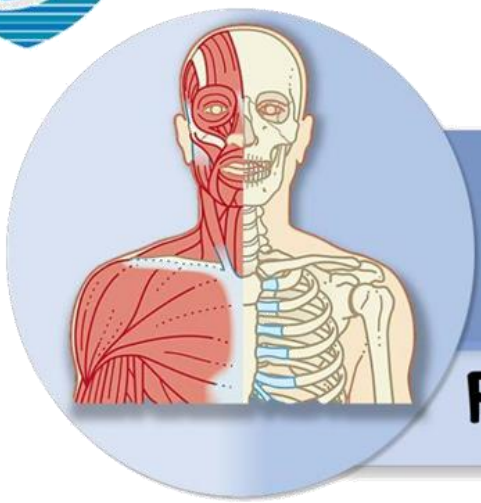


MSS system

Pathology

◉ Sheet ○ Slide

Number:	#1
Done by:	Yara saddam
Corrected by:	Mohammad Alfarra
Doctor:	Mousa Al Abbadi

BONE

Note: the sheet contains the videos about ossification (2 videos) and rank/OPG video that's why it's a little bit long.

*Functions of Bone:

1.Mechanical support
2. transmission of forces produced by muscles
3. protection of viscera
4. mineral homeostasis
5. Hematopoiesis: production of blood cells

*Structure of bone:

1) Extracellular Matrix

*The extracellular matrix is composed of:

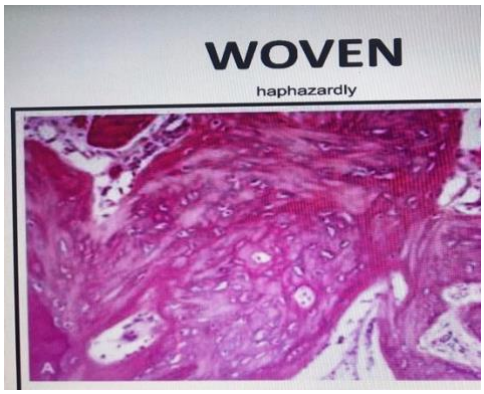
A) Osteoid (35%): organic type 1 collagen and glycosaminoglycans & other proteins.
B) Minerals (65%)

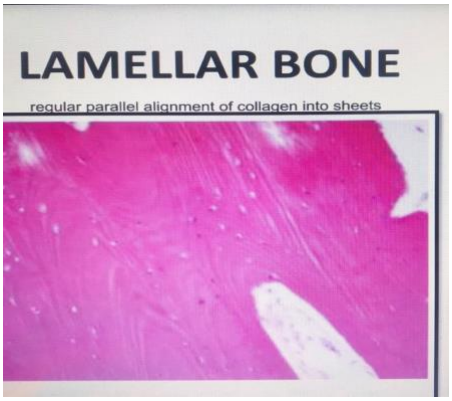
*The unique feature of the ECM of bone is hardness and this feature is provided by the inorganic compound (hydroxyapatite) and its formula is Ca5(Po4)3OH but since it exists as a dimer (multiply everything with 2) so we express it as: Ca10(Po4)6(OH)2.

*The bone matrix is synthesized in 2 histological forms:

A) Woven: produced rapidly, like in fetal development and in fractures repair. Collagen is arranged haphazardly so it has less structural integrity than lamellar bone.
*Note: the presence of woven bone in adults is ALWAYS abnormal but it's not specific for a particular bone disease.

B) Lamellar Bone: more organized and collagen is arranged in a parallel shape, so it have more integrity than woven.
* Note that the lamellar bone is organized as sheets while woven is disorganized.





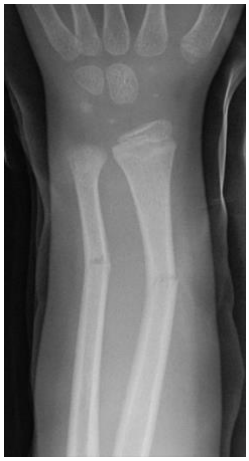
2)specialized cells:

1)OsteoBLAST (small, usually mononuclear and very active cell) (High N/C ratio)
*exist on: the surface of the matrix
*Function: Synthesize, transport and assemble bone matrix
*Derived from: mesenchymal stem cells

2)OsteoCYTE (mature bone cell)
*they are osteoblast that are trapped in the calcified bone matrix and they are surrounded by lacunae
*they are interconnected by network of cytoplasmic processes through tunnels known as Canaliculi
*Function: 1. Control Ca levels 2. Mechanotransduction
-Mechanotransduction: detection the mechanical force and translating it into biological response

3)OsteoCLAST (lower N/C ratio) (bigger than osteoblast)
*they are specialized multinuclear macrophages
* located on the surface of bone
*derived from: circulating monocytes
*Function: resorb bone so they make more spaces and less trabeculae

*Greenstick fracture: fracture of a young, soft bone in which the bone is bent because the children's bone isn't fully mature
-treatment? You deal with it like it's a normal fracture and after 2-3 days you will do an X-ray picture and it will show you some calcification and this is an indicator for the right diagnosis
Below there is a picture of how these fractures look like on Xray



note how the bone is bent, you might be confused that it's not a fracture while actually it is ☺

*Development of Bone (Ossification):

There are 2 types: 1. Endochondral ossification
2. Intramembranous ossification

1.Endochondral Ossification:

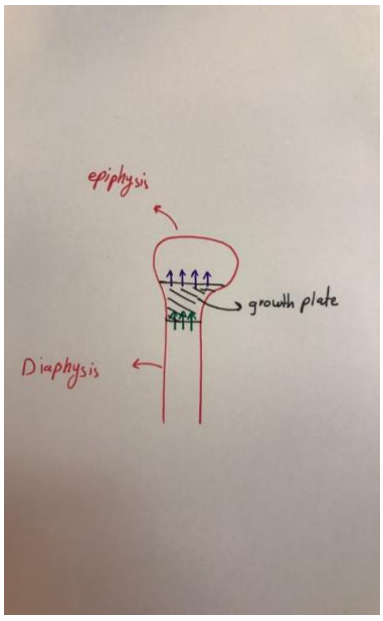
-endo= inside, chondral=cartilage so this type happens inside the cartilage, so we should have first a cartilage mold (قالب) made of mesenchymal precursor cells.

*STEPS:

1.at 8 weeks of gestation, the central portion of the cartilage mold resorbs and create the medullary canal and the osteoblasts appear and start to deposit bone below the periosteum making the 1ry ossification center and growing the bone radially.

-periosteum: the outermost layer of connective tissue that surrounds bone and its inner most layer is composed of fibrous connective tissue which allows the bone to increase in width (appositional growth)

2. After birth, the secondary ossification center appears in the epiphysis and endochondral ossification proceed in Centrifugal direction بعيدا عن المركز and eventually a plate of cartilage become entrapped between epiphysis and diaphysis forming a physis (growth plate).The black portion in the picture which is full of chondrocyte (cartilage making cells) and their direction of making cartilage in purple . while osteoblast direction in making bone shown in green and this process make the bone to increase in length. So as long as the bone increase in length then you do need active chondrocytes ☺



3. the chondrocyte within the growth plate undergoes proliferation, hypertrophy and apoptosis, and at the apoptosis region, the matrix mineralizes and is invaded by vessels to provide nutrients for the osteoblasts. when the bone stops growing in length there is no cartilage and the growth plate becomes the growth line or epiphyseal line.

2. Intramembranous ossification:

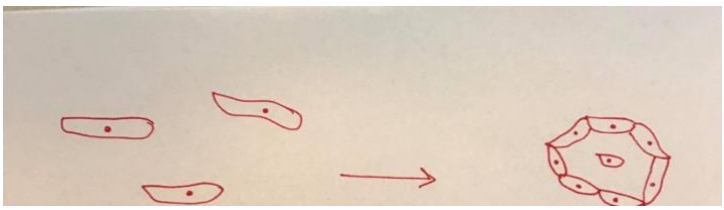
Intra=in between so it's in between connective tissues

*responsible for making flat bone:

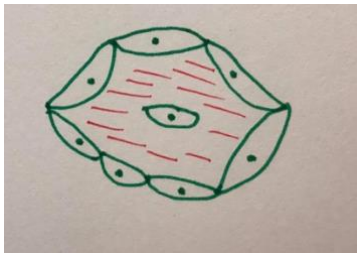
1. The skull
2. Mandible
3. Clavicle

*STEPS:

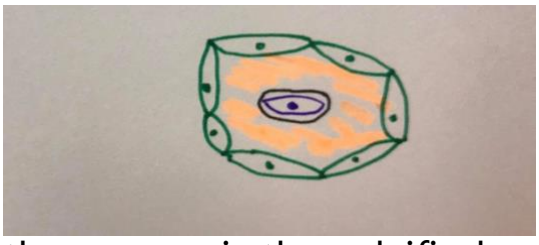
1.there are mesenchymal cells that aggregate and replicate



2. after sufficient replication they differentiate & become osteoblasts that secrete un-calcified osteoid, in the picture the color became green as an indicator of differentiation

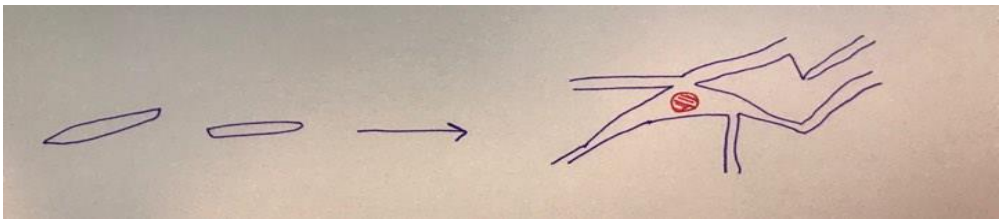


3. Alkaline phosphatase enzyme then add calcium salt& other minerals and calcify the osteoid and the osteoblast become osteocyte when it's surrounded by calcified osteoid



the orange is the calcified osteoid and the black portion is lacunae (home of osteocyte) note that the cell in center have different color bcz it's osteocyte.

4.As intramembranous ossification continues then there is osteobranches called Spicules are formed and eventually they touch each other and fuse and grow around a blood vessel for nutrients and waste exchange and the initial bone formed by this step is SPONGY BONE



note that the red is the blood vessel

5. through bone remodeling osteocytes at the edge on the spongy bone are re-organized and become packed bundles known as Osteon which is the building block of the compact bone that is formed at the edges of the spongy bone and this arrangement (compact->spongy->compact) = Flat BONE ☺

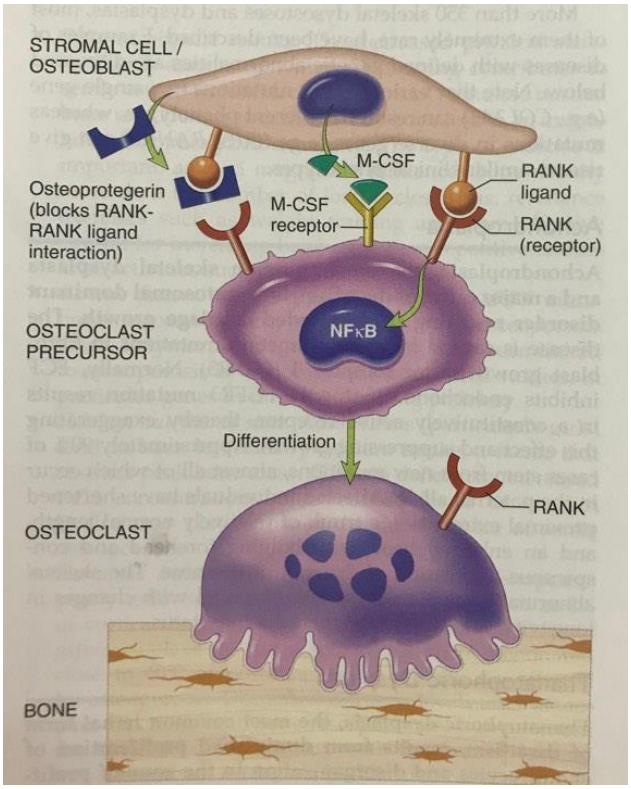
6. through another remodeling process the middle layer of the spongy can be removed and If happened it become medullary cavity ! Ta-daaaaa

In the next page I'm going to talk about the last topic which is bone remodeling but I'm not writing it in this page bcz it needs space and I only wrote this sentence to give the page a nice shape so it wouldn't look creepy , thanks for understanding me now let's move on to the next topic , lol I'm still filling the spaces but I'm going to stop now to make u feel comfy when u see the empty part of the page
:p اه صح كيف الرسم بس؟

*Bone Remodeling & Homeostasis:

-Remodeling: continuous dynamic process even in adults.
It takes place at-> microscopic locus known as (Bone multicellular unit) BMU which consist of a unit of a coupled osteoblast & osteoclast activity on the bone surface.

*Pathways that control remodeling, look at the picture thoroughly then I'm going to explain them one by one:



There is RANK receptor present on osteoclast precursor cell (2nd cell in pic) and its ligand which is RANKL present on osteoblast and marrow stromal cells (1st cell in pic) and when RANKL bind to its receptor it activates the transcription factor (NF-Kb) which is (in the middle of the 2nd cell in pic) and this factor is important for generation & survival of osteoclast.

*Osteoprotegrin: a receptor that is secreted by osteoblast and blocks binding of RANK with RANKL and its production is activated by the binding of WNT proteins secreted by various cells to the LRP5 and LRP6 receptors present on the osteoblast

2)Monocyte colony-stimulating factor

This factor is produced by osteoblast and binds to its receptor that is on the osteoclast precursor cell (2nd cell) and activate its differentiation into osteoclast. so, note here that osteoblast can secrete things that activate osteoclast differentiation and things that blocks it so. So, osteoclasts differentiation depends on the RANK-to-OPG ratio.

*Systemic factors that affect this ratio:

1) INCREASE osteoclast differentiation:

A) PTH (parathyroid hormone)

B) Steroids (endogenous or exogenous as drugs)

C)IL-1 (cytokine)

2) DECREASE osteoclast differentiation

A) sex hormones (estrogen and testosterone) [post-menopausal women are at higher risk of developing osteoporosis; because their estrogen level is low. They should take estrogen combined with progesterone, known as hormone replacement therapy (HRT), to prevent hyperplasia]

B) BMPs (bone morphogenic proteins)

*NOTE: (peak bone mass) is achieved in early adulthood after cessation of skeletal growth (~20 years old) and this point is determined by many factors -> polymorphism in vitamin D, LRP5, LRP6 receptors, nutrition and physical activity. Resorption > bone formation on 4th decade.

*Congenital disorders:

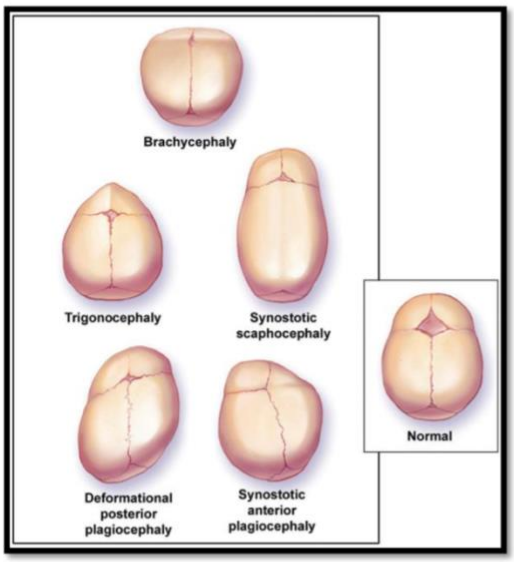
The spectrum of developmental disorders of bone is broad, and the classification system is not standardized. Here we will categorize the major diseases according to their perceived pathogenesis into 2 major groups:

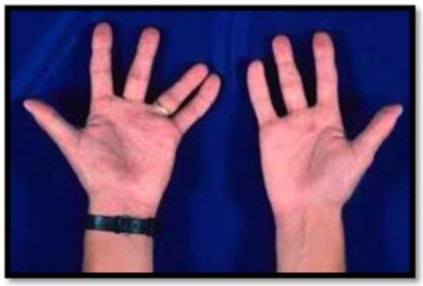
A) Dysostosis (dys= bad (abnormal), ostosis= bone formation)

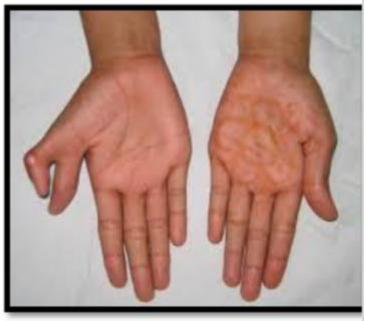
- It's defined as abnormal condensation and migration of mesenchyme.
- Genetic abnormalities that affect homeobox genes, cytokines and its receptor are especially common among dysostoses.
- The most common forms include: complete absence of a bone or a digit (aplasia), extra bone or digit (supernumerary digit), and abnormal fusion of bones (syndactyly & craniosynostosis)

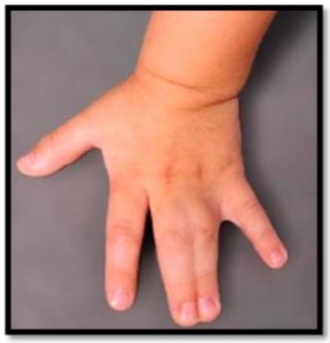
B) Dysplasia (will be discussed in the next lecture)

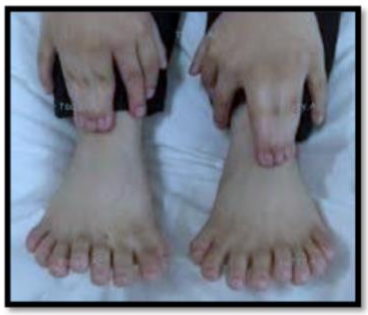
DYSOSTOSIS











THE END OF THE SHEET ☺