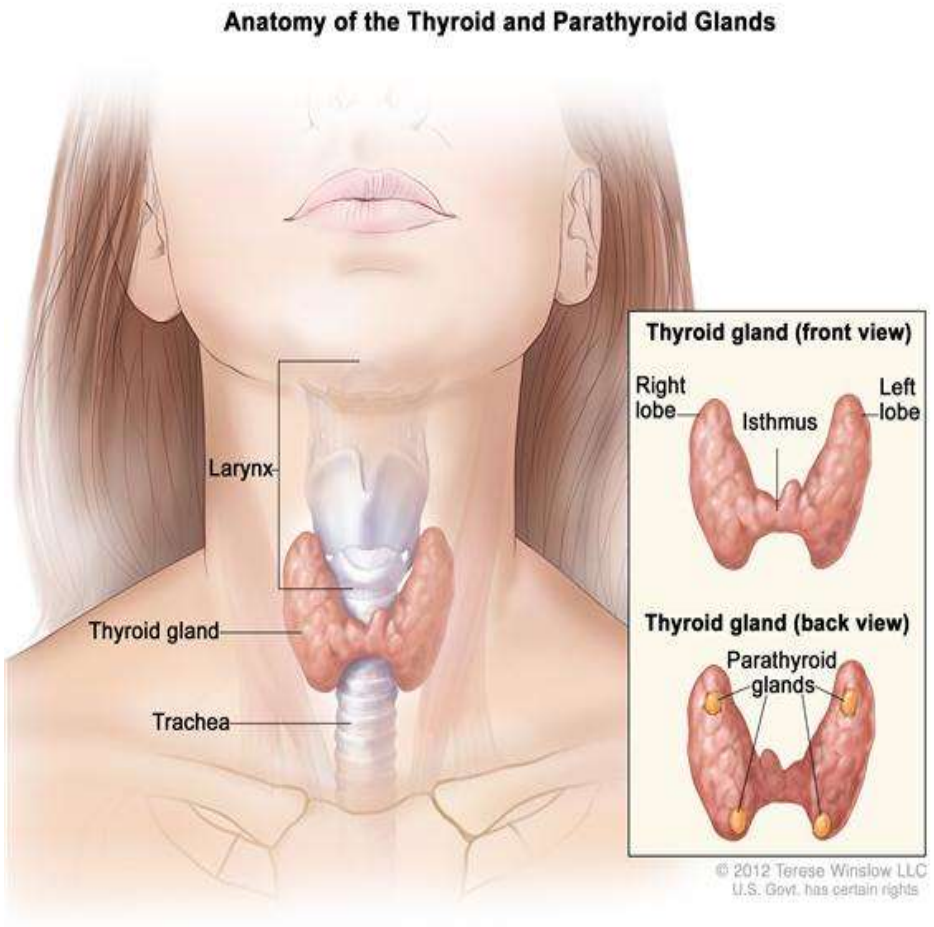
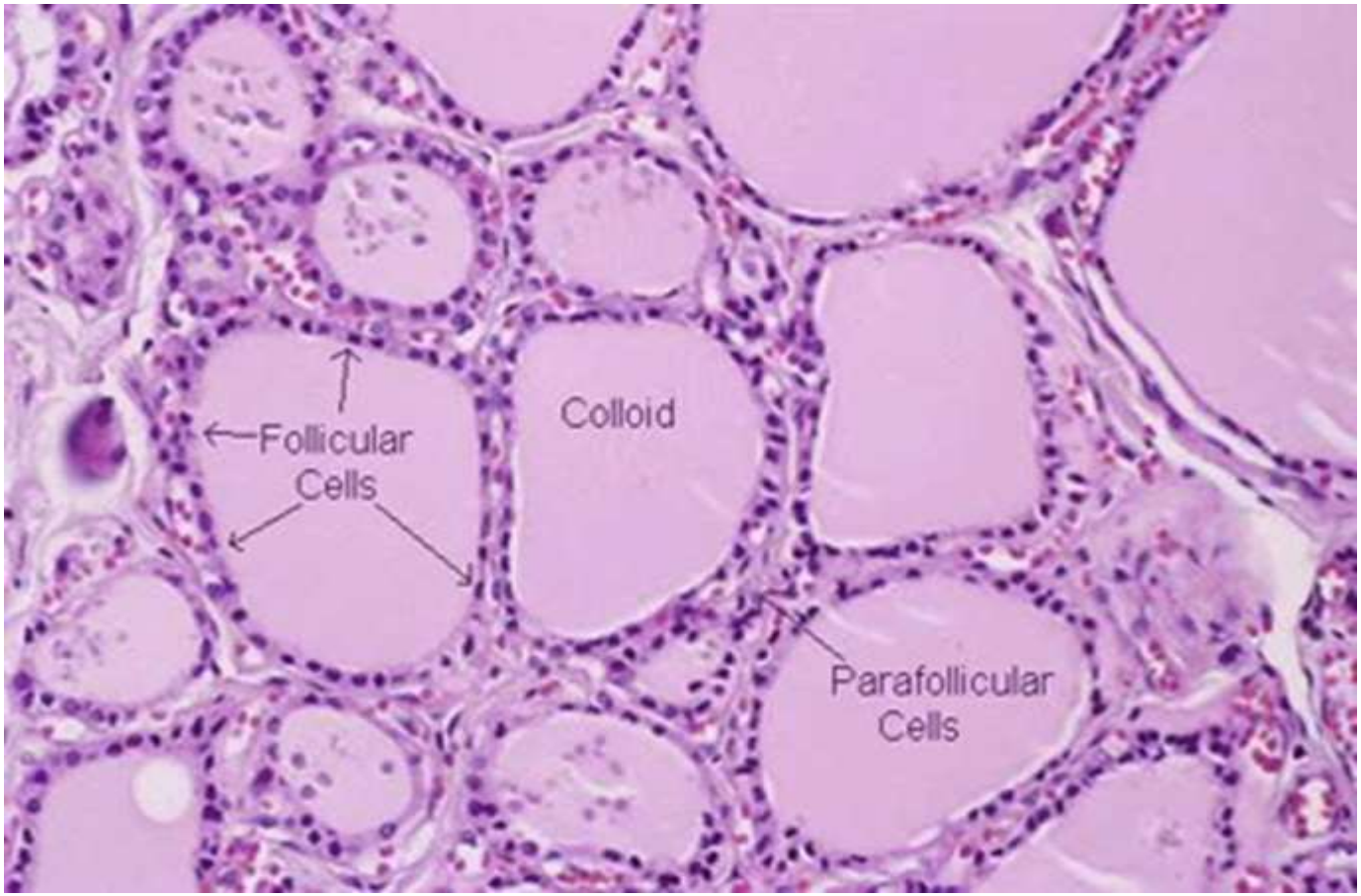
Introduction

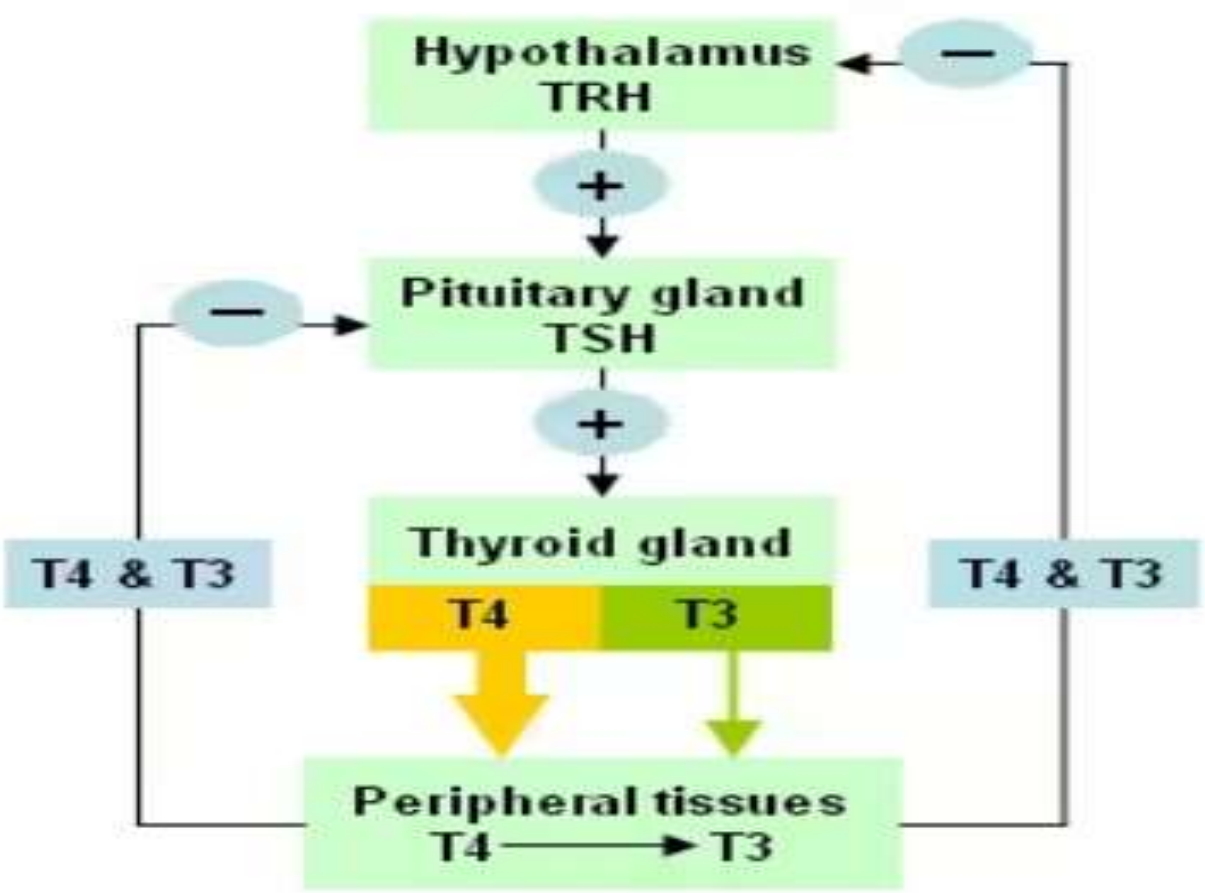
- The thyroid is one of the largest of the endocrine organs, weighing approximately 15 to 20 g.
- It has a tremendous potential for growth → termed a *goiter*, can weigh many hundreds of grams.



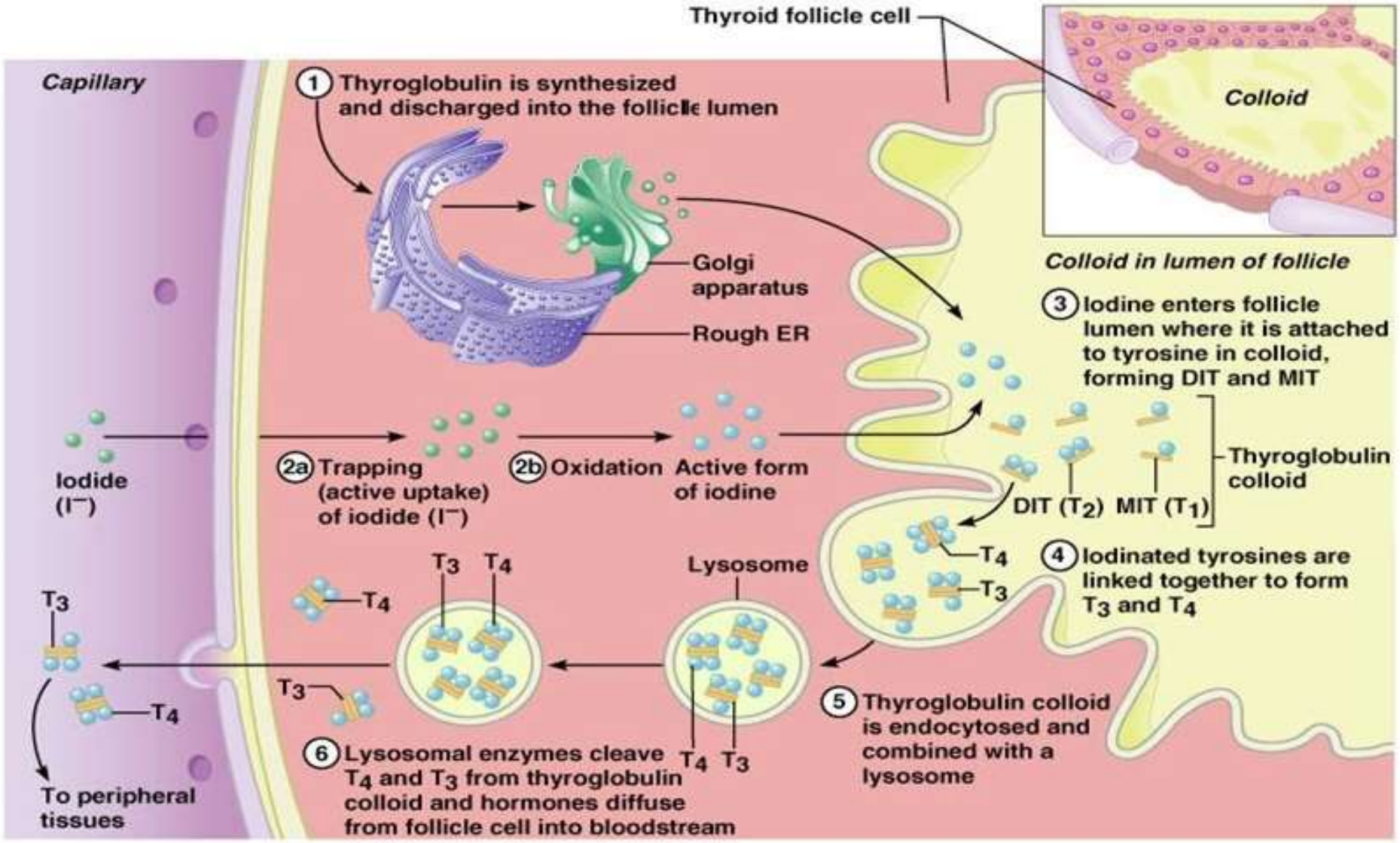

Follicular
Cells
Colloid
Parafollicular
Cells

- The gland is composed of closely packed spherical units termed *follicles,*
- He thyroid follicles are the structural and functional unit of the thyoid
- The interior of the follicle is filled with the clear proteinaceous colloid that normally is the major constituent of the total thyroid mass.
- The thyroid also contains para-follicular cells, or C cells, that are the source of calcitonin.

HPT AXIS


Hypothalamus
TRH
+
Pituitary gland
TSH
+
Thyroid gland
T4
T3
Peripheral tissues
T4 ⟶ T3
T4 & T3
T4 & T3
−
−

SYNTHESIS OF THYROID HORMONES



- Approach to thyroid disorders :

History

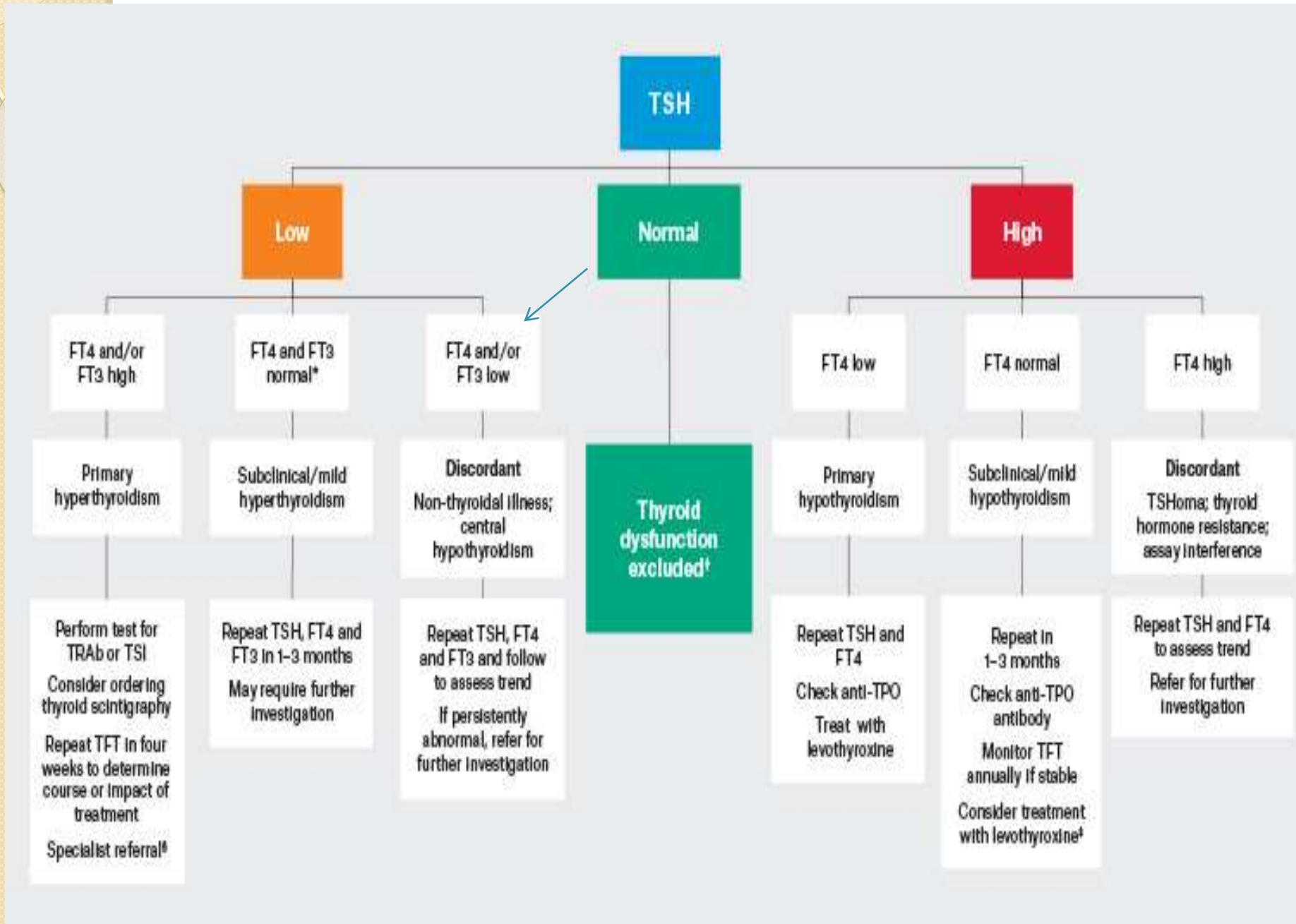
Physical examination

Blood tests(Depending on HX and PE) :
TSH , T4 , T3 , Thyroid antibodies

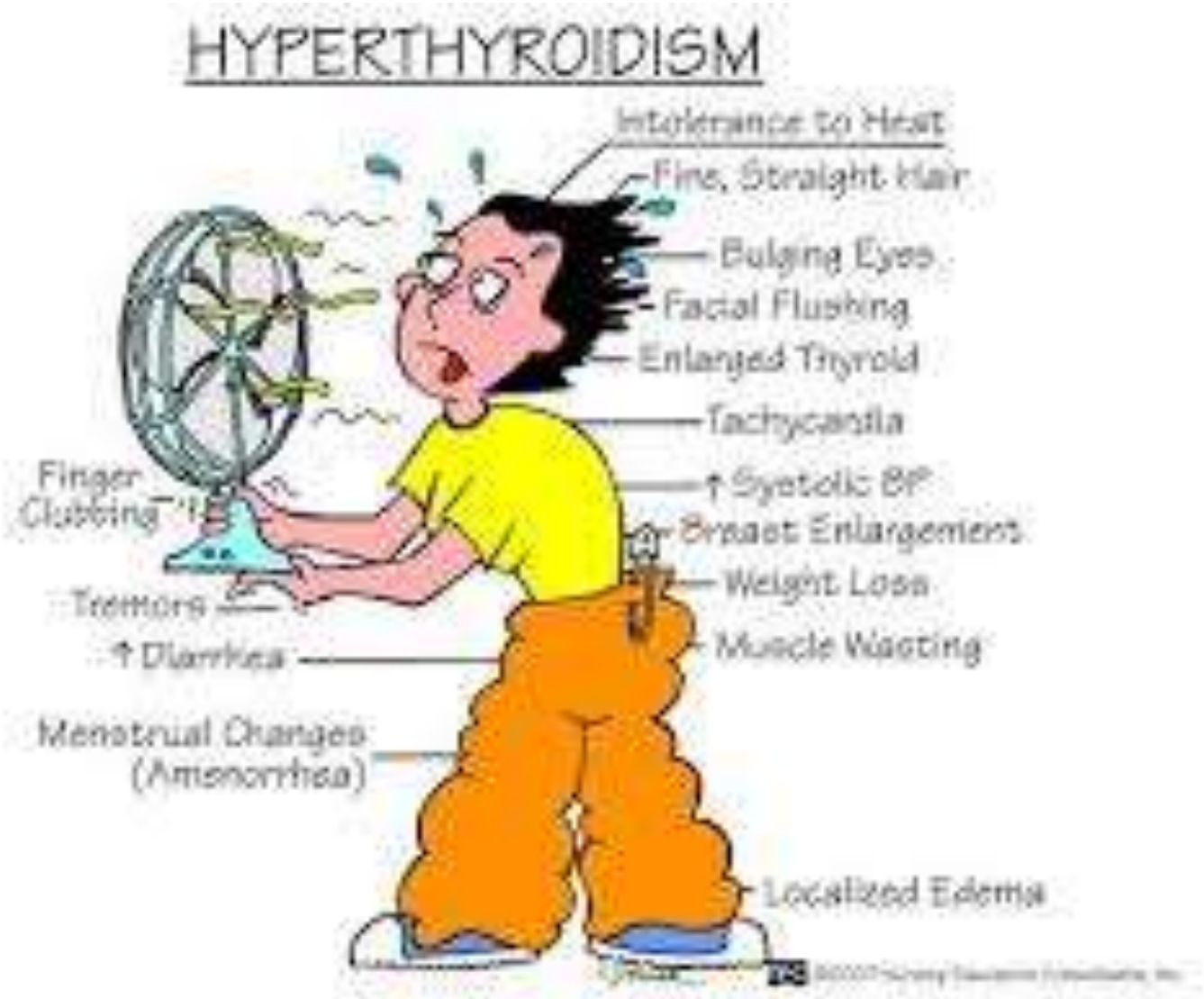
Imaging : Ultrasound , Nuclear imaging , CT

HYPOTHYROIDISM VS HYPERTHYROIDISM

Feature	Hypothyroidism	Thyrotoxicosis
General	**Weight gain**	**Weight loss**
	Lethargy	'Manic', restlessness
	Cold intolerance	Heat intolerance
Cardiac	Bradycardia	**Palpitations**, may even provoke arrhythmias e.g. atrial fibrillation
Skin	Dry (anhydrosis), cold, yellowish skin	Increased sweating
	Non-pitting oedema (e.g. hands, face)	Pretibial myxoedema: erythematous, oedematous lesions above the lateral malleoli
	-	Thyroid acropachy: clubbing
Hair	Dry, coarse (خشن) scalp hair, loss of lateral aspect of eyebrows	Fine (ناعم)
Gastrointestinal	Constipation	Diarrhoea
Gynaecological	Menorrhagia	Oligomenorrhea
Neurological	Decreased deep tendon reflexes Carpal tunnel syndrome	**Anxiety** **Tremor**


TSH
Low
Normal
High
FT4 and/or FT3 high
FT4 and FT3 normal*
FT4 and/or FT3 low
FT4 low
FT4 normal
FT4 high
Primary hyperthyroidism
Subclinical/mild hyperthyroidism
Discordant
Non-thyroidal illness; central hypothyroidism
Thyroid dysfunction excluded†
Primary hypothyroidism
Subclinical/mild hypothyroidism
Discordant
TSHoma; thyroid hormone resistance; assay interference
Perform test for TRAb or TSI
Consider ordering thyroid scintigraphy
Repeat TFT in four weeks to determine course or impact of treatment
Specialist referral‡
Repeat TSH, FT4 and FT3 in 1–3 months
May require further investigation
Repeat TSH, FT4 and FT3 and follow to assess trend
If persistently abnormal, refer for further investigation
Repeat TSH and FT4
Check anti-TPO
Treat with levothyroxine
Repeat in 1–3 months
Check anti-TPO antibody
Monitor TFT annually if stable
Consider treatment with levothyroxine‡
Repeat TSH and FT4 to assess trend
Refer for further investigation

THYROTOXICOSIS



Thyrotoxicosis

Symptoms	SIgns
Weight loss despite normal or increased appetite	Weight loss Tremor
Heat intolerance	Palmar erythema
Palpitations	Sinus tachycardia
Dyspnoea	Lid retraction, lid lag
Irritability, emotional lability	
Fatigue, Sweating, Tremor	
Less common	
Osteoporosis, Diarrhoea, steatorrhoea	Goitre with bruit Atrial fibrillation, HF
Muscle weakness, Pruritus, Ankle swelling Alopecia	Systolic hypertension/increased pulse pressure
Amenorrhoea/oligomenorrhoea Infertility, spontaneous abortion	Hyper-reflexia, Ill-sustained clonus, Proximal myopathy

Graves' ophtholmopathy
Graves dermopathy
Thyroid acrpoachy

Causes of Thyrotoxicosis

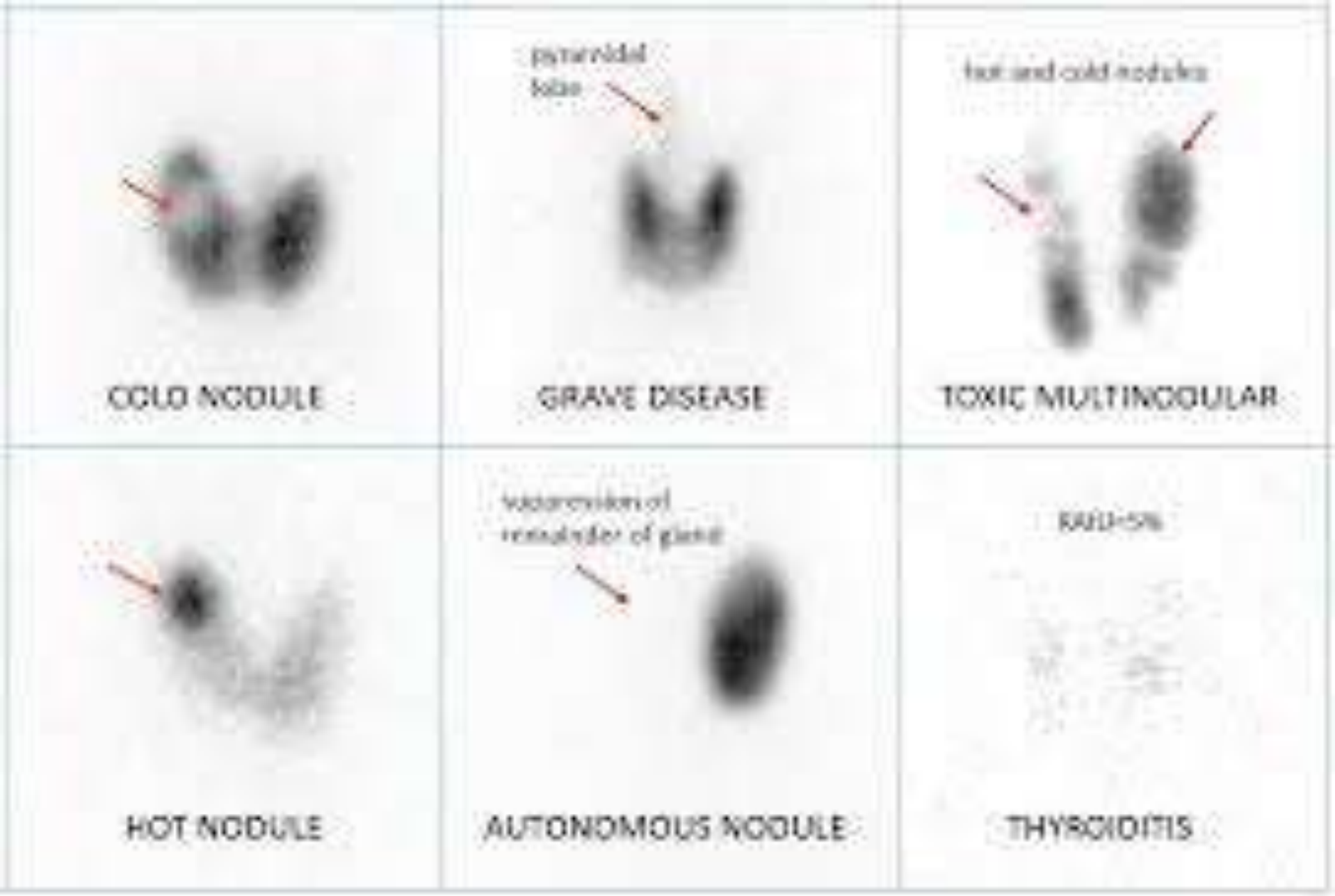
- **Disorders with increased Iodine uptake:**
- **(thyrotoxicosis with hyperthyroidism)**

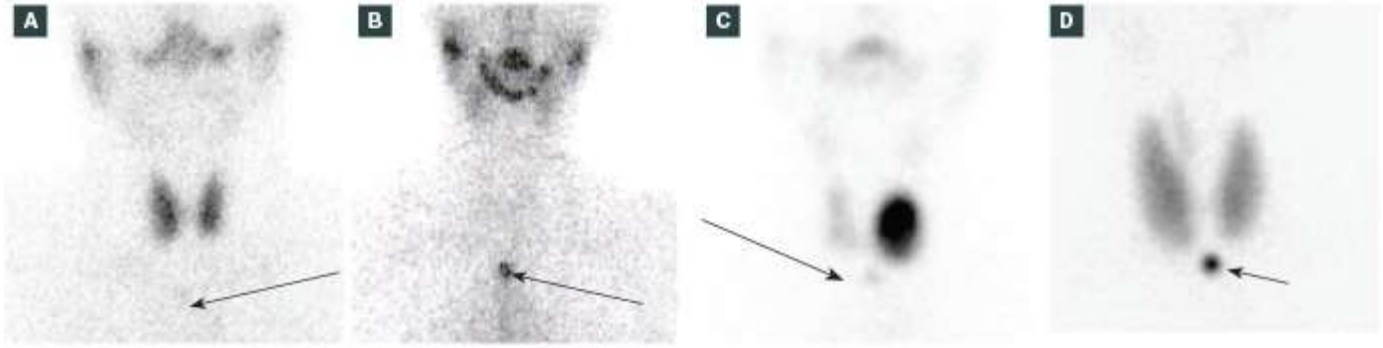
1. Graves' disease
2. Toxic MNG/adenoma
3. Inherited non-immune hyperthyroidism
4. Hyperthyroidism due to thyrotropin secretion (TSH-oma).
5. HCG-induced hyperthyroidism – Associated with pregnancy or Trophoblastic Tumors

- **Disorders with decreased Iodine uptake (Thyrotoxicosis without hyperthyroidism)**

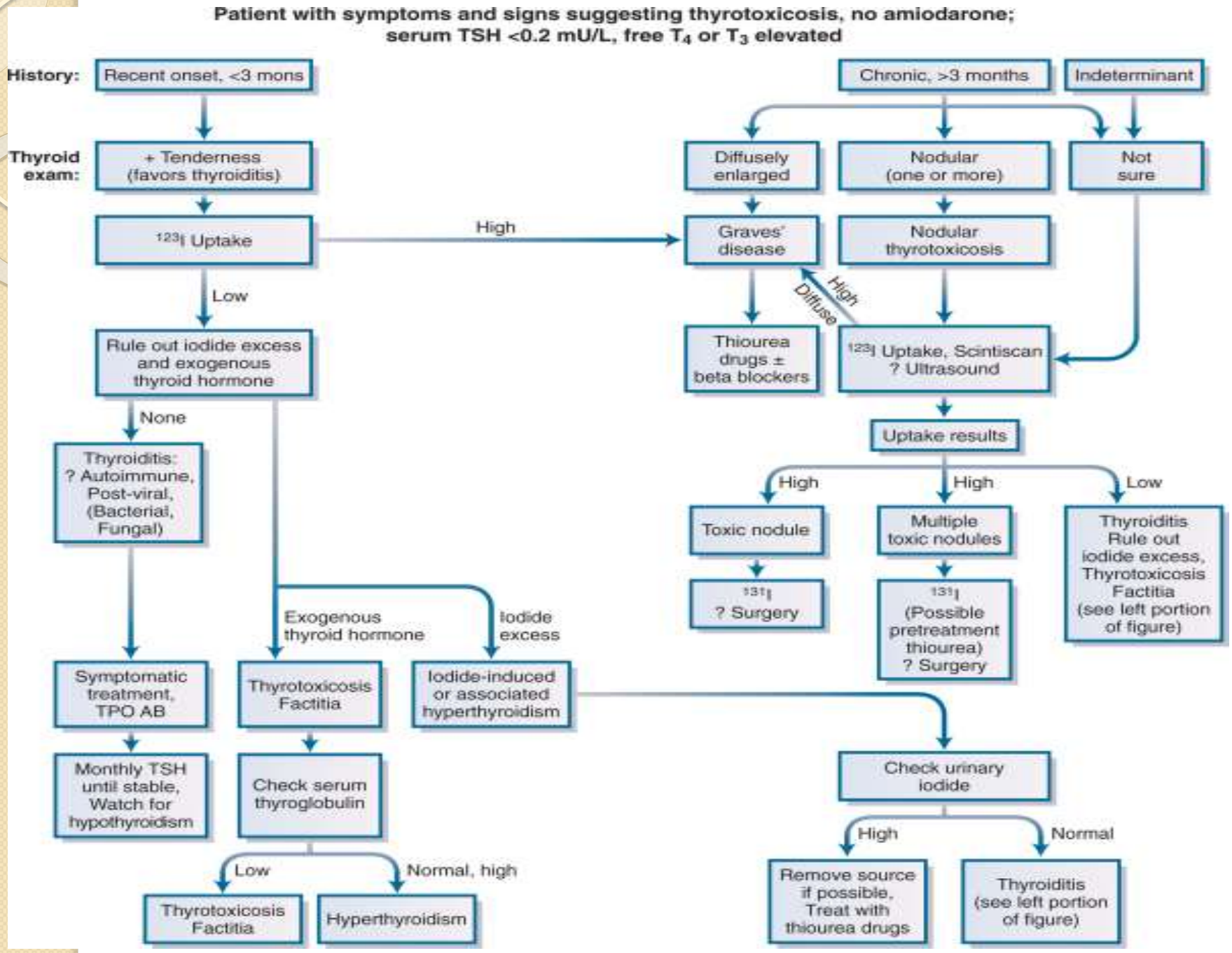
1. Thyroiditis!!!!
2. Iatrogenic thyrotoxicosis
3. Strauma ovarii
4. Metastatic thyroid carcinoma

DO NOT DO THYROID UPTAKE AND SCAN DURING PREGNANCY.


pyramidal lobe
COLD NODULE
GRAVE DISEASE
TOXIC MULTINODULAR
HOT NODULE
AUTONOMOUS NODULE
THYROIDITIS



Diagnosis	Normal thyroid	Thyroiditis	Left toxic adenoma	Graves' disease
Thyroid uptake	Diffuse, symmetrical	Low or absent	Increased in nodule Contralateral reduced	Diffuse, symmetrical
Salivary gland uptake	Normal	Appears prominent	Appears reduced	Appears reduced


Patient with symptoms and signs suggesting thyrotoxicosis, no amiodarone; serum TSH <0.2 mU/L, free T_4 or T_3 elevated
History:
Recent onset, <3 mons
Chronic, >3 months
Indeterminant
Thyroid exam:
+ Tenderness (favors thyroiditis)
Diffusely enlarged
Nodular (one or more)
Not sure
^{123}I Uptake
High
Graves' disease
Nodular thyrotoxicosis
Low
High
Diffuse
Rule out iodide excess and exogenous thyroid hormone
Thiourea drugs ± beta blockers
^{123}I Uptake, Scintiscan ? Ultrasound
None
Uptake results
Thyroiditis: ? Autoimmune, Post-viral, (Bacterial, Fungal)
High
High
Low
Toxic nodule
Multiple toxic nodules
Thyroiditis Rule out iodide excess, Thyrotoxicosis Factitia (see left portion of figure)
^{131}I ? Surgery
^{131}I (Possible pretreatment thiourea) ? Surgery
Exogenous thyroid hormone
Iodide excess
Symptomatic treatment, TPO AB
Thyrotoxicosis Factitia
Iodide-induced or associated hyperthyroidism
Monthly TSH until stable, Watch for hypothyroidism
Check serum thyroglobulin
Check urinary iodide
Low
Normal, high
High
Normal
Thyrotoxicosis Factitia
Hyperthyroidism
Remove source if possible, Treat with thiourea drugs
Thyroiditis (see left portion of figure)

THYROID AUTOANTIBODIES

Table 1 Antibodies described in AITD, frequency of presentation and detection method.

THYROID ANTIBODY	DETECTION METHOD	HT (%)	GD (%)	GENERAL POPULATION (%)
TPOAb	Radioimmunoassay (most sensitive)	>90	40 – 70	20
	ELISA			
	Hemagglutination			
TgAb	ELISA (most sensitive)	50–90	20 – 40	10
	Hemmagglutination			
TRAb	Immunoassays (detects presence and titer) Bioassays (determine activity)			
Stimulating		NA	90	10
Blocking		10	NA	NA

Subclinical Hyperthyroidism:

- normal serum free thyroxine and triiodothyronine levels
- with a thyroid stimulating hormone (TSH) below normal range (usually < 0.1 mu/l)

- The importance in recognising subclinical hyperthyroidism lies in the potential effect on the **cardiovascular system (atrial fibrillation) and bone metabolism (osteoporosis).**

Treatment?

- **In cases of Graves' disease, toxic MNG or adenoma:**

1. Anti-thyroid medications, i.e carbimazole
2. 1131 treatment
3. Surgery
4. Temporary beta blockers for symptoms control.

- **In cases of subacute thyroiditis →** Temporary beta blockers, NSAID's and/or steroids for symptoms control.

Case 1

- A 42-year-old woman presents to to the Endocrinology Clinic with feelings of anxiety. She has lost weight over the past few months , she also c/o palpitations, fine tremor and she noticed eye bulging.
- Pulse 120 regular Labs : t4 18 (11-22) , tsh less than .005 , ESR 10
- What to do next ??
- 1. reassurance
- 2.b.blocker and rtc after 2 months
- 3.order T3
- 4.thyroxine

- T3 15 PMOL/L (3.5-5)
- Thyroid uptake and scan shows increased uptake consistent with graves
- TRAB POSITIVE
- She received anti thyroid drug carbimazole and b .blockers

- One month later pt present with fever and sore thraot ,TFT within normal range ???
- 1.perscribe antibiotic and Reassurance
- 2.discontinue anti thyroid durg (ATD)
- 3. cbc
- 4.increase dose of ATD

Case 2

- A 48-year-old woman presents to her General Practitioner (GP) with a two-week history of malaise and anterior neck pain. She explains that she has been suffering from what seems like a severe flu-like illness.
- her pulse 118 (bpm) regular. (BP)is 132/74 mmHg. She has a fine tremor and her palms are moist. She has a slightly enlarged,smooth tender thyroid.
- labs : (T 4) 40 nmol/l 11–22 pmol/l,, (TSH) <0.01 µU/l 0.17–3.2 µU/l ,Erythrocyte Sedimentation Rate (ESR) 40 mm/hour 1–20 mm/hour
- DX ???? TREATMENT????

Case

- A 24-year-old woman presents to her General Practitioner (GP) for a 12 week early pregnancy check. She complains of mild lethargy and he checks some thyroid function tests. Her (TSH) is 0.3 mU/l (0.4–5 mU/l) (T 4) is 27 pmol/l (0–22 pmol/l). He diagnoses thyrotoxicosis and refers her to you for an opinion.
- Whatt is tthe best next management step for this patient?
- A Observation
- B Start carbimazole therapy
- C Start propylthiouracil therapy
- D Refer for radioiodine
- E Refer for thyroid uptake scan

Case

- A 37-year-old woman known to have GRAVES DX non compliant to TX has been brought to the ER ,with one day hx of agitation , fever , palpitation , abdominal pain , vomitting
- Pulse 180 irregular , bp 190/120 , tempreture 40.5
- Labs t4 120 (11-21) , tsh .001 ,
- Dx ????

THYROID STORM/THYROID CRISES

- An acute, life-threatening, hypermetabolic state induced by excessive release of thyroid hormones.
- Presentation: Fever, tachycardia, HTN , and neurological and GI abnormalities.

- Rapid diagnosis and aggressive treatment are critical.
- Diagnosis is primarily clinical
- Management: Supportive measures, Propylthiouracil and Beta blockers, steroids,pottasium iodide , plasmapheresis

Hypothyroidism

Signs	Symptoms[a]
Hypothermia	Fatigue
Bradycardia	Weakness
Delayed relaxation of deep tendon reflexes	Weight gain
Periorbital edema	Constipation
Enlargement of tongue	Cold intolerance
Diastolic hypertension	Dry skin
Hair loss	Hoarse voice
Pleural and pericardial effusions	Edema
	Cognitive dysfunction
	Depression
	Muscle cramps
	Paresthesias
	Menorrhagia
	Dry, griity-feeling eyes

Typica

Causes of hypothyroidism

1. Hashimoto's thyroiditis.
2. Post total thyroidectomy.
3. Post I131 treatment
4. Congenital, i.e Thyroid agenesis or dysplasia,
5. Medications, i.e Lithium and Amiodarone.
6. Iodine deficiency
7. Central hypothyroidism
8. Thyroid infiltration, i.e Riedel's thyroditis, amyloidosis, and hemochromatosis

Treatment

- Levothyroxine replacement.
- No need for additional T3 replacement.
- In older people with history of CAD, start with a low dose and then titrate dose up slowly.

- **Subclinical hypothyroidism**
- TSH raised but T3, T4 normal

- **Significance:**
- risk of progressing to overt hypothyroidism is 2-5% per year (higher in men)
- risk increased by presence of thyroid autoantibodies
- **Treat if:**
- TSH > 10
- Goitre
- Pregnancy or planning for pregnany
- Symptomatic

Physiologic state	Serum TSH	Serum Free T4	Serum T3	24-h radioiodine uptake
Hyperthyroidism, untreated	Low	High	High	High
Hyperthyroidism, T3 toxicosis	Low	Normal	High	Normal or High
Primary Hypothyroidism, untreated	High	Low	Low or Normal	Low or Normal
Hypothyroidism secondary to pituitary disease	Low or Normal	Low	Low or Normal	Low or Normal
Euthyroid, on exogenous thyroid hormone	Normal	Normal on T4, Low on T3	High on T3, Normal on T4	Low

case

- 45 yrs old female pt , brought to er , with GCS OF 11(E2,V4 , M5), her family states that she had seemed low over the past couples of month , and wearing more layers of clothes than seemed appropriate
- On P/E T 35 PULSE 38 REGULAR , CHEST CLEAR
- Labs: tsh 90 mu/l (.5-4.5) t4 2 pmol/l (11-21)
- DX???

Myxedema coma/Myxedema crises

- An uncommon but a life-threatening form of untreated hypothyroidism with physiological decompensation.
- The condition occurs in patients with long-standing, untreated hypothyroidism and is usually precipitated by a secondary insult, such as climate-induced hypothermia, infection, or another systemic condition, or drug therapy.

- Patients with myxedema coma have changes in their mental status, including lethargy, stupor, delirium, or coma.
- Treatment:

- Supportive measures
- IV levothyroxine
- In light of the possibility of adrenal insufficiency, stress steroid replacement *after* a cortisol level is obtained.

Euthyroid sick syndrome

- A.K.A non thyroidal illness
- Usually seen in critically ill patients
- Low total and free T3 with low or normal T4 and TSH

NONTOXIC DIFFUSE AND NODULAR GOITER AND THYROID NEOPLASIA

NONTOXIC GOITER: DIFFUSE AND NODULAR

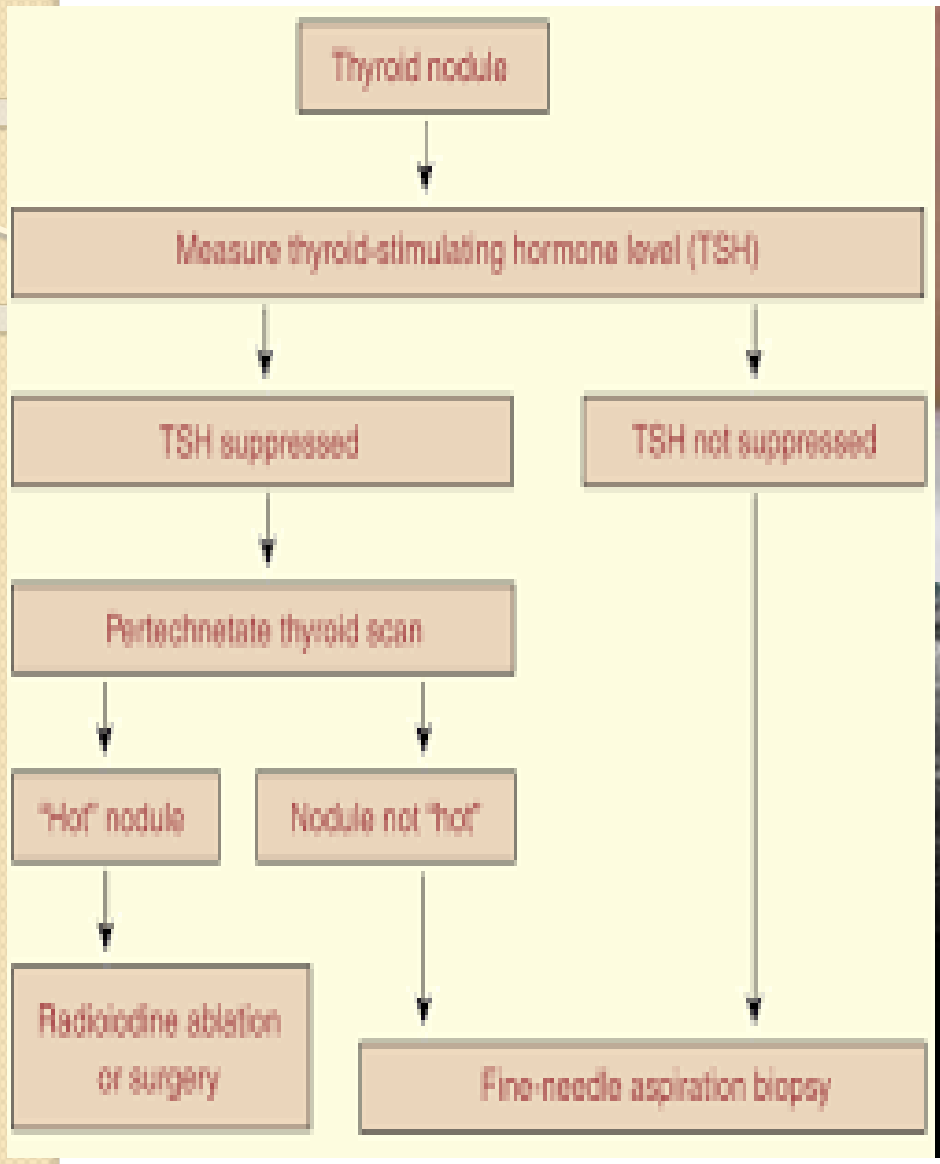
- Nontoxic goiter may be defined as any thyroid enlargement characterized by uniform or selective growth of thyroid tissue that is not associated with overt hyperthyroidism or hypothyroidism and that does not result from inflammation or neoplasia.
- A thyroid nodule is defined as a discrete lesion within the thyroid gland that is due to an abnormal focal growth of thyroid cells.
- **Risk factors:**

- Familial
- Iodine deficiency
- Smoking
- Alcohol
- Older age
- Female sex
- Hx of uterine fibroids

THYROID NODULE

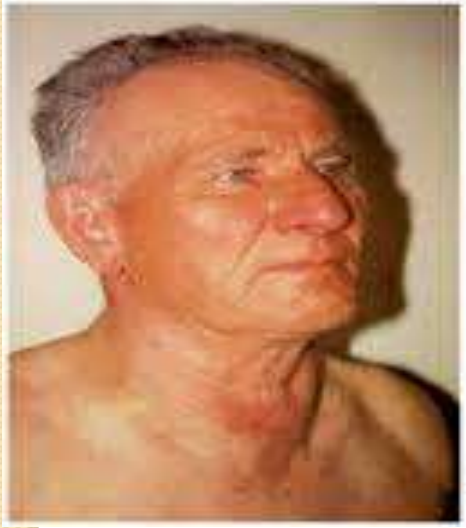
Ultrasound features associated with thyroid cancer risk in adults

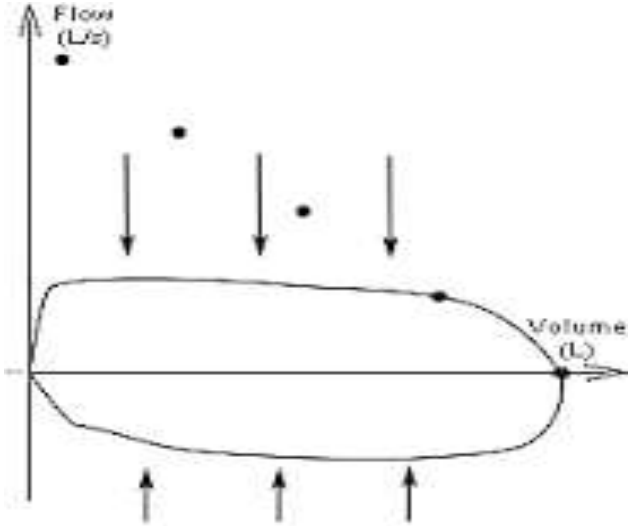
Ultrasonographic features that are associated with an increased risk of thyroid cancer
Hypoechogenicity
Solid composition
Punctate echogenic foci (microcalcifications)
Infiltrative/irregular margins
Taller-than-wide shape
Associated suspicious lymphadenopathy
Ultrasonographic features that are associated with a lower risk of thyroid cancer
Isoechoic or hyperechoic
Spongiform appearance
Simple cysts
Comet-tail artifact within a cystic nodule
Uninterrupted eggshell calcification


Thyroid nodule
Measure thyroid-stimulating hormone level (TSH)
TSH suppressed
TSH not suppressed
Pertechnetate thyroid scan
"Hot" nodule
Nodule not "hot"
Radioiodine ablation or surgery
Fine-needle aspiration biopsy

Indications for thyroid surgery

- Malignancy
- Indeterminate and/or repeatedly nondiagnostic FNA results
- Cosmetic, mostly in females
- Obstructive symptoms





Thyroid cancer

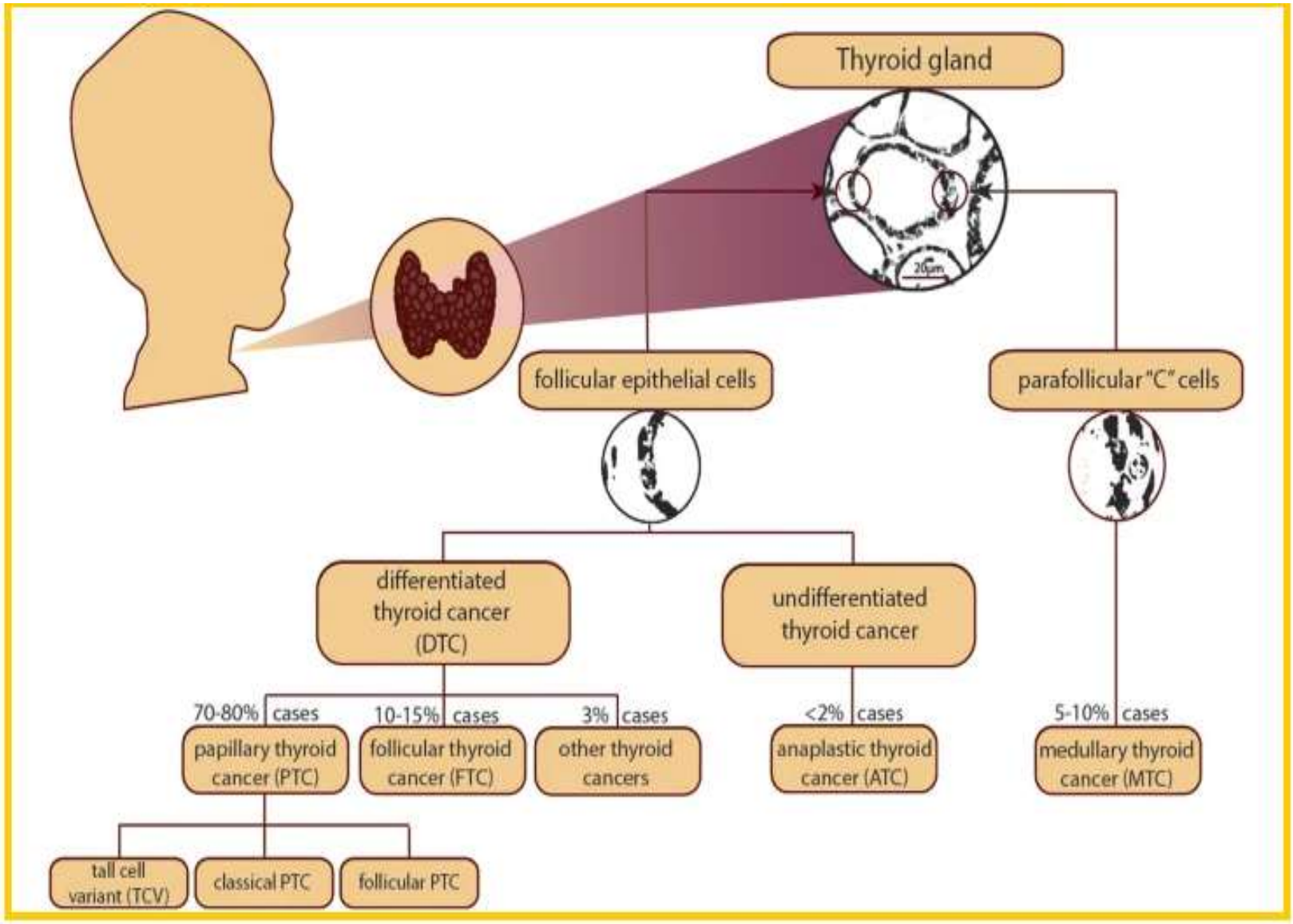
- The National Cancer Institute indicates that thyroid cancer is the most common type of endocrine-related cancer and estimates 60,220 new cases in 2013.

- Thyroid cancer represents approximately 3.6% of all new cancer cases.

- Although a diagnosis of thyroid or any type of cancer is frightening, the vast majority of thyroid cancers is highly treatable and in most cases curable with surgery and other treatments.

- Thyroid cancer is generally first suspected by a lump or nodule in the thyroid gland.

THYROID CANCER



1. Papillary Thyroid Cancer

- Most common type of thyroid cancer: 70% to 80% of all thyroid cancers are papillary thyroid cancer
- Commonly diagnosed between the ages of 30 and 50
- Females are affected 3 times more often than males
- Usually not aggressive
- May spread(lymphatic), but usually not beyond the neck

2. Follicular Thyroid Cancer

- Makes up about 10% to15% of all thyroid cancers
- Often diagnosed between the ages of 40 and 60
- Females are affected 3 times more often than males
- Cancer cells may invade

  blood vessels and travel

  to other body parts such

  as bone or lung tissues

3. Medullary Thyroid Cancer

- Makes up about 5 % to 10% of all thyroid cancers
- More likely to run in families and associated with other endocrine disorders
- Develops from the *C Cells or parafolicullar cells* that produce calcitonin
- An elevated calcitonin level can indicate cancer

- Often diagnosed between the ages of 40 and 50
- Females and males are equally affected
- Forms of medullary thyroid cancer include sporadic (not inherited), MEN 2A and MEN 2B, and familial (genetic, but not linked to other MEN-related endocrine tumors)

4. Anaplastic Thyroid Cancer

- Very rare—affects fewer than 5% of thyroid cancer patients
- Usually occurs in

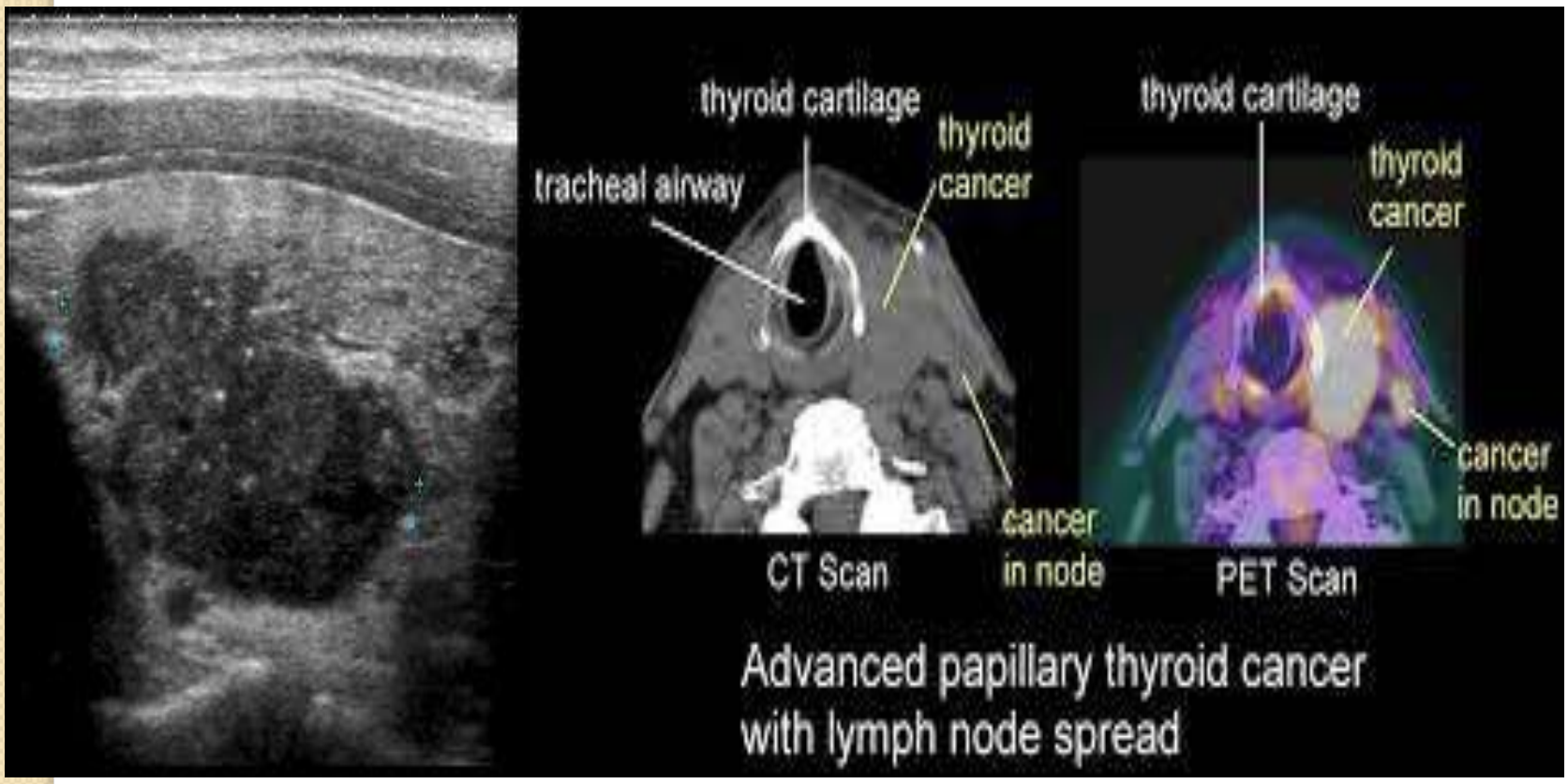
  patients older than

  65 years
- Females are affected

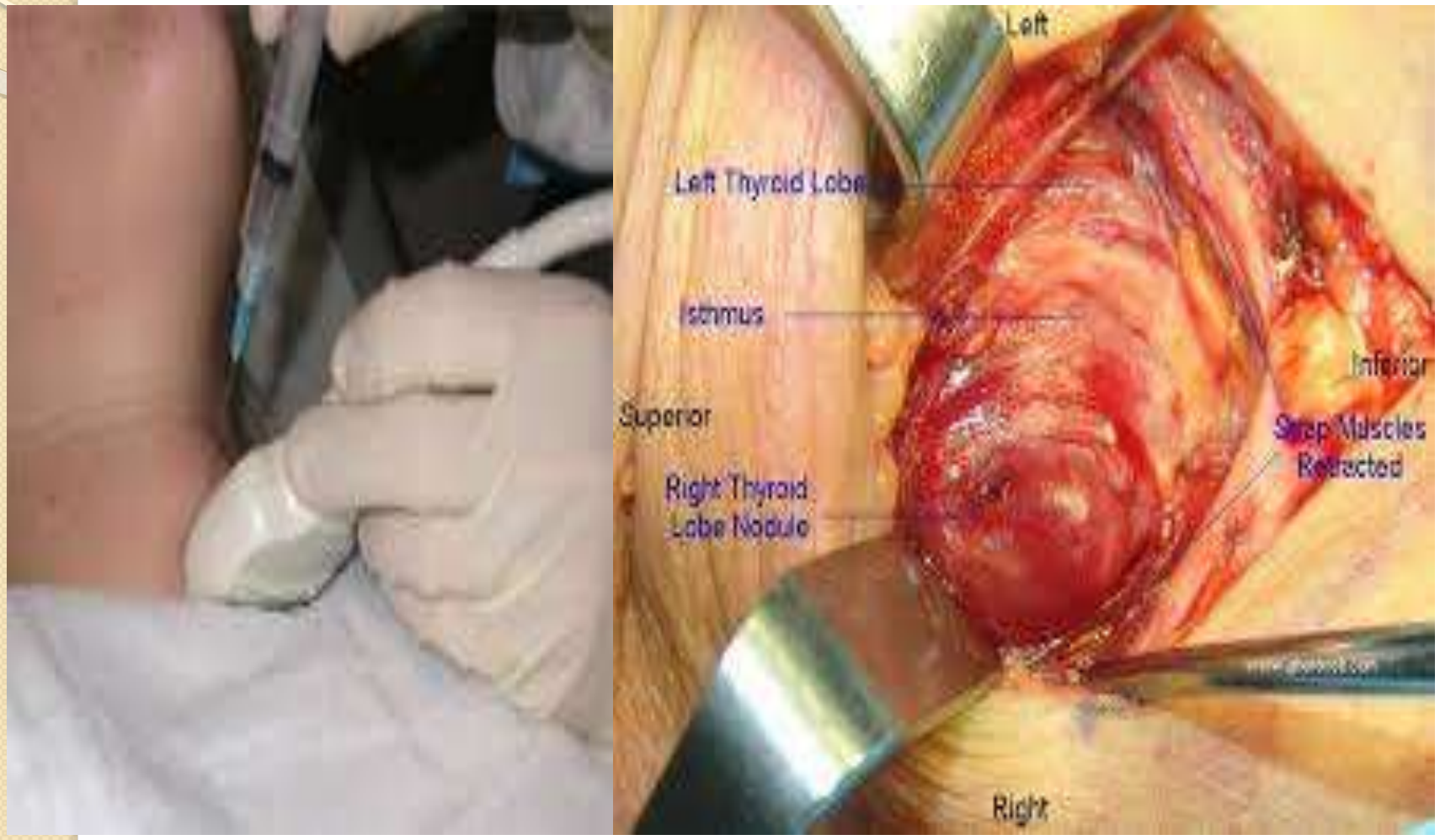
  more often than males
- Aggressive and invasive
- Least responsive to treatment

Diagnostic tests

1. Imaging studies (thyroid ultrasound, CT neck, PET scan).

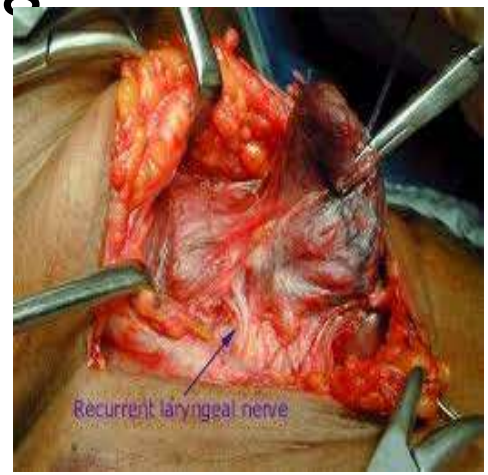


2. The gold standard is thyroid FNA or surgery.



Treatment

1. Surgery (total, subtotal or hemi-thyroidectomy)→ Need an experienced thyroid surgeon.



2. I131 ablation

3. External beam radiation

4. Chemotherapy

Secondary thyroid tumors

1. Thyroid lymphoma

1. Metastasis (Kidney, Lung, Bone, Melanoma)

1. Williams Textbook of Endocrinology
2. Medscape.com
3. UpToDate.com