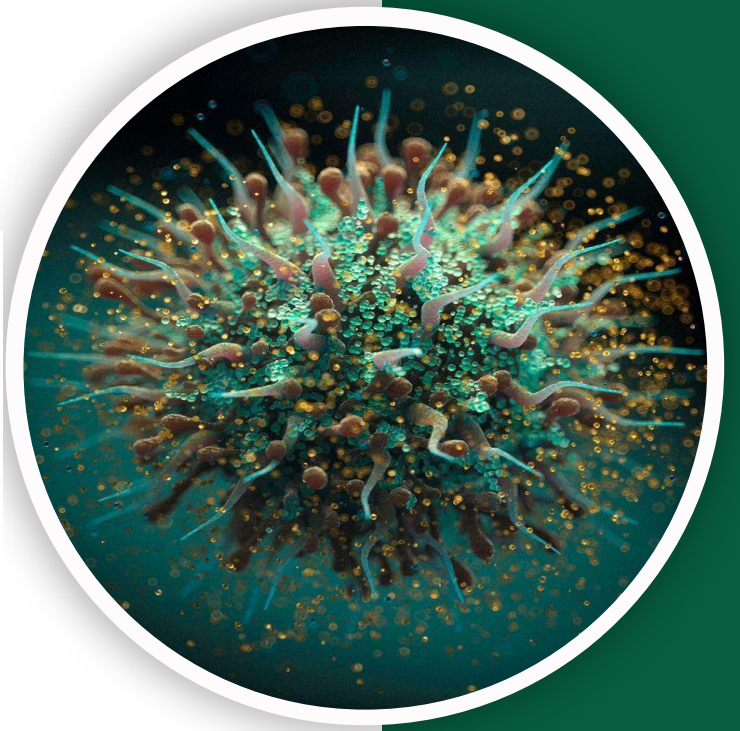
بسم الله الرحمن الرحيم

(وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ)

Pathology | MID #3

MSS -Skin tumors pt(3)



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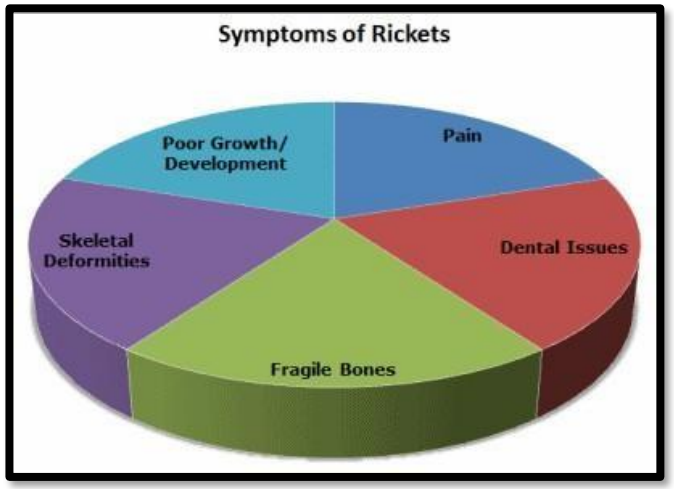
Continuation of the metabolic disorders of the bone from lecture 2:

RICKETS s OSTEOMALACIA



- **Vitamin D deficiency or abnormal metabolism of vitamin D.**
- **Children: Rickets**
- **Adults: osteomalacia**
- **Decreased mineralization of bone, unmineralized matrix.**
- **Increase risk of fractures.**

Rickets and osteomalacia share the same primary cause but differ in terms of the affected population. Rickets affects children, while osteomalacia affects adults.

Rickets & Osteomalacia:

- Rickets and Osteomalacia are both rare disorders that occur due to deficiency of vitamin D, that is either caused by:
    1. Insufficient intake of vitamin D.

       OR

    2. Abnormal metabolism of vitamin D.

- Vitamin D deficiency causes decreased mineralization of bone and an accumulation of unmineralized matrix, leading to the symptoms of rickets and osteomalacia, such as:
    1. Increased risk of fractures (fragile bone).
    2. Weakness of the bones which causes bowed bones in the legs (1) and arms (2).

- The prevalence of Rickets and osteomalacia has become very low recently, due to the availability of vitamin D supplements.

(2)

(1)

HYPERPARATHYROIDISM (HPT) (Common metabolic disorder)

This table is required

Hyperparathyroidism classification

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

Types of HPT:	primary	secondary	tertiary
pathology	Hyperfunction of parathyroid cells due to hyperplasia, adenoma or carcinoma. (1)	Physiological stimulation of parathyroid in response to hypocalcaemia. (3)	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. (2)	Treatment of underlying cause.	Usually cinacalcet or surgery in those that don't respond.

NICE have issued guidance for the use of cinacalcet in what they call refractory secondary hyperparathyroidism which is classified as tertiary hyperparathyroidism in this tblable. http://www.nice.org.uk/TA117

tblable.com

- Cinacalcet is a drug that lowers PTH levels.

The points labeled with numbers are further explained in the next slide.....

HYPERPARATHYROIDISM (HPT)

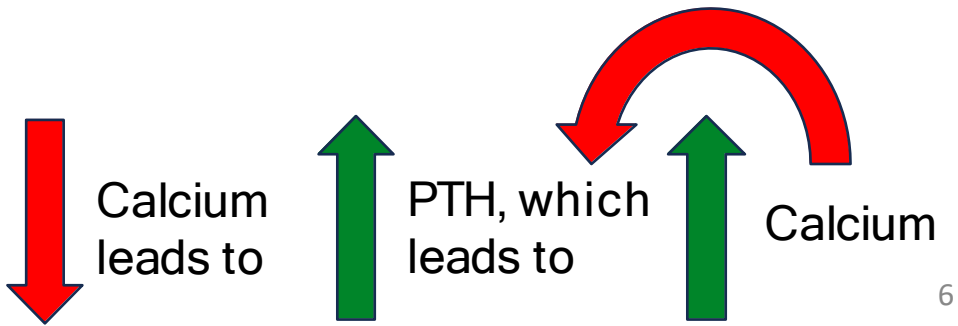
Primary HPT (most common type of HPT):

1) Hyperplasia, adenoma or carcinoma of parathyroid cells leads to hyperfunction and over secretion of parathyroid hormone, leading to high Calcium and low/normal phosphorus levels. Also, the altered parathyroid cells **stop** responding to the feedback inhibition response of the parathyroid hormone caused by **hypercalcemia**.
    - In normal conditions, hypercalcemia **decreases** parathyroid hormone release.
2) By surgery we mean surgical removal of overactive parathyroid glands.

Secondary HPT:

3) Secondary HPT is due to **chronic** hypocalcemia, which can be caused by:
    1. Chronic renal failure (over excretion of calcium in the urine).
    2. Vit.D deficiency.

- Remember, high calcium ->low PTH/ low calcium ->high PTH



HPT clinically

Clinically, Patients with HPT can present with:

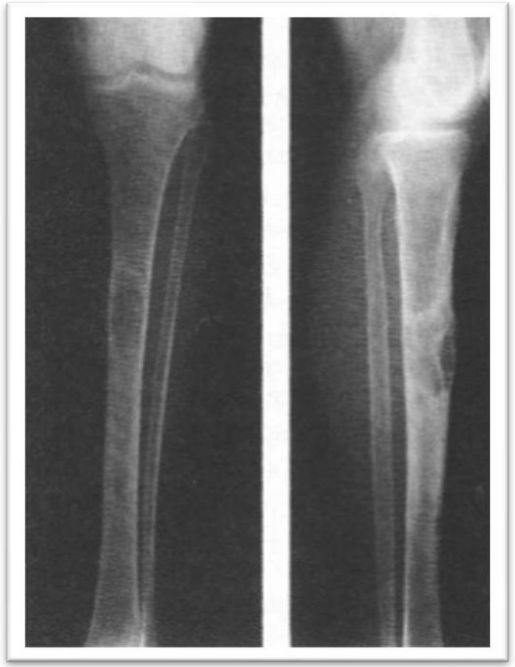
1 **Osteoporosis** causing the weakening of the bone.

2 **Brown tumors,** due to osteoporosis, which can cause fractures and bleeding. This bleeding becomes contained in a localized area known as a brown tumor.

- A brown tumor is not a true tumor; it is a collection of hematomas (closed wounds where blood collects) and cystic spaces (abnormal fluid-filled sacs) - see picture.

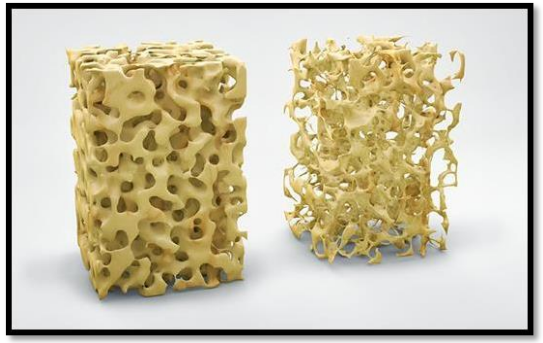
3- In *severe* cases of HPT, **OSTEITIS FIBROSA CYSTICA** can occur either locally or generally. This rare clinical presentation is characterized by severe osteoporosis and microcystic structures on bones.

OSTEITIS FIBROSA CYSTICA



Abbreviated OFC, also knownas osteitis fibrosa, osteodystrophia fibrosa, and von Recklinghausen's disease of bone (not to be confused withvon Recklinghausen's disease, neurofibromatosis type I) – not an –itis.

OSTEOPOROSIS



BROWN TUMOR

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.

Lecture 3

PAGET DISEASE OF BONE (OSTEITIS DEFORMANS)

- In Paget disease, abnormalities in both osteoblast and osteoclast function, along with a lack of coordination between them, lead to disturbances in bone formation and resorption, resulting in **Increased badly formed bone structure.**
- In paget disease there are **3 phases (lytic, mixed, sclerotic),** these phases take place in random order.
  - If osteoblast activity > osteoclast activity = sclerotic (bone formation) phase.
  - If osteoblast activity < osteoclast activity = lytic phase.
  - If osteoblast activity = osteoclast activity = mixed phase.

More common in North America and North Europe

- **1% in USA; geographic variations** in prevalence have been observed between countries.
- Unknown etiology. (Nobel prize awaits ☺)
- **Genetic and environmental factors** play an important role.
- **50% of familial Paget and 10% of sporadic have SQSTM1 gene mutations,** which are believed to stimulate the RANKs and inhibit the OPGs (osteoprotegerin), **(+RANK s -OPG)**
- **Viruses (measles and RNA viruses)??**

+ Stimulate.
- Inhibit.

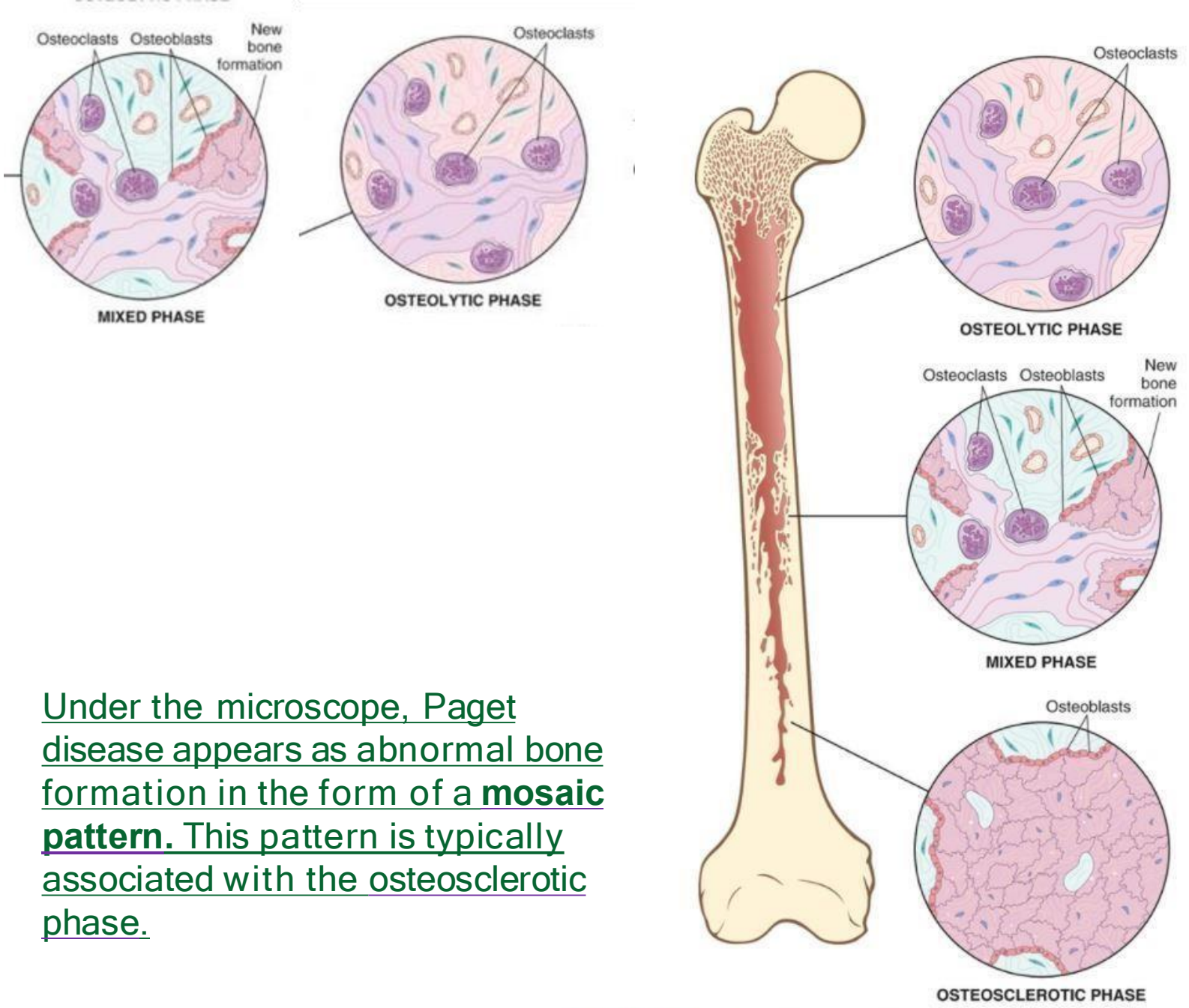


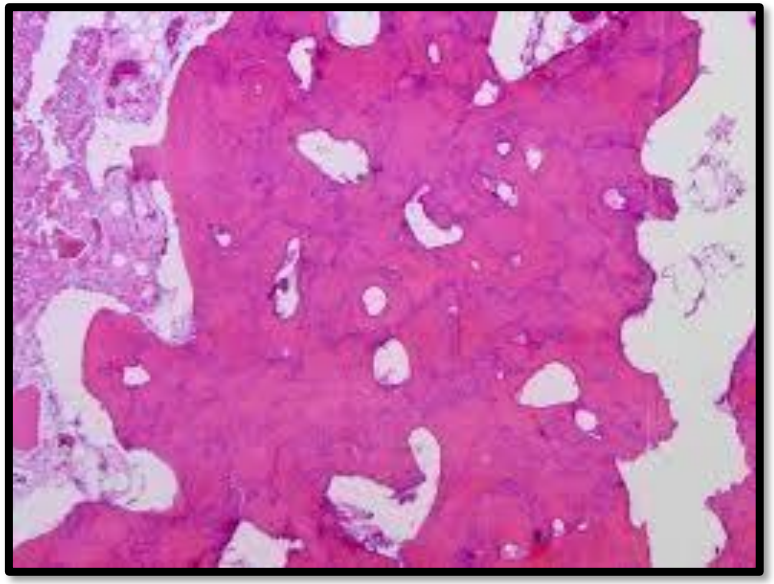
FIG. 21.10 Diagrammatic representation of Paget disease of bone demonstrating the t...

Increased activity of osteoclasts → more lytic lesions → decreased bone opacity in the **osteolytic** phase.

Under the microscope, Paget disease appears as abnormal bone formation in the form of a **mosaic pattern.** This pattern is typically associated with the osteosclerotic phase.

More activity of osteoblast → **osteosclerotic** phase

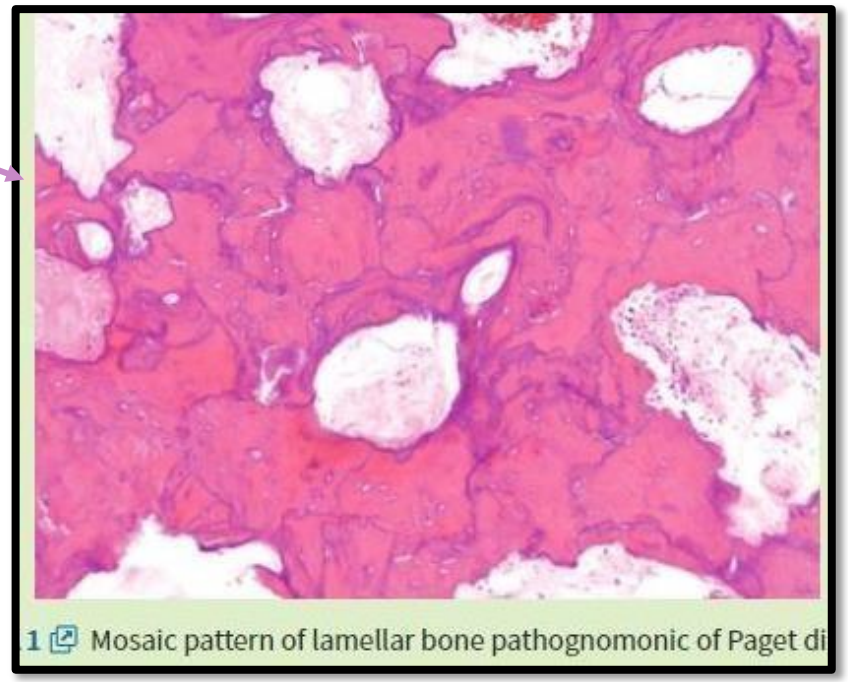
Some pathologic fractures can be treated by ORIF (open reduction internal fixation) - see slide 19.



X-ray of a pelvic bone affected by Paget disease.

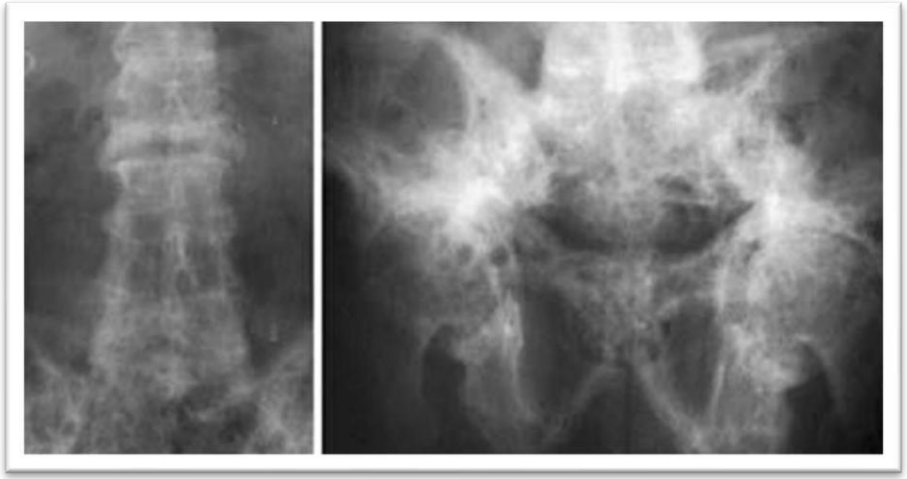
More common in the vertebral column and the proximal axial skeleton.

Mosaic Abnormal bone formation



The area which has whiter views on the x-ray has more osteoblastic activity (osteosclerotic), while lesser white indicates more osteoclastic activity (osteolytic).

Mosaic pattern under the microscope is only related to paget disease of the bone



Didn't get it?
See lecture...
13:30-16:23

Most of the time, a biopsy is done to rule out other causes.

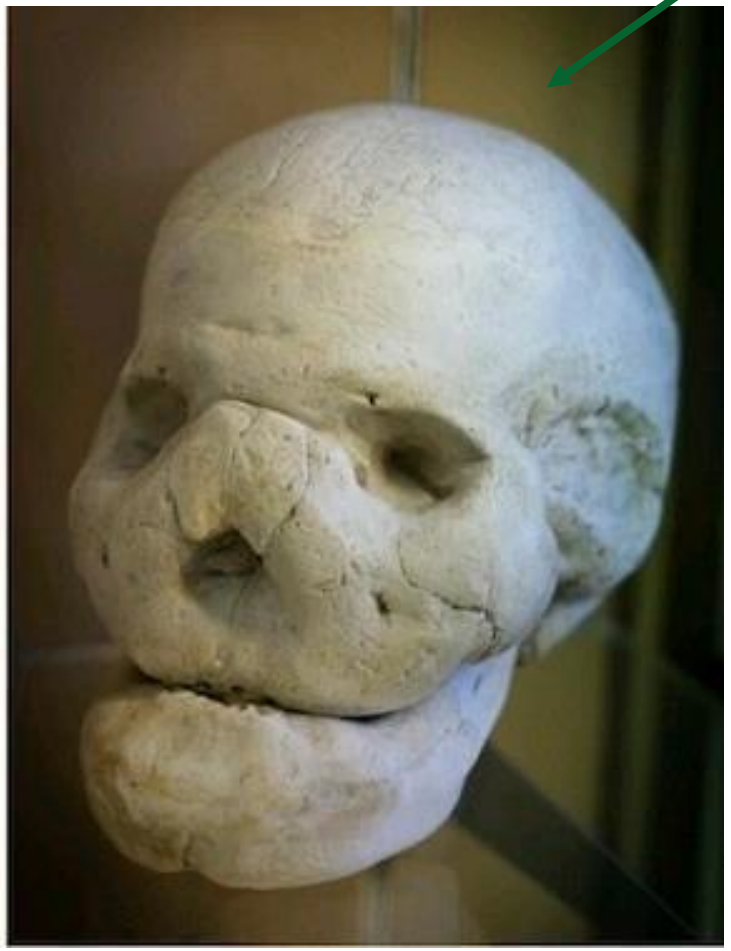
PAGET CLINICALLY:

High serum alkaline is a feature of paget disease of the bone

(more than one bone)

- **85% polystotic or 15% monostotic.**
- **Axial skeleton more affected (prox.Femur)** and is rarely found at distal bones.
- **Most are mild and asymptomatic** - no symptoms (if there are symptoms, **pain** is the major one).
- Causes of **Pain;**
    1. **Microfractures** (an excessive number of microfractures can progress to 2. nerve compression).
    2. **Nervecompression** (Similar to a vertebral disc, where a slipped disc compresses nerves, causing intense pain).
- The intensity of pain depends on the location and severity of the underlying cause.
- **Leontiasis ossea (lion face),** severe paget disease of the skull; **platybasia (invagination of skull base); secondary osteoarthritis; fractures; osteosarcoma (1%)**
- **DX: x-ray; ⇧ serum Alk P,** because of the commotion that occurs in the bone between osteoclasts and osteoblasts, **Normal Ca and PO4** → so you **exclude** the vitamin D deficiency and **hyperparathyroidism**.

Leontiasis ossea (**lion** face); platybasia

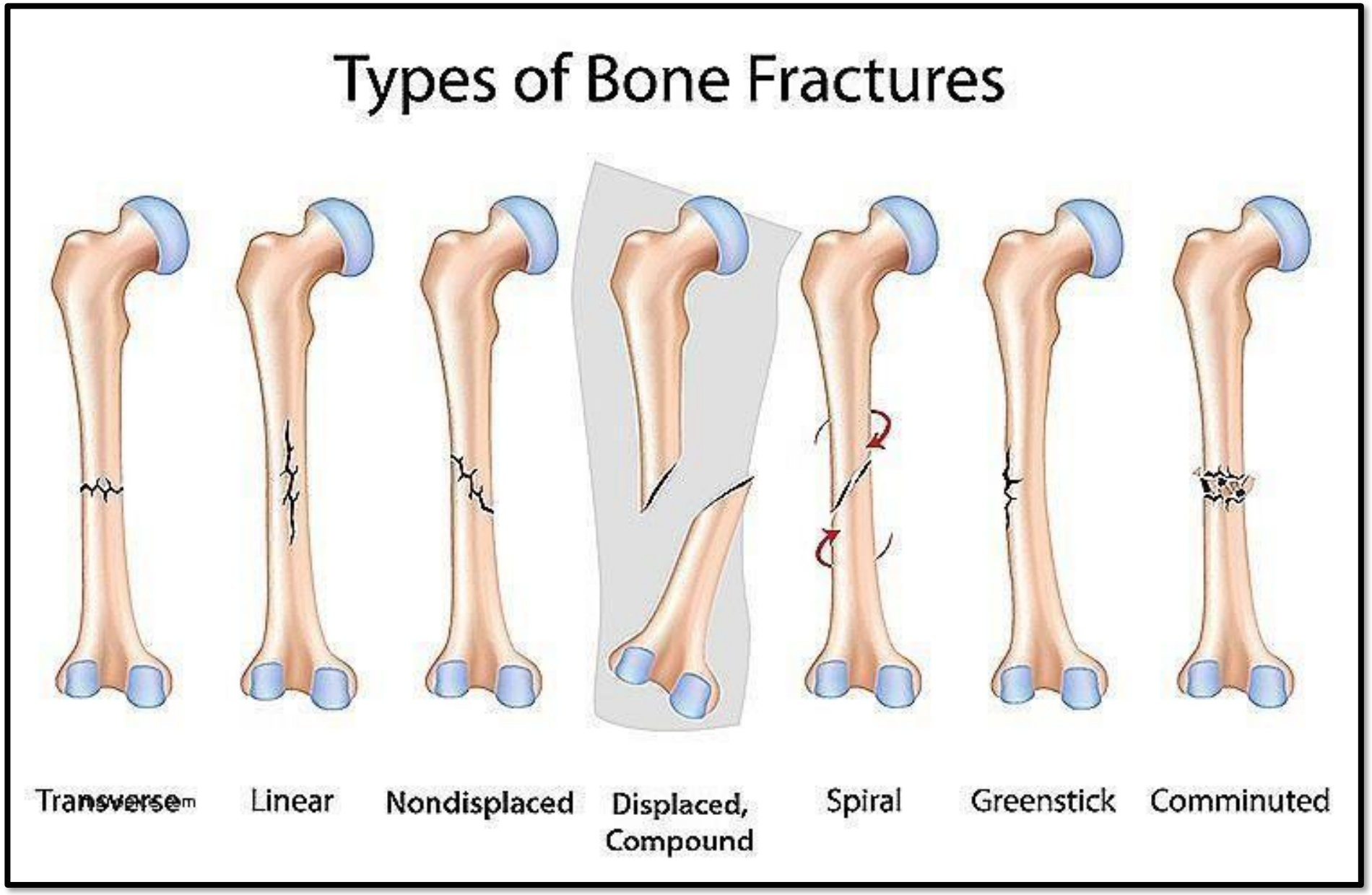


The base of the skull is flat cuz the severe formation of the skull wall by severe paget disease of the skull

FRACTURES #:

- **Loss of bone integrity from mechanical injury** (trauma)**&/or diminished bone strength.**
- **Most common pathology of bone.**
- Fractures are classified into multiple variants, as each type indicates **how it occurred** and determines the appropriate **treatment**:

1. **Simple #:** the overlying **skin is intact,** the fractured bone **doesn't** penetrate the skin, there's no communication with the skin.
2. **Compound #: communicates with overlying skin.**
3. **Displaced #: ends are not aligned**
4. **Stress #: repetitive slowly progressive** (often occurs in Paget disease / osteoporosis)
5. **Greenstick #: soft bone fracture** (mostly in children) **-**
6. **Pathologic #: bone abnormal (tumor),** occurs when there are abnormal bones, such as: in Paget, osteoporosis, or metastatic cancer.



Try to analyze each case then look at the following slide

Can a fracture be both, simple and nondisplaced?

- Simply, yes.

1. 

Transverse

-

Horizontal

2. 

Linear

-

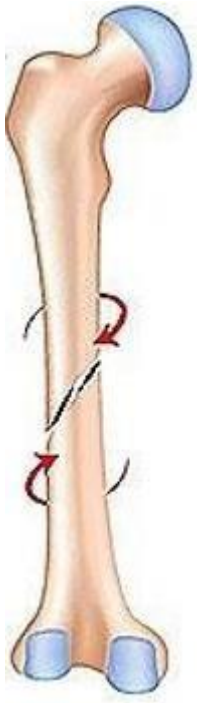
Vertical

3. 

Oblique

-

Diagonal

4. 

Spiral

Can be caused by twisting.

Treatment: no need for reduction or surgery, only immobilization to aid in repair/ healing and localizing the bone. For spiral fractures, it depends.

What about being both compound and displaced?

Also, yes

Compound, displaced. Penetrating the skin, it requires open reduction and surgery (internal fixation) and sometimes closed reduction.

What if the bone is fractured into small pieces?

Comminuted

More than 2 parts, it may be comminuted nondisplaced, comminuted displaced or comminuted compound (healing is more challenging and requires internal fixation - ORIF).

What if the periosteum was dented, and the bone is still soft and not fractured?

- The bone is still soft, no fracture.
- Clinical advice: if greenstick fracture is suspected, it must be treated as a normal fracture and to be checked after 2-3 days as the hematoma appears then callus formation to diagnose the case.

Green stick
At children in immature bone

EXTRA SLIDE – CLINICAL INFO.

- Simple + nondisplaced fractures are very easy to heal (2-3 weeks) after healing bone regain 90-99% of its original state.
- ***Open Reduction*** **& Internal Fixation (ORIF)** - Surgery is done to **realign the bone**, using screws, plates, or rods to stabilize it.
- **Closed Reduction** - If the bone can be **manually realigned** without surgery, a cast or brace is used for healing.

Skip if in a hurry, DON'T if you care about being an extraordinary physician.

FACTORS IMPACTING PROPER HEALING:

- **Displaced and comminuted fractures**
- **Inadequate immobilization (delayed union or nonunion)**
- **Pseudoarthrosis** - joint takes place of the fracture site, affecting bones and movement.
- **Infection (open** or compound fractures**)**
- **Malnutrition.**
- **Steroids/AIDrugs.** → Disrupting the bone remodelling balance by decreasing the bone formation and increasing the bone breakdown

✓ Healing is faster for younger (2-3 weeks) than older (5-6) patients.

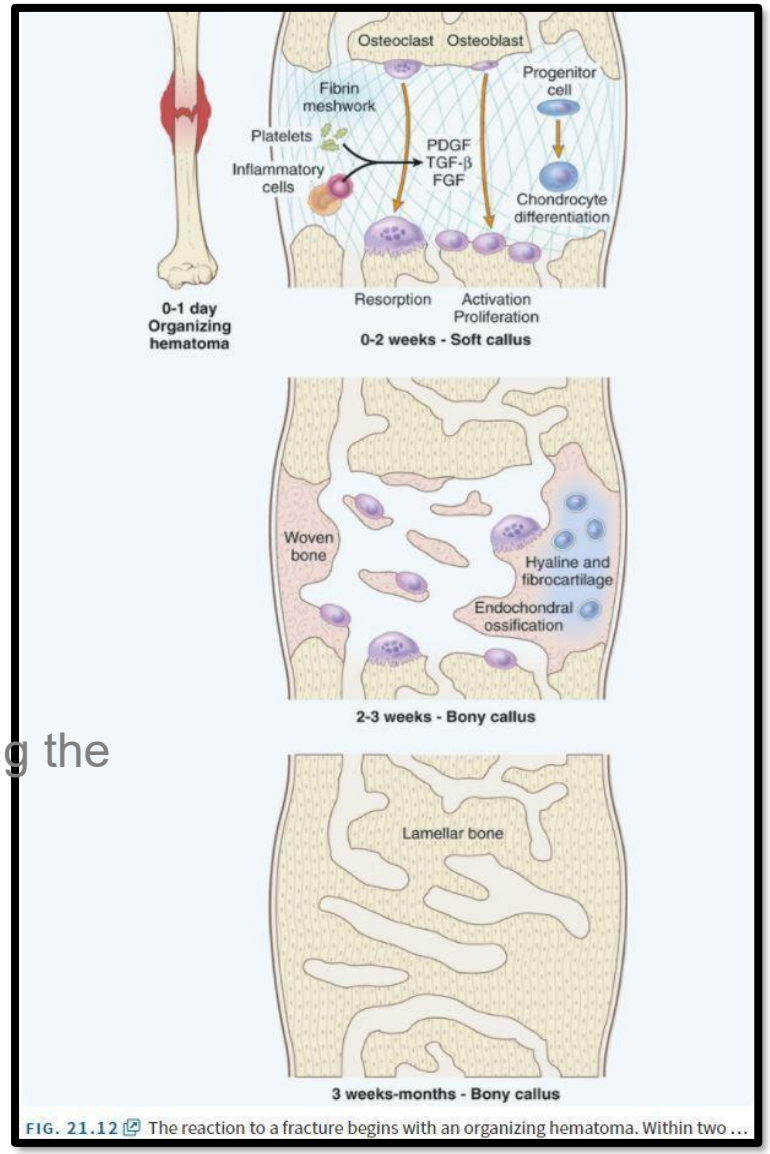


FIG. 21.12 The reaction to a fracture begins with an organizing hematoma. Within two …

Death of the bone

OSTEONECROSIS (AVASCULAR NECROSIS)

Why named avascular? Because the main cause is the interruption of the blood supply.

Infarction (ischemic necrosis) of bone and marrow

Blockage of the blood supply leads to thrombosis

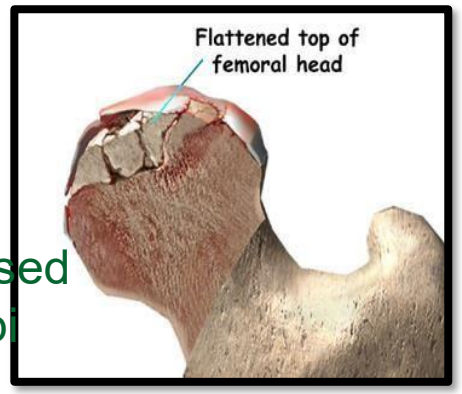
ASSOCIATED CONDITIONS:

- **Vascular injury: trauma, vasculitis**
- **Drugs: steroids**
- **Systemic disease: Sickle**
- **Radiation**

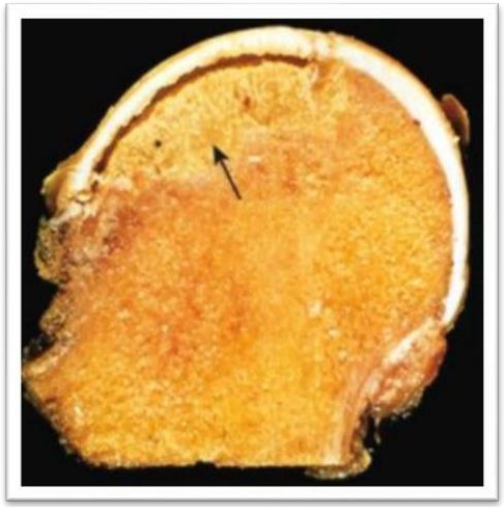
Sicklers are exposed to develop thrombi

MECHANISM:

- **Mechanical disruption**
- **Thrombotic occlusion**
- **Extravascular compression**



- Most common bone affected by OSTEONECROSIS is the **head of the femur.**



Pyramidal shape necrosis, the base of the pyramid is in the articular joint.

Additional Resources:

رسالة من الفريق العلمي:

أَتَعْرِفُ مَا مَعْنَى الْيَقِينِ بِاللَّهِ؟

الْيَقِينُ بِاللَّهِ هُوَ الَّذِي يُحقِّقُ الْمُسْتَحِيلَ، الْيَقِينُ بِاللَّهِ هُوَ أَنْ تَكُونَ كُلُّ الْأَبْوَابِ مُعْلَقَةً وكل الظروف صعبة وكل المؤشرات تُوحِي بِعَكْسِ مَا تَتَمنَّاهُ لَكِنَّكَ عَلَى يَقِينٍ بِأَنَّ الله سيصلح كل شيءٍ وسيتكَفْلُ بِكُلِّ شَيْءٍ .. يَقُولُ ابْنُ القيم متحدثا عَنْ الْيَقِينِ بِاللَّهِ "لو أَنْ أَحَدَكُمْ هُم بِإِزَالَةِ جَبَلٍ وَهُوَ وَاثِقٍ بِاللَّهِ لَأَزَالَهُ.. فَثِقْ بِاللَّهِ، وَثِقْ بِتَدَابِيرِهِ واجعل يقينك بِاللهِ هو سر الرِضا بِكُلِّ شَيءٍ يحدثُ لَكَ.

For any feedback, scan the code or click on it.

Corrections from previous versions:

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