Hyperparathyroidism

BY

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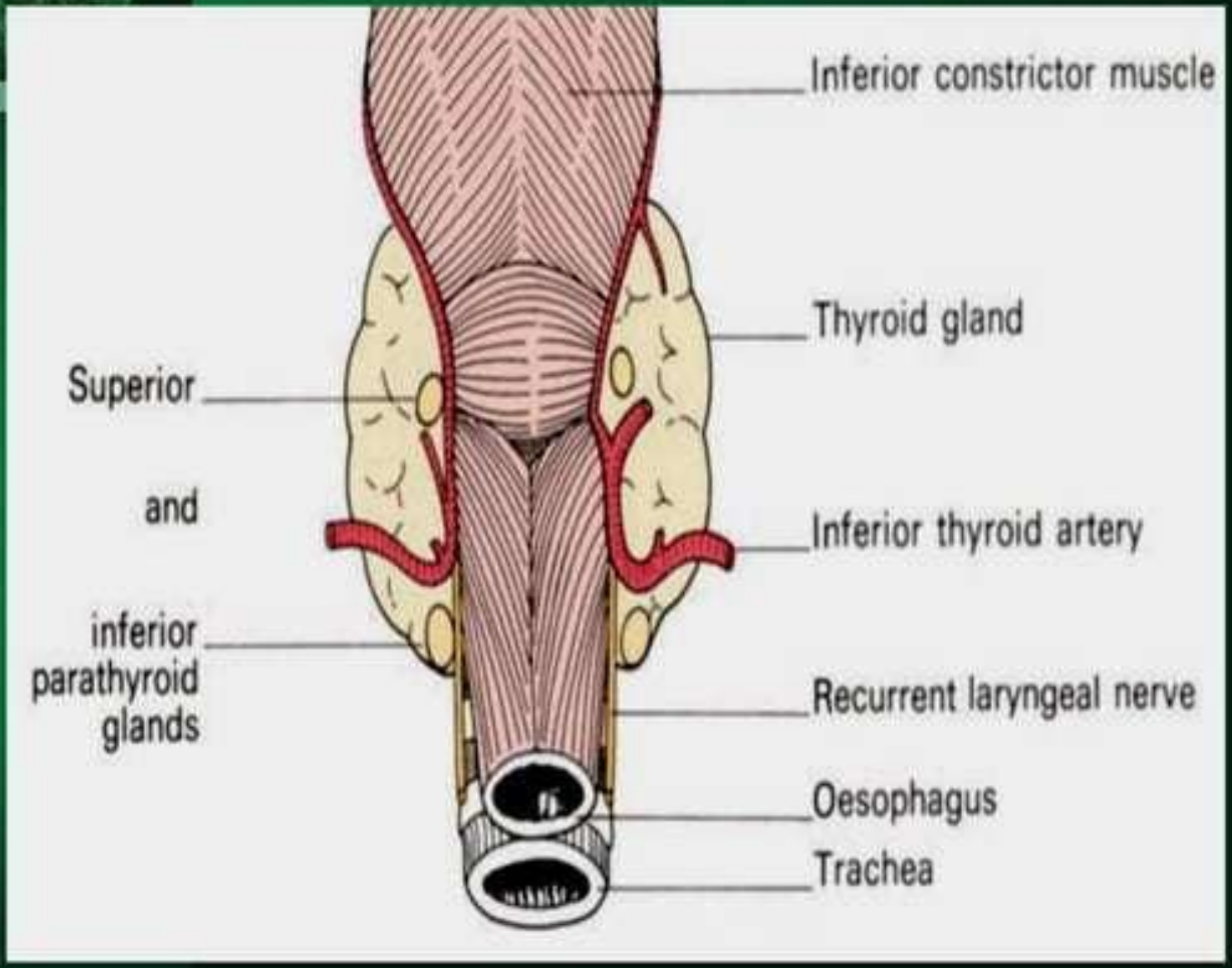
Parathyroid glands were discovered by **Ivar Victor Sandström** (1852-1889), a Swedish medical student in 1880. It was the last major organ to be recognized in humans.


Inferior constrictor muscle
Thyroid gland
Superior
and
inferior
parathyroid
glands
Inferior thyroid artery
Recurrent laryngeal nerve
Oesophagus
Trachea

ANATOMY

* 4 small yellowish brown bodies.

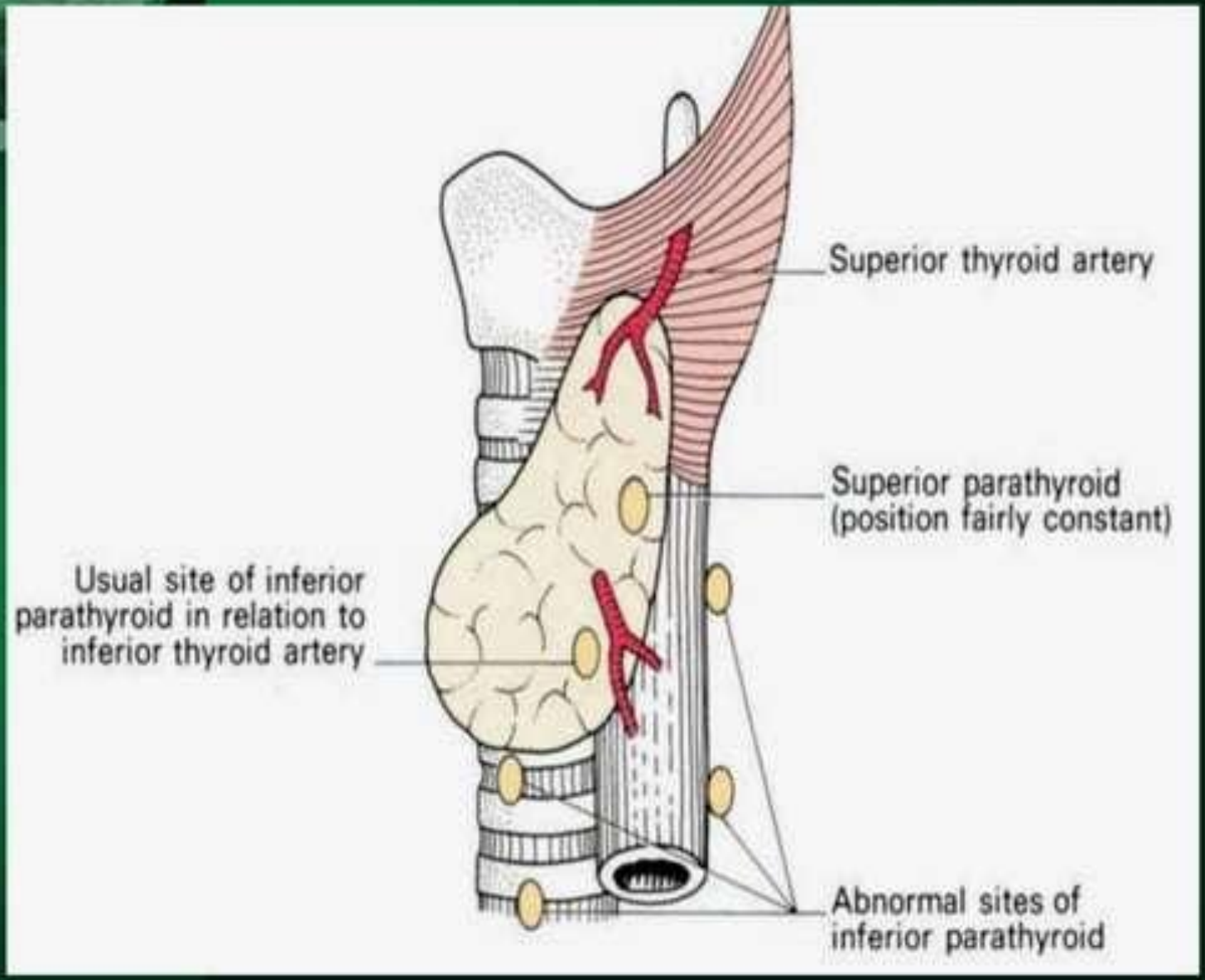
* situated posterior to lateral lobes of thyroid gland.

* In 1% of population, number is < 4
  > 4 is the number in about over 33 %.

* divided, according to their situation, into *superior* and *inferior*.

* superior parathyroids are more constant in position, and are situated, one on either side, at the level of the lower border of the cricoid cartilage.

* the inferior, may be applied to the lower edge of the lateral lobes, or placed at some little distance below the thyroid gland, or found in relation to one of the inferior thyroid veins.


Superior thyroid artery
Superior parathyroid
(position fairly constant)
Usual site of inferior
parathyroid in relation to
inferior thyroid artery
Abnormal sites of
inferior parathyroid

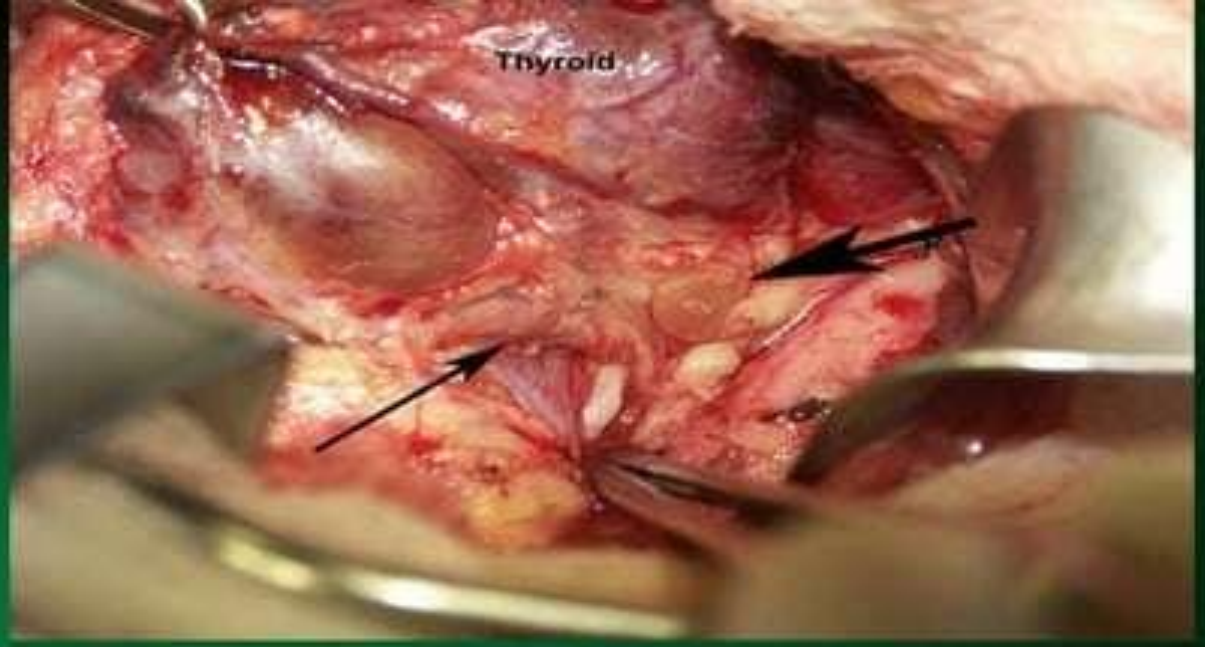
APPEARANCE

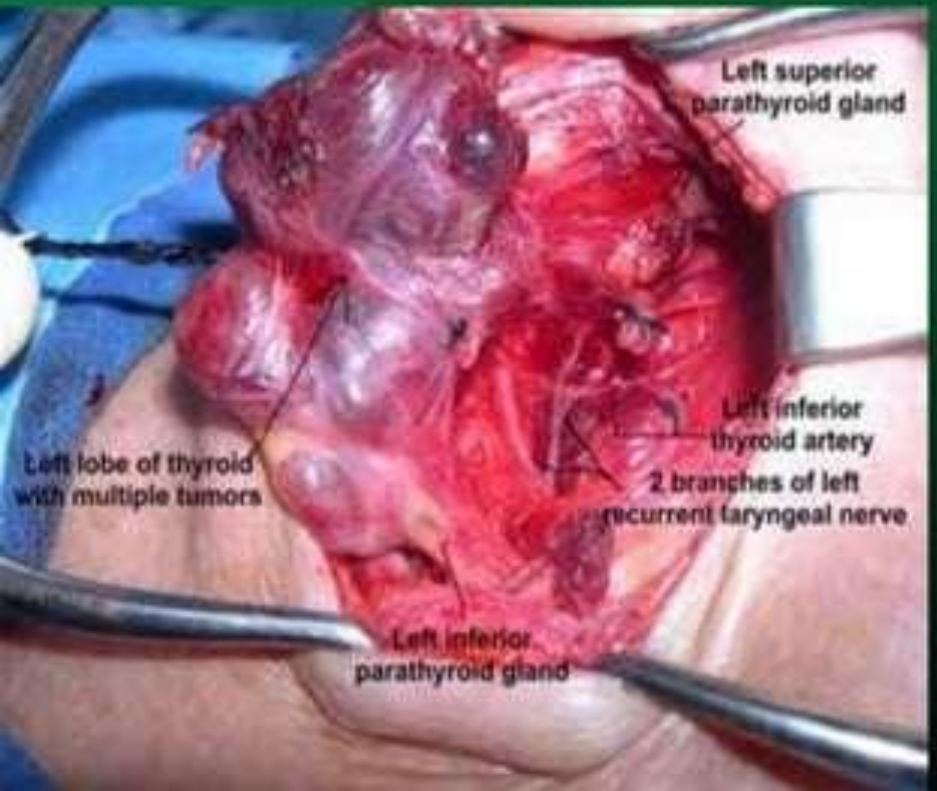
*shape: ovoid, polypoid or spherical.

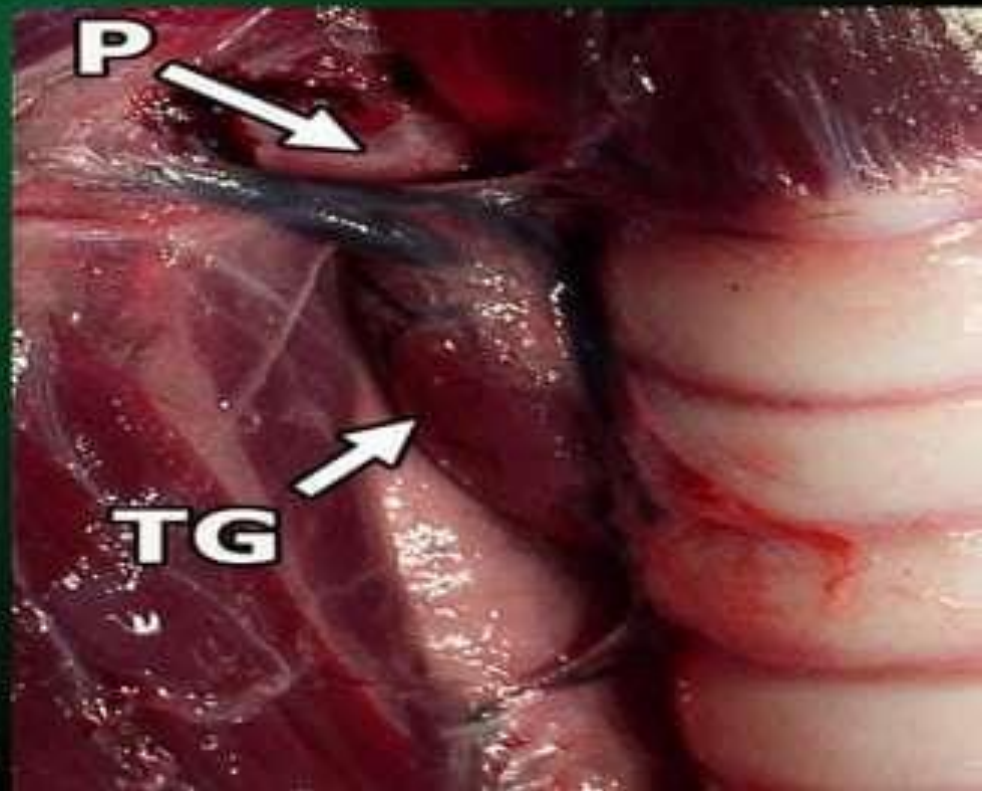
*colour: yellowish brown.

*size :6 x 3 x 2 millimeters.

*Wt :35 - 40 milligrams.


Thyroid


Left superior parathyroid gland
Left inferior thyroid artery
2 branches of left recurrent laryngeal nerve
Left lobe of thyroid with multiple tumors
Left inferior parathyroid gland


P
TG

Blood supply ?

*Each parathyroid gland is supplied by a branch from the inferior thyroid artery.

*Superior parathyroids are sometimes supplied by superior thyroid artery.

STRUCTURE

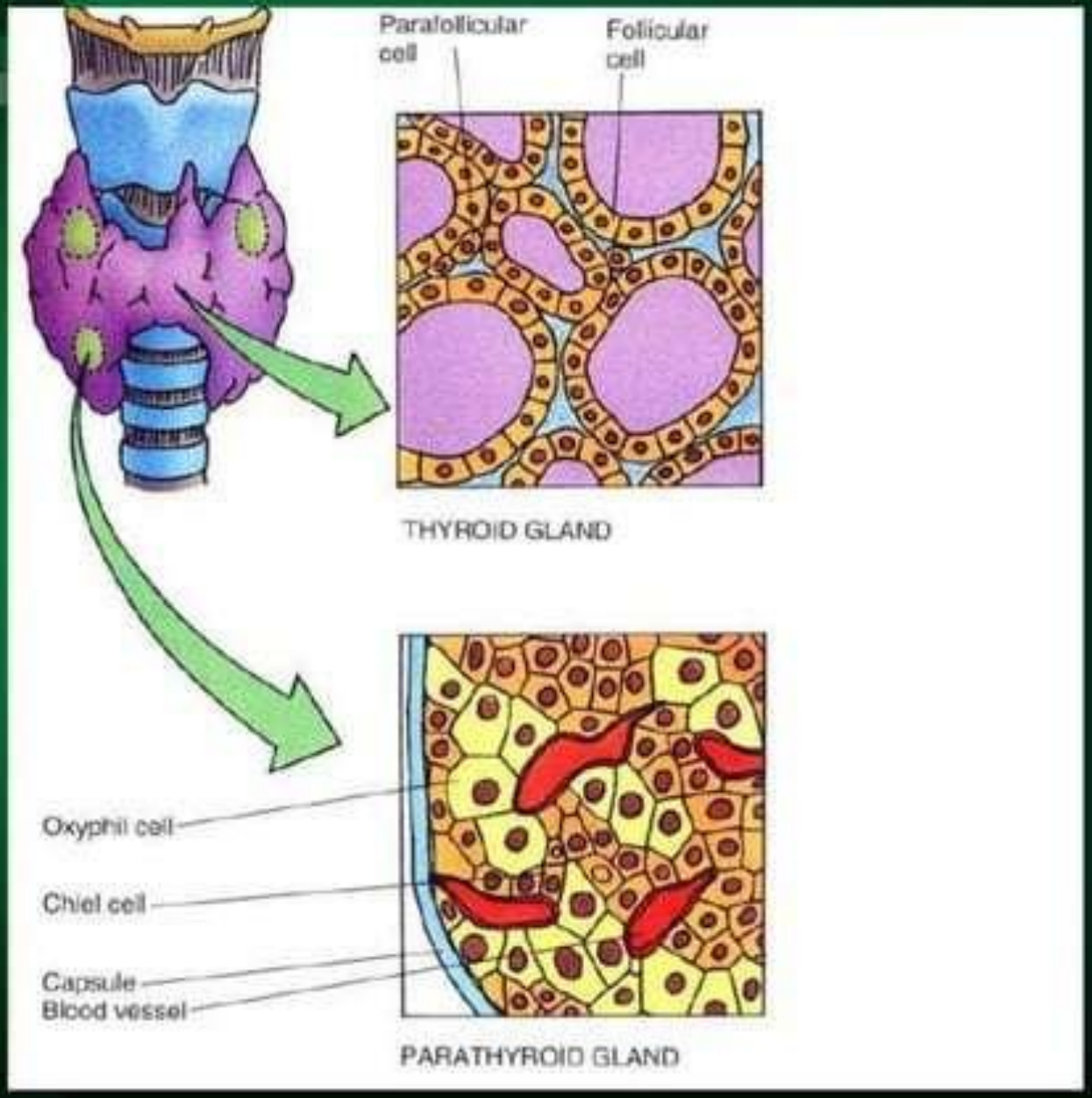
***Connective tissue stroma.**

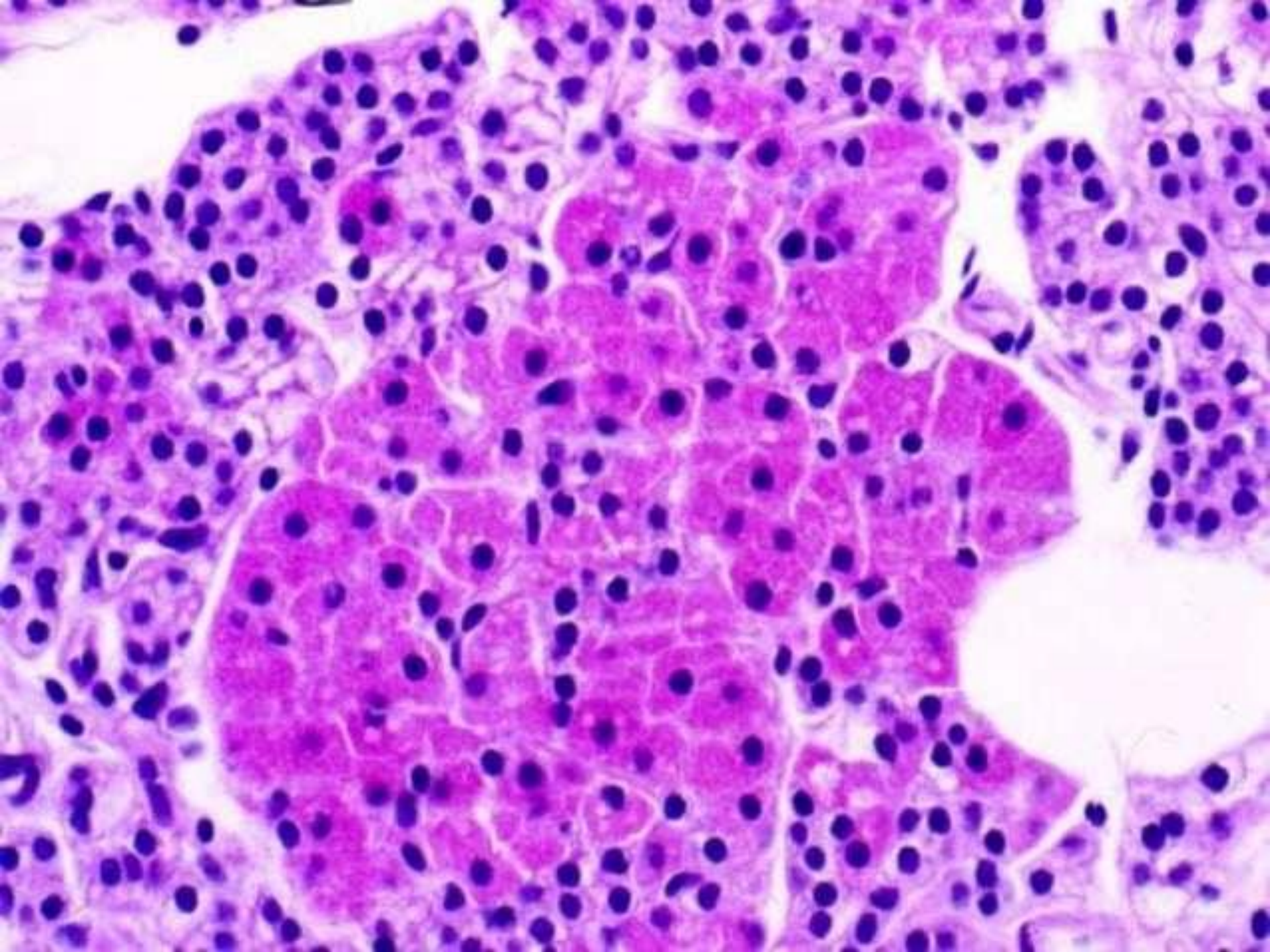
***Parenchyma:**

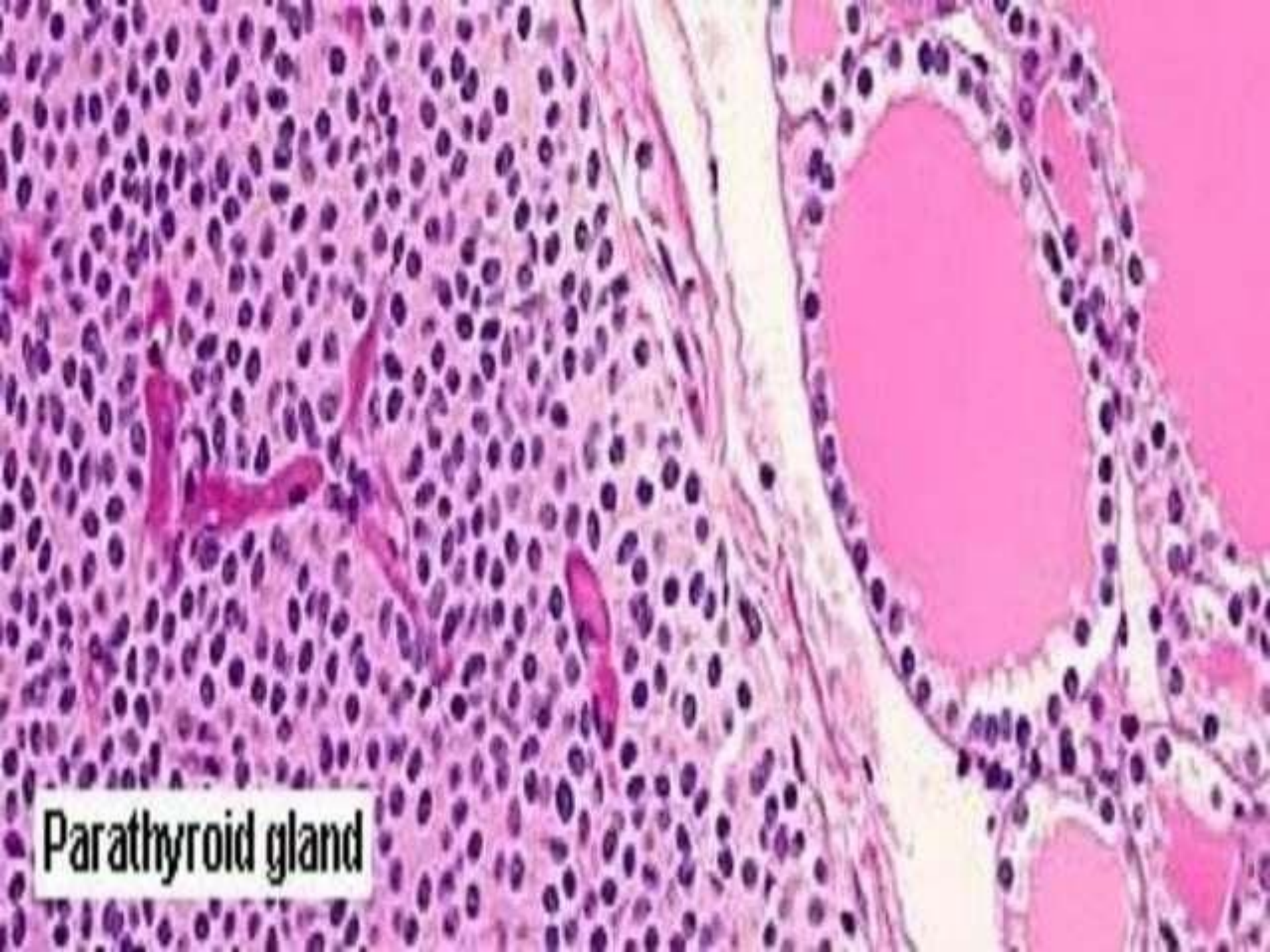
1- Chief cells: small closely packed cells secreting PTH.

2- Oxyphil cells: - larger in size but fewer in number

- their function is not yet known.


Parafollicular cell
Follicular cell
THYROID GLAND
Oxyphil cell
Chief cell
Capsule
Blood vessel
PARATHYROID GLAND

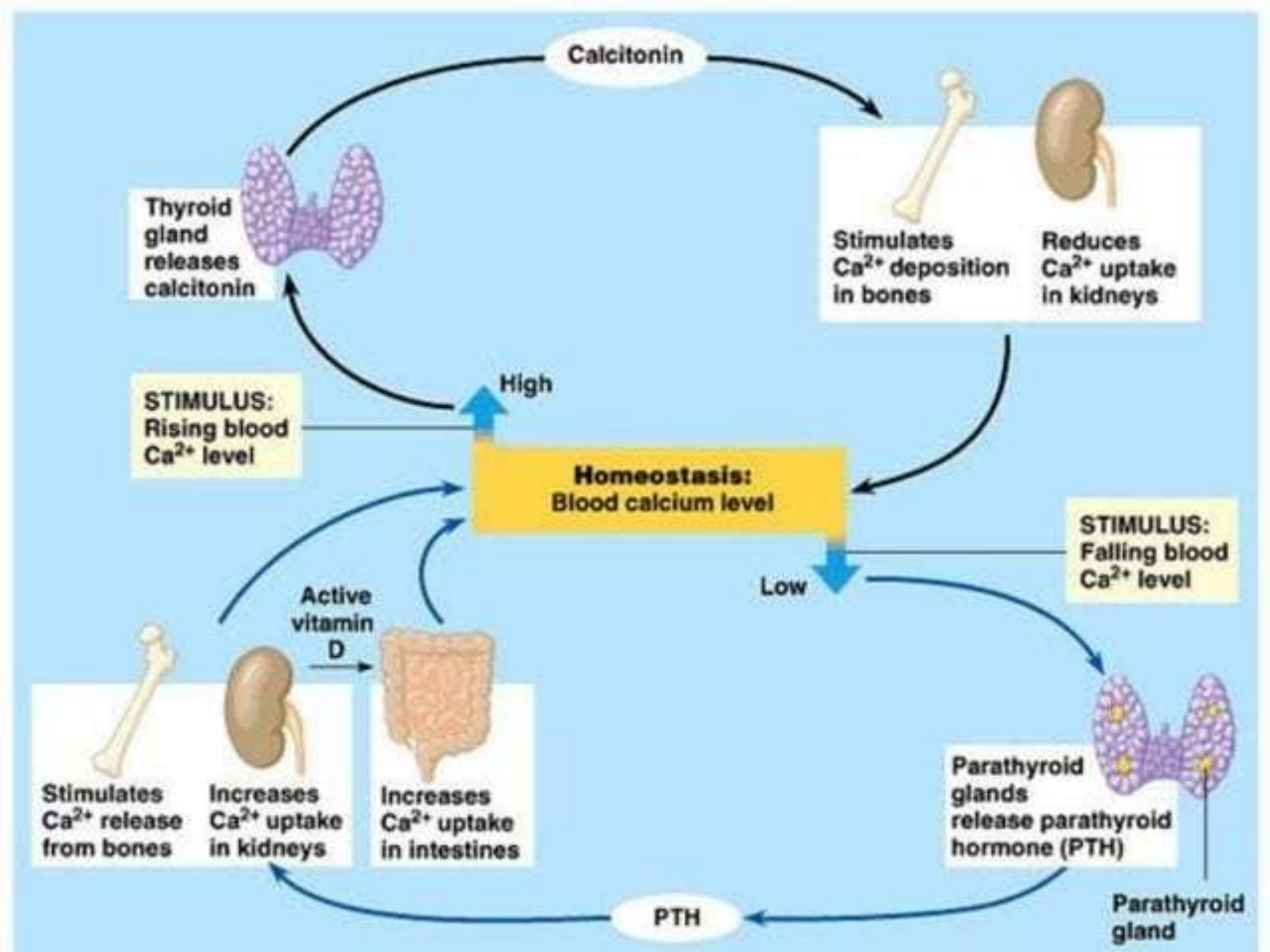



Parathyroid gland

FUNCTION OF THE PARATHYROID GLANDS

*Despite its name, parathyroid gland carries out a different task compared to thyroid gland.

*Thyroid gland is mainly responsible for regulation of mental and physical development, while parathyroids regulate calcium (Ca) and phosphorus (PO_4) metabolism.


Calcitonin
Thyroid gland releases calcitonin
Stimulates Ca^{2+} deposition in bones
Reduces Ca^{2+} uptake in kidneys
STIMULUS: Rising blood Ca^{2+} level
High
Homeostasis: Blood calcium level
STIMULUS: Falling blood Ca^{2+} level
Low
Active vitamin D
Stimulates Ca^{2+} release from bones
Increases Ca^{2+} uptake in kidneys
Increases Ca^{2+} uptake in intestines
Parathyroid glands release parathyroid hormone (PTH)
Parathyroid gland
PTH

Ca Metabolism

*Importance of Ca in body:

1- Bone mineralization.

2- Blood coagulation.

3- Neuromuscular transmission.

4- Neurotransmitter release.

5- Contraction of all muscle types.

6- Cell membrane permeability and excitability.

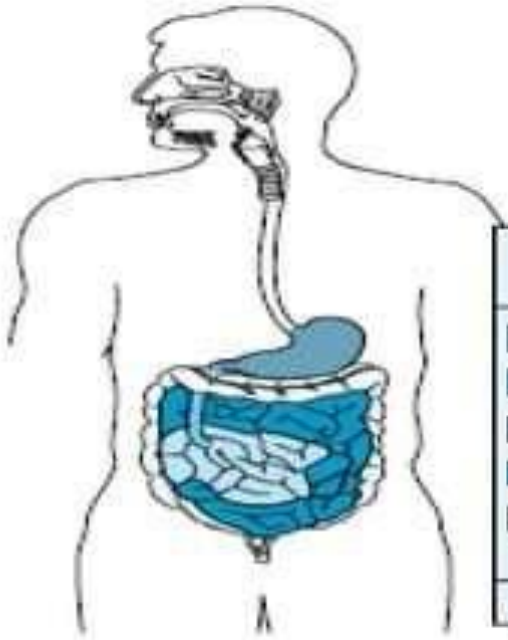
7- Secretion of glands.

*Daily requirements: **1gm /day.** (+ve Ca balance)

*Normal plasma Ca concentration: **9-11 mg%**

*Absorption: ↓↑

*Excretion: **75% in stool, 25% in urine.**



Gastrointestinal absorption of dietary calcium (Ca)

Site	Net Ca absorption		% of intake absorbed
	mmol/d	mg/d	
Stomach	0	0	0
Duodenum	0.75	30	3
Jejunum	1.0	40	4
Ileum	3.25	130	13
Colon	0	0	0
Total*	5	200	20

*Normal dietary Ca intake =1000 mg (25 mmol) per day

Control Of Ca Homeostasis

1- Parathormone hormone (PTH):

raises plasma Ca level if it is lowered by:

- -Vit. D activation→↑ Ca absorption.
- -↑ Ca reabsorption in DCT.
- -↓ PO4 reabsorption in PCT.
- -↑ Ca mobilization from bone.

2- CALCITONIN:

lowers plasma Ca level if it is raised by:

- -↓ Ca absorption.
- -↑ PO4 reabsorption in PCT.
- -↓ Ca mobilization from bone.

3- VITAMIN D:

- -↑ Ca absorption.
- -↑ Ca bone uptake and deposition.

Hyperparathyroidism

DEFINITION:

Overproduction of the parathyroid hormone (PTH) resulting in abnormal calcium homeostasis.

CAUSES (TYPES):

Hyperparathyroidism

primary	(this case)	autonomous secretion
secondary		response to normal regulatory stimuli
refractory secondary		nonsuppressible secretion after correction of metalolic abnormalities
tertiary		refractory secondary with hypercalcemia

I. Primary Hyperparathyroidism

Def.

uncontrolled (autonomous) PTH production with loss of feedback mechanism by extracellular Ca.

Incidence

0.1 – 0.3%

more in ♀ (3 :1), may be *familial*

esp. between 45-60 years

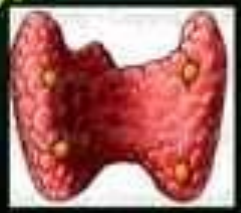
Aetiology

-Single parathyroid adenoma (85%)

-In 15% of cases, multiple glands are involved (either multiple adenomas or hyperplasia).

-Parathyroid carcinoma (rare)

-Paraneoplastic syndromes (rare)



The aetiology of adenomas or hyperplasia remains unknown in most cases.

Familial cases can occur either as part of the multiple endocrine neoplasia syndromes (MEN 1 or MEN 2a)

Or familial isolated hyperparathyroidism

Feature	MEN I (3p)	MEN IIA	MEN IIB
Eponym	Wermer's syndrome	Sipple's syndrome	-
Pituitary Adenoma	+	-	-
Medullary thyroid cancer	-	+	100%
Parath. hyperplasia	+	-	-
Pheochromocytoma	-	+	50%
Pancreatic tumours	Insulinoma-gastrinoma	-	-
Marfanoid body	-	-	80%
Multiple neuromata	-	-	95%

Pathophysiology :

- In parathyroid adenomas: change in the set point of PTH release (normal feedback on PTH production by extracellular calcium seems to be lost and the adenoma considers normal level of Ca as being low)

- In parathyroid hyperplasia: increase in the number of cells producing PTH.

- Symptoms of hyperparathyroidism are due to:
  * chronic excessive resorption of Ca from bone.
  * hypercalcaemia.

Symptoms:

" Disease of *bones, stones, abdominal groans* and *psychic moans*"

1-Skeletal manifestations:

Bone and joint pain esp. in hand and feet (pseudogout).

2-Renal manifestations:

polyuria, dysuria, renal colics or stone passage.

3-Gastrointestinal manifestations:

anorexia, nausea, vomiting, abdominal pain, constipation.

4-Neuromusculopsychologic manifestations:

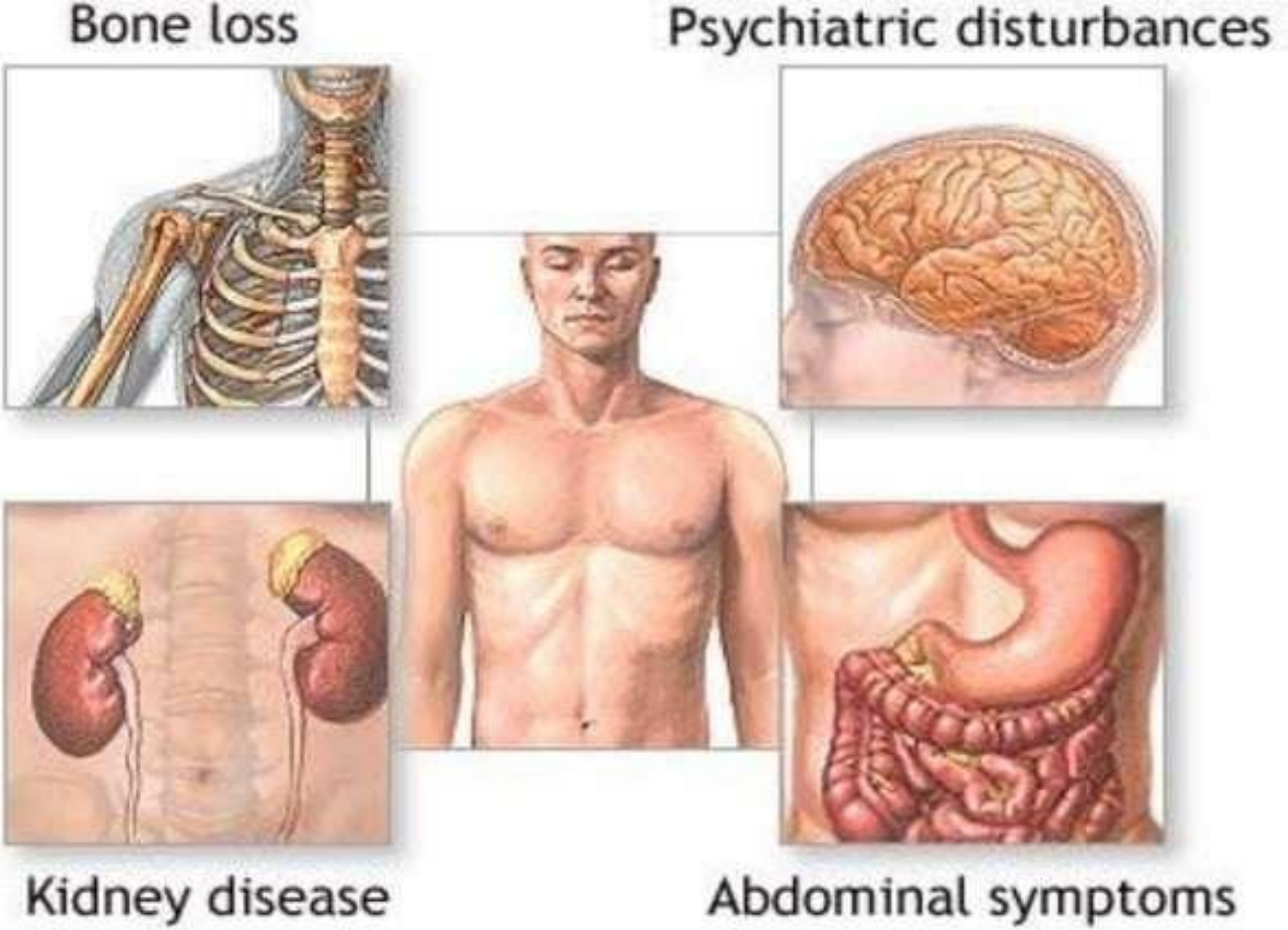
proximal muscle weakness, easy fatigability, depression, inability to concentrate, and memory problems that are often poorly characterized and may not be noted by the patient.

5-Cardiovascular manifestations :

palpitation and hypertensive symptoms.

6-Hyperparathyroid Hypercalcaemic crisis

7-Asymptomatic hypercalcaemia in most cases.


Bone loss
Psychiatric disturbances
Kidney disease
Abdominal symptoms
ADAM.

Physical Signs:

Examination is usually noncontributory but may reveal:

1- muscle weakness.

2- depression.

3- hypertension and bradycardia.

4- palpable neck mass is not usually expected with hyperparathyroidism, although in rare cases, it may indicate parathyroid tumour.

Diagnostic Workup (based on lab data)

A- Laboratory Studies:

1-Parathormone immuno-assay
(core of the diagnosis).

2-Total or ionized serum calcium levels.

3- 24-hour urine calcium.

4-Dent's test:

an elevated PTH level with an elevated ionized serum Ca level is diagnostic of 1ry hyperparathyroidism.

normocalcemic hyperparathyroidism
(? 2ry)

B- Imaging studies:

imaging studies are not used to make the diagnosis of primary hyperparathyroidism (which is based on laboratory data) or to make a decision for surgical therapy (which is based on clinical criteria).

Imaging studies are used to: .

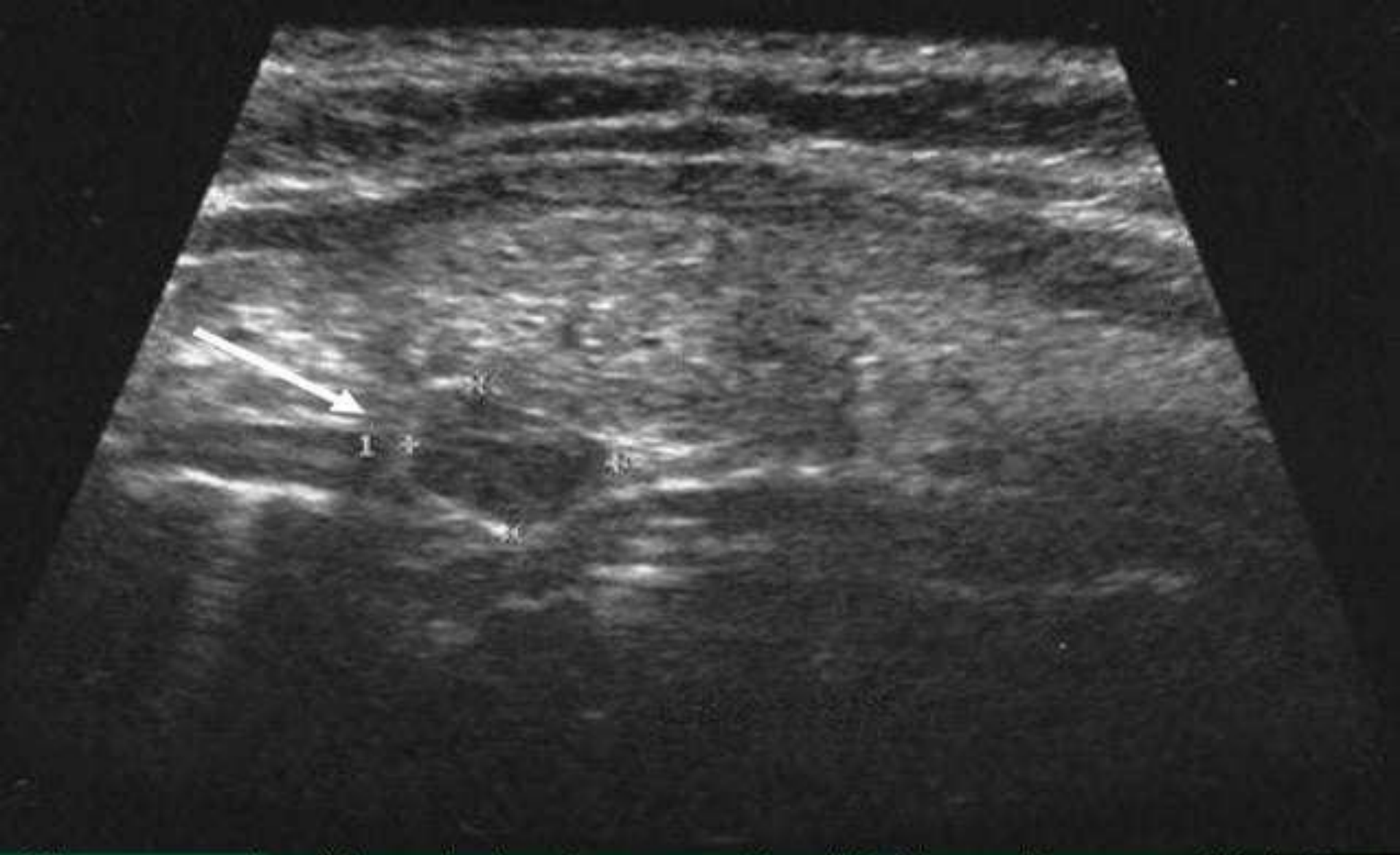
1- guide the surgeon once surgical therapy has been decided.

2- detect skeletal manifestations.

1-Neck Ultrasonography:

***operator-dependent.**

***not reliable in multigland disease.**



Ultrasonography of the neck showing an extrathyroidal 10-mm diameter nodule below the left thyroid lobe (white arrow) consistent with a parathyroid mass.

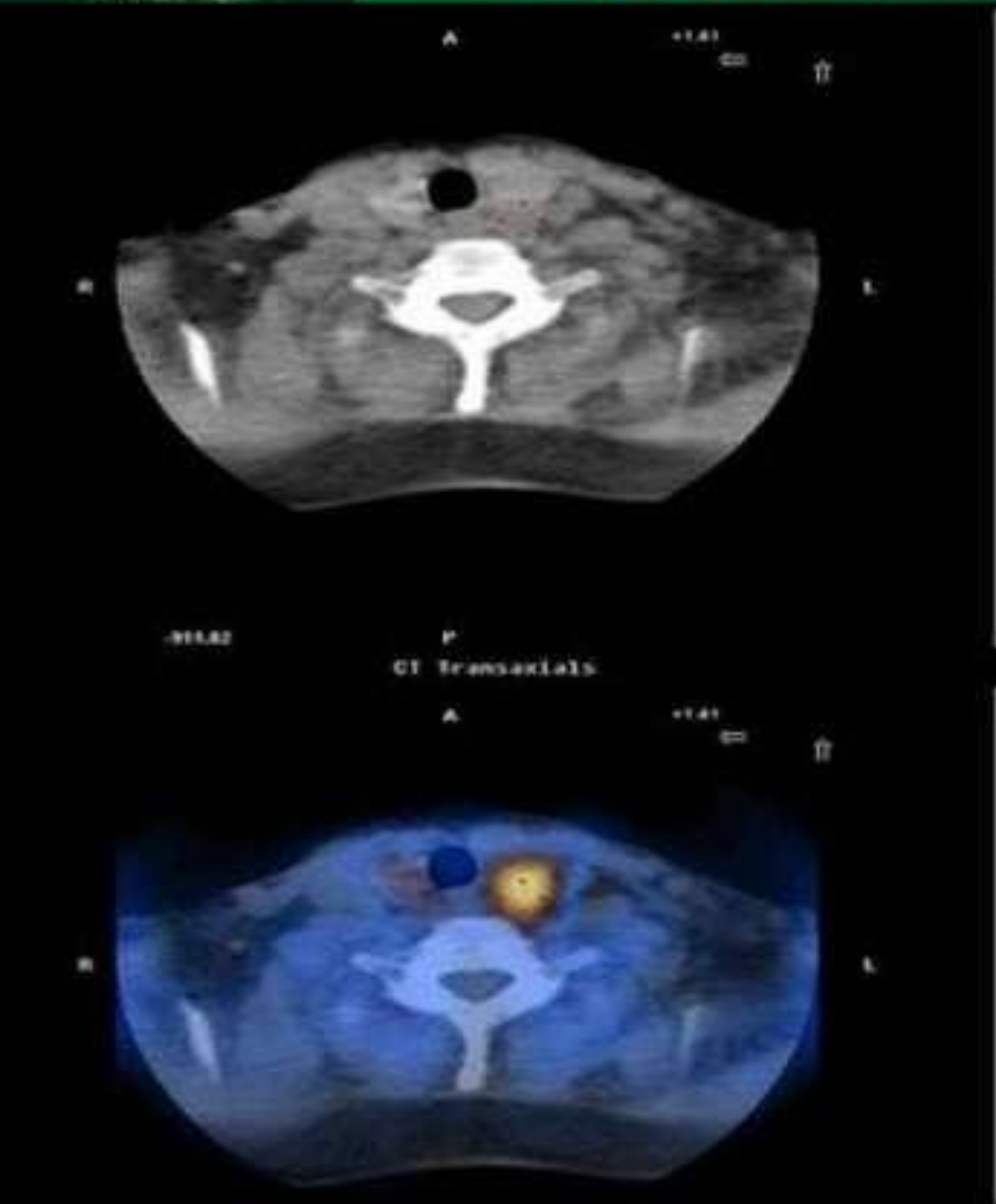
2-Nuclear scanning: (Sestamibi scan)

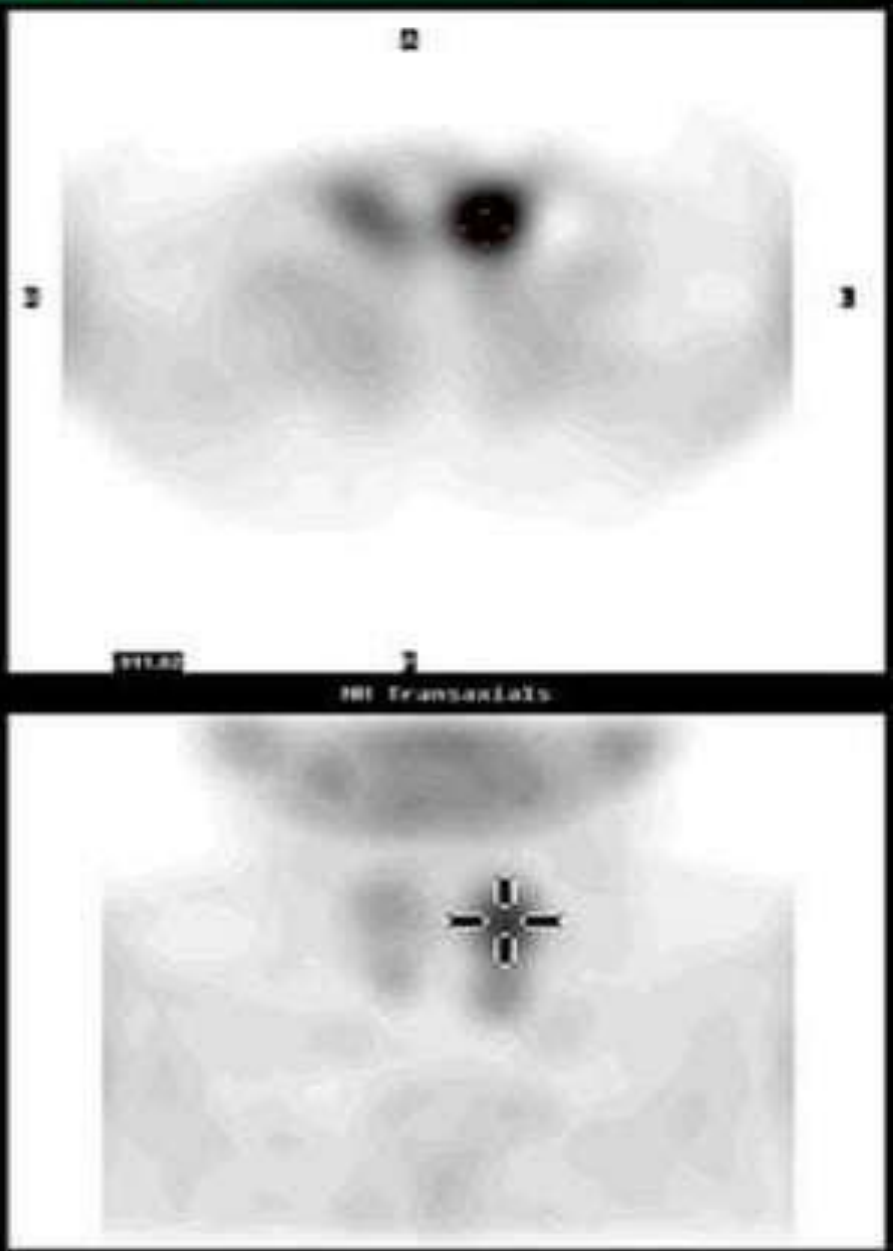
*Radiolabeled Sestamibi is concentrated in thyroid and parathyroid tissues but usually washes out of normal thyroid in under an hour and persists in abnormal parathyroid tissue that can be seen as a persistent focus of activity on delayed images.

*Sensitivity for solitary adenomas ranges between 60-90%.

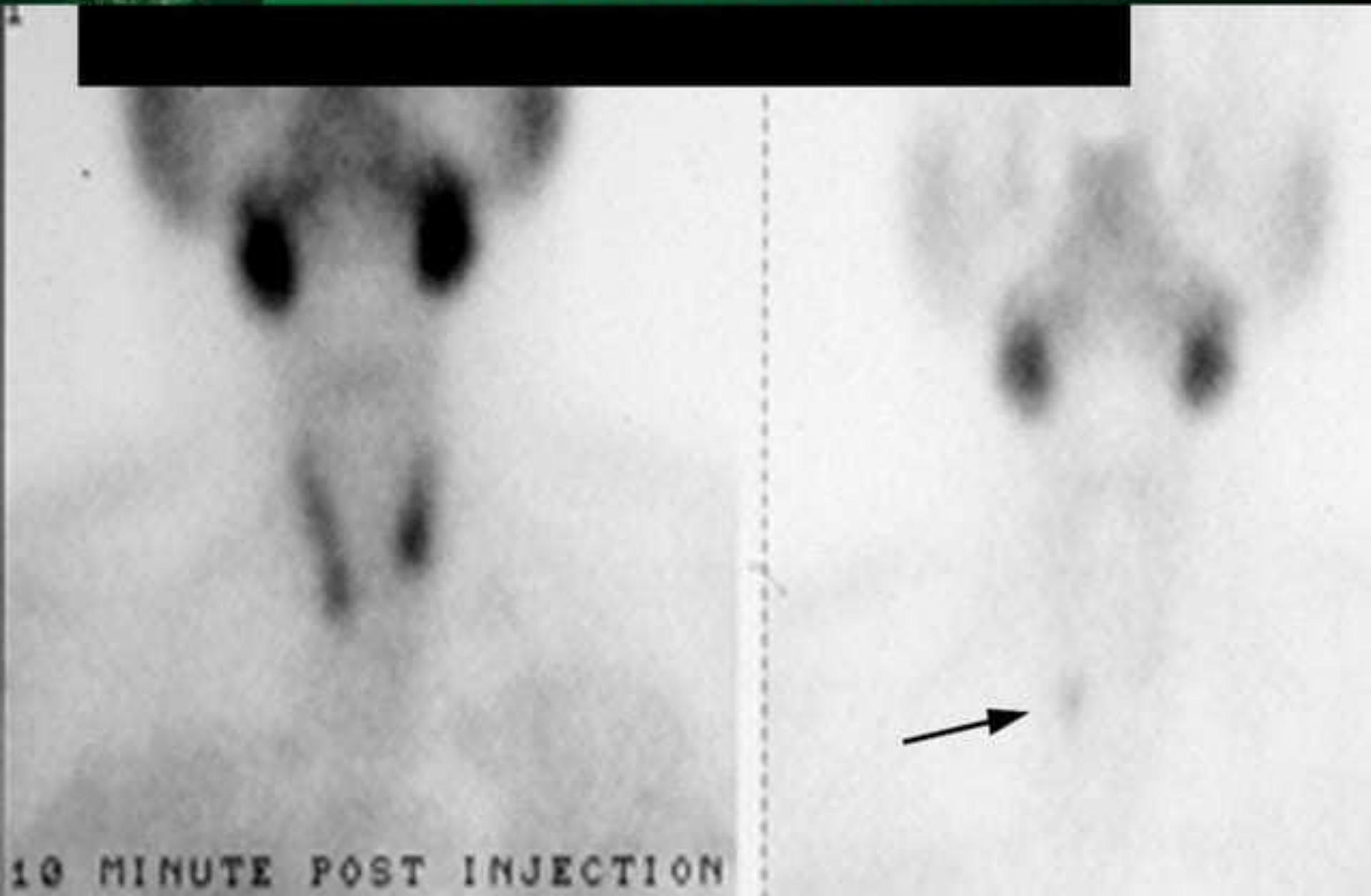
* Scan can include the mediastinum and, thus, is extremely useful in cases of an ectopic adenoma or previously failed surgical exploration.

Sestamibi scan





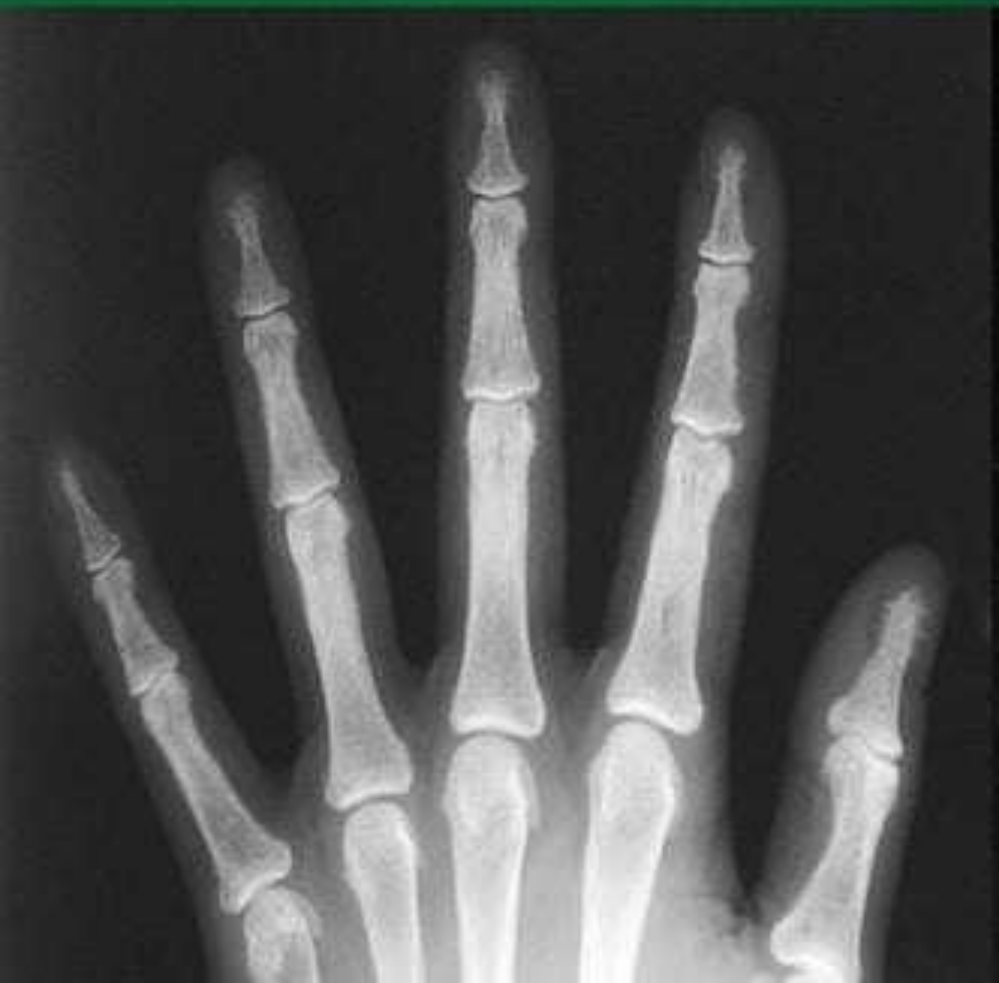
Sestamibi scan



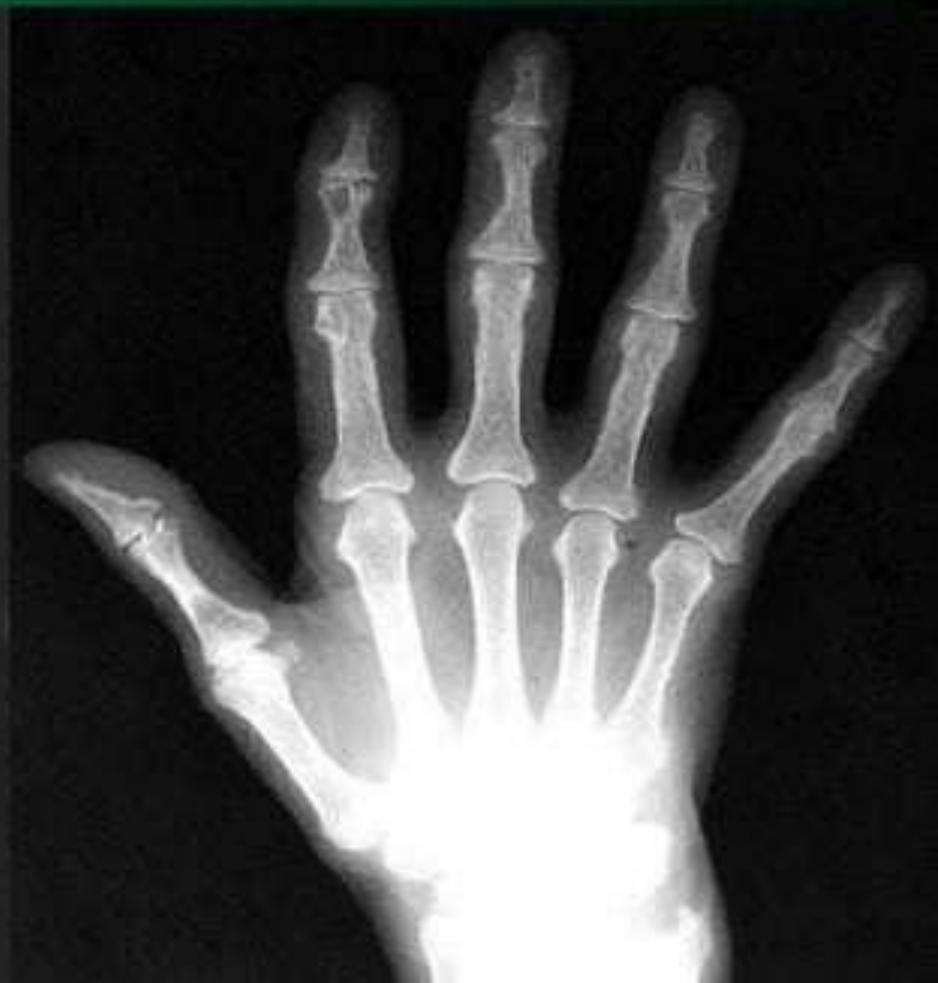
3-CT and MRI scanning.

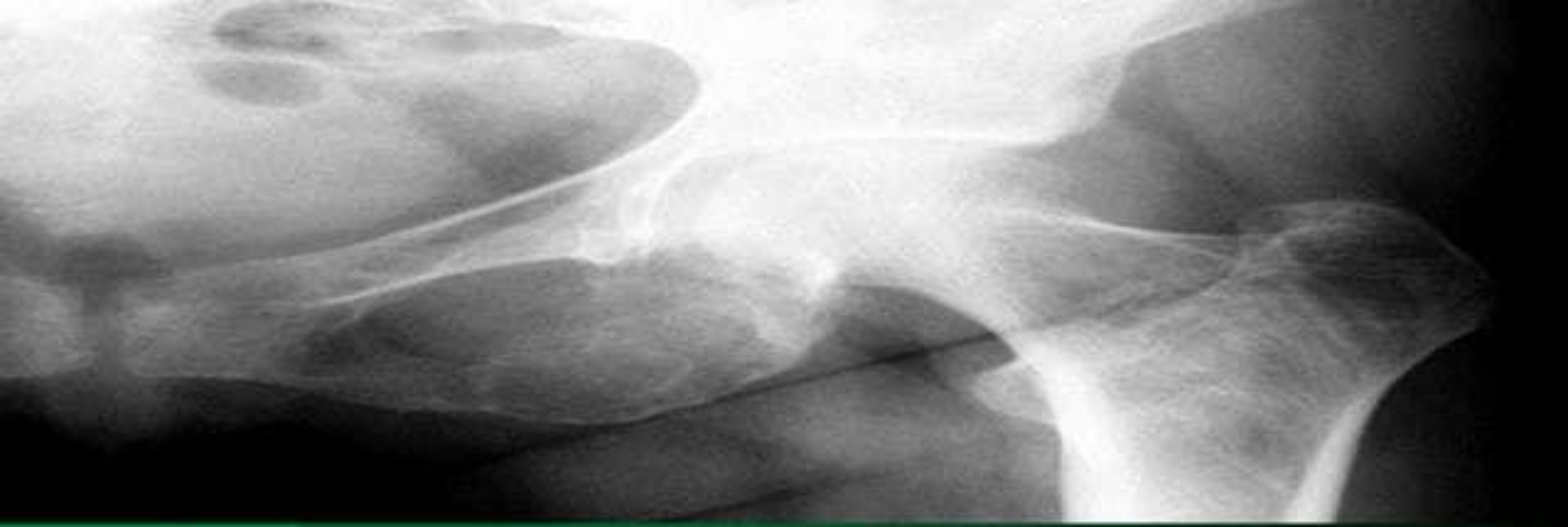
4- X-ray and DXA.

Subperiosteal resorption
as well as acroosteolysis

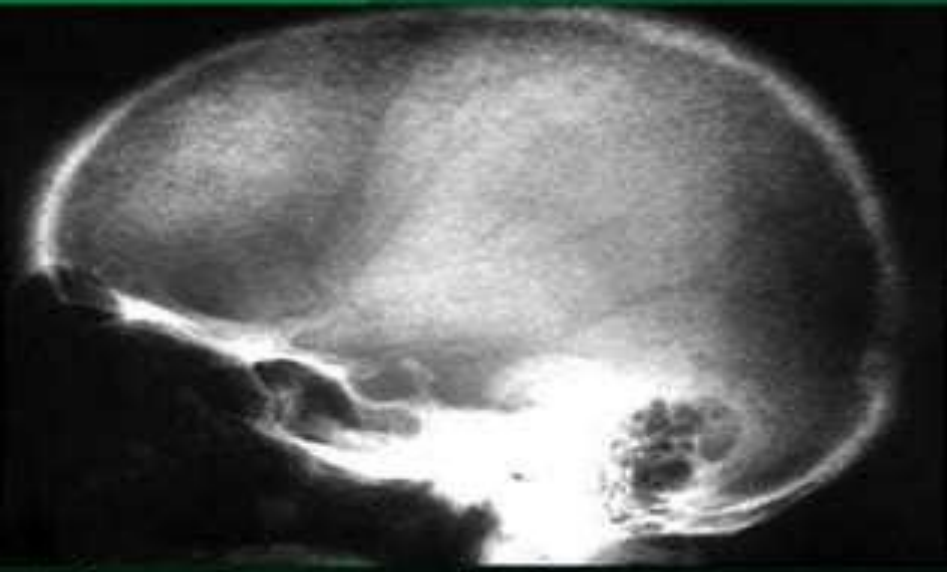


Brown tumor in the phalanx
with subperiosteal resorption

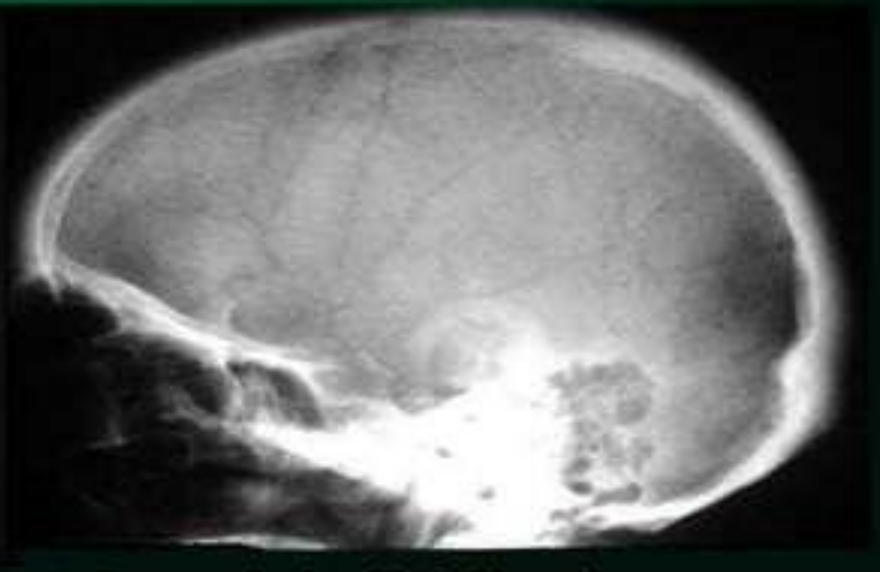




Brown tumor in the inferior obturator ramus



Salt and pepper skull



Normal skull following treatment

TREATMENT OF 1RY HYPERPARATHYROIDISM

MEDICAL CARE:

For asymptomatic patients and those who choose not to have surgery

-Lifestyle:

***regular exercise.**

***avoidance of immobilization.**

-Diet:

***good hydration.**

***moderate daily Ca intake of 800-1000 mg.**

***vitamin D intake appropriate for age and sex.**

-Drugs:

***Calcimimetics (e.g. cinacalcet)**

***Oestrogen therapy (postmenopausal).**

***Bisphosphonates.**

***PPA (percutaneous parathyroid ablation) Techniques.**

***avoid thiazides, diuretics, lithium, …etc.**

SURGICAL CARE:

-Since 1925, the gold standard treatment for Primary Hyperparathyroidism is *Parathyroidectomy.*

-There is universal agreement that surgical treatment should be offered to all patients with symptomatic disease. Some controversy exists regarding the optimal management of asymptomatic patients.

Indications Of Surgery in asymptomatic primary hyperparathyroidism: National Institutes of Health (NIH) Workshop (2002)

1) Any age younger than 50 years.

2) 1.0 mg/dL above the upper limit serum Ca.

3) 24-hour urinary Ca excretion > 400 mg.

4) Bone Mass Density (BMD) score below -2.5 at any site.

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3) 24-hour urinary Ca excretion > 400 mg.

4) Bone Mass Density (BMD) score below -2.5 at any site.

5) A 30% reduction in creatinine clearance

-Choice of the procedure:

*identification of all parathyroid glands and removal of all abnormal glands.

*In the case of 4-gland hyperplasia, a 3.5-gland is performed (subtotal parathyroidectomy).

Preoperative Localization of abnormal parathyroid

Sestamibi Scan.

HRUS

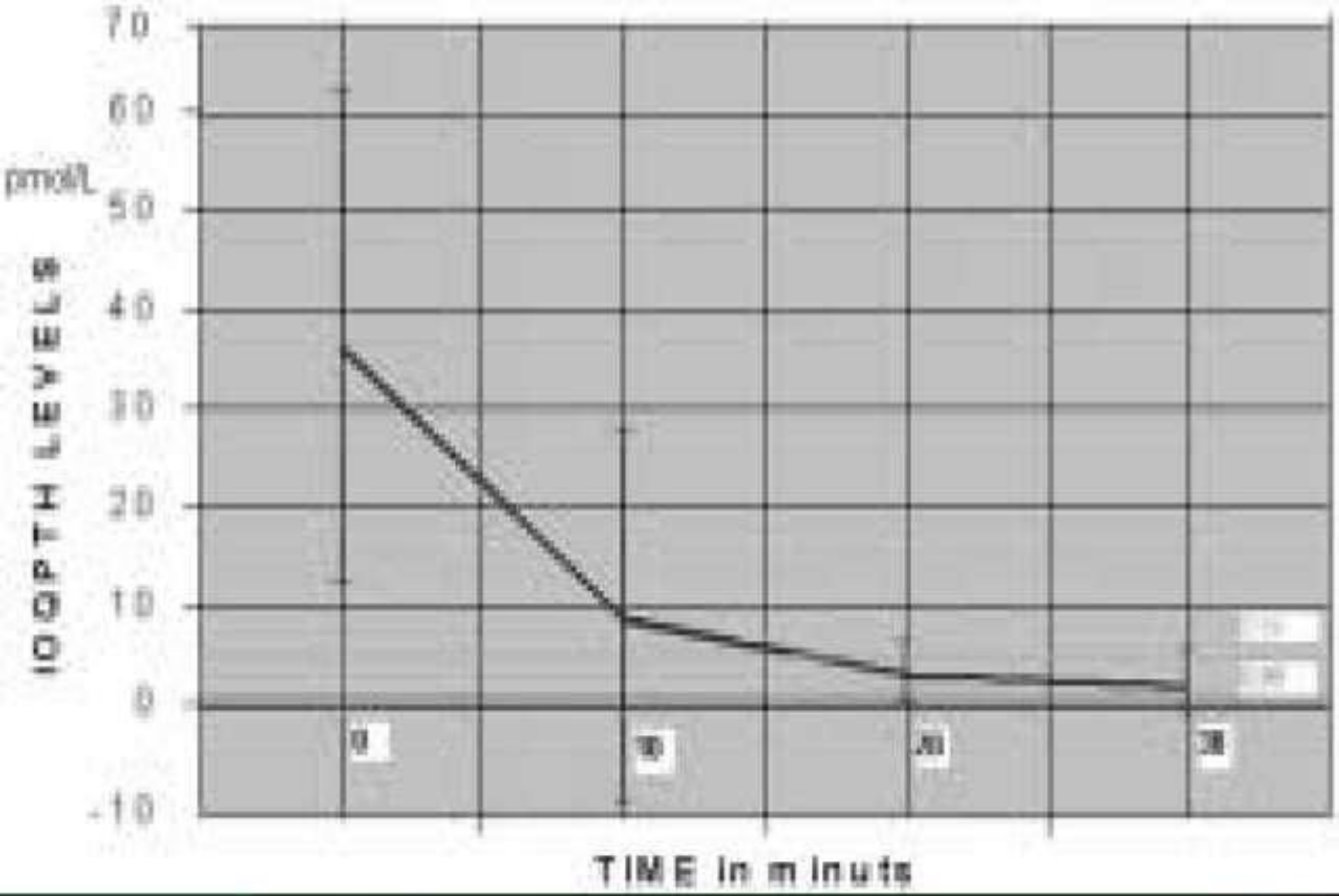
CT.

MRI.

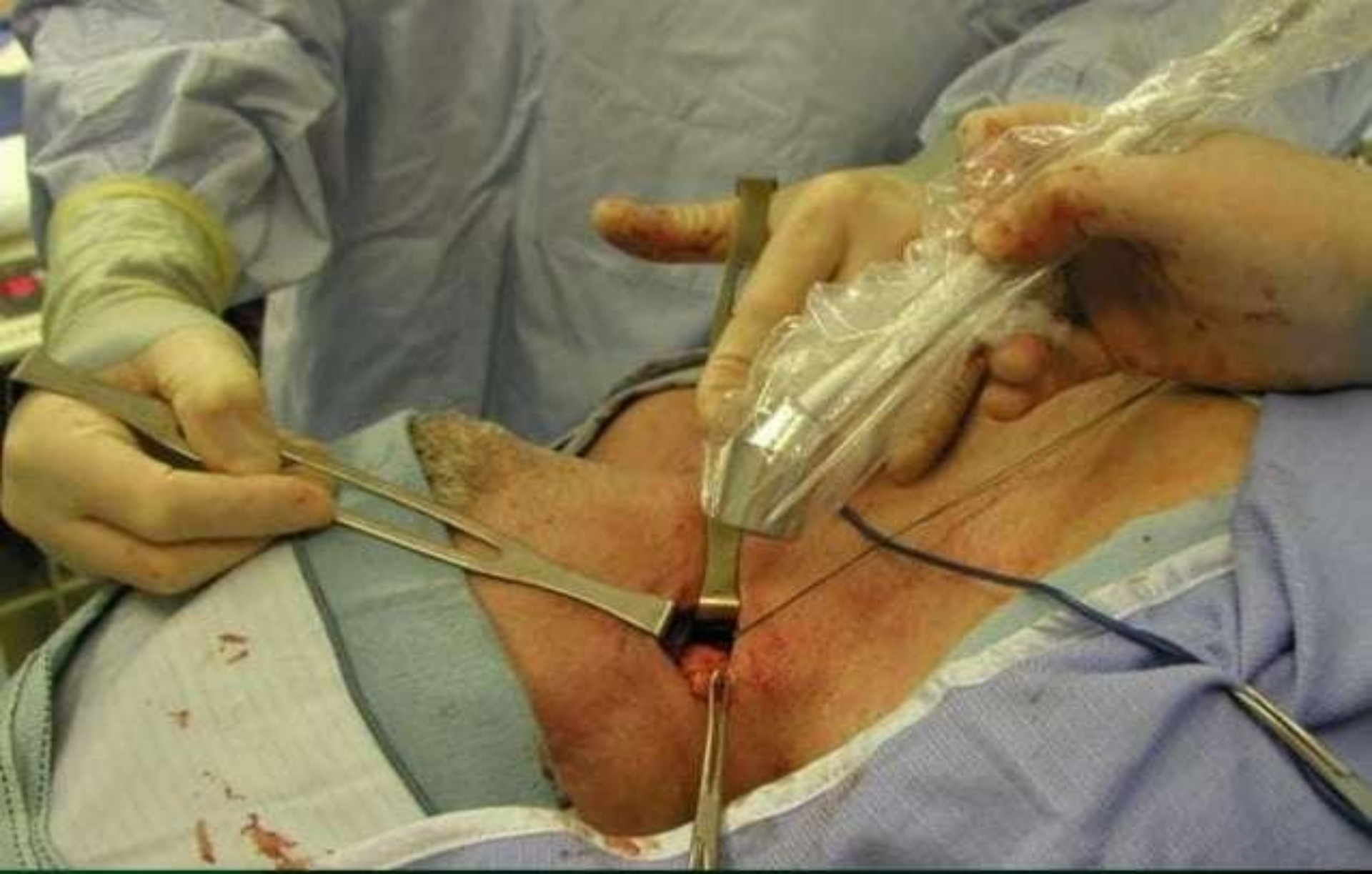
Intraoperative Localization

Intraopartive PTH assay

Radioguided parathyroidectomy



Intraopartive PTH assay



Radioguided parathyroidectomy


adenoma

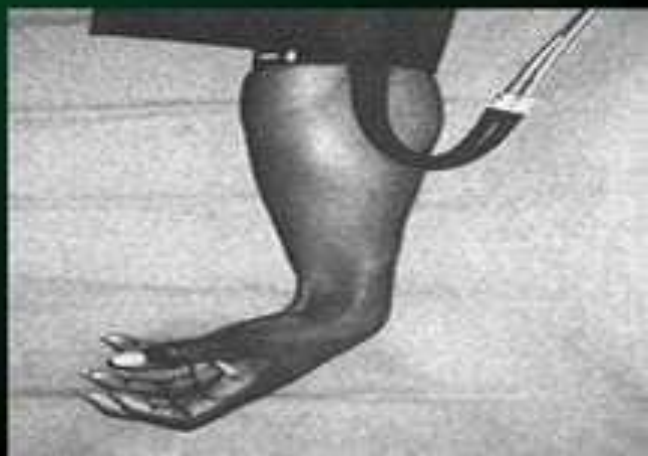
POSTOPERATIVE CARE &COPMPLICATIONS

-If a directed parathyroidectomy is performed successfully, most of these patients may be safely discharged the day of surgery.

-For a full parathyroid exploration, Ca levels must be monitored postoperatively every 12 hours until stabilization. (24-72 hrs pop). Many patients become hypocalcemic, but few become symptomatic.

Chvostek's sign

Trousseau's Sign



- Recurrent L. Nerve injury.

- A potential life-threatening emergency in the postoperative period is the development of an expanding hematoma in the pretracheal space.

- Regular follow up in the early pop period (2 wks) for estimation of PTH and Ca levels after surgery.

II. Secondary Hyperparathyroidism

Definition & aetiology:

Overproduction of PTH secondary to prolonged or intense hypocalcaemia as in:

- chronic renal failure
- malabsorption
- rickets

Diagnosis:

low-normal calcium and elevated PTH

Treatment:

Unlike 1ry hyperparathyroidism, medical management is the mainstay of treatment:

- treatment of the cause.
- vit D, Ca and PO4 binding agents.
- surgery if other measures failed.

III. Tertiary Hyperparathyroidism

Definition:

Overproduction of PTH after longstanding secondary hyperparathyroidism and resulting in hypercalcaemia

Aetiology

Prolonged (refractory) 2ry type→ chief cell hyperplasia→ ↑ PTH + ↑ Ca. Four-gland involvement occurs in most patients.

Treatment:

Total parathyroidectomy with autotransplantation or subtotal parathyroidectomy is indicated.

THANKS

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