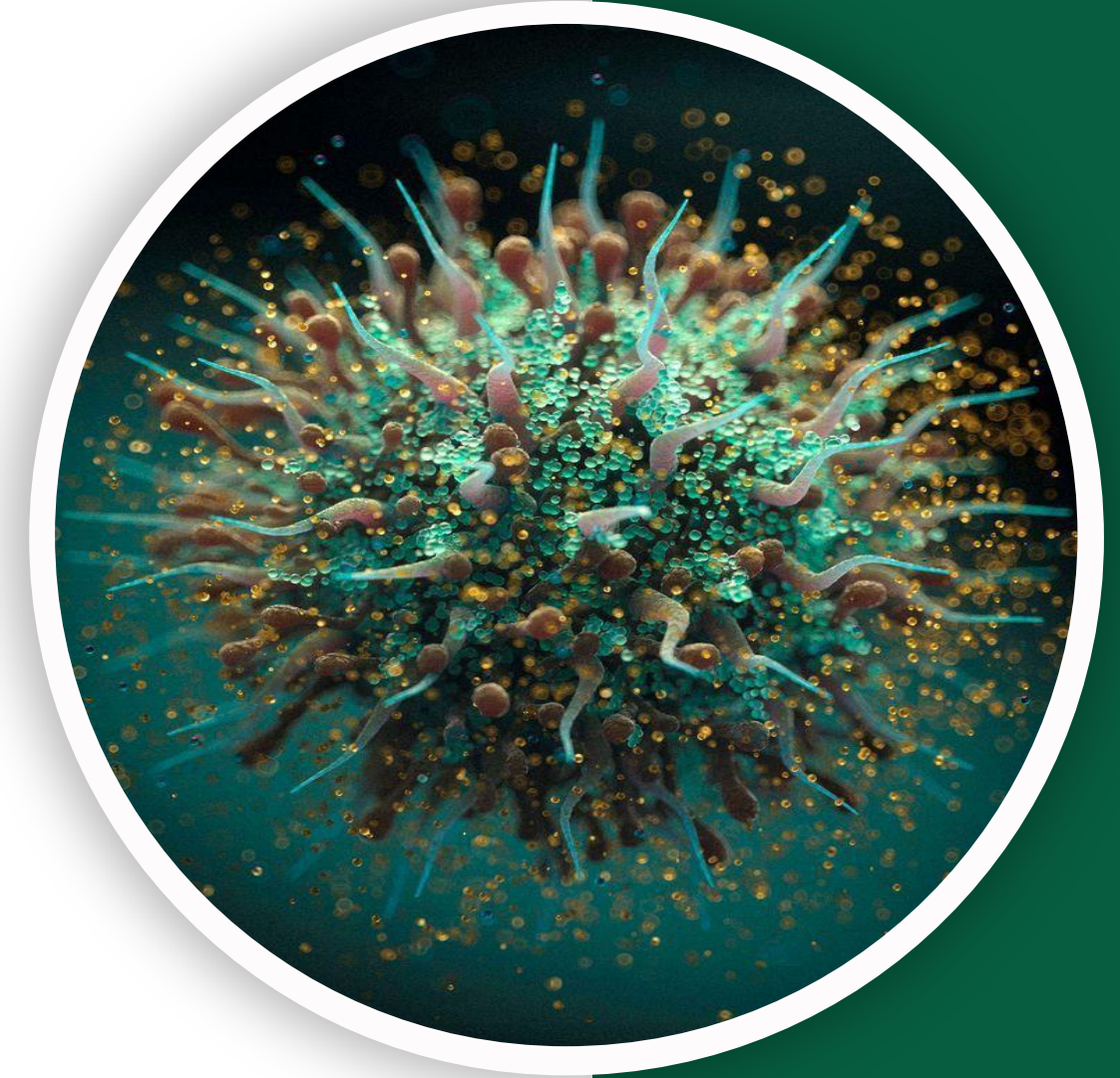


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Endocrine Pathology | FINAL 3

Diseases of Parathyroid Glands



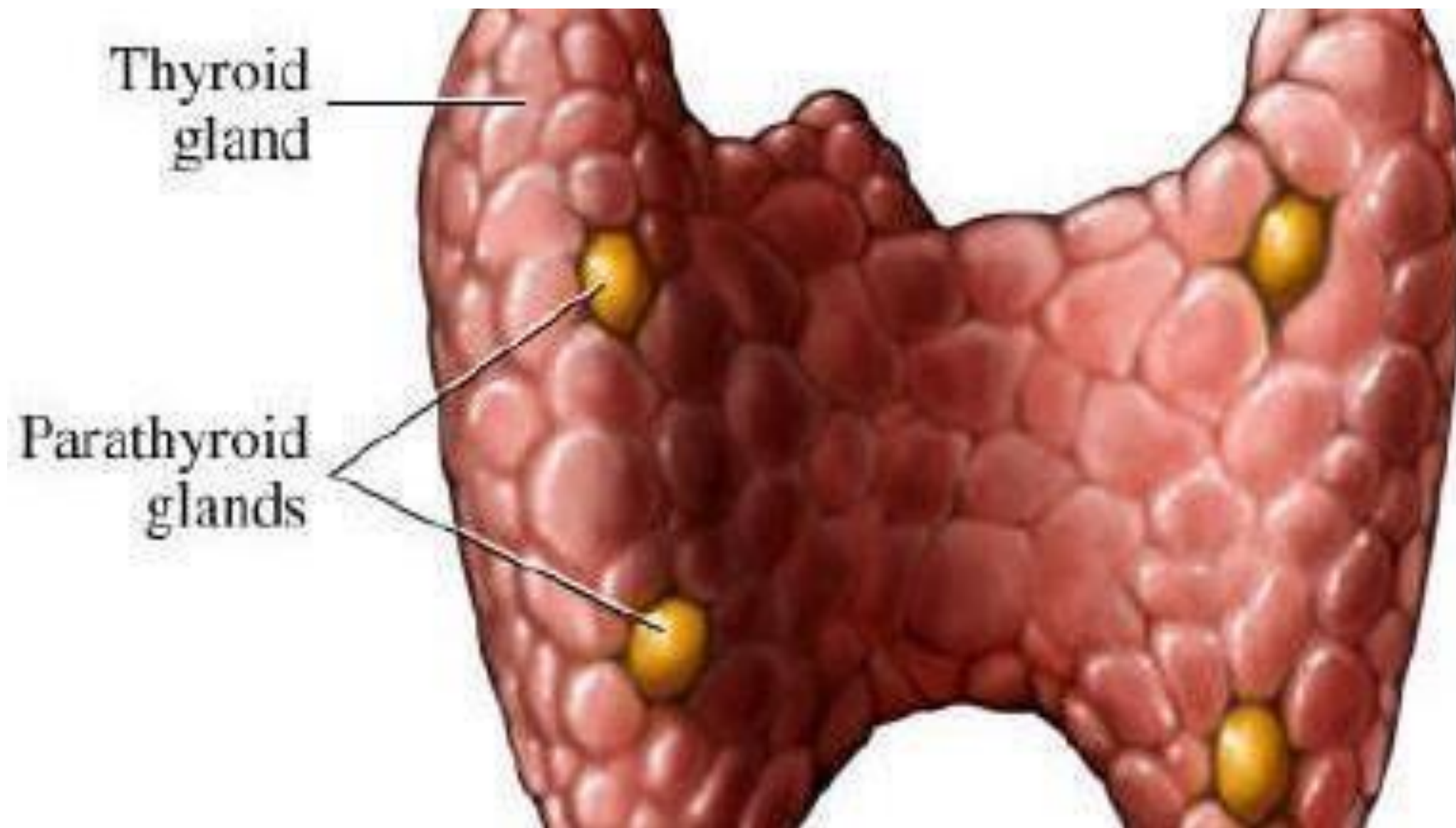
Reviewed by : Mohammad Al-Amawi

Diseases of the Parathyroid Glands

Dr Heyam Awad

FRCPath

Parathyroid gland:



Parathyroid glands:

- There are **four** parathyroid glands
- They are derived from the **pharyngeal pouches**
- (**Usually**) Located in close proximity to the upper and lower poles of each thyroid lobe.
- Each gland is yellow-brown in color and resemble lentil seed **in size - very small -**.

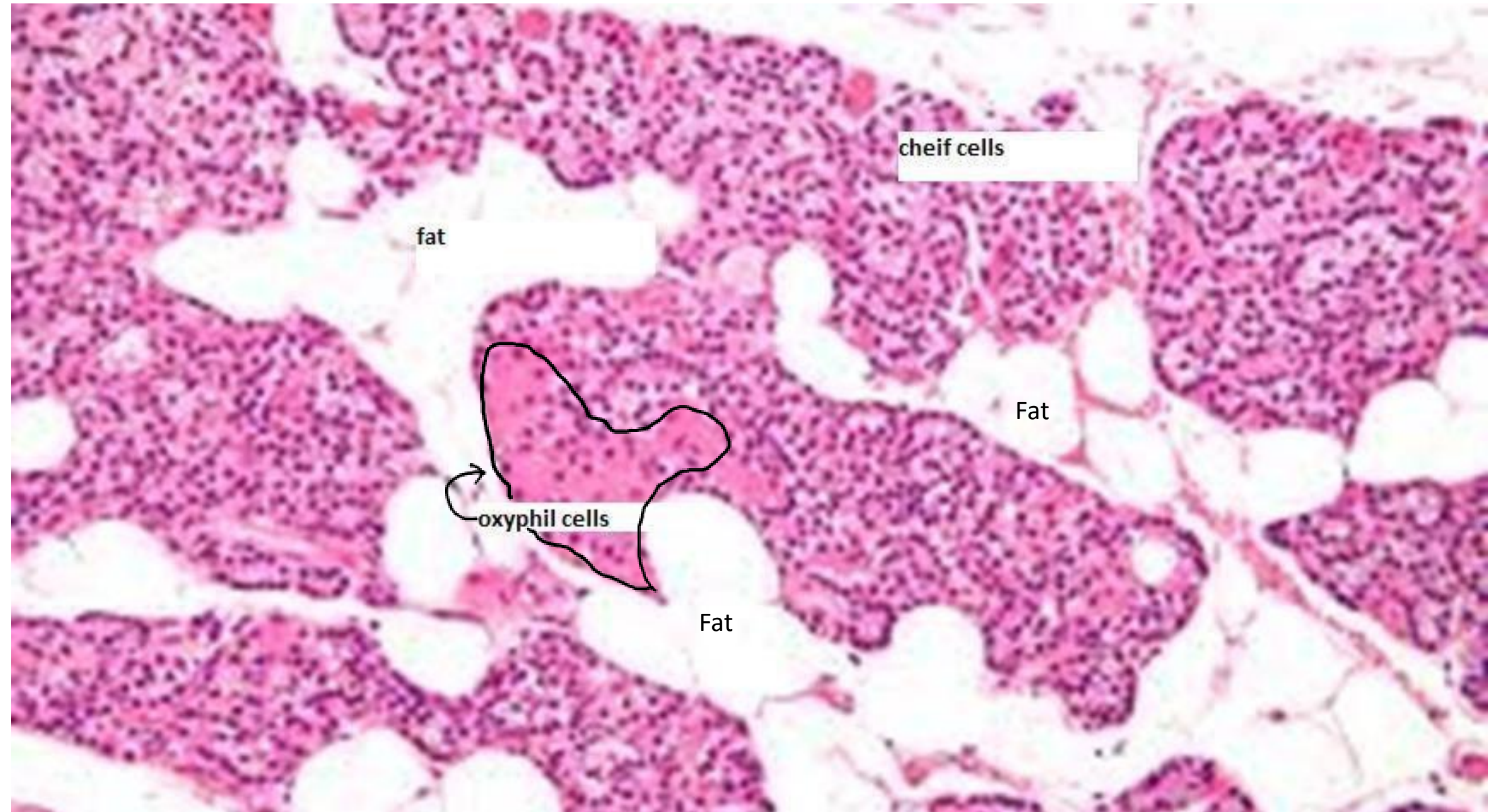


Histology:

- **It composed of 2 type of cells :**
- Parathyroid glands are composed of **Chief cells** that secrete parathyroid hormone (PTH).
- **Oxyphil cells** are **eosinophilic** and contain mitochondria (in large numbers). Their function is unknown. Some research suggests that they can secrete PTH in some cases of hyperparathyroidism.
- **Normal parathyroid glands contain fat as well.**
- SEE NEXT IMAGE FOR DETAILS..

Parathyroid gland:

- The majority of the gland consists of **Chief cells**, which are characterized by their small nuclei and the pale, almost white cytoplasm.
- In contrast, **Oxyphil cells** differ in appearance due to their eosinophilic (pinkish) cytoplasm, which is larger in size -the cytoplasm is more abundant-.
- This pink coloration is due to the high number of **mitochondria** present in these cells.
- In a normal gland, fat is typically visible as areas with a whitish color. The absence of fat can be a sign of abnormality, such as hyperplasia, adenoma, or carcinoma. Therefore, when trying to distinguish between a normal and abnormal gland, it's important to look for the **presence of fat within the tissue**.

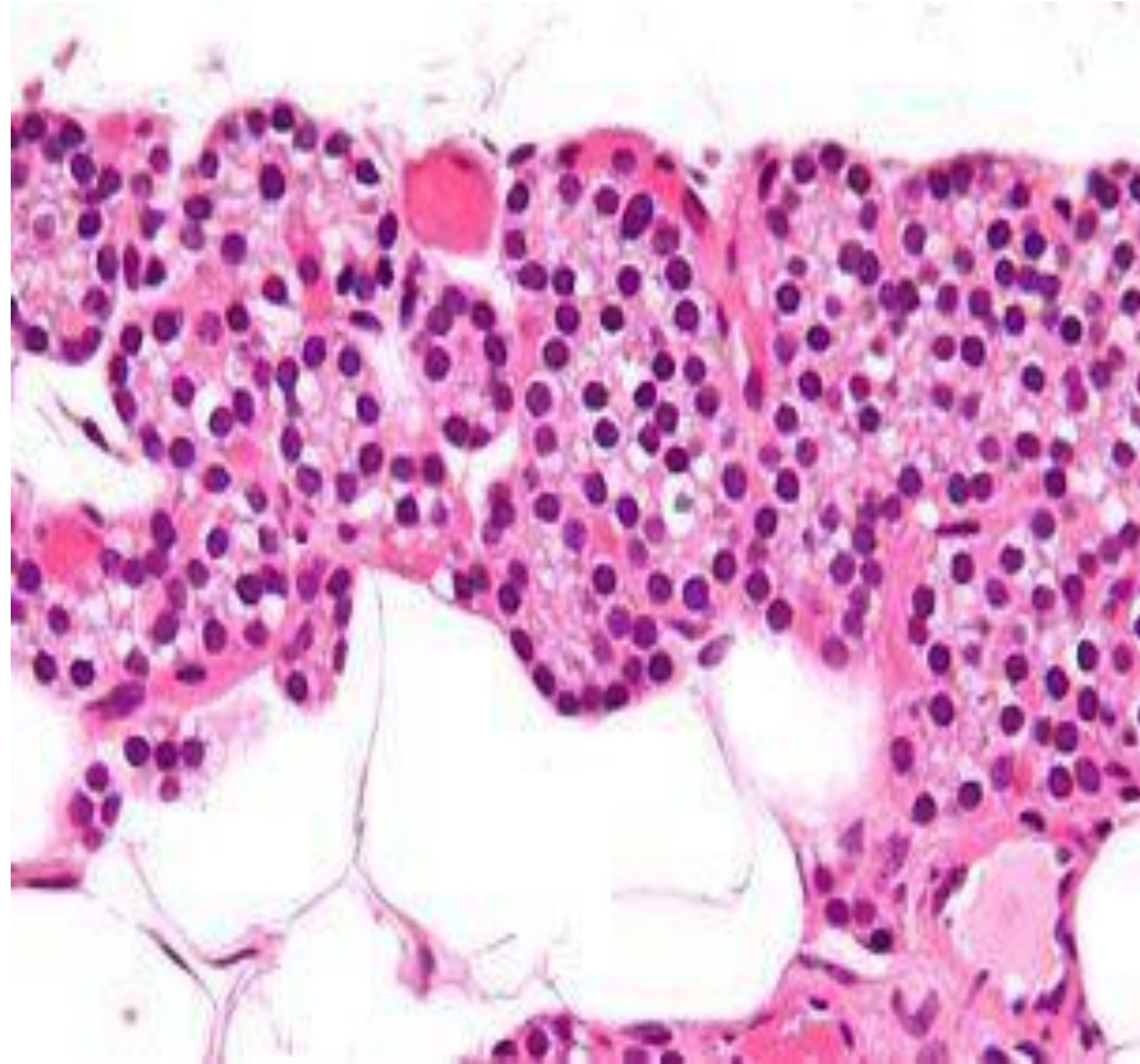


Note:

- **As we said normal parathyroid contains fat.**
- **This is important to know because parathyroid hyperplasia and adenoma usually do not contain fat and this is an important feature to distinguish between them histologically.**

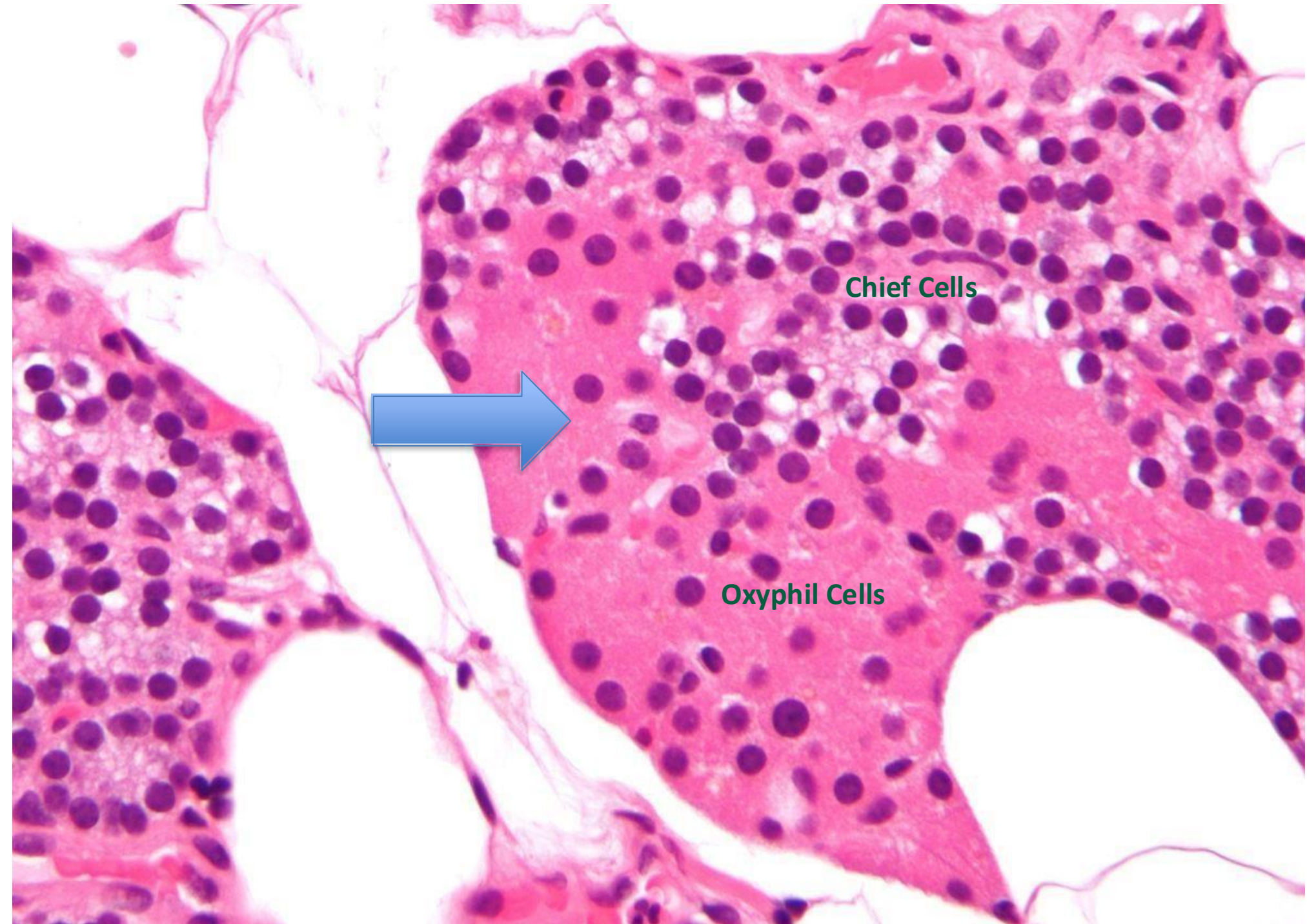
Parathyroid chief cells:

Light pink cytoplasm



Oxyphil cells:

Larger cells
(filled with dark pink cytoplasm)



Regulation of PTH:

- **PTH regulates calcium level in blood.**
- If blood calcium decreases.. Parathyroid gland secretes PTH...
- **NOTE:** the regulation of PTH secretion is NOT under control of the pituitary BUT is regulated by calcium levels in the blood, Unlike most endocrine glands, which function under the regulatory control of the pituitary gland.

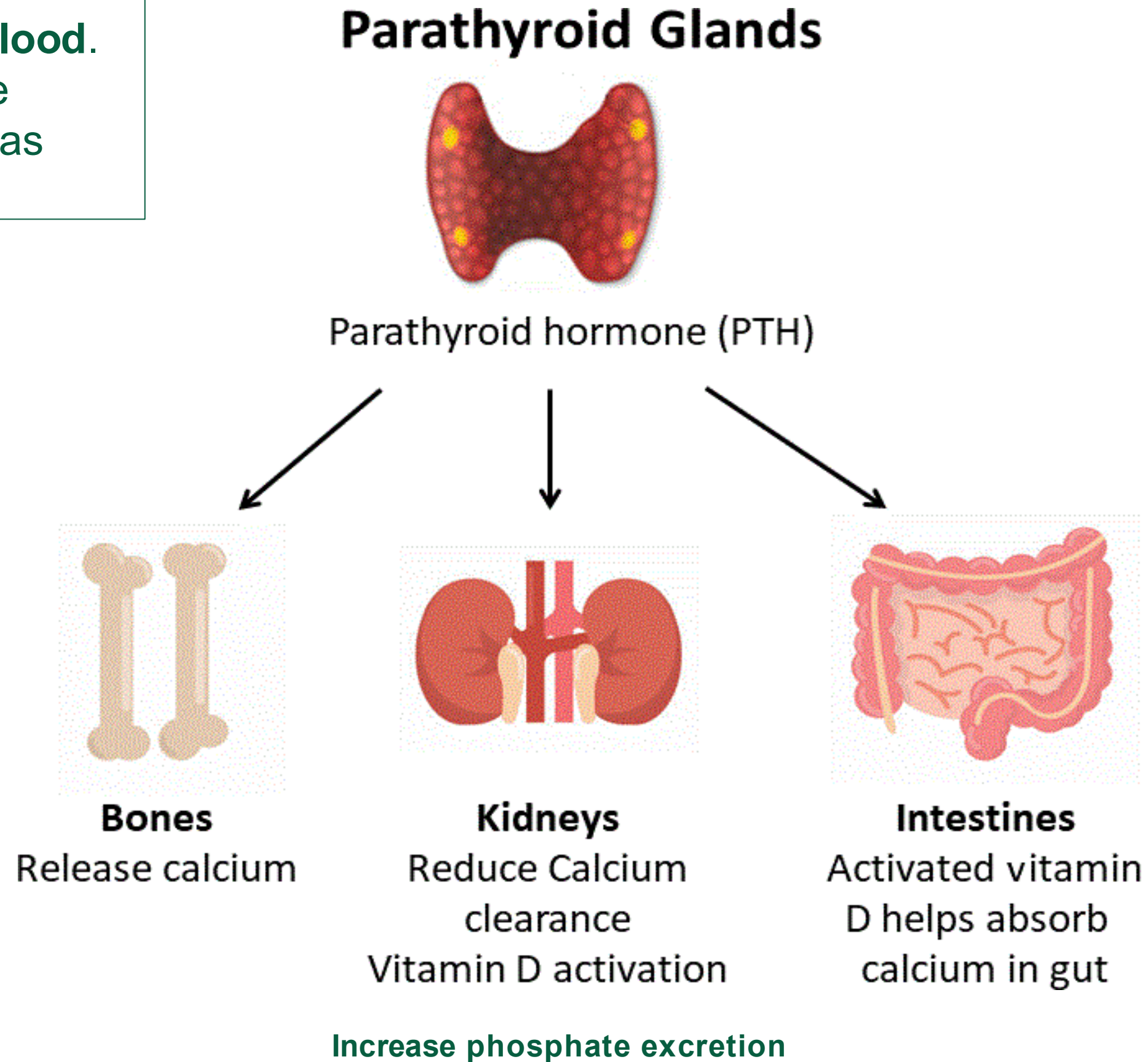
Functions of PTH:

- PTH increases blood calcium by its effects on the kidneys, GIT and bone. **See Next Slide..**

PTH Functions:

- **Kidney:** Increases renal tubular reabsorption of calcium, accordingly, serum calcium concentration is increased (**direct effect**).
- **GI:** Increases conversion of vitamin D to its active form. Which increases gastrointestinal absorption of calcium (the effect in GI is **indirectly** through activation of vit D).
- **Bones:** Increases osteoclastic activity (increases bone resorption) so releasing calcium from bone to blood.
- **Increases phosphate excretion in urine..** So phosphate level is decreased.. So less calcium binds to phosphate.. So more free calcium in blood, **How?**
- ✓ **Answer:** Some calcium in the blood is bound to phosphate, When phosphate levels decrease, free calcium increases. We focus on free calcium because it's the active form that performs physiological function (PTH → ↓ Phosphate in blood → ↓ Calcium-phosphate binding → ↑ Free (ionized) calcium in blood)

➤ The only function of this hormone is to **increase calcium levels in the blood**. It does so through three different mechanisms, as previously mentioned.



Diseases of the parathyroid:

- Hyperparathyroidism
 - Hypoparathyroidism
 - Mass lesions: adenomas and carcinomas.
- 
- Related to hormone secretion disorder

➤ Note: Mass lesion refers to an abnormal mass of tissue within the body that can be either benign or malignant.

HYPERPARATHYROIDISM :

1. **Primary Hyperparathyroidism:** **autonomous** increase in parathyroid hormone not caused by decreased calcium (the problem is in the parathyroid gland or there is ectopic secretion of parathyroid hormone as a paraneoplastic syndrome)
2. **Secondary Parathyroidism:** parathyroid hormone increases **due to decreased calcium level**. The most common cause is **renal failure**.
3. **Tertiary hyperparathyroidism:** in some patients with secondary hyperparathyroidism, the increased parathyroid hormone production becomes autonomous and not regulated by calcium levels.

- ❖ Normally, when calcium levels decrease, PTH increases. **In primary hyperparathyroidism**, PTH is elevated due to gland overactivity, not low calcium. This can result from hyperplasia, adenoma (mostly), or carcinoma of the parathyroid gland.
- ❖ **Secondary hyperparathyroidism** occurs due to low calcium levels, often from chronic kidney disease, leading to increased PTH secretion. If calcium levels normalize, PTH typically returns to normal.
- ❖ **In tertiary hyperparathyroidism**, after prolonged stimulation, the parathyroid glands become autonomous and continue to secrete high levels of PTH even when calcium levels are normal.

Primary Hyperparathyroidism:

- Primary: means **autonomous** secretion of PTH.. That is not caused by decreased calcium level
- Primary hyperparathyroidism is a common disorder and important cause of hypercalcemia.

Causes of primary hyperparathyroidism:

1. **Parathyroid adenoma** (85% to 95%) **most common**
2. Primary parathyroid hyperplasia-5% to 10%.
3. Parathyroid carcinoma-(1%) **Very rare**

- **What's the difference between the Parathyroid adenoma and hyperplasia?**

Adenoma is a benign tumor in one gland (solitary). **Hyperplasia** is the enlargement of multiple glands, often all four.

Parathyroid adenoma:

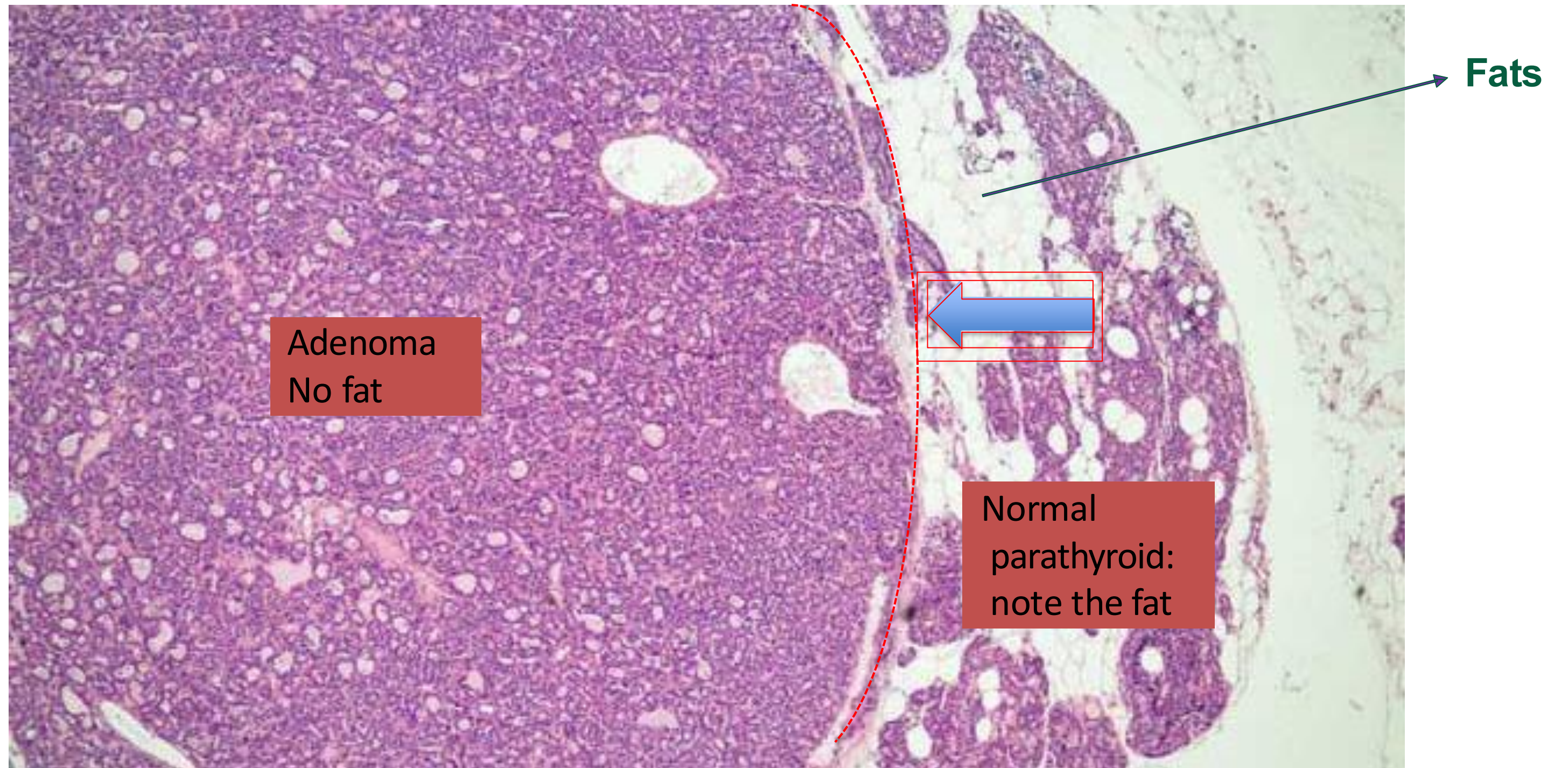
- Most parathyroid adenomas weigh between 0.5 and 5 g (significant enlargement)
- They are **encapsulated, soft and solitary** (only one gland is usually affected and the other three are normal or atrophic (read the green box)).
- A rim of compressed, normal, non-neoplastic, parathyroid tissue, separated by a fibrous capsule, is visible at the edge of the adenoma. (See next slide)
- Cells with pleomorphic nuclei may be seen (**endocrine atypia**) and must not be taken as a sign of malignancy.
- Mitotic figures are rare .
- Inconspicuous adipose(fatty) tissue .

The healthy parathyroid glands shrink (atrophy) due to a negative feedback loop triggered by the adenoma...

Because the abnormal parathyroid gland secretes excessive amounts of parathyroid hormone (PTH), the body senses this hormone overload and suppresses the activity of the remaining normal parathyroid glands. As these healthy glands cease hormone production and remain dormant, they gradually shrink from disuse.

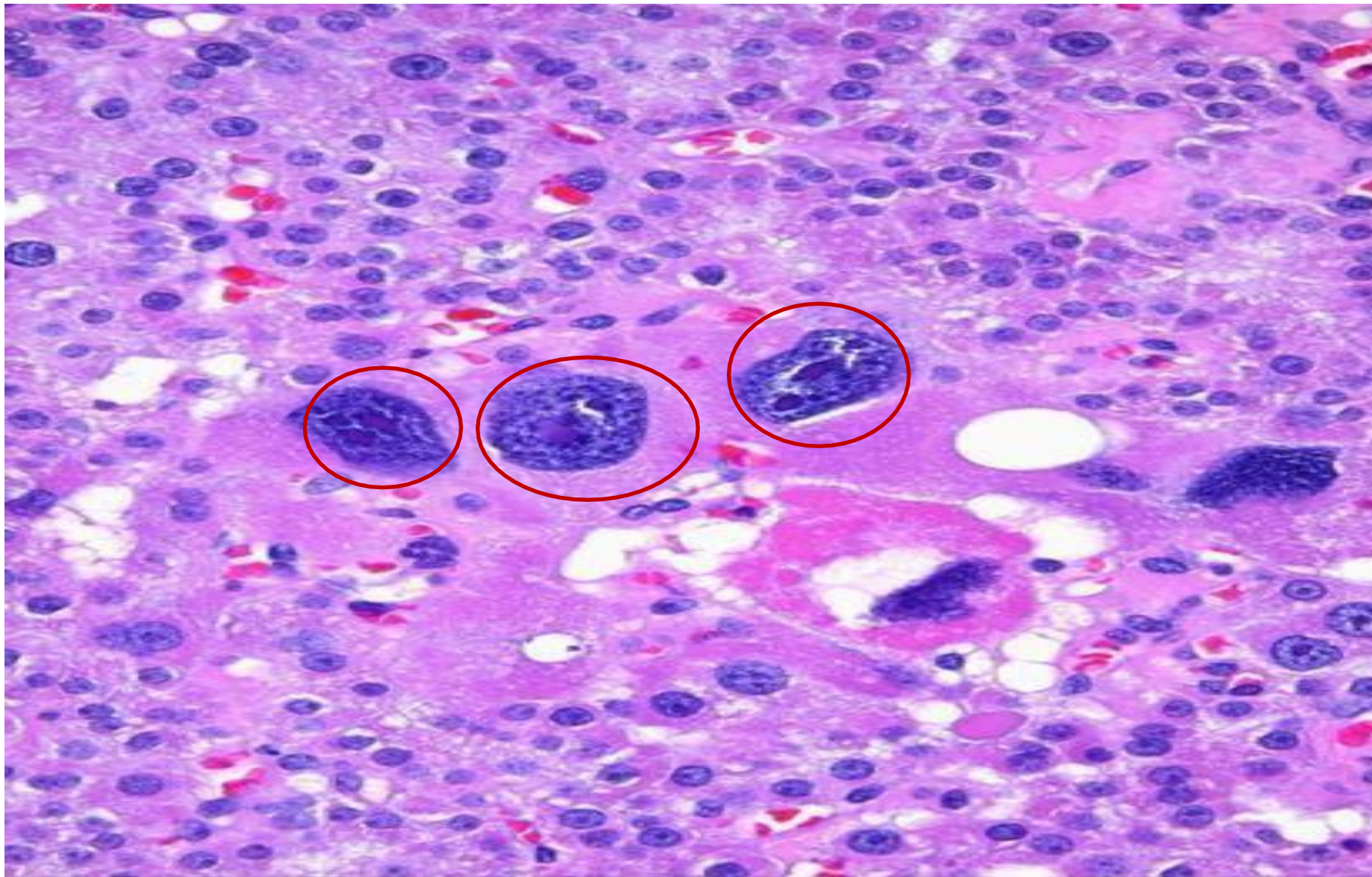
Parathyroid adenoma:

Note the **thin capsule**(**arrow**) separating the adenoma from the normal tissue



Endocrine atypia:

This is not necessarily a malignant feature (**benign**)



- The most important cytological feature of neoplasia is **nuclear pleomorphism**, which refers to the variability in the size and shape of the nuclei. However, in endocrine glands, the presence of endocrine atypia does not necessarily indicate malignancy. These nuclear abnormalities may be seen in benign endocrine tumors as well.

Parathyroid hyperplasia:

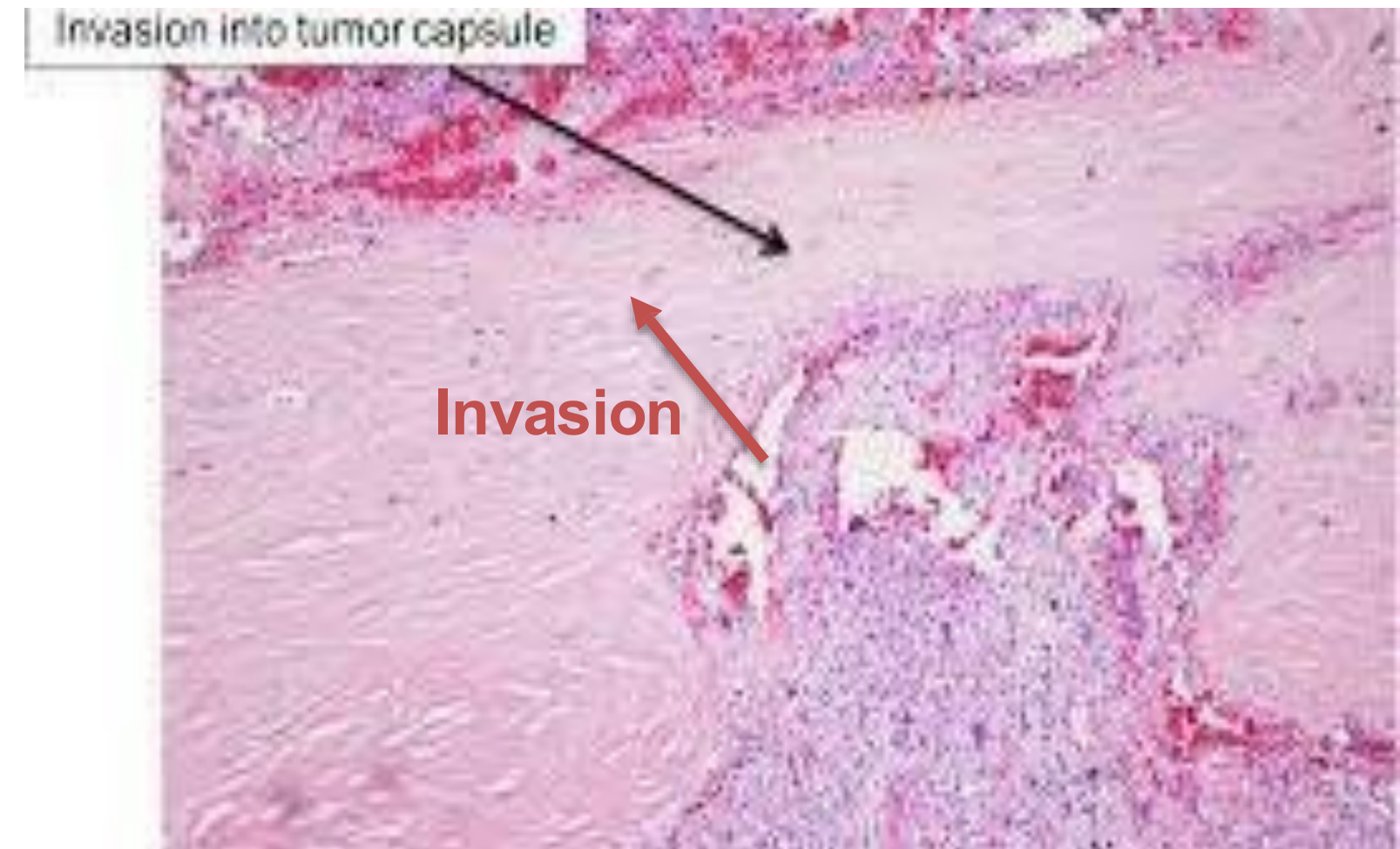
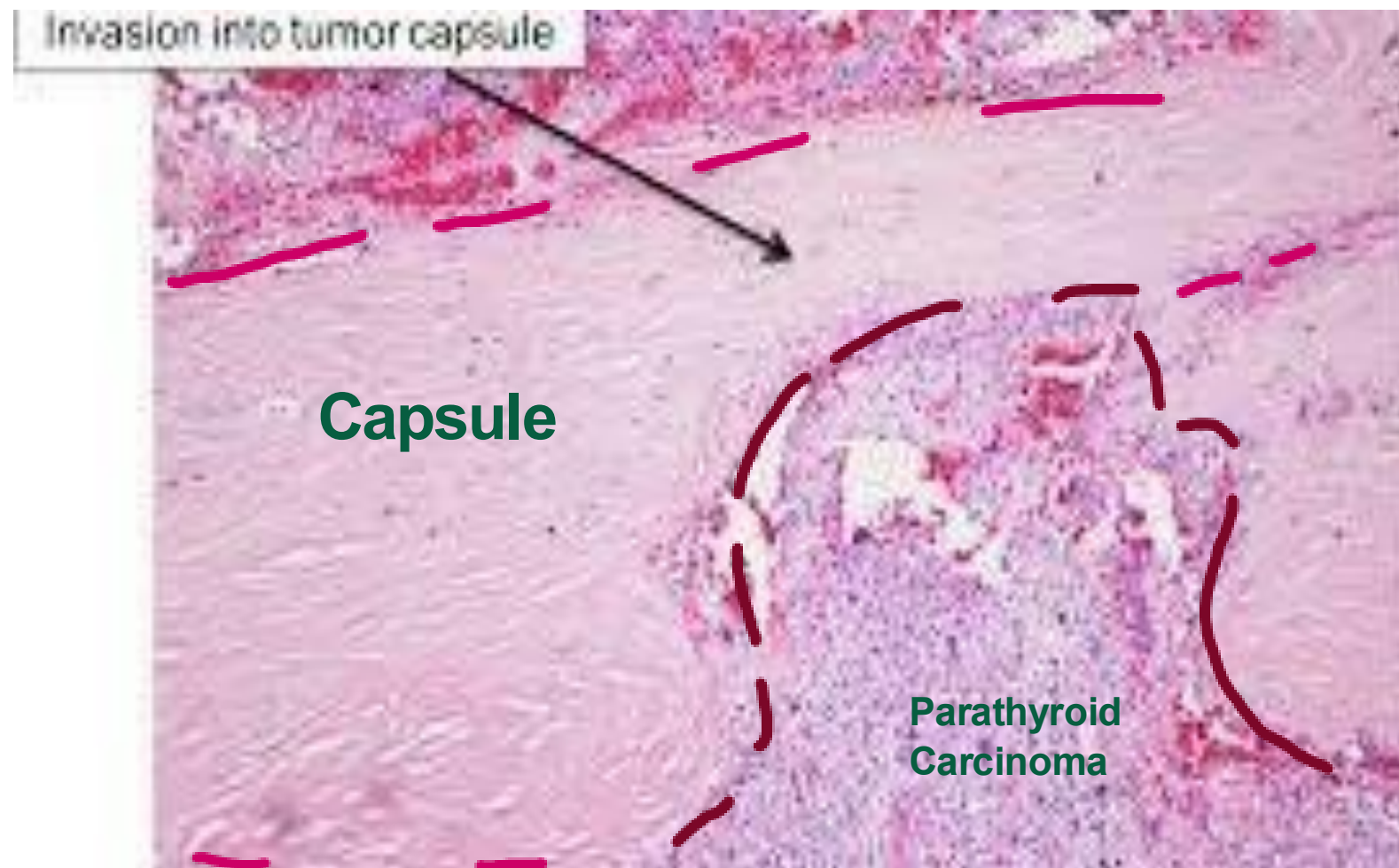
- **Multi-glandular process** (more than one gland enlarged)
- The combined weight of all glands rarely exceeds 1.0 g (**very small**)
- Stromal fat is inconspicuous within foci of hyperplasia.

✓ This contrasts with parathyroid adenoma, in which a single gland is affected and may enlarge significantly, reaching a weight of up to 5 grams.

Parathyroid carcinomas :

- one gland affected (**Solitary**)
- Consist of irregular masses that sometimes **exceed 10 g** in weight (**Very large**)
- The diagnosis of carcinoma based on cytologic detail is unreliable, and **invasion of tissues and metastasis** are the **only definitive criteria**
- *Local recurrence occurs in one third of cases,*
- *Distant dissemination (metastasis) occurs in another third*

Parathyroid carcinoma:



- ✓ The boundary of the tumor **invades** the capsule this is called mushroom-shaped invasion. To diagnose parathyroid carcinoma, we rely on two main features: invasion and metastasis.

Important Note:

- **In hyperplasia, adenoma and carcinoma..
Amount of fat in the gland decreases.**

Comparison Between Parathyroid Adenoma, Hyperplasia, and Carcinoma

Feature	Parathyroid Adenoma	Parathyroid Hyperplasia	Parathyroid Carcinoma
Nature	Benign tumor	Non-neoplastic proliferation	Malignant tumor
Number of glands affected	One gland (solitary)	All four glands	one gland (solitary)
Capsule invasion	Absent	Absent	Present (mushroom-shaped invasion)
Metastasis	Never	Never	Possible
Weight	0.5-5 g	Rarely exceeds 1 g	Usually large (>10g)

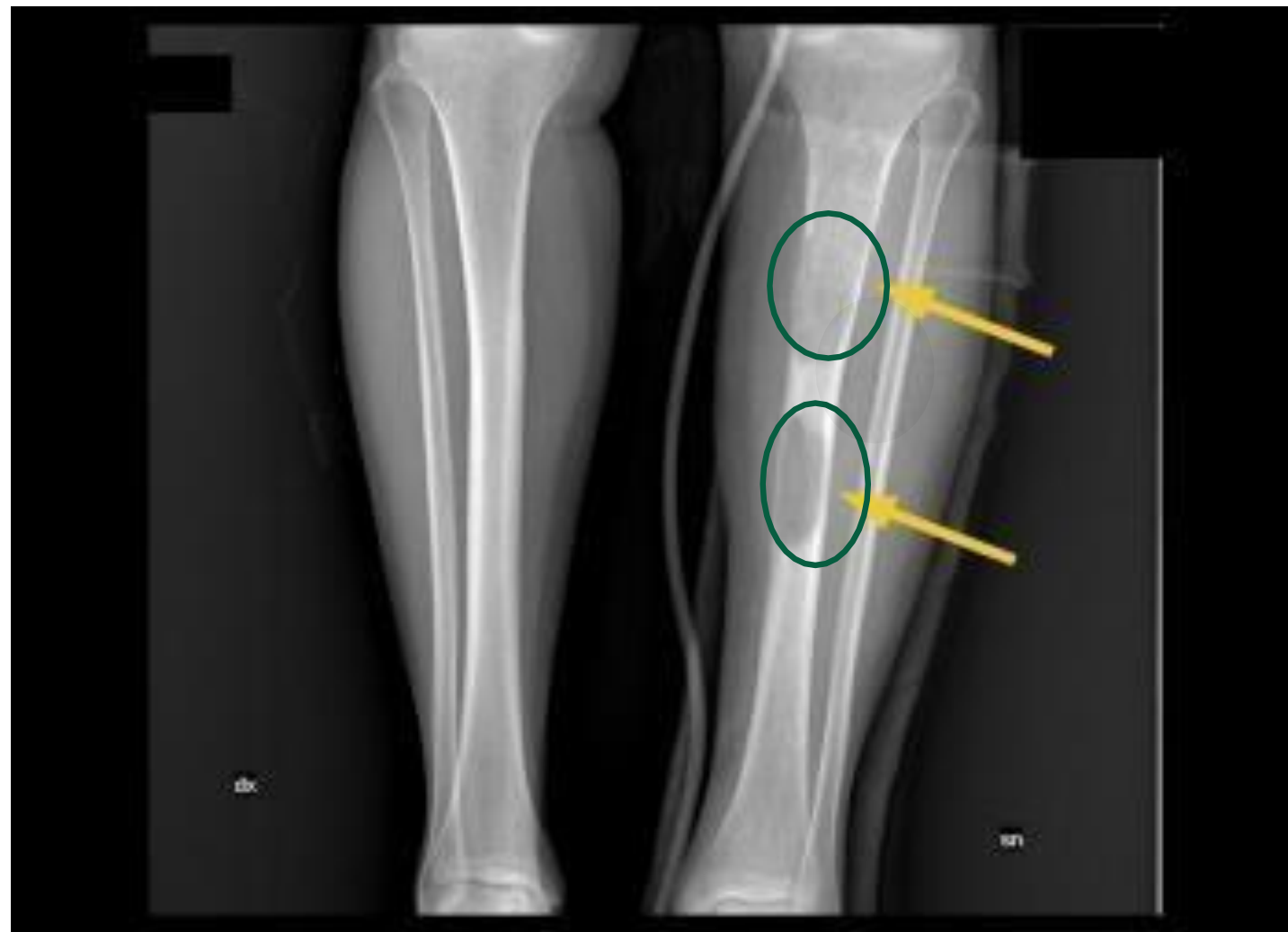
Morphologic changes in other organs in hyperparathyroidism:

- **Hyperparathyroidism** (primary, secondary, or tertiary) **affects many organs and can result in:**
 1. skeletal changes
 2. kidney changes
 3. metastatic calcifications

1. Skeletal changes:

- **Increased osteoclastic activity, resulting in erosion of bone and mobilization of calcium salts:**
 - In severe cases, the cortex is grossly thinned and the marrow contains increased amounts of fibrous tissue accompanied by foci of hemorrhage and cysts (**Osteitis fibrosa cystica**)
- **Brown tumors of hyperparathyroidism:**
 - Aggregates of osteoclasts, and hemorrhage (**due to bone loss**) occasionally form masses that may be mistaken for neoplasms

Osteitis fibrosa cystica:

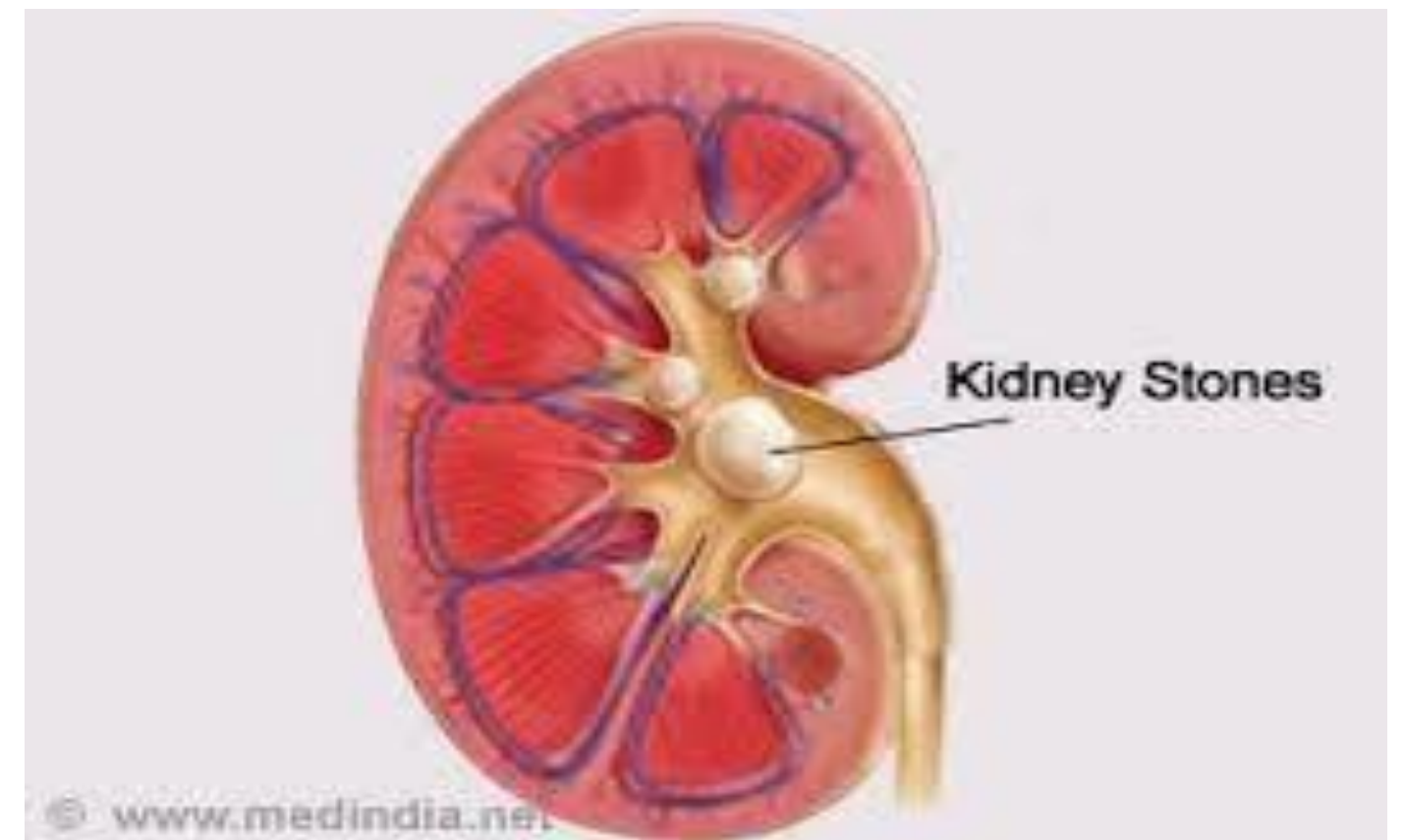


- ✓ In these regions, the bone is eroded and replaced by fibrous tissue and hemorrhagic foci.



2. Kidney changes:

- a. Increased calcium favours formation of urinary tract **stones** (nephrolithiasis)
- b. **Calcification** of the renal interstitium (nephrocalcinosis)



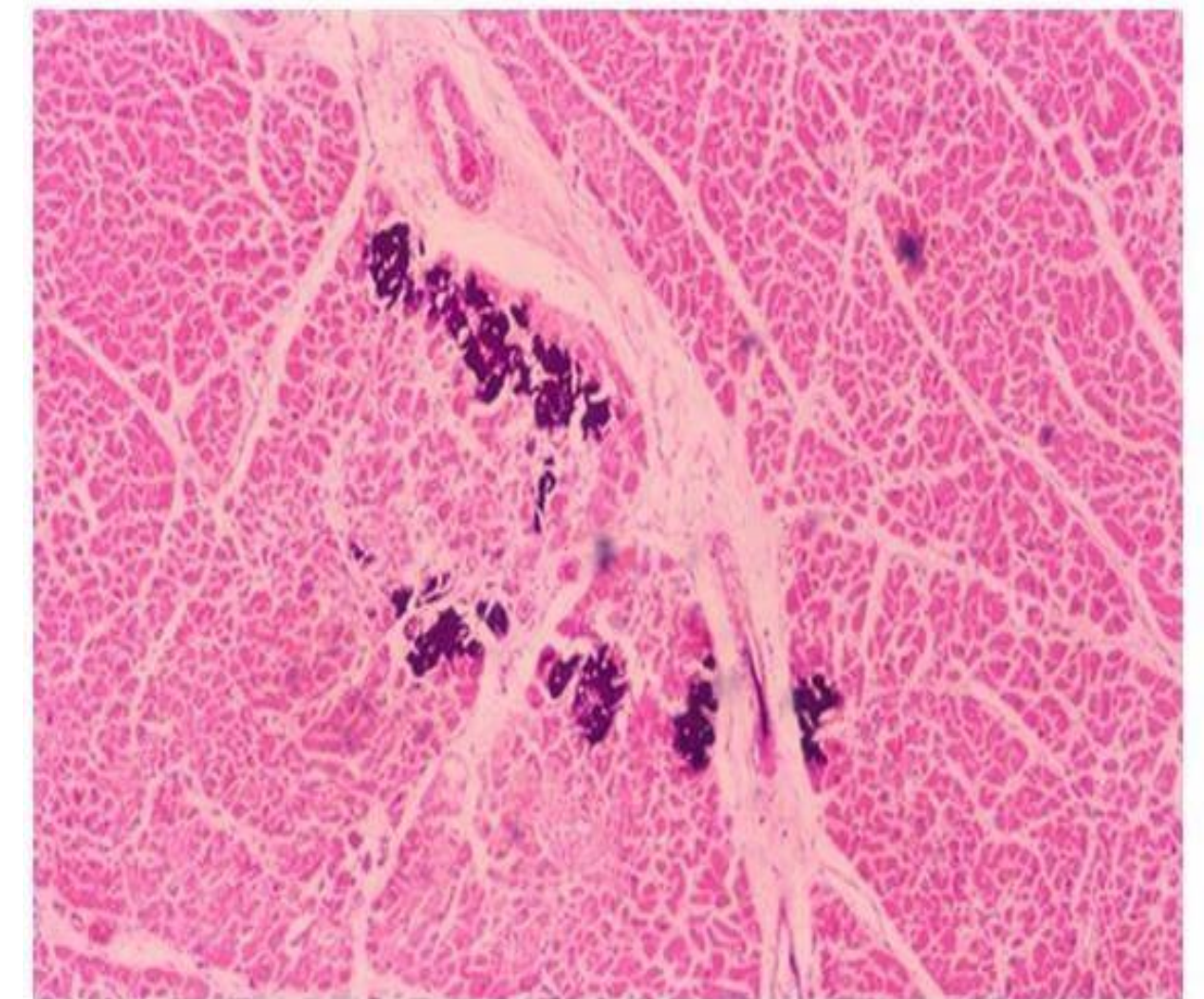
3. Metastatic calcification:

- May be seen in the stomach, lungs, myocardium, and blood vessels

➤ Types of Calcification in Tissue Damage:

Type	Dystrophic Calcification	Metastatic Calcification
Serum Calcium Level	Normal	Increased
Cause	Tissue death, degeneration	Hypercalcemia
Calcium Deposition	In damaged or dead tissue	In normal tissue

See next slide:



Dystrophic and Metastatic Calcification:

There are two primary types of calcification associated with tissue damage: **Dystrophic calcification** and **Metastatic calcification**...

Dystrophic calcification occurs locally in damaged or dead tissue as a direct result of tissue death or degeneration, and it develops even while a person's overall serum calcium levels remain completely normal. In contrast, **Metastatic calcification** is caused by hypercalcemia—an elevated level of calcium in the bloodstream—which forces excess calcium to deposit throughout otherwise normal, healthy tissue.

Clinical features of primary hyperparathyroidism:

- Primary hyperparathyroidism is a disease of **adults** and is much more common in **women** than in men.
- *The most common manifestation is an increase in serum calcium*

Clinical Manifestations:

painful bones due to fractures

renal stones, (severe pain due to calcification)

abdominal groans (pain)

Psychic moans, (calcium levels affect mood)

Why the abdominal groans (abdominal pain) reasons include:

peptic ulcers,  due to increased calcium levels

pancreatitis,  due to

Gallstones

Renal stones

- **Painful bones: due to fractured bones(bones become weak due to osteoporosis and osteitis fibrosa cystica and this causes fractures)**

Secondary Hyperparathyroidism :

Caused by chronic decreases in the serum calcium level

- Renal failure is the most common cause

Chronic renal insufficiency results in:

- 1. Decreased phosphate excretion**, which in turn results in hyperphosphatemia. Which depresses serum calcium levels and so stimulates parathyroid gland activity.
- 2. Reduced availability of α 1-hydroxylase enzyme** necessary for the synthesis of the active form of vitamin D, (so if there is no activation of VitaminD, no calcium absorption from the GIT will occur) which in turn reduces intestinal absorption of calcium.

Clinical Features:

- Are dominated by those related to chronic renal failure
- Bone abnormalities (*renal osteodystrophy*) are less severe than those seen in primary type
- **Serum calcium remains near normal because compensatory increase in PTH levels sustains serum calcium.**

Tertiary Hyperparathyroidism:

In a minority of patients, parathyroid activity may become autonomous and excessive, with resultant hypercalcemia, a process sometimes termed **tertiary hyperparathyroidism**.

In a small percentage of patients, secondary hyperparathyroidism—often associated with chronic renal failure and decreased blood calcium—can transition into an excessive and autonomous state. When this occurs, parathyroid hormone activity no longer suppresses itself in response to elevated blood calcium levels. This unregulated function ultimately leads to hypercalcemia, a condition referred to as tertiary hyperparathyroidism.

HYPOPARATHYROIDISM:

Is less common than hyperparathyroidism and the major causes are:.

- a. Surgically induced hypoparathyroidism:* inadvertent removal of parathyroids during thyroidectomy.
- b. Congenital absence(rare):* This occurs in conjunction with thymic aplasia (Di George syndrome) and cardiac defects,
- c. Autoimmune hypoparathyroidism (autoimmune destruction):*
this is a hereditary polyglandular deficiency syndrome
 - Any condition that leads to the removal or destruction of all four parathyroid glands will, of course, result in hypoparathyroidism.
 - However, if only one or two glands are affected, the remaining glands can usually compensate adequately.

Hypoparathyroidism



Causes:

- absent parathyroid from birth
- accidental removal upon thyroid removal

Symptoms:

- decreased Ca levels in blood (hypocalcemia)
- sensitive nerves
- uncontrollable spasms of the limbs

Treatment

- daily calcium and vitamin D supplements

رسالة من الفريق العلمي:

وليس شيء من الأسباب أنفع من الدعاء، ولا أبلغ في حصول المطلوب.

ولمّا كان الصحابة -رضي الله عنهم- أعلم الأمة بالله ورسوله -صلى الله عليه وسلم- وأفقههم في دينه كانوا أقوم بهذا السبب وشروطه وآدابه من غيرهم، وكان عمر بن الخطاب -رضي الله عنه- يستنصر به على عدوّه، وكان أعظم جنده به، وكان يقول لأصحابه: "لستم تُنصرون بكثرة، وإنّما تُنصرون من السماء"، وكان يقول: "إني لا أحمل همّ الإجابة، ولكن همّ الدعاء، فإذا ألهمتم الدعاء فإن الإجابة معه".

وأخذ الشاعر هذا المعنى فنظمه، فقال:
لو لم ترد نيل ما أرجو وأطلبه ... من جود كفيك ما عودتني الطلبا

فمن ألهم الدعاء فقد أريد به الإجابة، فإنّ الله سبحانه يقول: ﴿ادْعُونِي أَسْتَجِبْ لَكُمْ﴾. وقال: ﴿وَإِذَا سَأَلَكَ عِبَادِي عَنِّي فَإِنِّي قَرِيبٌ أُجِيبُ دَعْوَةَ الدَّاعِ إِذَا دَعَانِ﴾.

• العلامة ابن القيم -رحمه الله-

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Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			