MSS

Musculoskeletal System

Doctor 2019 | Medicine | JU

Pathology

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Hey guys,
In this sheet we will continue talking about
metabolic bone disorders
Smile & Have fun💜

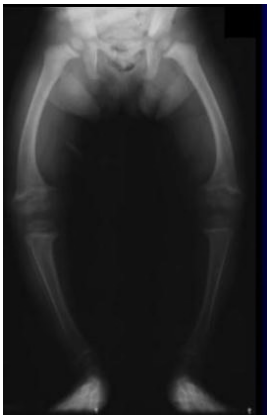
Rickets and Osteomalacia

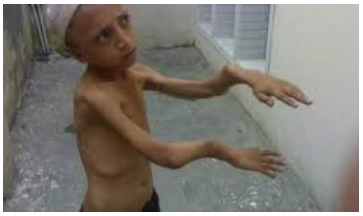
- In children, we call this disorder **Rickets**, while in adults it is called **Osteomalacia**.
- Due to vitamin D deficiency or abnormal metabolism of vitamin D.
- low levels of vitamin D, decreases the concentration of calcium in matrix, causing decreased mineralization of bone, unmineralized matrix.
- Inadequate mineralization results in weak bone with an increased risk for fracture.
- Children's bones become fragile, they suffer from pain in their bone , dental issues , poor development and growth & skeletal abnormalities .

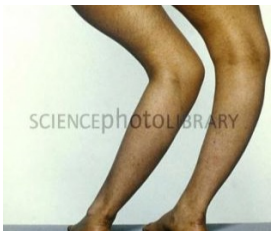
You should not see patient like this because people notice vitamin D deficiency early & get treatment early

Bowing of the bone

Notice HOW curved are these bones.







HYPERPARATHYROIDISM (HPT)

- Thyroid gland regulates serum calcium via parathyroid hormone (PTH) secretion, that raises blood calcium by increasing calcium absorption in GI tract ,stimulating conversion of inactive vitamin D to active form & breaking down the bone (⬆️resorption of the bone) to stabilize calcium level in the blood.

- Calcium concentration is important & affect the Electrical system of the heart.

Hyperparathyroidism classification

Different causes and features of hyperparathyroidism - raised parathormone (PTH).

	primary Imp	secondary	tertiary
pathology	Hyperfunction of parathyroid cells due to hyperplasia, adenoma or carcinoma.	Physiological stimulation of parathyroid in response to hypocalcaemia.	Following long term physiological stimulation leading to hyperplasia.
associations	May be associated with multiple endocrine neoplasia.	Usually due to chronic renal failure or other causes of Vitamin D deficiency.	Seen in chronic renal failure.
serum calcium	high	low / normal	high
serum phosphate	low / normal	high	high
management	Usually surgery if symptomatic. Cincacalcet can be considered in those not fit for surgery.	Treatment of underlying cause.	Usually cinacalcet or surgery in those that don't respond.

Both are high

- Normally, we have(3-4) parathyroid glands around thyroid gland (upper left , lower left, upper right,lower right)
- Usually we depend on the conc. of calcium & phosphate in serum because many labs can not measure PTH level in the blood

Primary HPT

Primary HPT is a cause of hyperplasia (increase number of cells> increases the function > increases Parathyroid hormone > increases calcium level in the blood) adenoma or carcinoma of PTH gland.

Primary HPT is more common and the disorder is in the parathyroid gland itself .

🔼 calcium concentration in blood,🔽 calcium concentration in bone ➡️ weaken the bone

Secondary and tertiary HPT

In both Secondary and tertiary HPT, parathyroid glands are normal and the problem is the positive feedback due to hypocalcemia.

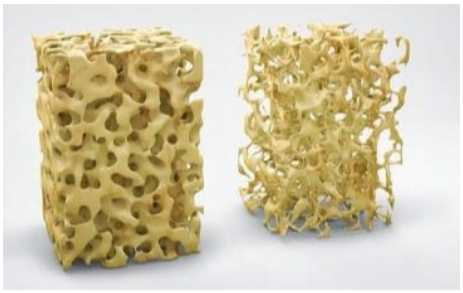
HPT Clinically

Brown tumor

Not really cancer , It's a **mass** of collection of blood (blood hematoma) with fractures of bone that suffer from osteoporosis .

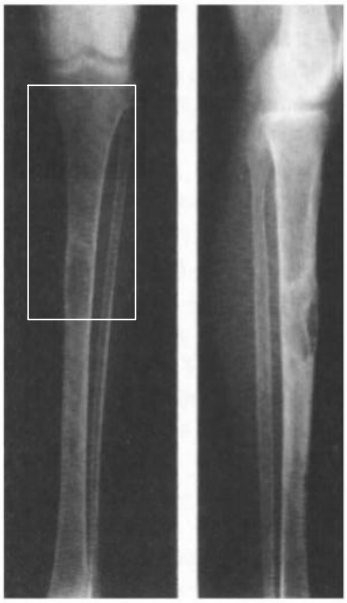
Extra : Its called brown tumor because The lesions localize in areas of extensive bone resorption, which is replaced by fibrovascular tissue and giant cells with abundant deposits hemorrhage and hemosiderin which impart the brown color .

Osteoporosis



HPT is one of the causes of **secondary** osteoporosis .

OSTEITIS FIBROSA CYSTICA (OFC)



Very rare condition, also called (osteitis fibrosa, osteodystrophia fibrosa, and von Recklinghausen's disease of bone)

Not to be confused with von Recklinghausen's disease, neurofibromatosis type I

It's an inflammatory response causes weakening of the bone by resorption of the bone , **fibrosis and cyst formation** .

The bones appear **less white** in color under X-ray

You should catch & diagnose the HPT before it develops to these conditions

Summary

Metabolic Disorders of Bone

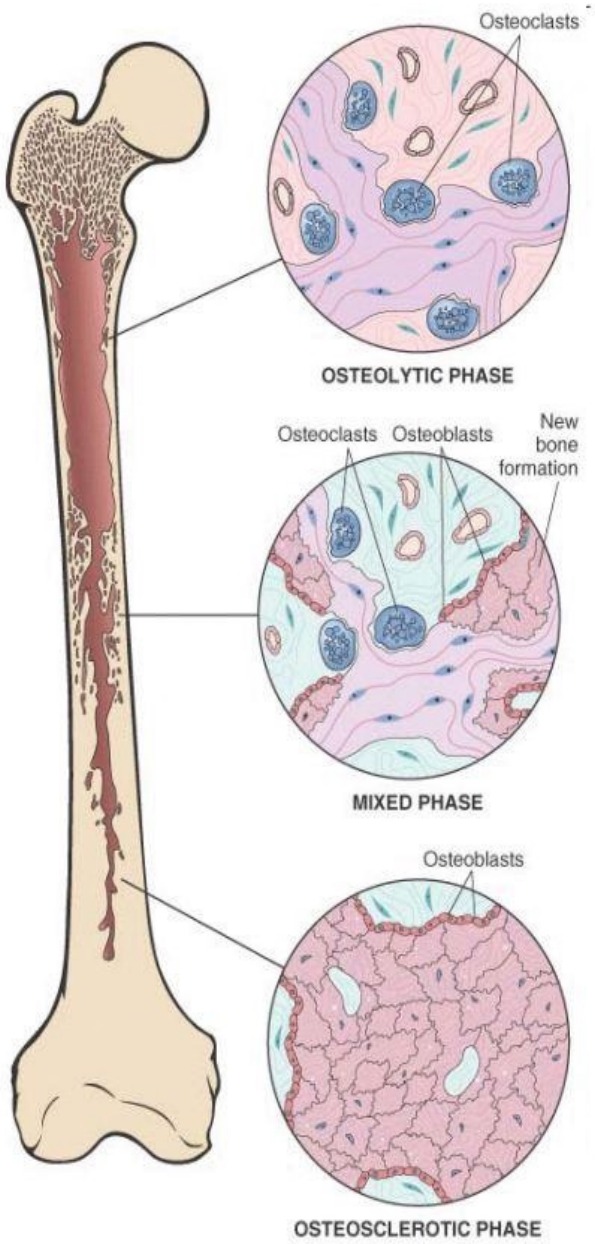
- **Osteopenia** and **osteoporosis** represent histologically normal bone that is decreased in quantity. In osteoporosis the bone loss is sufficiently severe to significantly increase the risk of fracture. The disease is very common, with marked morbidity and mortality from fractures. Multiple factors including peak bone mass, age, activity, genetics, nutrition, and hormonal influences contribute to its pathogenesis.
- **Osteomalacia** is characterized by bone that is insufficiently mineralized. In the developing skeleton, the manifestations are characterized by a condition known as **rickets.**
- **Hyperparathyroidism** arises from either autonomous or compensatory hypersecretion of PTH and can lead to **osteoporosis**, **brown tumors,** and **osteitis fibrosa cystica**. However, in developed countries, where early diagnosis is the norm, these manifestations are rarely seen.

Paget disease (Osteitis Deformans)

It is badly formed bone structure (increase the amount of abnormal bone structure).

- Bone is deformed & there is a little inflammatory response.

Can be divided into 3 phases



Osteolytic phase

More osteoclastic activity; bone is being resorbed and lytic lesions will be formed.

Mixed phase

Osteoblastic and Osteoclastic activity at the same time.

osteosclerotic phase

High Osteoblastic activity (increased bone density) like Marble bone disease

Some times the 3 phases happened in the same bone so if you see that , make sure that it's a paget disease case

Etiology

We don't know the etiology (the cause) of Paget disease, some scientists blame viruses such as measles and RNA viruses, but if you are asked about the cause you will answer that the cause is unknown but there are some geographic variations (1% in USA).

There are many Factors:

1-Environmental and acquired factors

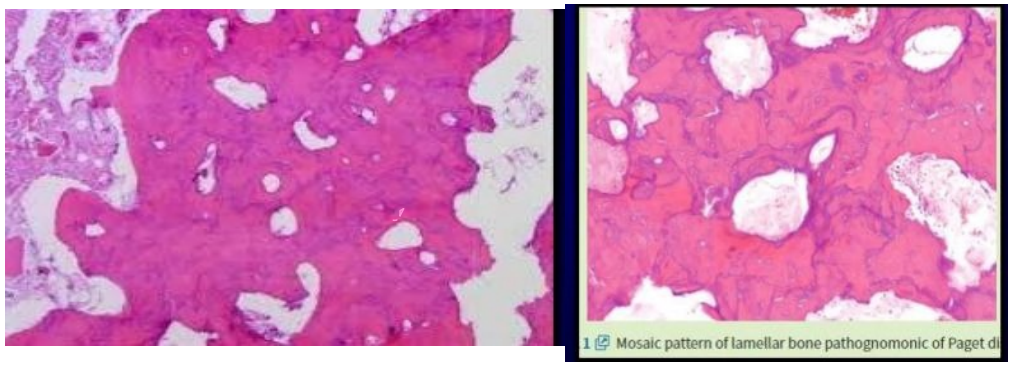
Like RNA Viruses

2-Genetic factor

50% of familial Paget regardless of the severity and 10% of sporadic have SQSTM1 gene mutations

The mutation Causes increase in RANK expression (stimulation), and decrease in OPG (osteoprotegerin) expression "inhibition" which will increase the osteoclastic activity

Radiograph & histological sections

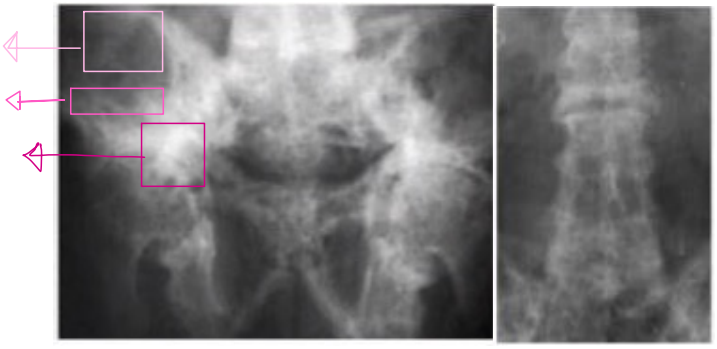


Very abnormal bone appearance (mosaic lamellar bone)

more black so it is in osteolytic phase.

mixed area

more white so it is in osteosclerotic phase



Paget Clinically

- Paget is polystotic (more than one bone is involved (generalized)) in 85% of patients; 15% Monostotic (one bone is affected only).

- Axial Skeleton (vertebral body, pelvic bone, shoulder bone) is more affected than other distal extremities (femur & tibia)

- Most are mild and asymptomatic and Pain is caused by micro fractures & repair during physical activity or nerve compression.

Clinical features

- **Leontiasis ossea (lion face) or platybasia** : characteristic of severe Paget disease by invagination of skull base

- secondary osteoarthritis &fractures

- osteosarcoma (primary bone sarcoma) (1%)
  🔼 risk of cancer in chronic paget disease patients

- DX:
  Clinically with pain fractures , x-ray ,increase in serum Alkaline Phosphatase, Normal Ca and PO4

Note : you can differentiate between hyperparathyroidism's patients and Paget's patients by the amount of alkaline phosphatase (increased in Paget's patients)

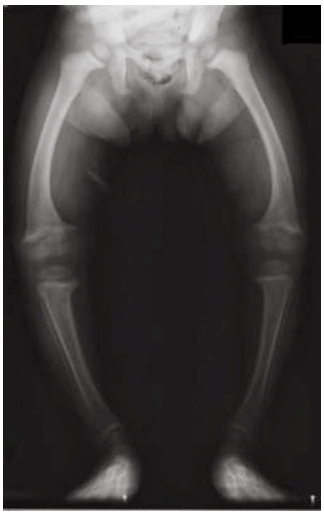
🩺It's important clinically to distinguish between the pain of nerve compression & the pain of micro fractures

Test yourself

1- A 4-year-old girl is brought to the pediatrician's office. Her mother says that she noticed that her legs seem unsteady and bowed when the girl stands. She noticed this for the first time 2 months ago. What is the most likely diagnosis?

A)Osteopenia
B)Osteoporosis
C)Paget disease
D)Rickets

2- A 3-year-old boy is brought to his pediatrician's office for a well-child exam. His family emigrated from Kenya last year and he is fully vaccinated. Up until the age of 8 months, he was exclusively breastfed. Since that time, he has consumed a diet consisting primarily of vegetables, fruits, and eggs. He is otherwise healthy with no past medical conditions. On physical examination, the physician notes the patient's dark skin as well as widening of the wrist bones and wide-spacing of the cranial sutures that is easily reducible by pressure. An x-ray of the child's lower extremities is shown



A)Decreased alkaline phosphatase (ALP)
B) Deficiency of parathyroid hormone
C) Impaired bone mineralization
D) Malabsorption of fat-soluble vitamins
E) Mutation of type I collagen

3- A 65-year-old man comes to the clinic because of a persistent headache, dizziness, and severe hip pain during the past year. He says that his hat no longer fits him. He also reports ringing in his ear and some hearing loss. He has a history of hypertension and diabetes mellitus controlled with lisinopril and metformin. His paternal grandfather had osteosarcoma. Temperature is 37.5° C (99.6° F), blood pressure is 126/82 mm Hg, pulse is 79/min, and respiratory rate is 16/min. Physical examination elicits bone pain. Serum calcium, parathyroid hormone, and phosphorus levels are within reference ranges. Elevation of which of the following markers is associated with this patient's most likely cause of bone pain?

A) Alkaline phosphatase
B) Calcitonin
C) Gamma-glutamyl transferase
D) Tartrate resistant acid phosphatase

4- A patient was diagnosed with renal failure in early stage. Parathyroid glands are noticed to be stimulated with no hyperplasia. Which if the following may be found in serum?

A)High levels of Alkaline phosphatase
B)Low levels of Phosphate
C)Low levels of Calcium
D)Low levels of parathyroid hormone (PTH)

Answers :
1- D
2-C
3-A
4-C