MSS & Skin Tumors Pathology 2022 Lecture 1

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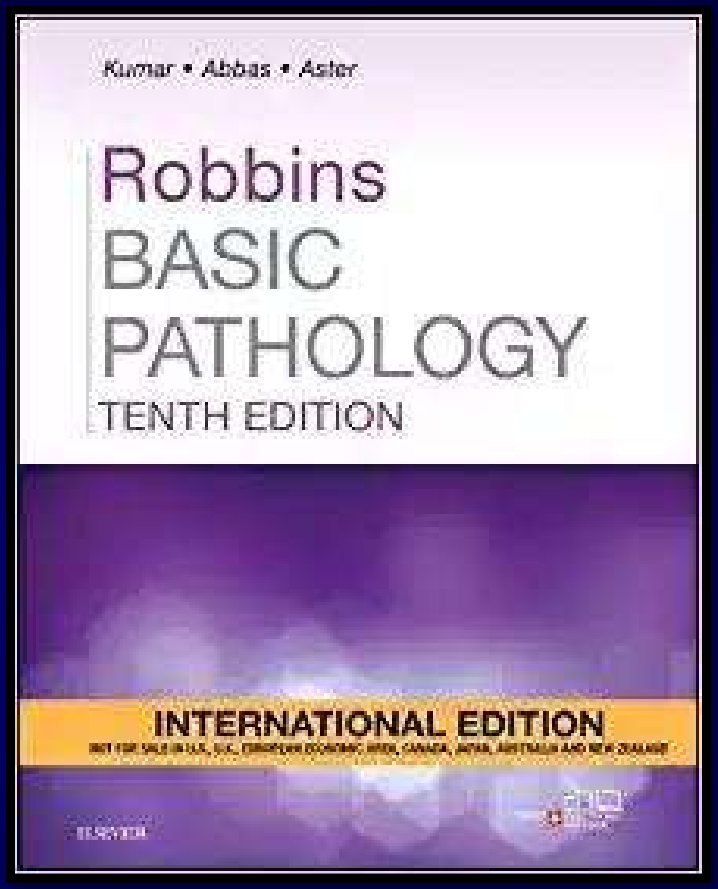
MY DUTIES

- 10 lectures
- Simplify
- Short Videos



YOUR DUTIES

- **Understand the concepts**
- **Help U all Understand…understand… understand X 10…only then memorize**
- **Answer questions (exception) & inquiries**
- **Respect the whole process…I paid my dues…it is your future**
- **No inquiries about the nature of the exam…I don't answer questions of the exam…don't even try**

PLEASE DON'T ASK THESE QUESTIONS AT ALL

- How many questions on my material?
- What should we concentrate on?
- Are the slides enough?
- Should we memorize this or that?
- Is this or that required?

[YOU SHOULD NOT ONLY STUDY FOR THE EXAM]

[YOU ARE NOT STUDYING FOR ME EITHER]

[YOU ARE LEARNING SO THAT YOU WILL BE A GOOD CARING & THOROUGH PHYSICIAN WHO WILL APPLY THE STNADRAD OF CARE]

OUTLINE & OBJECTIVES

- ✓ Remember the basic structure & function of bone
- ✓ Congenital diseases of bone and cartilage
- Metabolic disorders of bone
- Paget disease of bone
- Fractures
- Osteonecrosis
- Osteomyelitis
- Bone tumors and tumor-like conditions

CONTINUE…OUTLINE AND OBJECTIVES

- **Arthritis:**
  - **Osteoarthritis; RA; Juvenile Idiop A**
  - **Seronegative Spondyloarthropathies**
  - **Infectious arthritis; Lyme arthritis**
  - **Crystal-induced arthritis**
- **Joint tumors & tumorlike conditions**
- **Soft tissue tumors:**
  - **Adipose tissue; fibrous tissue; skeletal muscle**
  - **Smooth muscle; tumors of uncertain origin**

  Skin neolpasms

E learning (will be sent to you too)

Bone development	**https://www.youtube.com/watch?v=xXgZap0AvL0&ab_channel=INTELECOM**
Osteoporosis	https://youtu.be/eT_G9NHIyV0 https://youtu.be/VwCkyf0lQwo
Osteoarthritis	https://youtu.be/BBqjltHNOrc https://youtu.be/pnKaBMvVUs0
Rheumatoid arthristis	https://youtu.be/Yc-9dfem3lM https://youtu.be/ld8PhyAHov8
Osteoarthristis vs rheumatoid arthritis	https://youtu.be/6lx_774GuTw
Osteomyelitis	https://youtu.be/mpUq6Ui6yew
Gout	https://youtu.be/bznoU5bke4U
Bone tumors	https://youtu.be/wezFzUX-UWY
Bone and soft tissue tumors	https://youtu.be/gPCzAdD6mIw
Soft tissue tumors	https://youtu.be/qpkPKk3HxUQ
Ossifications	https://youtu.be/Vwethc4jt7U https://youtu.be/vOKLFdP4pjE
Skin neoplasms	https://www.youtube.com/watch?v=Too2MtxEFoQ&ab_channel=MedFlix https://www.youtube.com/watch?v=-uf1mOu98V8

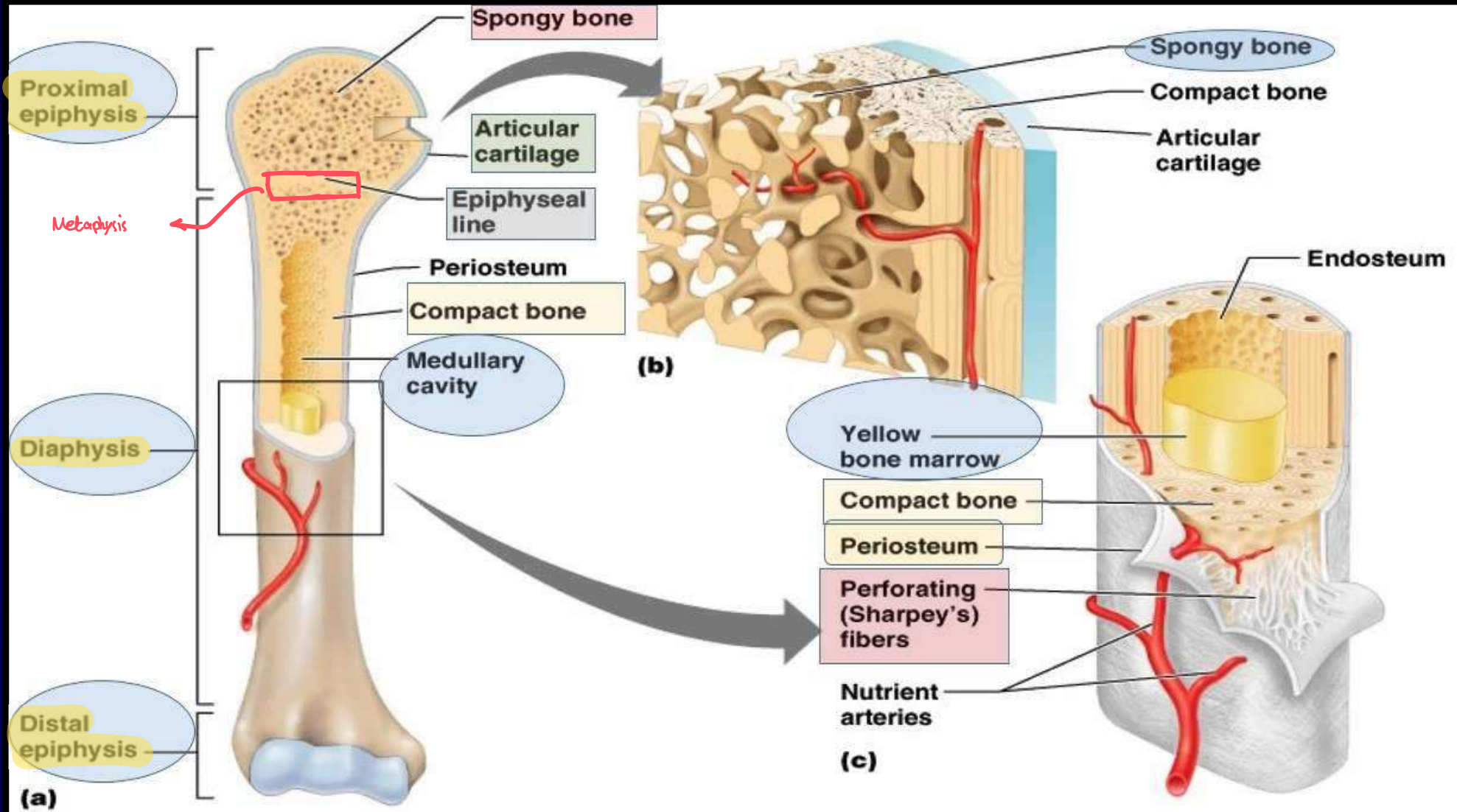
BONE FUNCTIONS

- Mechanical support
- Forces transmission
- Protection
- Mineral homeostasis especially Ca^{++} PO_4^{-3}
- Hematopoiesis → formation of Blood cells

* so any disease will effect on these functions

BONE STRUCTURE

- **Matrix (osteoid 35% and minerals 65%):**
  - Osteoid: organic type I collagen and glycosaminoglycans & other proteins
  - Inorganic hydroxyapetite $[Ca_{10}(PO_4)_6(OH)_2]$
  - Woven vs lamellar bone
- **Cells:**
  - Osteoblasts: forms bone
  - Osteoclasts: resorbs bone
  - Osteocytes: mature bone cells



Structure of a Typical Long Bone

but it's not specific for any particular disease

* abnormal in shape * Mature bone * organized (Collagen Fibers are parallel)

WOVEN VS LAMELLAR BONE

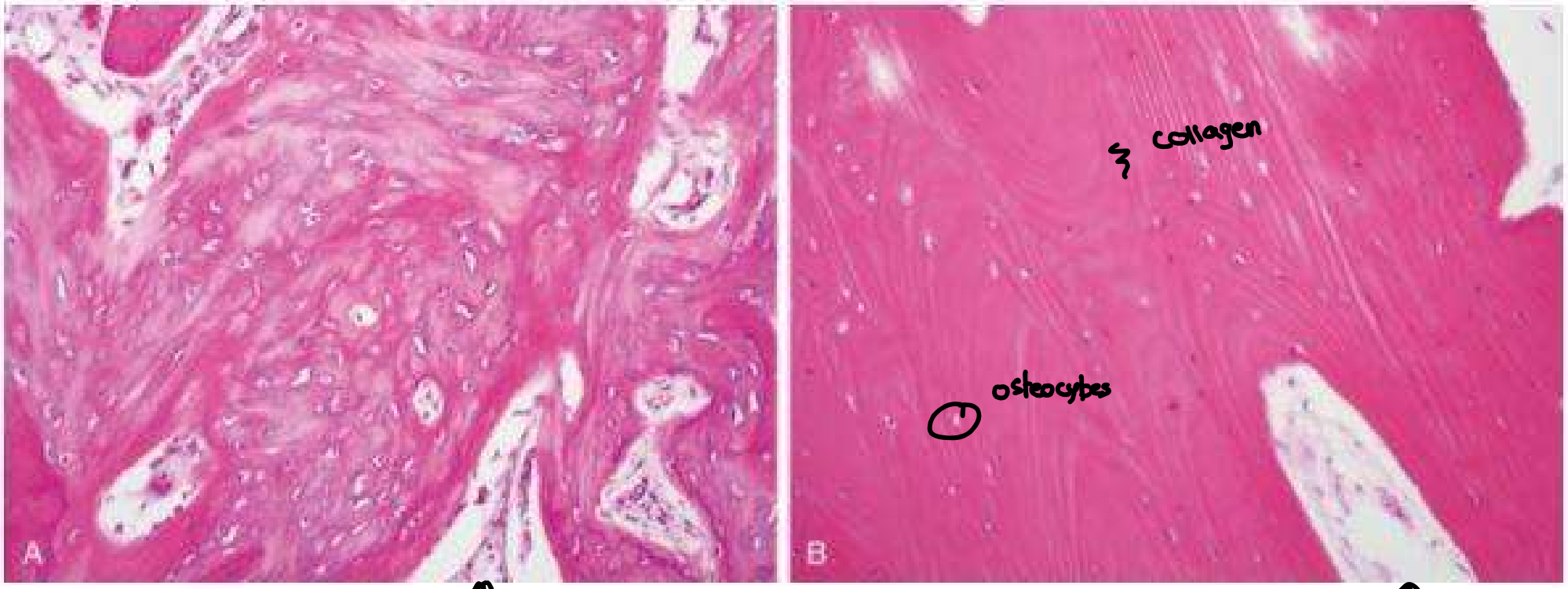


FIG. 21.1 Woven bone (A) is more cellular and disorganized than lamellar bone (B)

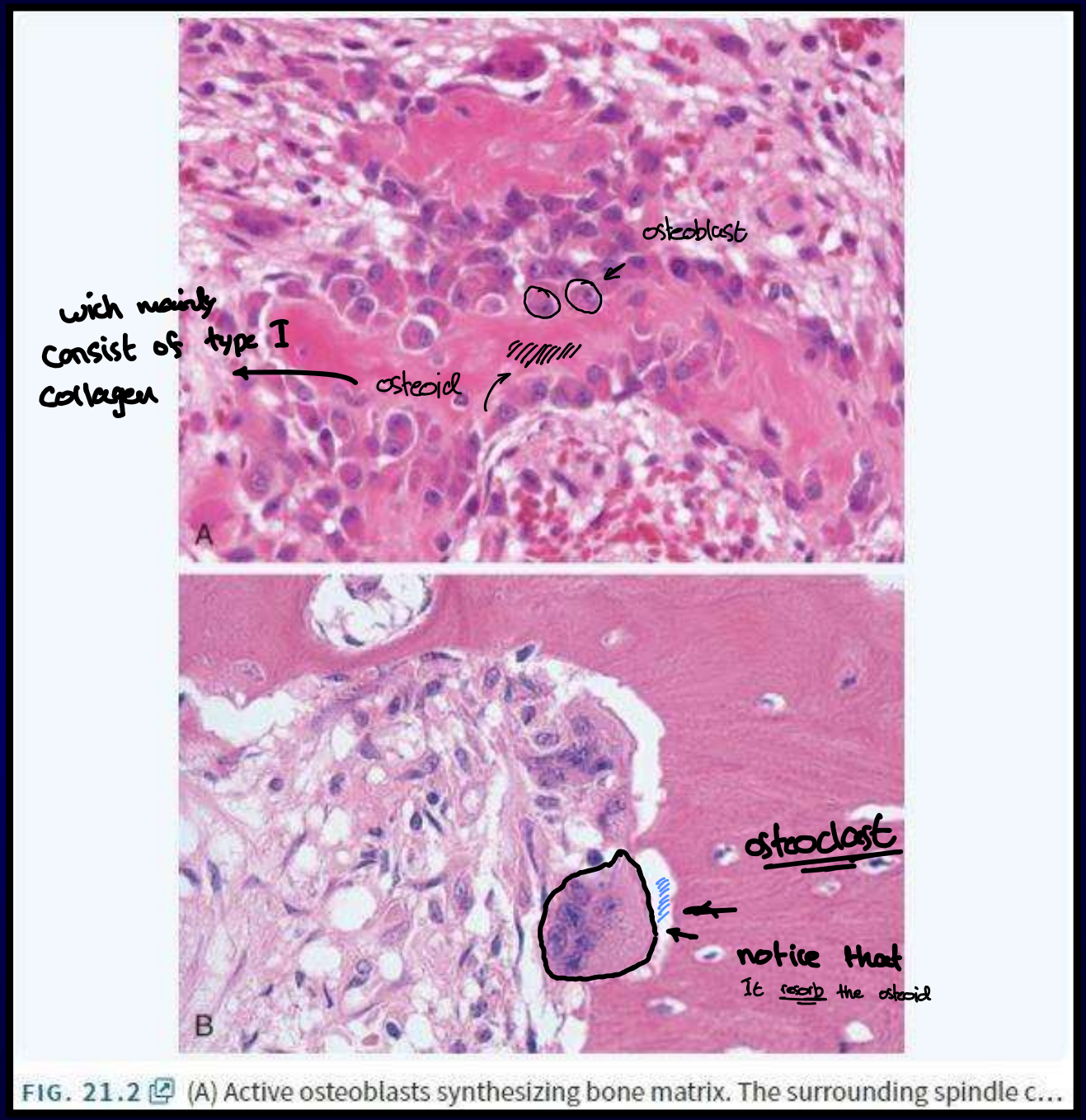


FIG. 21.2 (A) Active osteoblasts synthesizing bone matrix. The surrounding spindle c...

OSTEOBLASTS

↳ Form the bone (mainly here we mean the osteoid)

↳ $\frac{n}{c}$ ratio is small

OSTEOCLASTS

↳ resorb bone (osteoid)

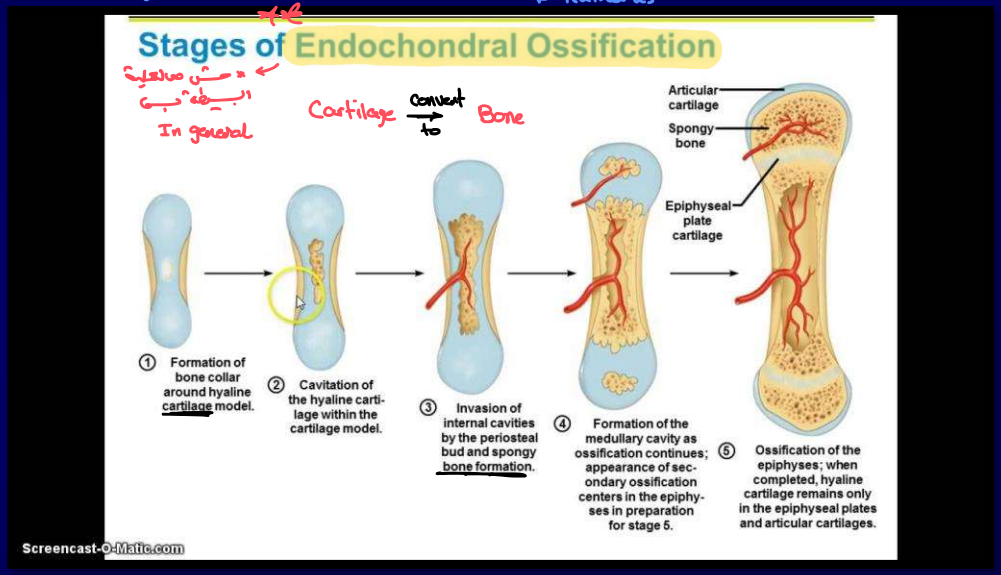
* multinucleated cell
* derived from circulating monocytes

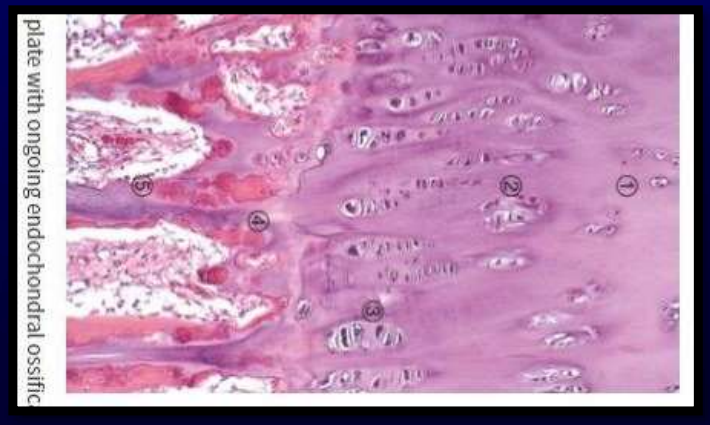
DEVELOPMENT

LONG BONES

develop through ??

Ex: * Femur
* humerus

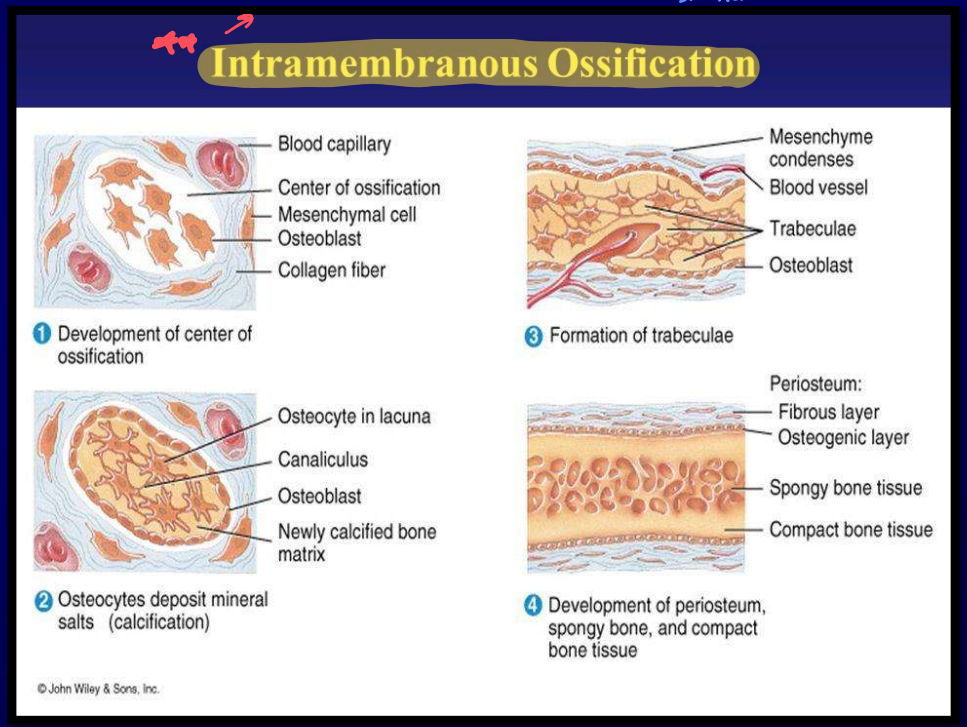




FLAT BONES

no cartilage Note

Ex :- * clavicle
* sternum



HOMEOSTASIS & REMODELING

- Continuous and dynamic complex process even in adult mature skeleton (microscopic level)
- Peak bone mass is reached in early adulthood after completion of skeletal growth
- Resorption > bone formation on 4th decade

osteoclast >> osteoblast

Activation ↑ + Osteoclast differentiation	inhibition ↓ - Osteoclast differentiation
PTH (para thyroid hormone) IL-1 Steroids	BMPs (bone morphogenic proteins) Sex hormones (estrogen & test.)

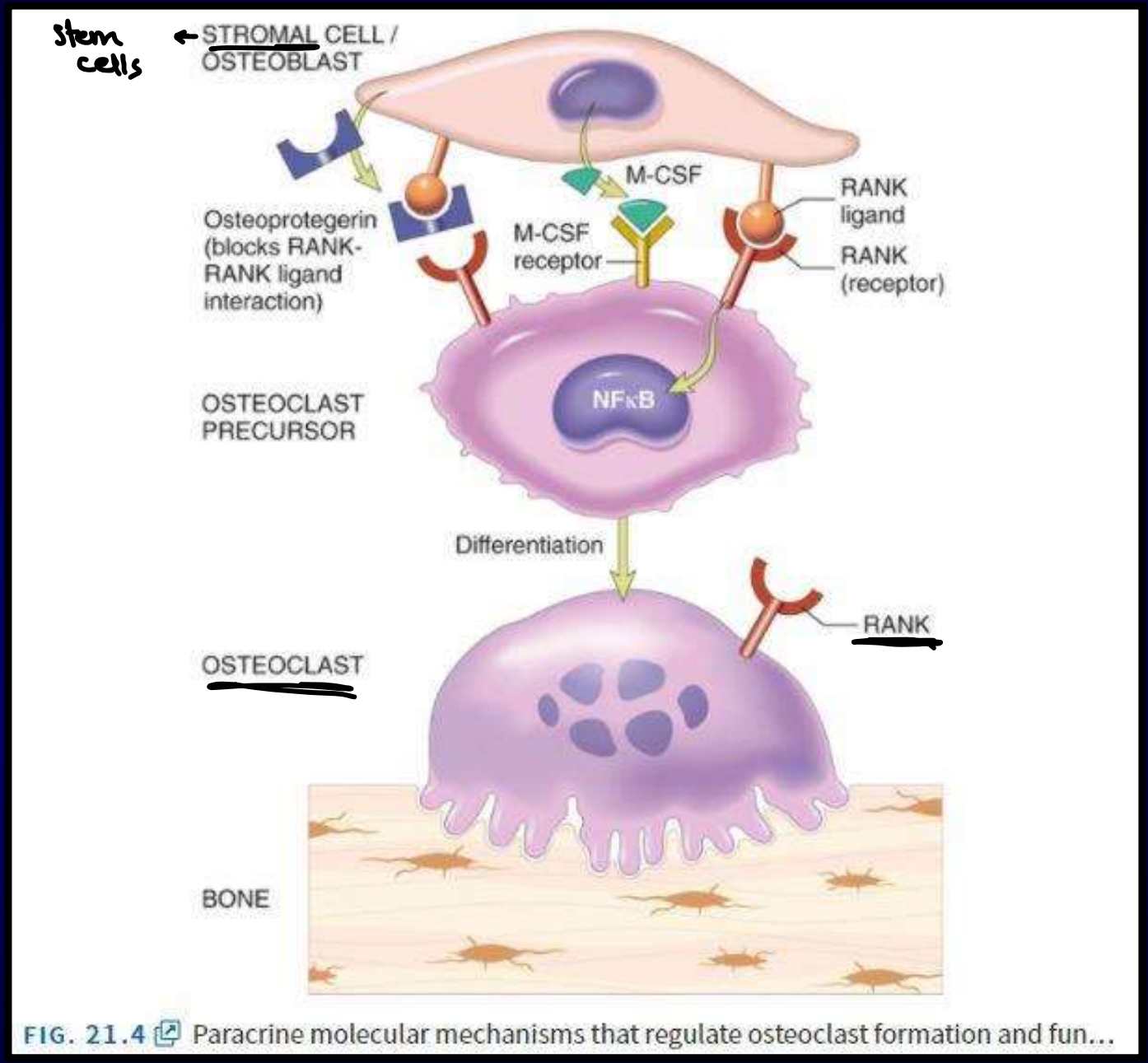


FIG. 21.4 Paracrine molecular mechanisms that regulate osteoclast formation and fun...

** CONGENITAL DISORDERS → classified into 2 groups ?!

① DYSOSTOSIS (bad bone)

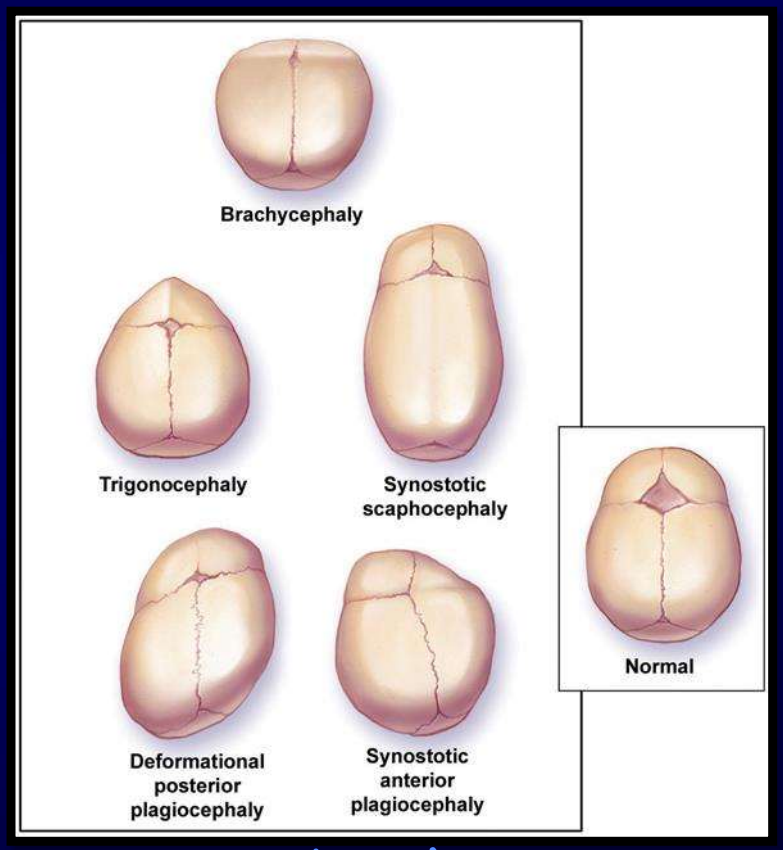
- Abnormal condensation & migration of mesenchyme
- Genetic abnormalities of homeobox genes, cytokines and its receptors
  - Aplasia (no formation) نقص بالأصابع
  - Supernumerary digit زيادة أصابع
  - Syndactyly & craniosynostosis → (الأصابع ملصقين / تأكل بالـ skull)

Ex

② DYSPLASIA

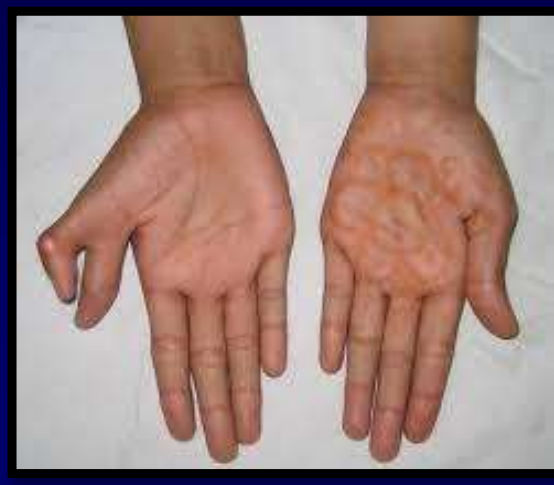
- Disorganized bone & cartilage
- Gene mutations that control development and remodeling
- Dysplasia here: not premalignant

DYSOSTOSIS



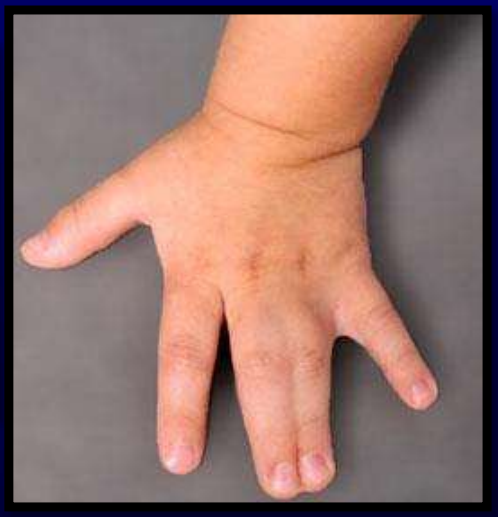
* craniosynostosis

↳ Aplasia



↳ * Supernumerary digit

* Syndactylyl



* Synda...

Lecture 2

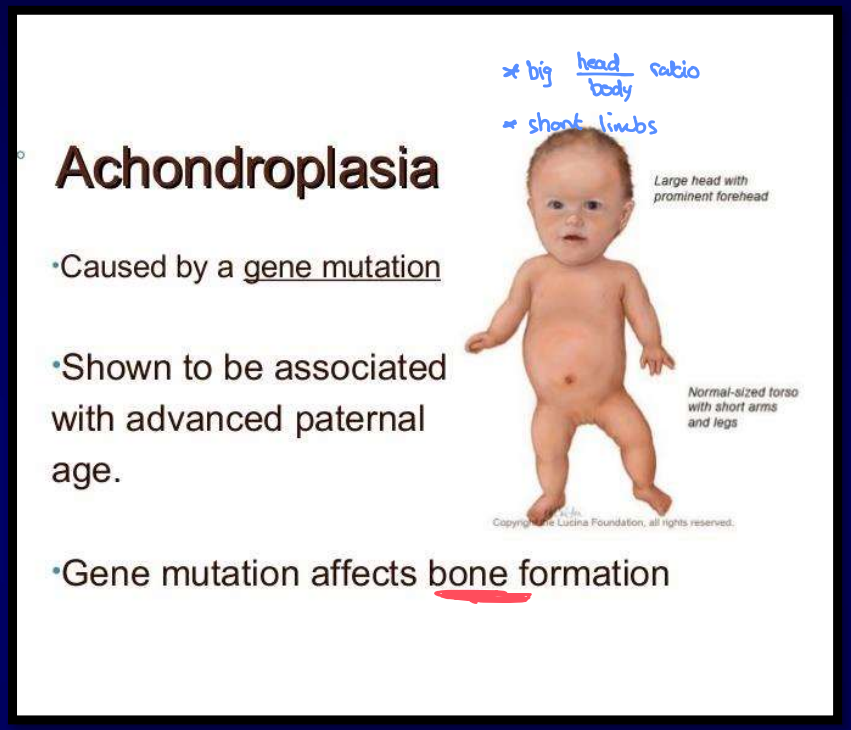
Ex of disordered related to it ?!

*DYSPLASIAS

usually because of point mutation

- **Achondroplasia (dwarfism): most common**
- **Mutations in FGFR3** (Growth Receptor; Fibroblast Factor)
- **No impact on longevity, intelligence or reproductive status**

*life expectancy

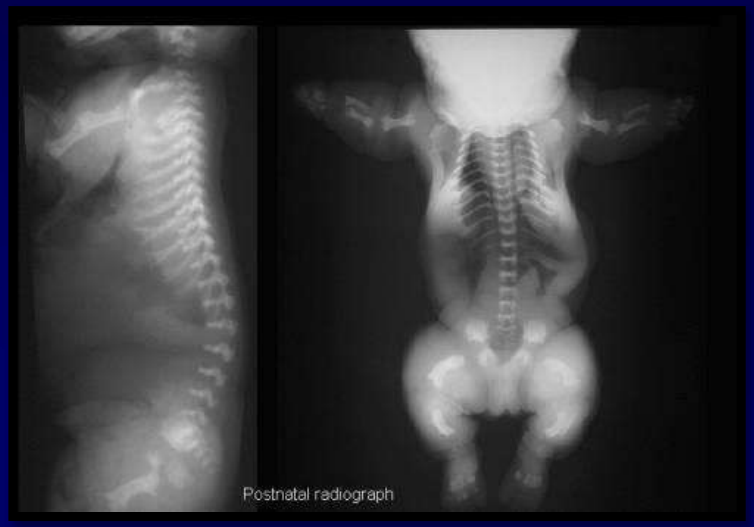


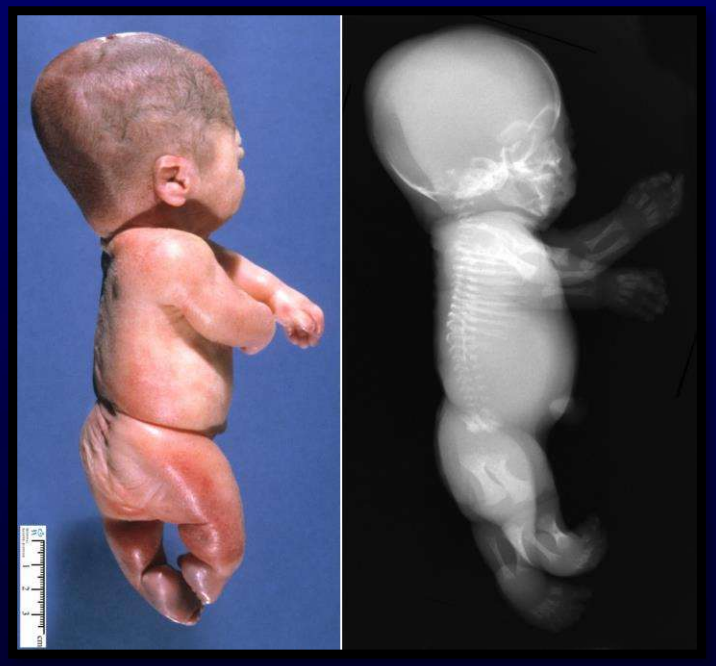
* big head/body ratio
* short limbs

Peter Dinklage: 48-years-old, married with 2 children from USA, New Jersey "Game of thrones"

THANATOPHORIC DYSPLASIA

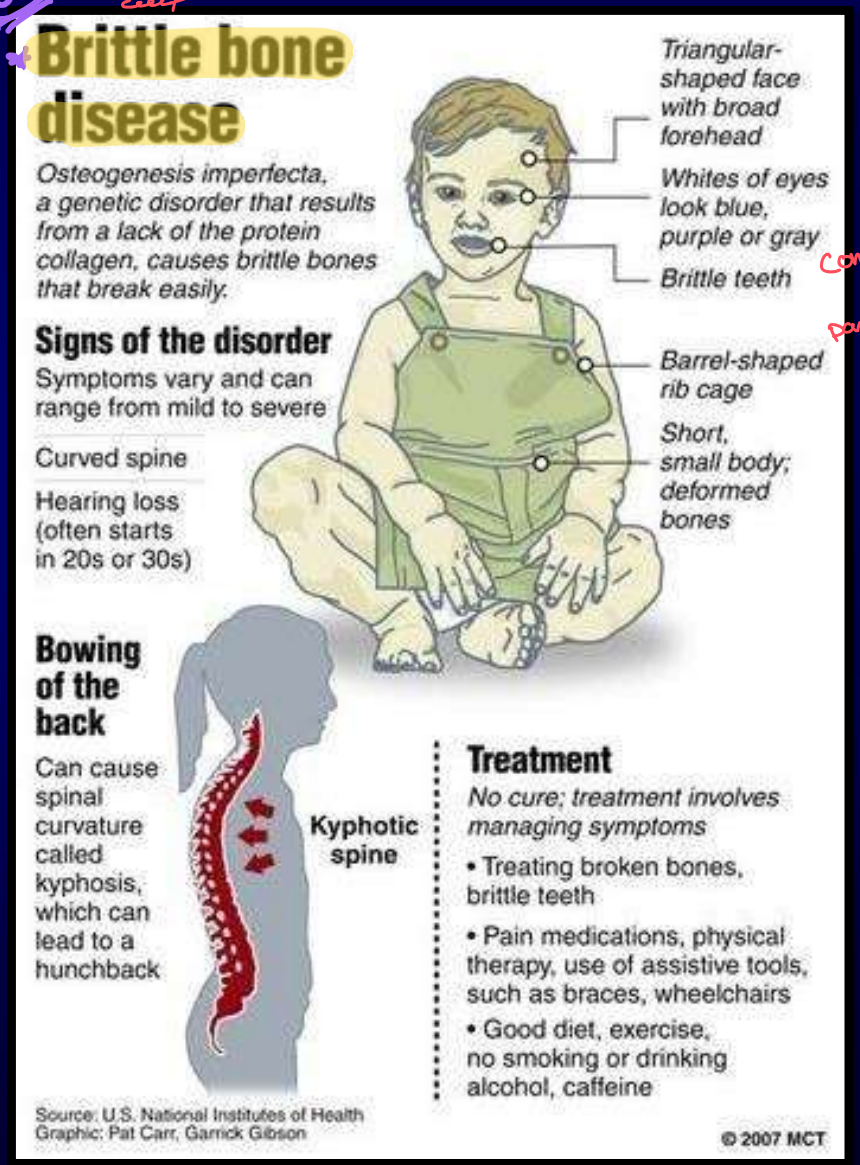
- Most common lethal form of dwarfism
- FGFR3 mutations (different from Achondroplasia)
- Die at birth or shortly after (small chest leading to resp. insufficiency)





← Focus on this pic →

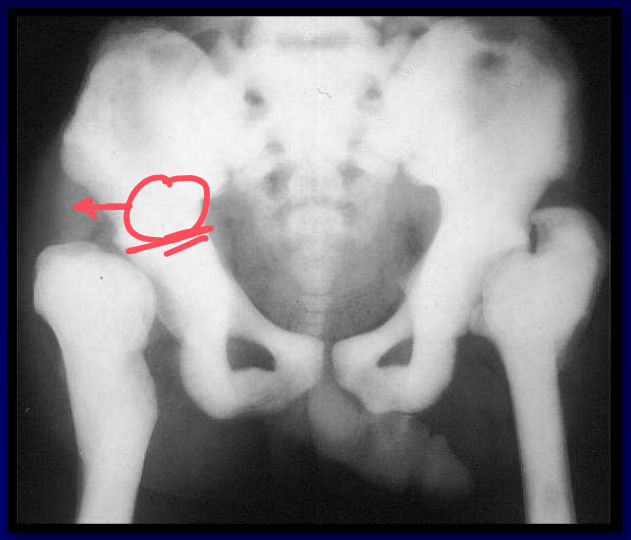
OSTEOGENESIS IMPERFECTA

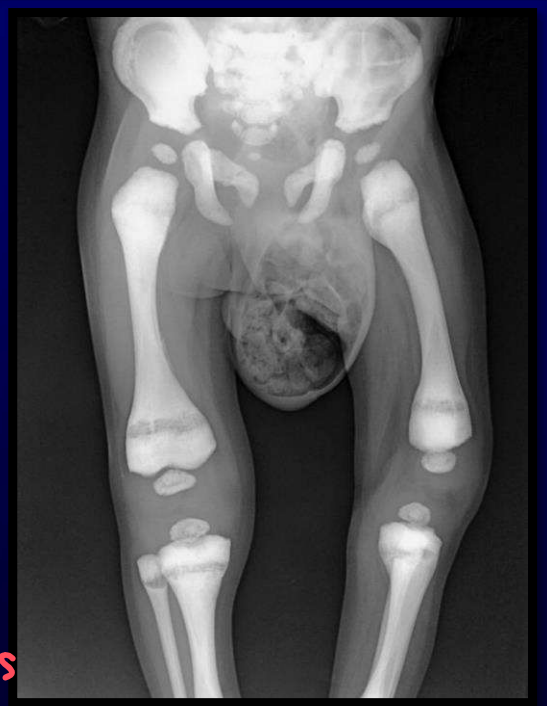


- Most common inherited disorders of connective tissue
- Group of disorders; AD: deficiency of type I collagen synthesis
- Too little bone; fragility
- Blue sclera; hearing loss; teeth abnormalities
- Type 2 (lethal) and type I (relatively normal life)

OSTEOPETROSIS

- **Marble bone disease** "stone bone" (group of disorders); rare
- Impaired osteoclast function: **reduced bone resorption** leading to diffuse sclerosis
- Dx: X-ray
- Fractures and leukopenia in severe forms





In normal bone there is an ability to absorb shocks

Summary

Congenital Disorders of Bone and Cartilage

Abnormalities in a single bone or a localized group of bones are called **dysostoses** and arise from defects in the migration and condensation of mesenchyme. They manifest as absent, supernumerary, or abnormally fused bones. Global disorganizations of bone and/or cartilage are called **dysplasias.** Developmental abnormalities can be categorized by the associated genetic defect.

- FGFR3 mutations are responsible for achondroplasia and thanatophoric dysplasia, both of which manifest as dwarfism.
- Mutations in the genes for type I collagen underlie most types of osteogenesis imperfecta (brittle bone disease), characterized by defective bone formation and skeletal fragility.
- Mutations in *CA2* and *TCIRG1* result in osteopetrosis (in which bones are hard but brittle) and renal tubular acidosis.