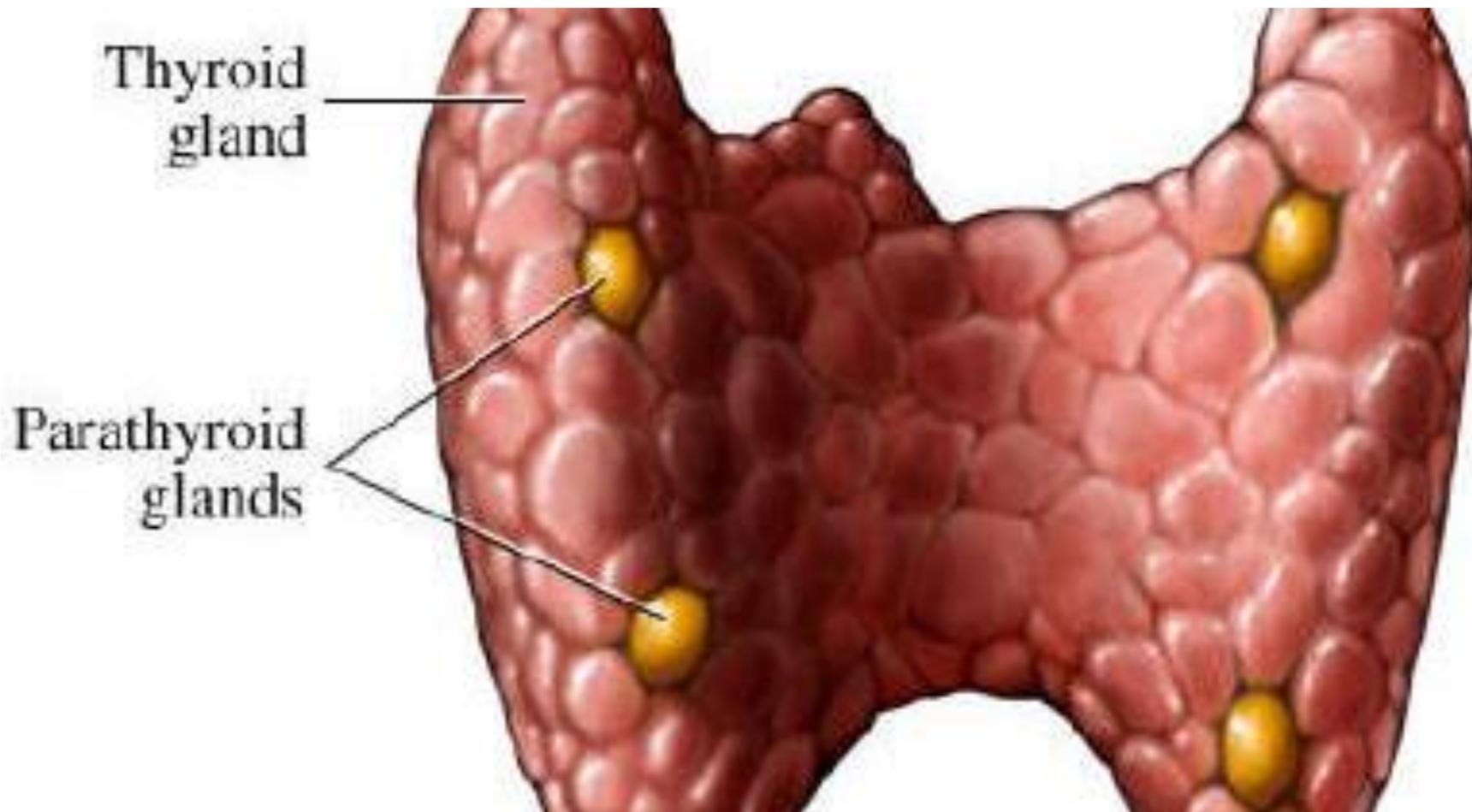


ENDOCRINE system 2019
Parathyroid gland and MEN
syndromes

Dr Heyam Awad

FRCPath

Parathyroid gland = جار درقية



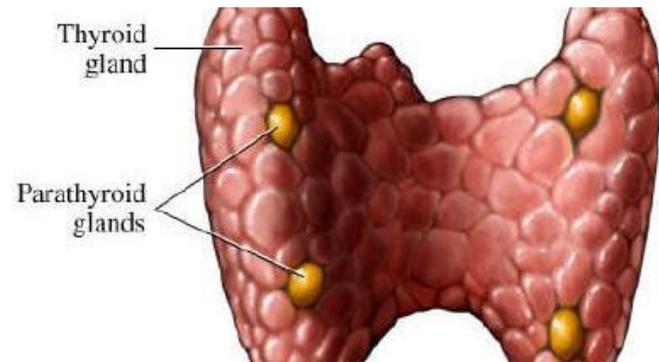
Parathyroid glands

- There are **four** parathyroid glands
- They are derived from the **pharyngeal pouches**
- 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



Parathyroid glands

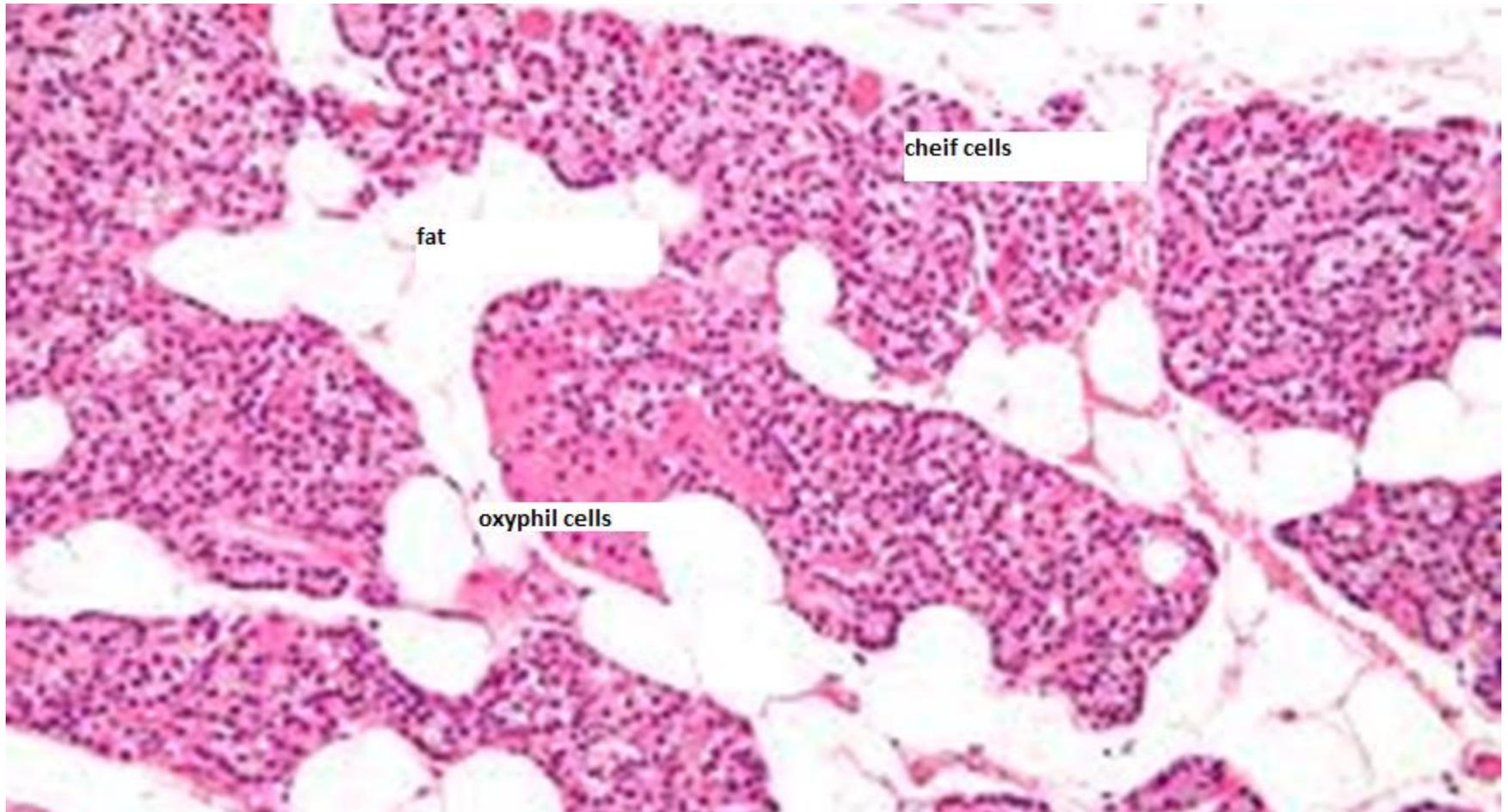
- Mostly located in close proximity to the upper and lower poles of the thyroid lobes. But can be seen anywhere along the path of descent of the pharyngeal pouches including the carotid sheath, thymus and anterior mediastinum.



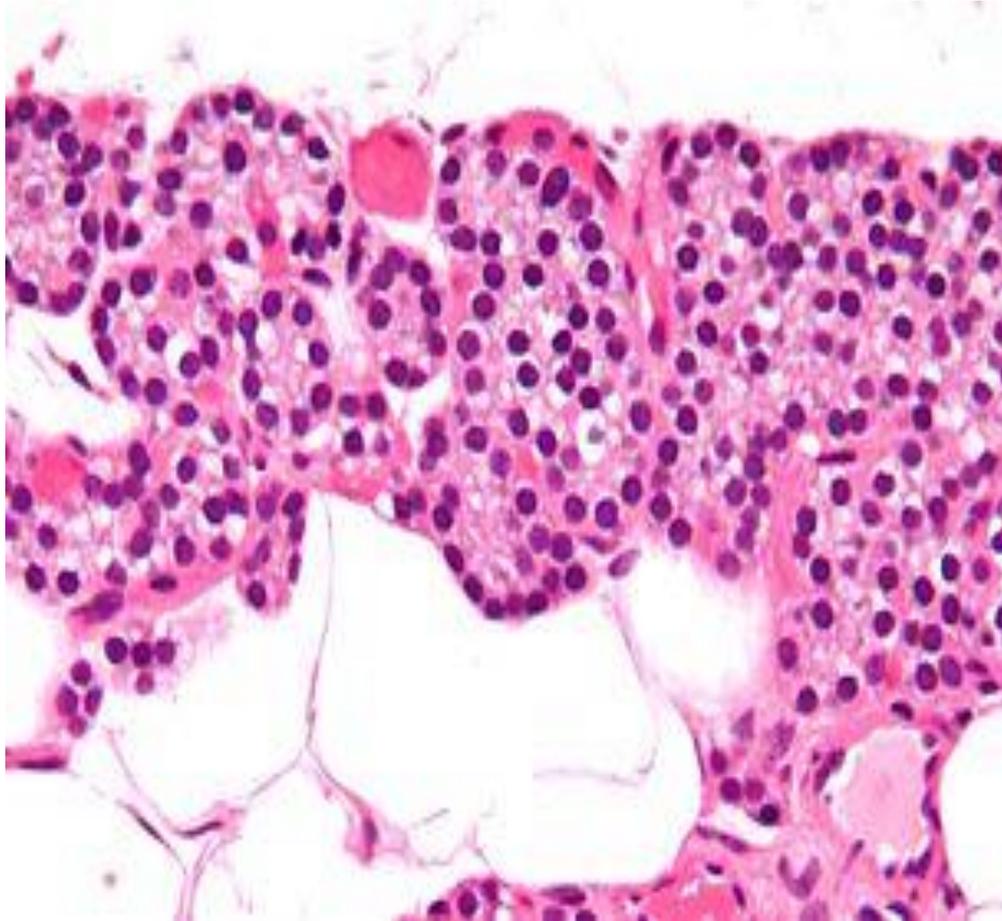
histology

- Parathyroid glands are composed of **chief cells** that secrete parathyroid hormone (PTH)
- **Oxyphil cells** are eosinophilic and contain mitochondria.. 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 IMAGES FOR DETAILS

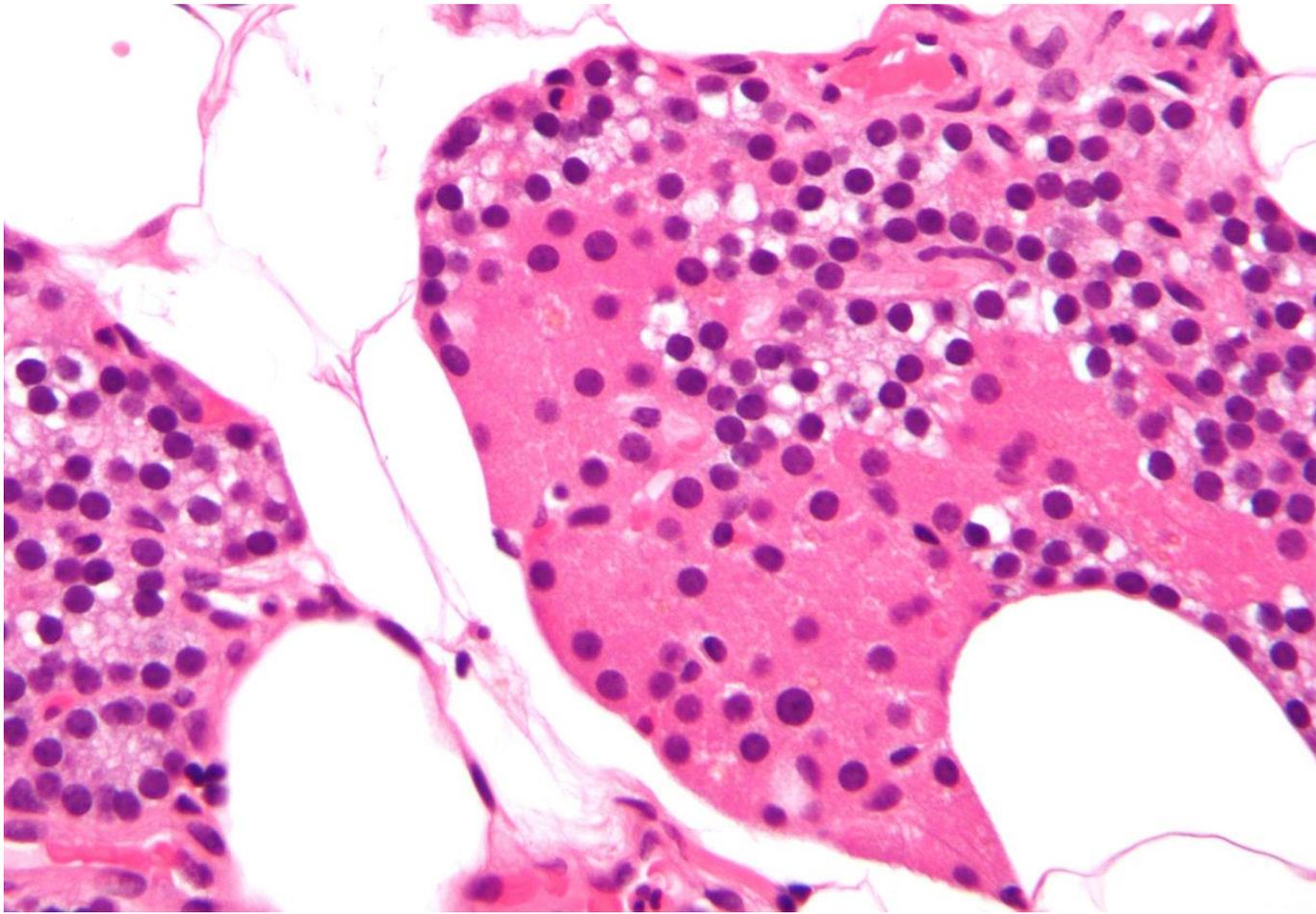
Parathyroid gland



Parathyroid chief cells



Oxyphil cells



Note:

- As we said normal parathyroid contain 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.

Regulation of PTH

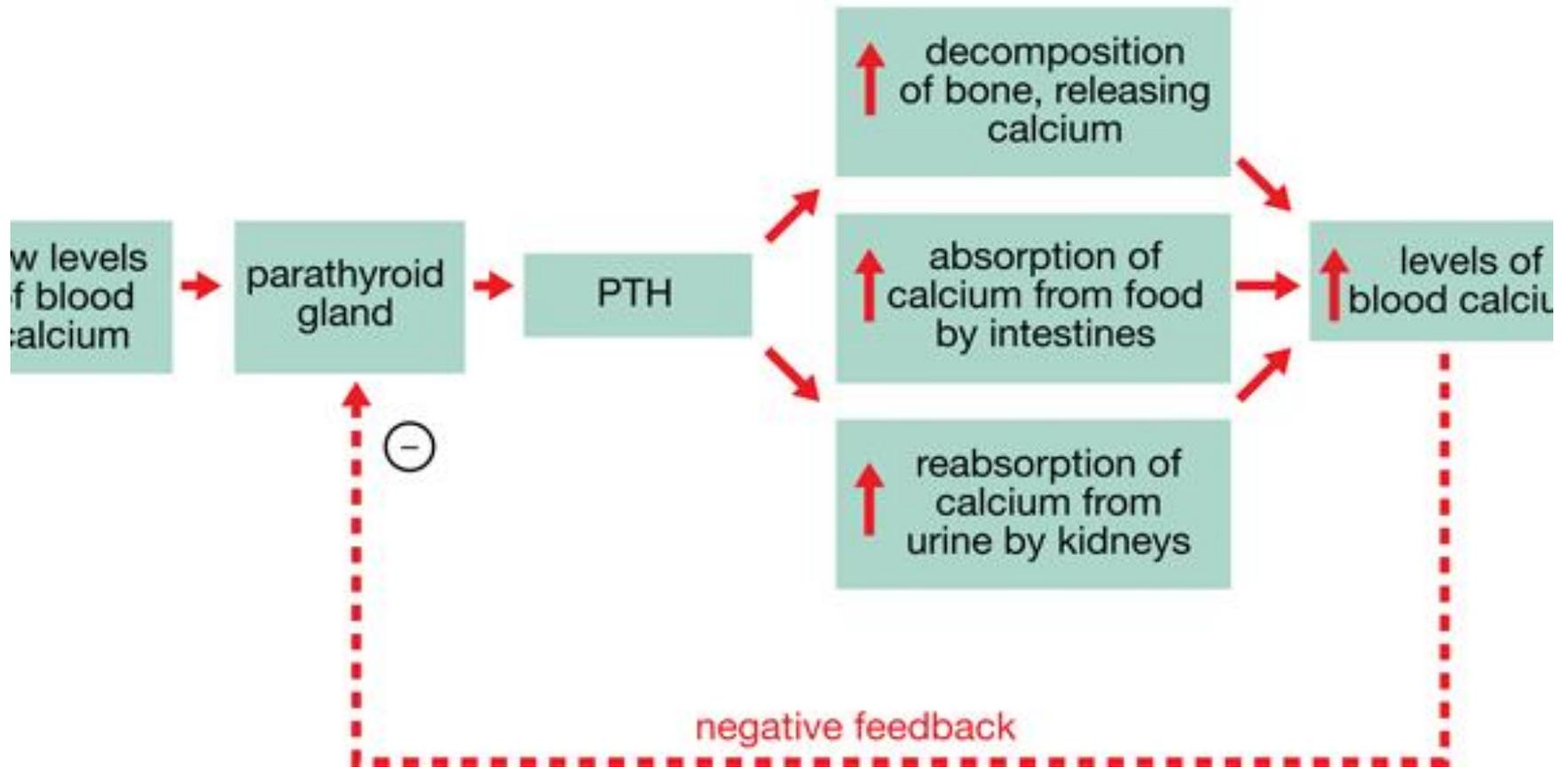
- PTH regulates calcium level in blood.
- If blood calcium decreases.. Parathyroid gland secretes PTH... NOTE: the regulation of PTH secretion is NOT under control of the pituitary BUT is regulated by calcium levels in the blood.

PTH/ functions

- Increases **renal** tubular reabsorption of calcium
- Increases conversion of **vitamin D** to its active form.. Which increases **gastrointestinal** absorption of calcium
- 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.

PTH

Regulation of Parathyroid Hormone (PTH) Levels



Diseases of the parathyroid

- Hyperparathyroidism
 - Hypoparathyroidism
 - Mass lesions.
-
- NOTE: mass lesions in parathyroid glands do occur but mass effect is usually not important clinically.. Because these glands are small and cannot cause actual compression.

HYPERPARATHYROIDISM :

- a. **Primary:** **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)
- b. **Secondary:** parathyroid hormone increases due to decreased calcium level. The most common cause is renal failure.
- c. **Tertiary** hyperparathyroidism: in some patients with secondary hyperparathyroidism, the increased parathyroid hormone production becomes autonomous and not regulated by calcium levels.

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%)
2. Primary parathyroid hyperplasia-5% to 10%.
3. Parathyroid carcinoma-(1%)

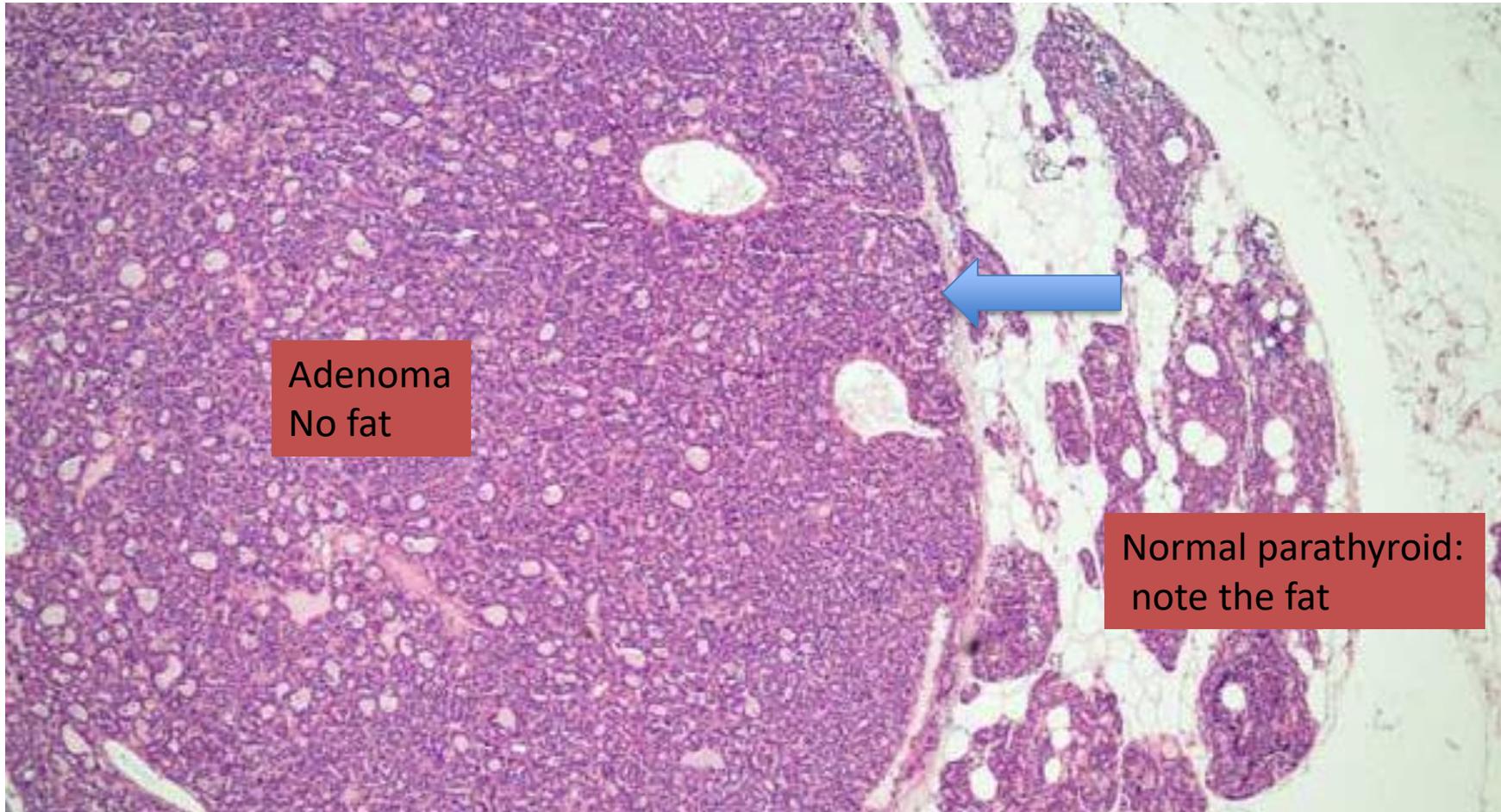
- Majority : **sporadic**

but: some familial cases associated with MEN syndromes.

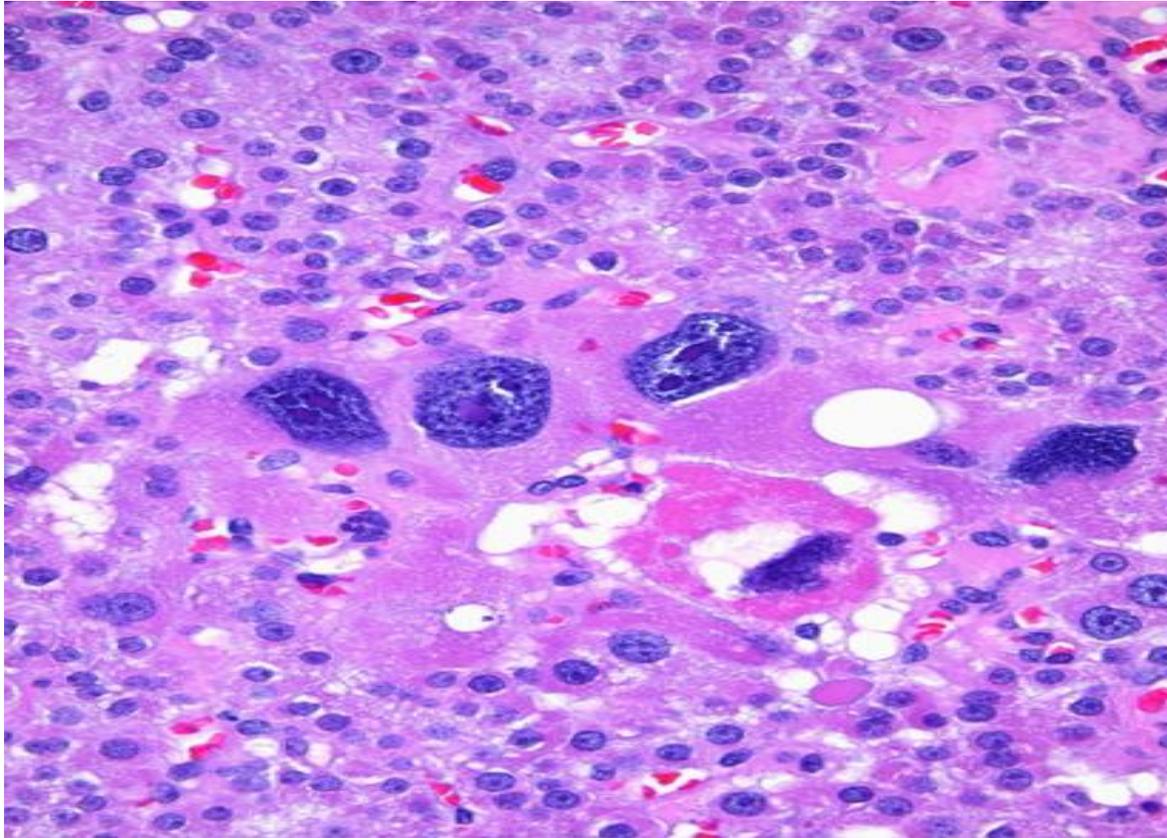
Parathyroid adenoma:

- Most parathyroid adenomas weigh between 0.5 and 5 g.
- They are encapsulated, soft and **solitary**.
- **One gland only is usually affected and the other three are normal or atrophic**
- A rim of compressed, normal, non-neoplastic, parathyroid tissue, separated by a fibrous capsule, is visible at the edge of the adenoma.
- 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 .

Parathyroid adenoma. Note the thin capsule (arrow) separating the adenoma from normal



Endocrine atypia.. This is not necessarily a malignant feature.



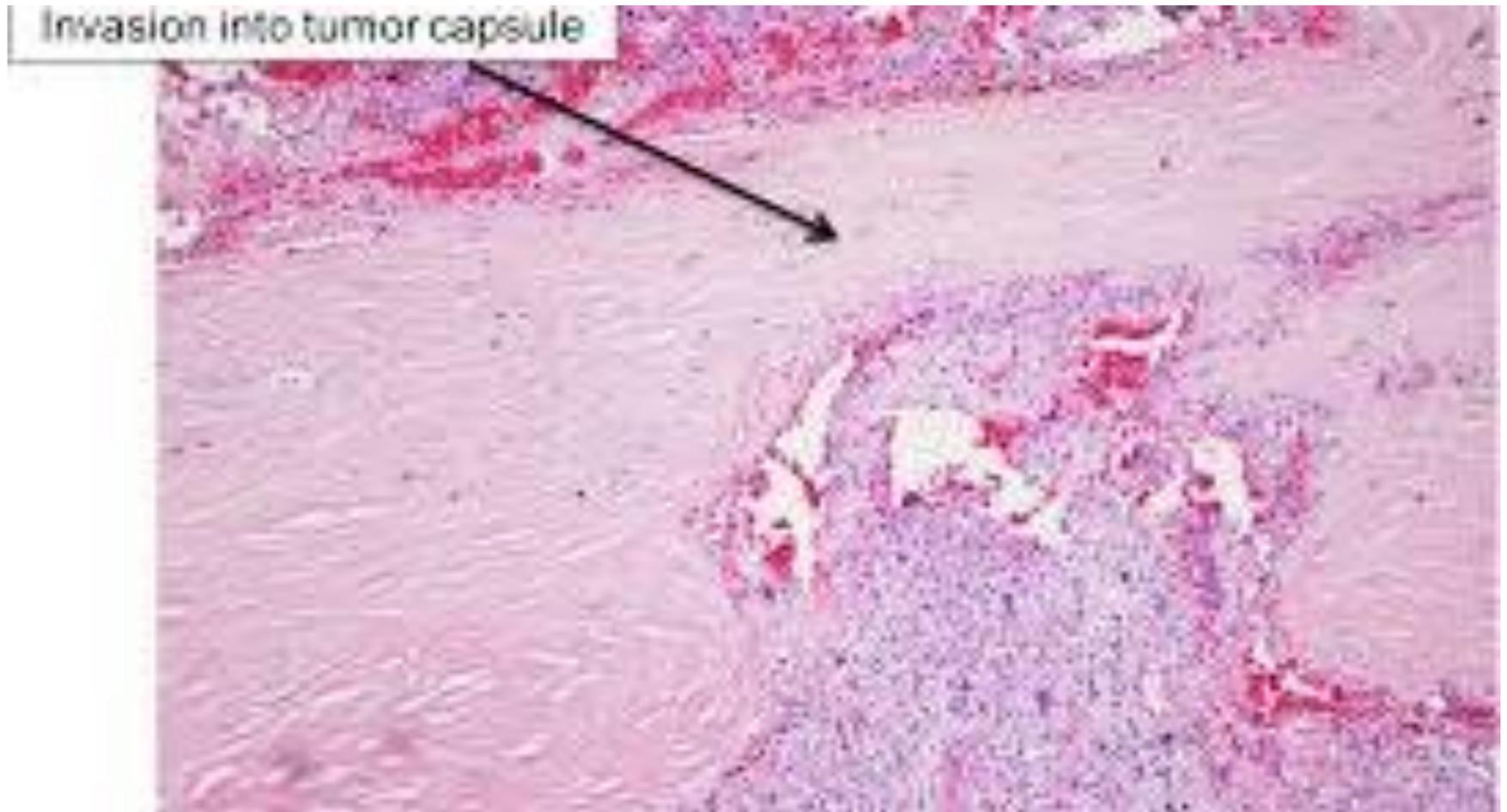
Parathyroid hyperplasia

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

Parathyroid carcinomas :

- one gland affected.
- Consist of irregular masses that sometimes **exceed 10 g** in weight .
- 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,**
- **More distant dissemination occurs in another third**

Parathyroid carcinoma



note

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

Morphologic changes in other organs in hyperparathyroidism

- Hyperparathyroidism affects many organs and can result in
 - 1. skeletal changes
 - 2. kidney changes
 - 3. metastatic calcifications

1. Skeletal changes

a. characterized by

- Increased osteoclastic activity, resulting in erosion of bone and mobilization of calcium salts.
- In more 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**)

b. Brown tumors of hyperparathyroidism)

- Aggregates of osteoclasts,, and hemorrhage occasionally form masses that may be mistaken for neoplasms

Osteitis fibrosa cystica



Osteitis fibrosa cystica



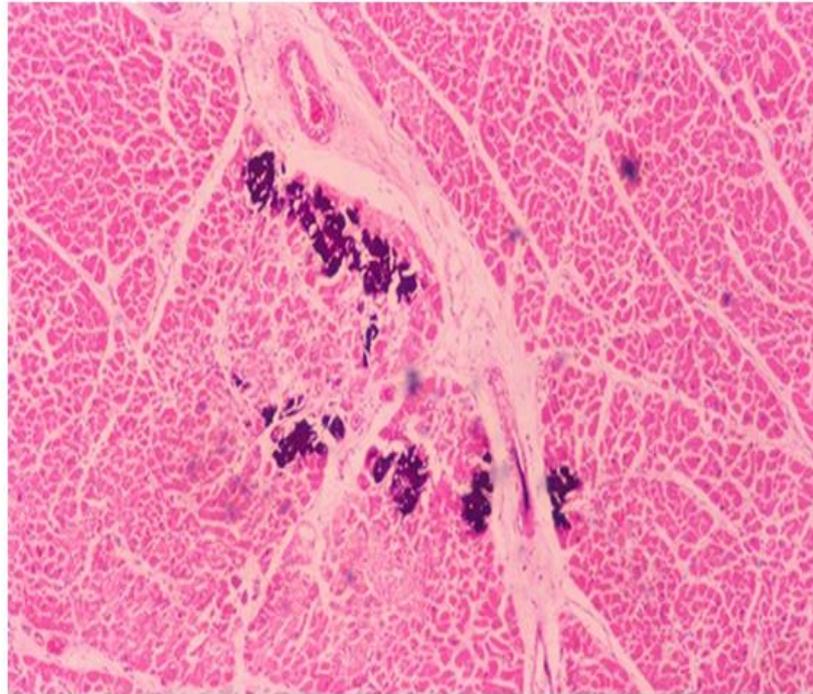
Image from Wikipedia.org licensed under available at wikipedia.org/wiki/File:Osteitis_fibrosa_cystica_08afr_Xray.jpg

2. **Kidney changes** in hyperparathyroidism:

- a. PTH-induced hypercalcemia favors the 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



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 **and is the most common cause of clinically silent hypercalcemia.***
- **The most common cause of clinically apparent hypercalcemia in adults is malignancy: paraneoplastic syndromes or bone mets.**

Clinical Manifestations :

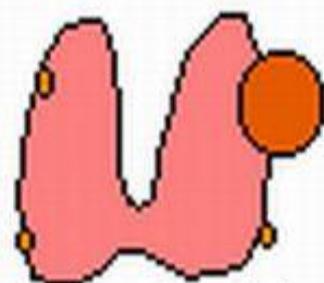
painful bones,
renal stones,
abdominal groans,
psychic moans.

Why the abdominal groans (abdominal pain)..reasons include:

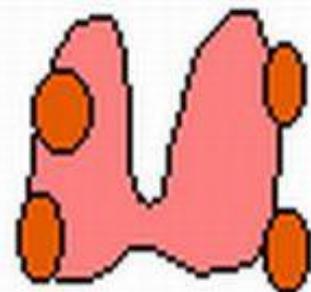
peptic ulcers,
pancreatitis,
Gallstones
Renal stones

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

Easy to diagnose and treat -- if you think of it.



parathyroid adenoma



pancreatitis
stomach ulcers
kidney stones



"osteitis fibrosa cystica"



It's all in your mind!

"depression"
and
"psychosis"

Secondary Hyperparathyroidism –

caused by chronic decreases in the serum calcium level

- *Renal failure is the most common cause*

1. Chronic renal insufficiency causes decreased phosphate excretion, which in turn results in hyperphosphatemia. Which depress serum calcium levels and so stimulate parathyroid gland activity
2. reduced the availability of α_1 -hydroxylase enzyme necessary for the synthesis of the active form of vitamin D, 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.**

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

HYPOPARATHYROIDISM:

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

- a. Surgically induced hypoparathyroidism:* inadvertent removal of parathyroids during thyroidectomy.
- b. Congenital absence:* This occurs in conjunction with thymic aplasia (Di George syndrome) and cardiac defects,
- c. Autoimmune hypoparathyroidism :* This is a hereditary polyglandular deficiency syndrome

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

- **MEN syndromes**

MULTIPLE ENDOCRINE NEOPLASIA SYNDROMES

- Are a group of **inherited** diseases resulting in proliferative lesions of multiple endocrine organs.
- Endocrine tumors arising in the context of MEN syndromes have distinctive features that are not shared with their sporadic counterparts:
 1. Occur at a *younger* age than that for sporadic cases.
 2. They arise in *multiple endocrine organs*.
 3. Even in one organ, the tumors *often are multifocal*.
 4. *Usually are preceded by an asymptomatic stage of endocrine hyperplasia involving the cell of origin of tumor.*
 5. Are usually *more aggressive* and *recur* in a higher proportion of cases than tumors that occur sporadically.

MEN type 1

- Is an autosomal **dominant** syndrome and the gene (*MEN1*) is located at 11 and is a tumor suppressor gene;.
- Organs most commonly involved are the parathyroid, the pancreas, and the pituitary-the "**3 Ps**."

a. Parathyroid: *Primary hyperparathyroidism* is the most common manifestation of MEN-1 (80% to 95% of patients)

.

- Abnormalities include both hyperplasia and adenomas.

b. Pituitary: The most frequent pituitary tumor in patients with MEN-1 is a prolactin-secreting macroadenoma.

- In some cases, acromegaly develops in association with somatotropin-secreting tumors

c. Pancreas: Endocrine tumors of the pancreas are the **leading cause of death** in MEN-1.

- Are aggressive tumors manifest with metastatic disease.
- May find multiple microadenomas" scattered throughout the pancreas in conjunction with the dominant lesions
- Pancreatic endocrine tumors often are functional
- Hypoglycemia, related to insulinomas, is also common.

MEN 2 syndromes

- MEN 2A
- MEN 2B

- Both : activation mutation of RET proto-oncogene.
- AUTOSOMAL DOMINANT.

MEN Type 2A

THYROID, PARATHYROID AND ADRENALS.

- a. Thyroid: **Medullary carcinoma** of the thyroid develops in virtually **all** untreated cases, and the tumors usually occur in the first 2 decades of life
- b. Adrenal medulla: **Pheochromocytomas** develop in 50% of the patients; and 10% of these tumors are malignant.
- c. Parathyroid: 10% to 20% of patients develop parathyroid **hyperplasia** resulting in primary hyperparathyroidism

Multiple Endocrine Neoplasia Type 2B

- a. Organs commonly involved include the thyroid and the adrenal medulla and the spectrum of thyroid and adrenal medullary disease is similar to that in MEN-2A,
- b. *Primary hyperparathyroidism does not develop in patients with MEN-2B.***
- c. Extraendocrine manifestations.*

Extraendocrine manifestations.

1. Ganglioneuromas of mucosal sites (gastrointestinal tract, lips, tongue)

a marfanoid habitus, in which overly long bones of the axial skeleton give an appearance resembling that in Marfan syndrome

*Thank
you*

