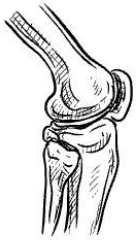
بسم الله الرحمن الرحيم



PATHOLOGY

MID | Lecture 1

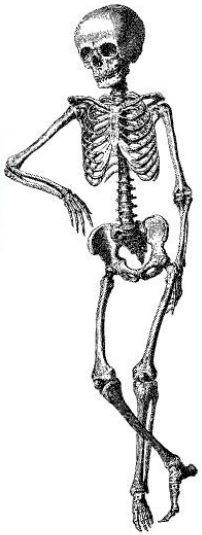
MSS & Skin Tumor – pt.1

Written by: Ansam Othman
Layan Fawarseh

Reviewed by: Mas Nafoukh

وَإِن تَتَوَلَّوْا يَسْتَبْدِلْ قَوْمًا غَيْرَكُمْ ثُمَّ لَا يَكُونُوا أَمْثَالَكُم

اللهم استعملنا ولا تستبدلنا



MSS & Skin Tumors Pathology 2025 Lecture 1

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Professor of Pathology & Cytopathology

University of Jordan

College of Medicine

BONE FUNCTIONS

- Mechanical support
- Forces transmission
- Protection
- Mineral homeostasis
- Hematopoiesis

BONE STRUCTURE

- **Matrix** (osteoid 35% and minerals 65% (calcium, phosphorous and others)):
  - Osteoid: organic type I collagen [the major component of osteoid and one of the strongest types of collagen] and glycosaminoglycans and other proteins
  - Inorganic hydroxyapatite [$Ca_{10}(PO_4)_6(OH)_2$]
  - Woven vs lamellar bone

- **Cells:** Will be discussed in the coming slides
  - Osteoblasts: forms bone

  the major component of bone cells , they lay and synthesize bone.
  - Osteoclasts: resorbs bone

  [the bone eating cells] ---> originate from the macrophage-monocyte system.
  - Osteocytes: mature bone cells

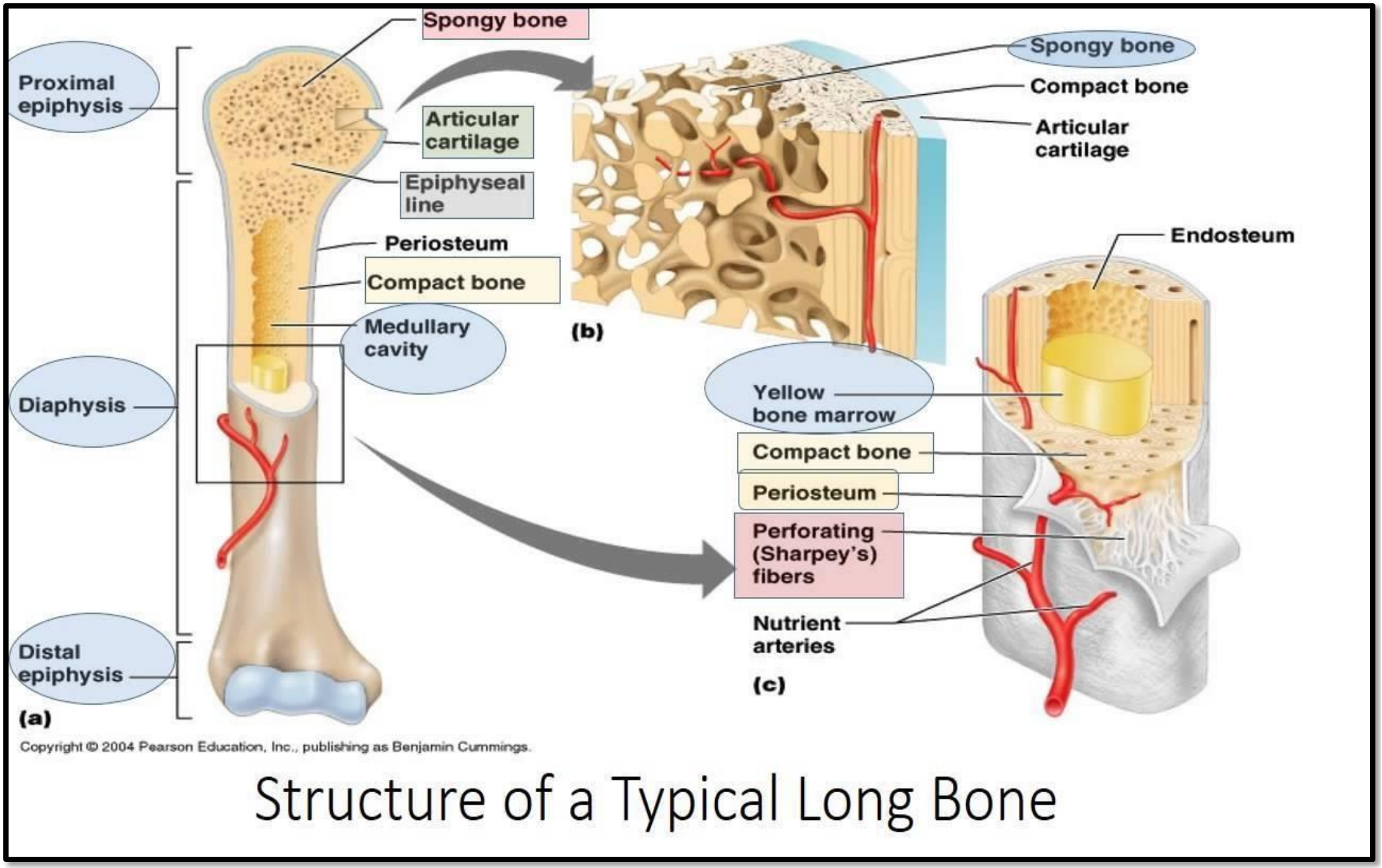
  less active, smaller in size than osteoclasts and osteoblasts and do not have too many cytoplasmic organelles for metabolic activity.

Notes regarding previous slide

- Recall types of collagen :

Collagen type 1 : bone forming
Collagen type 2 : cartilage forming
Collagen type 4 : basement membrane forming

- The Balance between bone formation [osteoblasts] and bone resorption [osteoclasts] is very critical in the understanding of many diseases like **osteoporosis** [the bone and the bone matrix gets less and the bone becomes weaker and exposed to many diseases and fractures].



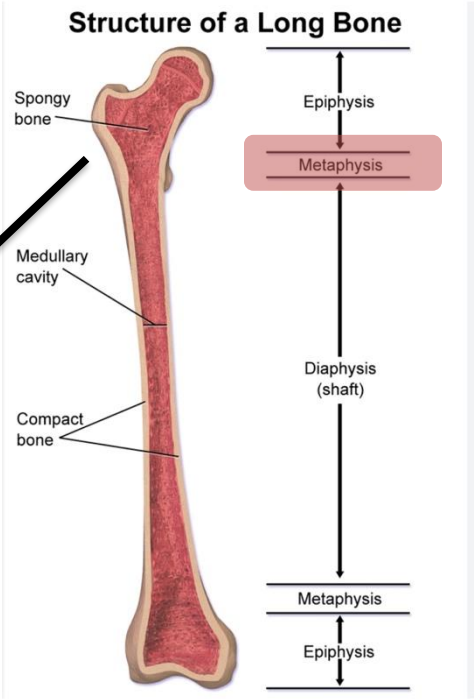
Structure of a Typical Long Bone

The histology of the bone

- Proximal and distal **Epiphysis**.
- **Epiphyseal plate**: where the growth occurs.
- **Periosteum**: the outer part of the bone which contains nerves [any irritation of periosteum will cause pain].
- **Compact bone**: below the periosteum and before getting into spongy bone marrow [it is very hard].
- **Medullary cavity**: which contains bone marrow particles where the major Hematopoiesis occurs.
- **Diaphysis**: the area located between proximal and distal epiphysis.
- **The endosteum**: The inner part of the compact bone.

Spongy bone = trabecular bone

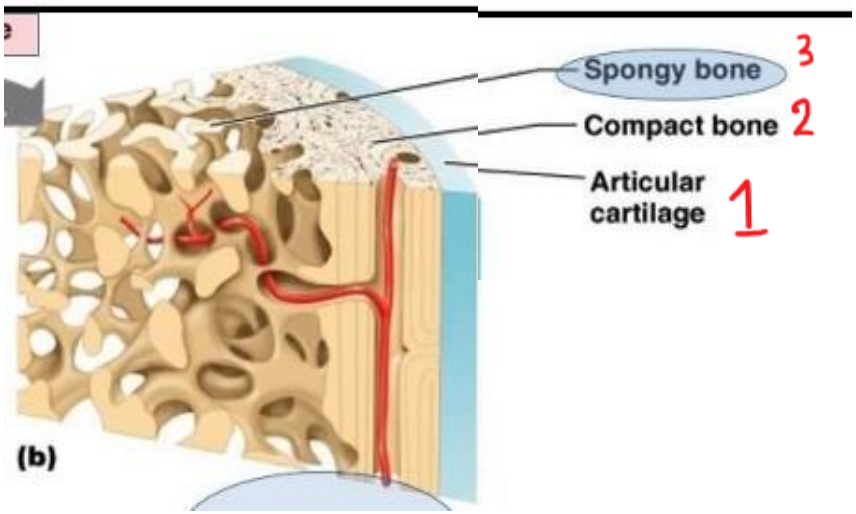
- There are certain fractures & diseases that affect the proximal epiphysis, some of them affect Diaphysis and some of them affect metaphysis.



An extra figure shows metaphysis which is the nick of the long bone (between epiphysis and diaphysis)

- As a summary

This high power figure shows the articular cartilage shown as number (1) below it we have compact strong bone shown as number (2) then trabeculae bone shown as number (3) , the blood supply comes from outside then goes to the penetrating arteries.



WOVEN VS LAMELLAR BONE

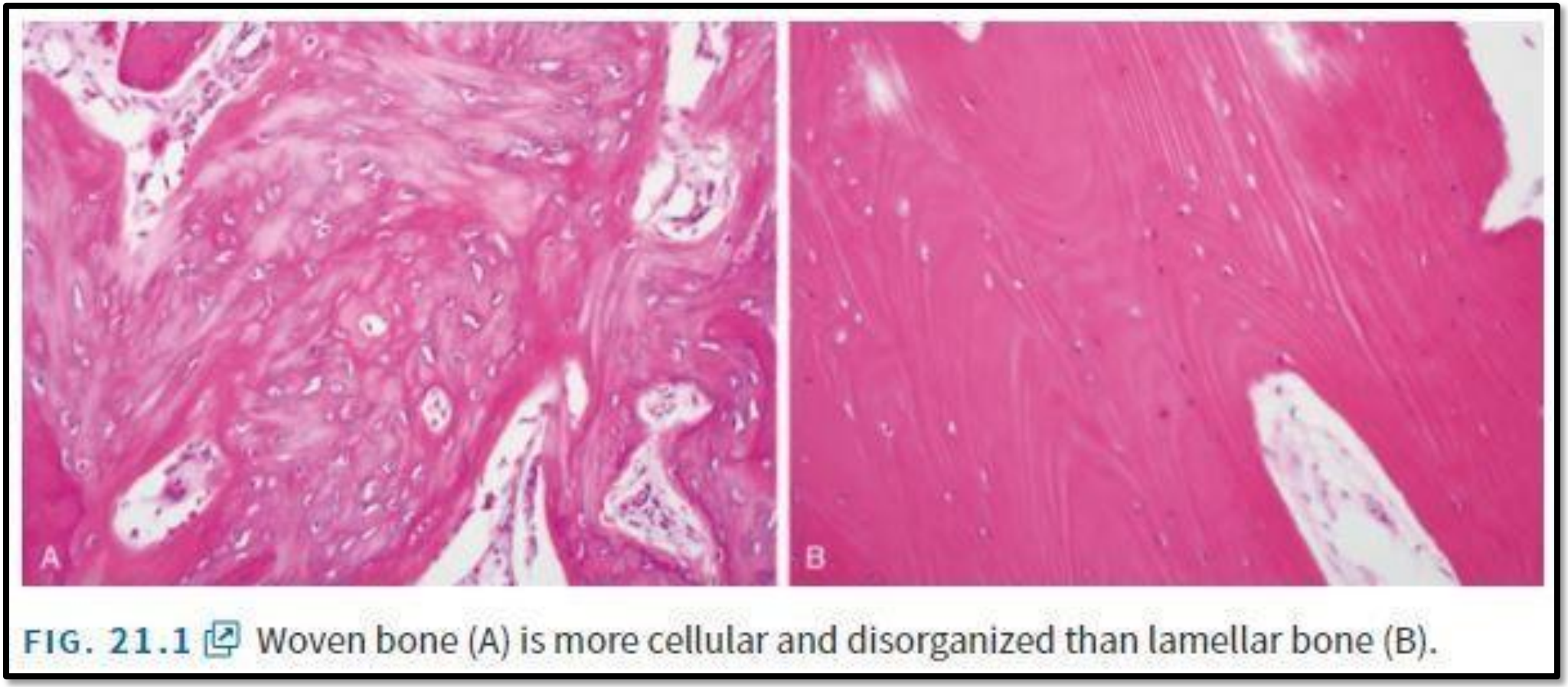
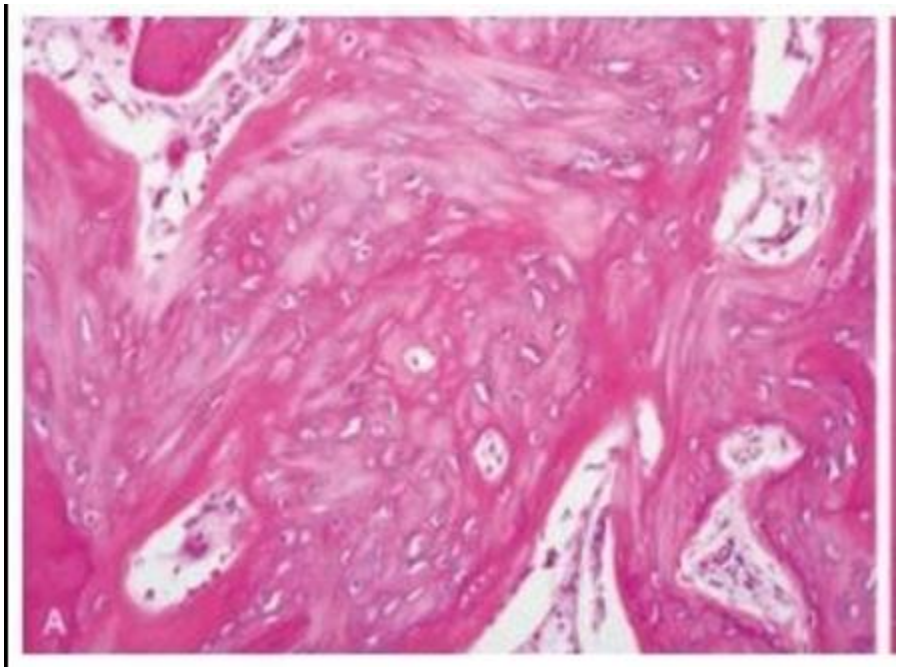


FIG. 21.1 Woven bone (A) is more cellular and disorganized than lamellar bone (B).

WOVEN VS LAMELLAR BONE

1- Woven bone

✓ More cellular and disorganized.
✓ The trabeculae are wider.
✓ The arrangement between cells
And type 1 collagen is haphazard.
✓ In early young born in children and in certain diseases.

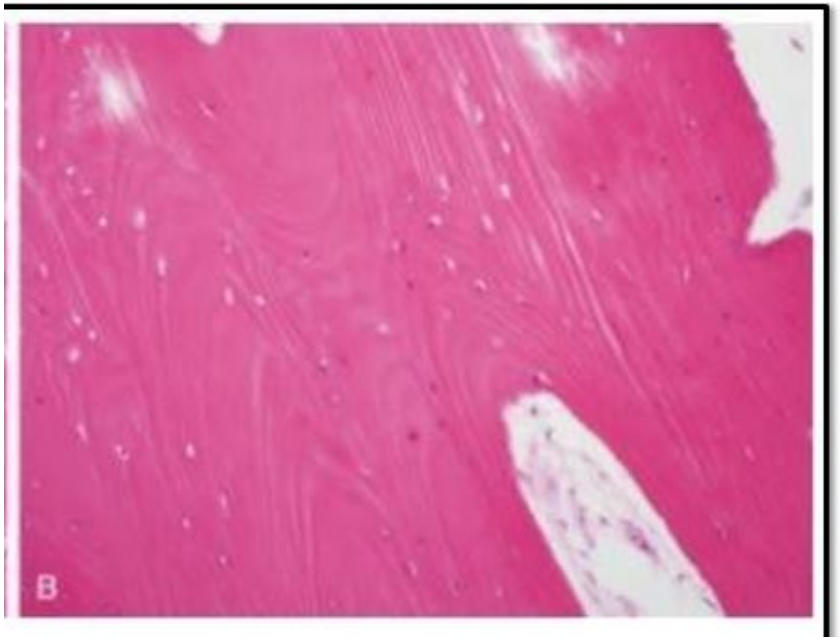


- In adults, if you see woven bone something wrong or abnormal is going on, whether it is malignancy or fracture site.

WOVEN VS LAMELLAR BONE

2- Lamellar bone

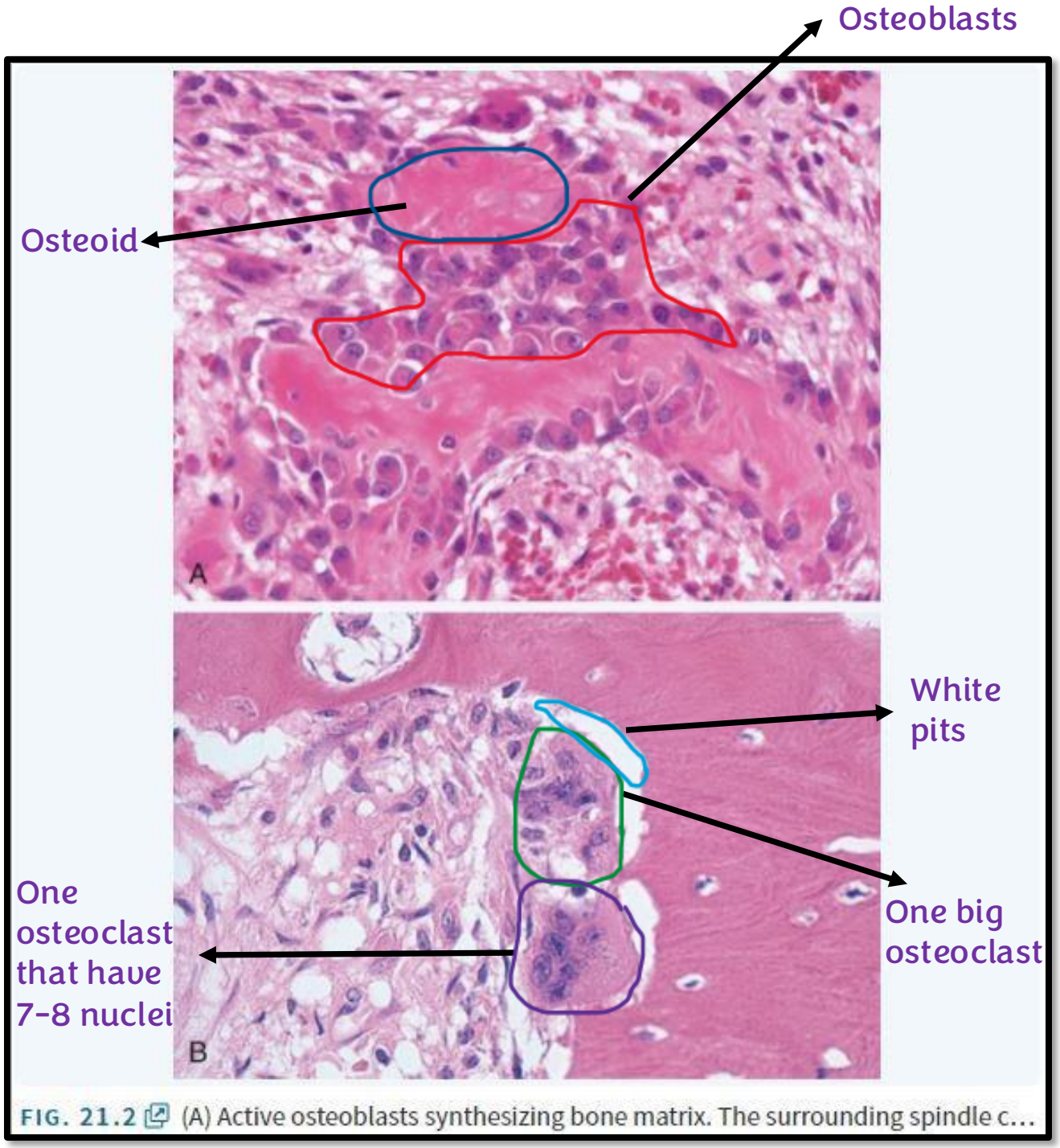
✓ The cells are more linear and organized
✓ Less cells
✓ main structure of mature long bones
✓ More collagen [strong]



Doctor said that he will give us the following pictures and ask which is lamellar and which is woven also ask when or where would you see this and that...

(Histological differences between osteoblasts and osteoclasts)

سبحان الله وبحمده



OSTEOBLASTS

- Smaller cells.
- They have higher nuclear cytoplasmic ratio than osteoclasts.
- Found around osteoid that are laid out and formed by osteoblasts.
- Mono-nucleus.

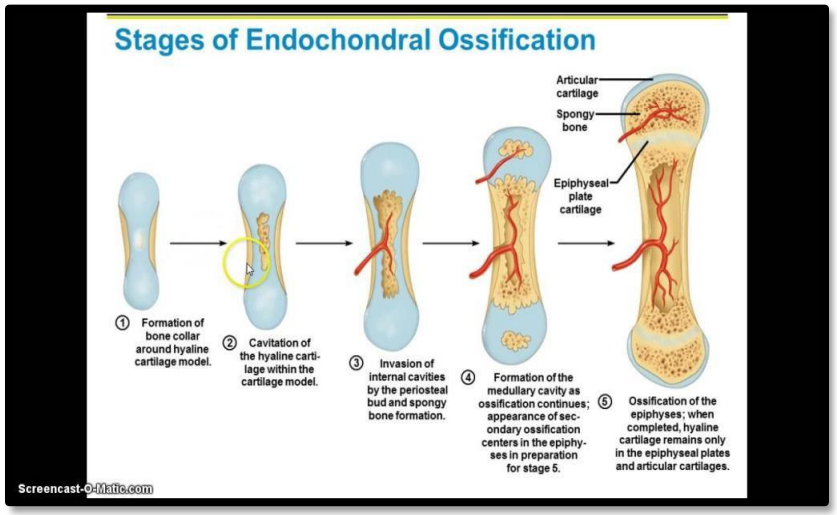
OSTEOCLASTS

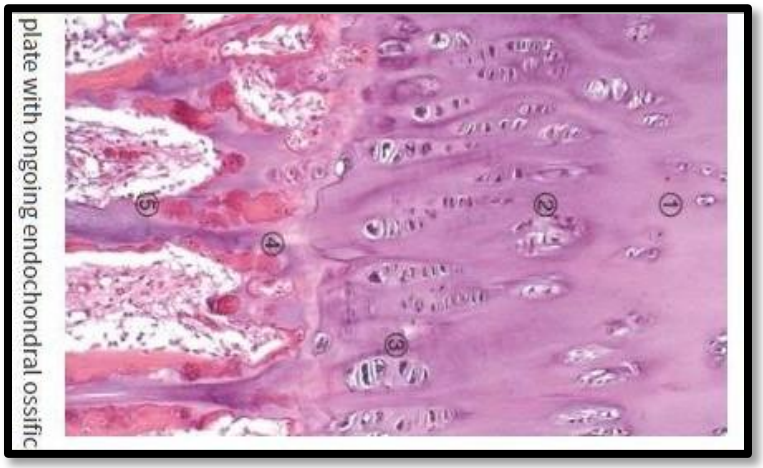
- Considered from the macrophages monocytic system.
- Its function is eating up mature bone (resorbs bone).
- White pits: where osteoclasts are eating mature bone.
- Multi-nucleated giant cells (may have 100-150 nuclei)

سبحان الله العظيم

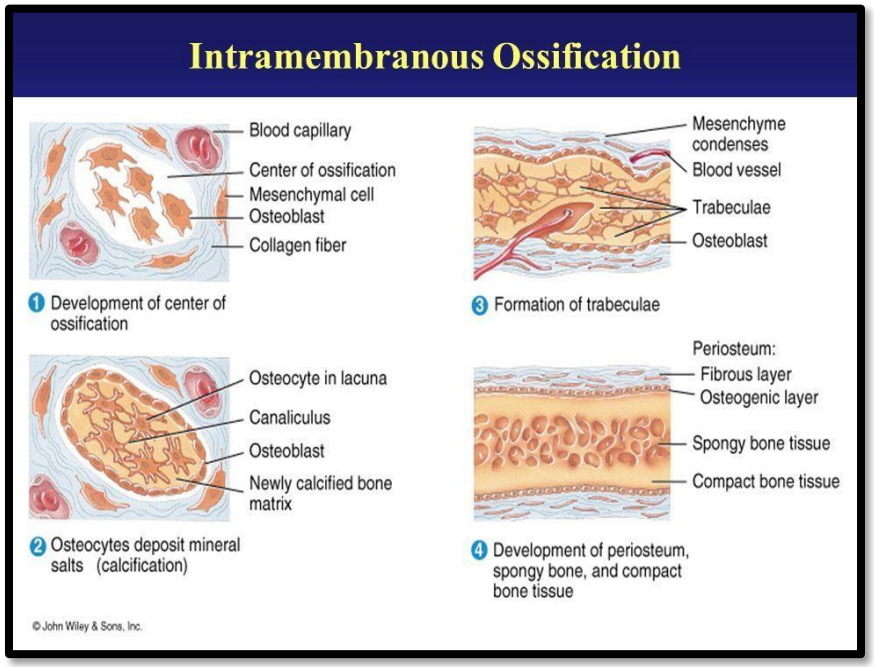
DEVELOPMENT

LONG BONES





FLAT BONES



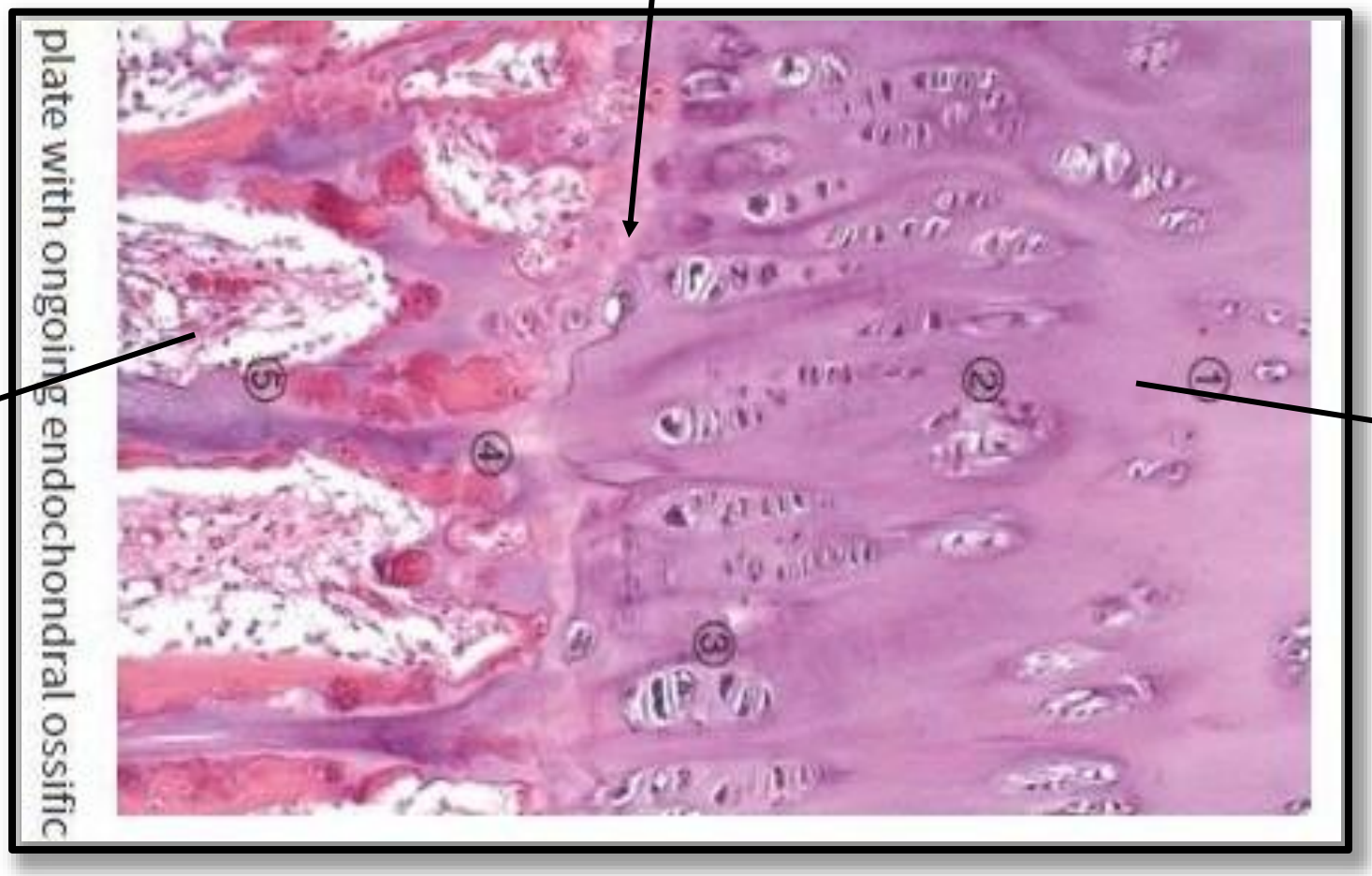
Take a deep look at the following pictures, then figure out the clarification in the next two slides.

There are two major ways for bone development (bone genesis):

	endochondral Ossification	Intramembranous Ossification
The need for cartilage:	Yes – Formation of bone from young mature cartilage in utero until mature bone in adults.	No – Doesn't require cartilage.
In which types of bone it happens?	Main process (method) in which **long** bones are formed.	Main method of **flat** bones formation ;e.g.: clavicle, scapular, pelvic bones, skull,...etc.
The progression of ossification:	cartilage → endochondral ossification starts in the center → most of long bone is replaced by mature bone	Basic mesenchymal cells start the process in the nidus and then bone formation continues without passing through ossification of cartilages.
Additional notes	there is only a remnant of articular cartilage at both ends.	___

Prof. Mousa indicated in the lecture that you have to see YouTube animation and other videos in order to understand both methods very well, he also advise you to reed this part from the book.

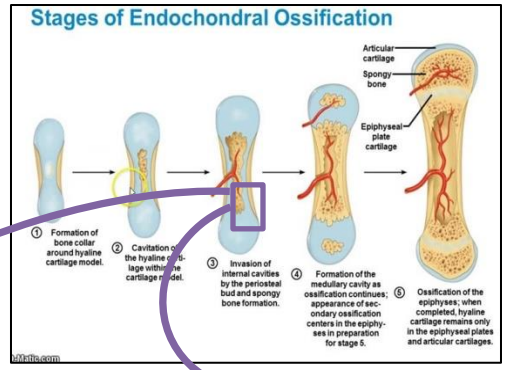
Growing process of endochondral ossification – histological view:

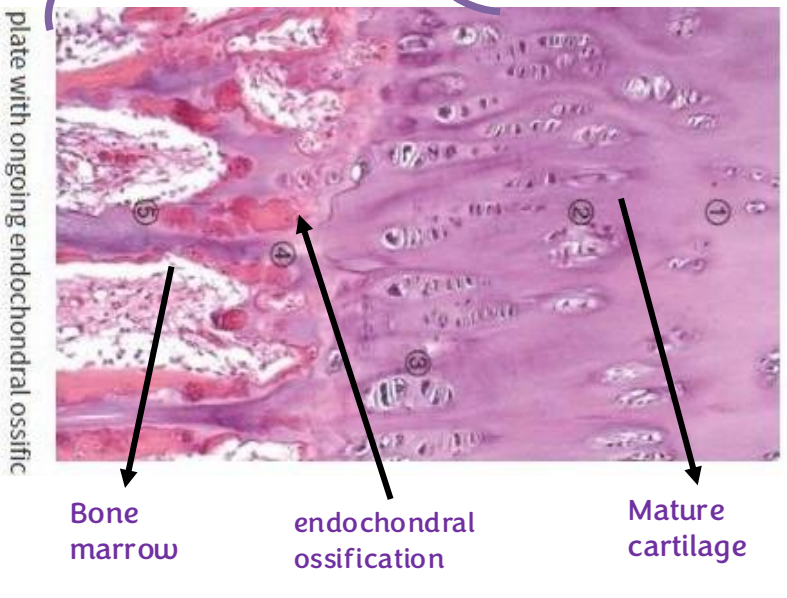


* This histological view indicates that this is a young bone which is being transformed by the process of endochondral ossification.

Extra slide – Regarding the controversial arrow :

- Prof.Mousa mentioned it in this direction, which already makes sense in this context:
- The arrow's direction means that bone is increasing, extending, spreading in this direction – just like a spill of water – so in this direction bone is increasing and cartilage is decreasing = (endochondral ossification (bone genesis) is increasing).
- As water is extending away from the bucket, the bone is extending from the center to the extremities.
- Regarding the numbers in the picture, these numbers are explaining it as separated tissues, but the arrow clarify the progression in the future.





"... وأنَّ غراسها: سبحان الله، والحمد
لله، ولا إله إلا الله، والله أكبر ..."

HOMEOSTASIS & REMODELING

- **Continuously** metabolizing **and dynamic** -not static- **complex process even in adult mature skeleton (microscopic level)**
- The balance between osteoblasts & osteoclasts function is changing continuously (+/-) depending on the age and the location of the bone.
- **Peak bone mass is reached in early adulthood after completion of skeletal growth,** in age 20 or 23 until 30, then it starts to decline depending on your athletic activity, movement, nutrition and supplies.
- **Resorption > bone formation on 4th decade;** main pathogenesis of the major metabolic syndrome of osteoporosis, this difference could be delayed or minimized.

EXTREMELY IMPORTANT TABLE

+ Osteoclast differentiation	- Osteoclast differentiation
Factors that activate it → tipping the balance toward more resorption: 1. PTH (parathyroid hormone) 2. IL-1 (interleukin-1) 3. Steroids (endogenous steroids production or exogenous steroid usage) (Steroid- taking patients may be advised to take vitamin-D and Calcium products)	Factors that de-activate it → tipping the balance toward less resorption: 1. BMPs (bone morphogenic proteins) 2. Sex hormones (estrogen & test.) (Some Athletes take androgenic sex hormones in order to increase their bone and muscle mass)

The Formation of Active Multinucleated Osteoclast

This cartoon is explained in the next slide.

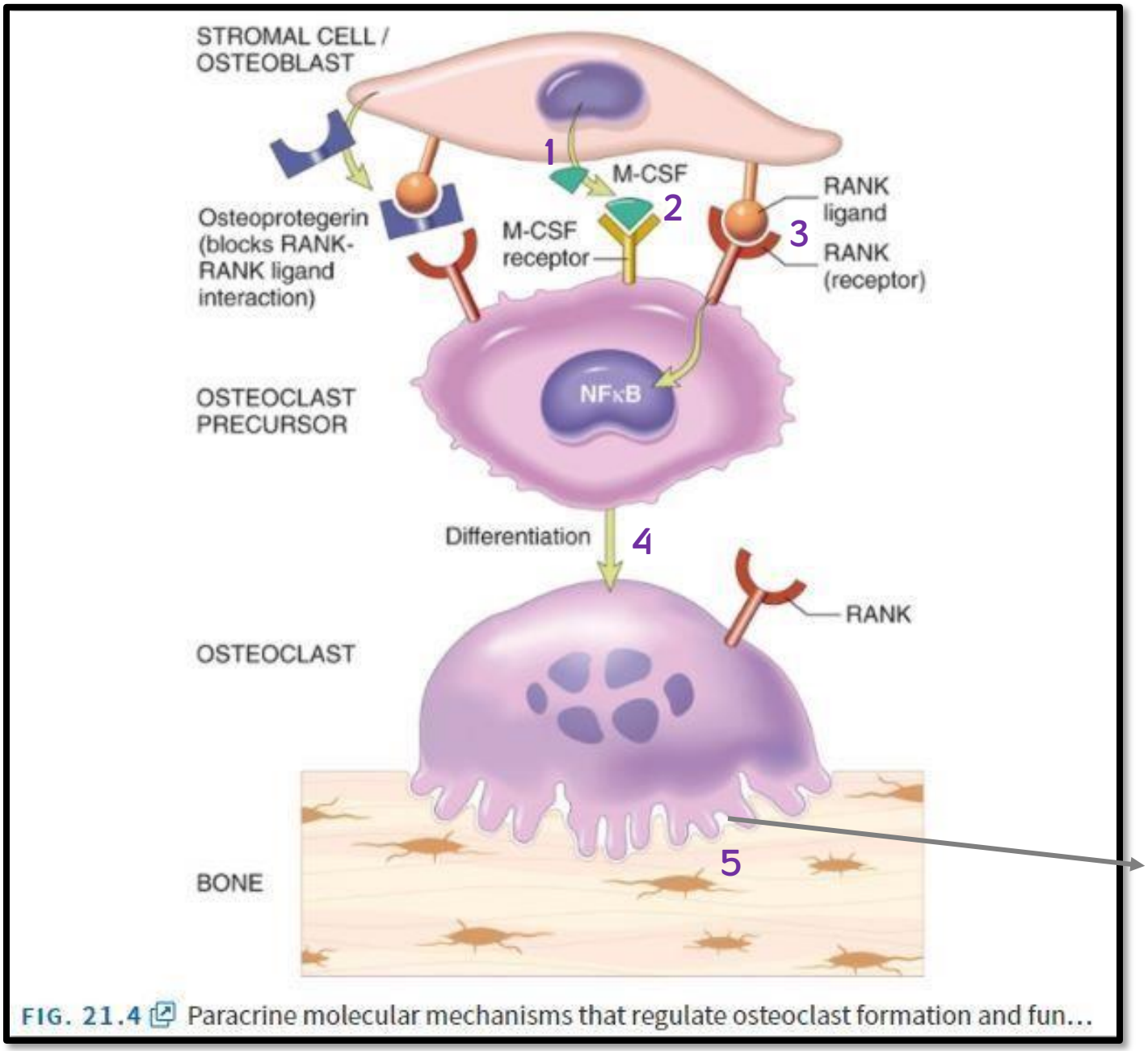


FIG. 21.4 Paracrine molecular mechanisms that regulate osteoclast formation and fun...

حسبي الله لا إله إلّا هو عليه توكّلت و هو رب العرش العظيم

Do you remember what is the name of the resorbed area around osteoclast? (: If no, go to slide 14 again.

☞ Process of Osteoclast Activation and Regulation:

1. M-CSF Secretion:

· Stromal cells secrete Monocyte Colony-Stimulating Factor (M-CSF).

2. Receptor Binding:

· M-CSF binds to receptors on osteoclast precursors, stimulating their production and maturation into osteoclasts.

3. RANKL-RANK Interaction:

· RANKL (Receptor Activator of Nuclear Factor Kappa-B Ligand), which is found on the surface of stromal cells, binds to the RANK receptor on osteoclast precursors.

· This interaction is crucial for the differentiation of osteoclast precursors into active osteoclasts.

4. Osteoclast Maturation:

· The binding of RANKL to RANK receptors triggers the maturation of osteoclast precursors into mature osteoclasts.

5. Bone Resorption:

· Activated osteoclasts begin resorbing bone tissue, leading to bone breakdown and weakening.

☞ Outcome of Excessive Osteoclast Activity:

· When osteoclast activity is too high, bone resorption exceeds bone formation, leading to osteoporosis, which results in weakened bones—which will be discussed later -.

☞ Therapeutic Intervention:

· Medications are developed to block the RANKL-RANK interaction by enhancing proteins-e.g.: osteoprotegerin) that prevent RANKL from binding to its receptor.

· This reduces osteoclast activation and bone resorption.

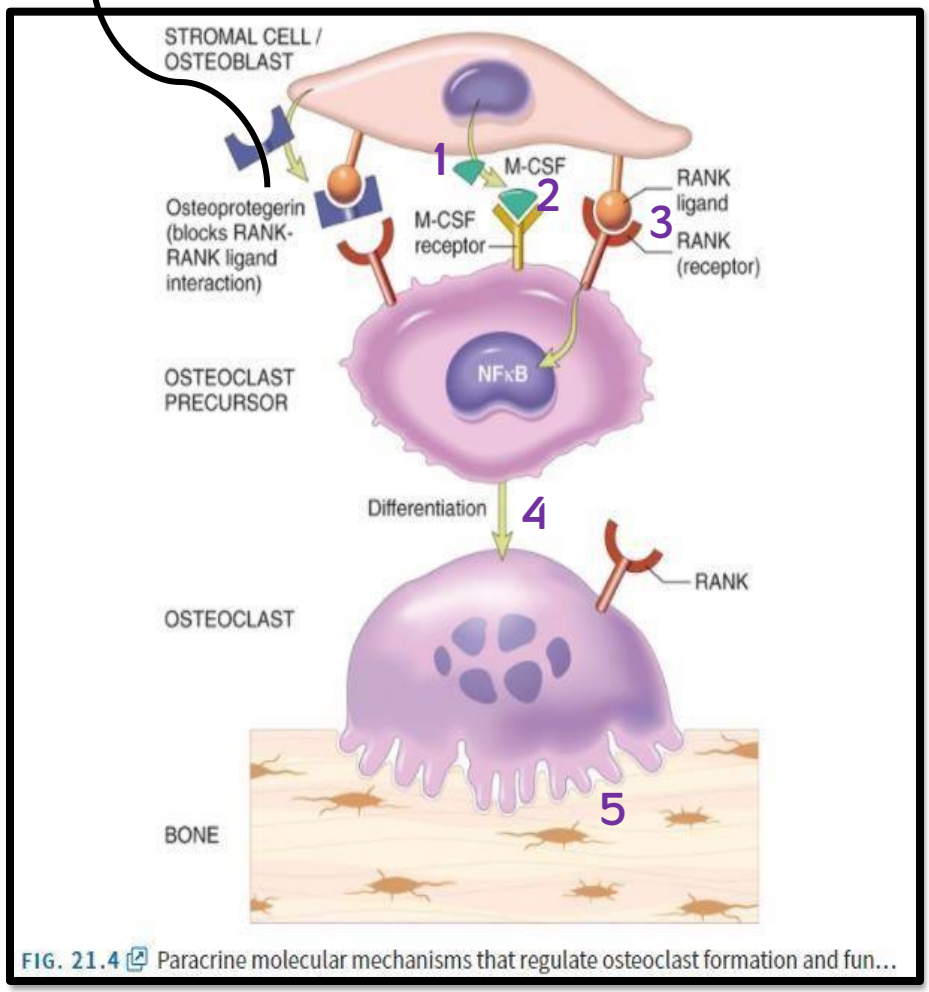
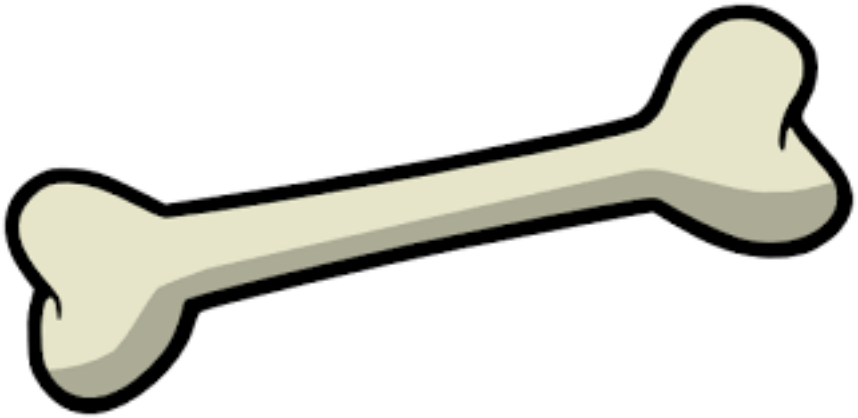


FIG. 21.4 Paracrine molecular mechanisms that regulate osteoclast formation and fun...

Each step is numbered with its place at the FIG, so plz Follow the order of steps to understand it.

Click on the diaphysis for a short quiz



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	---	---	slide 16 was added
V1 → V2			

Additional Resources:

Reference Used:

1. Robbins Basic Pathology 11th eddition

Extra Resources from Dr Mousa Alabbadi :

1. **Intramembranous Ossification**
2. **Ossification**

رسالة من الفريق العلمي:

صدق الله العظيم " أيامًا معدودات"، رمضان قصير لا يحتمل التقصير، وقدومه عبور لا يقبل الفتور ... فخالقك تبارك وتعالى وَهَبَك شهرين قبل رمضان، شهر تخلية من المعاصي (رجب) وشهر تحلية بالطاعات (شعبان)، فماذا أعددت لرمضان؟ وتذكّر قوله تعالى: " وَلَوۡ أَرَادُواْ ٱلۡخُرُوجَ لَأَعَدُّواْ لَهُۥ عُدَّةٗ وَلَٰكِن كَرِهَ ٱللَّهُ ٱنۢبِعَاثَهُمۡ فَثَبَّطَهُمۡ وَقِيلَ ٱقۡعُدُواْ مَعَ ٱلۡقَٰعِدِينَ" (التوبة-46)، سارع بحمل عدَّتِك وعتادك لرمضان فإنّ أبواب خيره ستُفتح قريبًا إن شاء الله، وتذكّروا أن من كانت بدايته مُحرقة كانت نهايته مُشرقة، وأنّ الخيل إذا شارفت على انتهاء السباق قدّمت كل قوتها لتظفر بالفوز، فعامل رمضان كأنّك مودّع ،واسعَ به كما كان يفعل القدوة الأولى حبيبنا المصطفى عليه الصلاة والسلام.

اللهم بلّغنا رمضان لا فاقدين ولا مفقودين وأعنّا على الصيام والقيام وتقبّله منا واجعلنا فيه من العُتقاء من النار واجعل أعمالنا كلها خالصةً لك.