Doctor 022

# Histology

## Sheet no.4


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# Types of bone:

**Table 8–1** Summary of bone types and their organization.

| Type of Bone | Histological Features | Major Locations | Synonyms |
|---|---|---|---|
| **Woven bone**, newly calcified | Irregular and random arrangement of cells and collagen; lightly calcified | Developing and growing bones; hard callus of bone fractures | Immature bone; primary bone; bundle bone |
| **Lamellar bone**, remodeled from woven bone | Parallel bundles of collagen in thin layers (lamellae), with regularly spaced cells between; heavily calcified | All normal regions of adult bone | Mature bone; secondary bone |
| **Compact bone**, ~80% of all lamellar bone | Parallel lamellae or densely packed osteons, with interstitial lamellae | Thick, outer region (beneath periosteum) of bones | Cortical bone |
| **Cancellous bone**, ~20% of all lamellar bone | Interconnected thin spicules or trabeculae covered by endosteum | Inner region of bones, adjacent to marrow cavities | Spongy bone; trabecular bone; medullary bone |

- Woven bone :the bone during it's formation ,lightly calcified and not organized ( can't get final organization and final mineralization. ) , and is formed during bone healing.

  Later on the body through osteoblast will digest woven and lay down newly bone (lamellar) which is more organized and mineralized

- Lamellar bone: woven bone transform into more organized form which is lamellar. Organization depends on how collagen is organized so lamellar is necessary. Most bone in adults, compact or cancellous, is organized as lamellar bone of calcified matrix.

- Compact bone : (is in the circumflex which is bigger lamellae outside the bone, but beneath the periosteum as we see in long bone ) tightly squeezed cells ,filled with lamellae (lamellae are sheets of the matrix) , no spaces (the only space present is central canal and filled with vessels and fluids that will go toward osteocyte). Compact is crowded by osteons, in other word it's crowded by lamellae. Compact represent 80% of all lamellar.

The orientation of collagen fibers (specifically collagen type 1) running in all direction into different lamellae -but not haphazardly- to cover all the axes to strengthen the bone in general. Collagen fibers look like lines while sectioning the osteon and looking at it's lamellae.

- Cancellous bone :20% of lamellar (the opposite of the compact)

  The more informal name is (spongy bone ). It's deep in the center, in the medullary cavity and in flat bones , cancellous has not concentric lamellae or interstitial fluid because there isn't any osteon. Between lamellae there are osteocytes. Lamellae form spicules or trabeculae which are interconnected together. Cancellous has spaces and the important thing is **bone marrow** (where monocytes originate in it then it give osteoclasts ) we have two types of bone marrow: 1*red (which contain a large amount of hematopoietic cells and of blood). 2*yellow bone marrow (has more fat cells, it increases with age and usually we see this marrow in medullary cavity).

## Compact and cancellous bone:

| | | |
|---|---|---|
| **Compact bone**, ~80% of all lamellar bone | Parallel lamellae or densely packed osteons, with interstitial lamellae | Thick, outer region (beneath periosteum) of bones |
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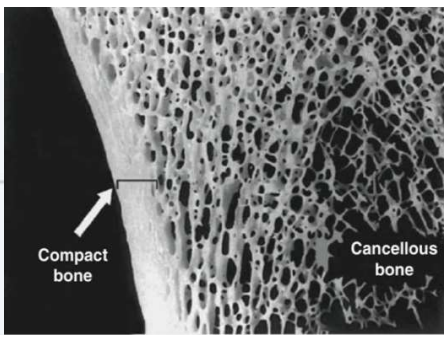


# The majority of the bone come from compact bone.

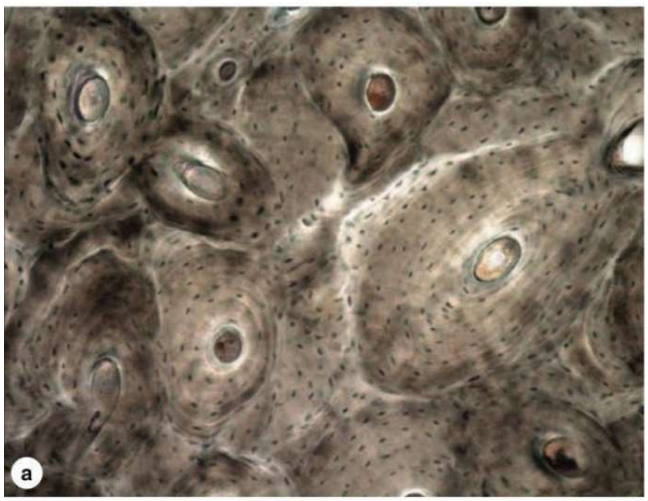
## Compact Bone osteons:

Each osteon **(Haversian canal)** is:

1. Formed of complexes of concentric lamellae.

2. 100-250 µm in diameter.

3. Surrounding a central canal that contains small blood vessels,





nerves and endosteum, it's lined by osteogenic cells.

**1) Cc: central canal**

**2) L:concentric lamellae**

**3) O:osteocytes in lacunae**

**4) c: canaliculi**

**5) I:interstitial lamellae.**

• It is **the characteristic structural unit** in compact bone, and only found in it.

Between concentric lamellae there is interstitial. Osteocytes in lacunae connect with each other, with central canal and periphery with osteon via dendritic processes inside canaliculi.

In the left picture a (ground bone specimen) decalcified; we know that since it's rounded cells that lack canaliculi in between. But the picture in the right side is calcified; since it's compact & it has canaliculi.

Slides in purple, doctor's speech in black

# Osteogenesis

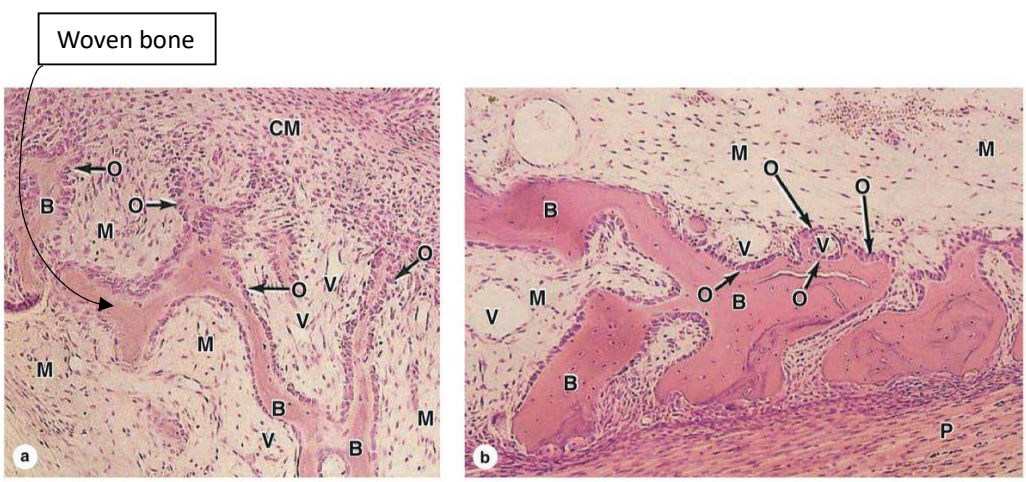
This the serious talk about bone formation.

When we talked about cartilage previously, we have seen it forms by one way which is chondrogenesis, **Intramembranous ossification** somehow close to what happen in cartilage (mesenchyme—bone—woven bone—remodelling—lamellar).

And the second one of the osteogenesis is **Endochondral ossification.**

**(Doctor here said that she recommends to read this topic from the book).**

## 1.Intramembranous:




Intramembranous means I have a pre-existing mesenchyme (which is connective tissue come from it), **(pic a)** these

condenses mesenchyme with good amount of blood coming, so we have a lot of blood vessels ( because this process require many resources, we need lots of nutrients, oxygen, energy in order to produce something new in the body), **this happens in the embryos,** so these mesenchymal stem cells will transform (differentiate) into osteoblast, and these osteoblast will start the deposition of the matrix, and they will lay down the matrix of the bone, and you will find woven bone and its beginning of its formation, its small amount of woven bone (because this is quit early), when you look at woven bone you should differentiate two types of cells, the ones in trapped (osteocytes), and those in the surface with larger number (osteoblast), and the majority cells in the field are mesenchymal cells.

**(pic2):** This more advanced (this photo tacked time after the first one), bigger amount of bone, and larger blood vessels, so we see more woven bone, more osteocytes in trapped, and we still see the osteoblast on the surface and only on the surface.

If you look in the bottom of the image you see **(P)**, it represents periosteum, where dose this periosteum come from?

Ans: from mesenchymal stem cells, (not all the mesenchymal cells they will become osteoblast), but some of them will differentiate to give us the elements of the periosteum, (dense irregular CT), what do I have to have it? We should have fibroblast, so some of mesenchyme will give us fibroblast, and some of them will remain in the inner cellular

of the periosteum (because in the future they will give us new fibroblast), and same thing will happen in the endosteum on the other side (that is not covered in this image).

some points related to **intramembranous ossification** from slides:

- Most flat bones form this way (bones of the skull, jaws, scapula and clavicle).
- Within the condensed mesenchyme begins in ossification centers----osteoblasts----woven bone with osteocytes in lacunae and canaliculi.
- The anatomical bone forms gradually as woven bone matrix is replaced by compact bone that encloses a region of cancellous bone with marrow and larger blood vessels.

- Mesenchymal regions that do not undergo ossification give rise to the endosteum and the periosteum.
- The fontanelles or "soft spots" on the heads of newborn infants are areas of the skull in which the membranous tissue is not yet ossified.
  (when we say bones of the skull, we says flat bones, but not all the cranial bone will form the final shape of the bone, because we have something called(fontanelles) (النافوخ), these are regions that the cranial bones do not completely approach each other and don't close the cranial cavity, and they have some spaces between them that are connected together by membranous tissue, and

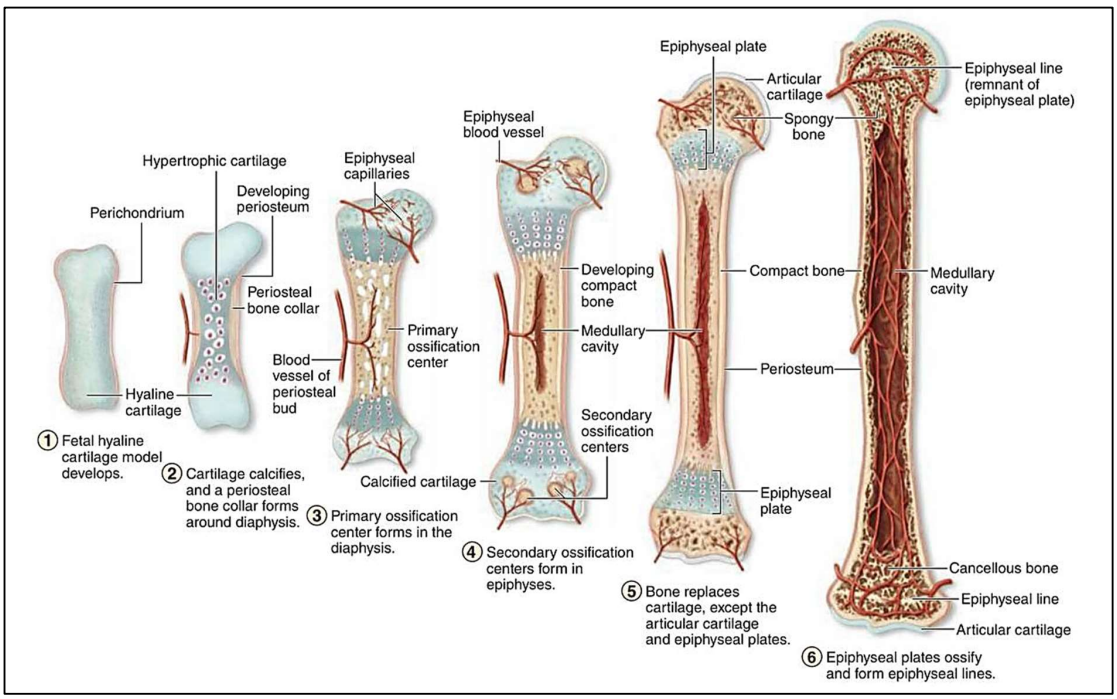
later on will complete final growth and then the two ends will fuse at a specific time point.

The other type of osteogenesis is the:

# 2. Endochondral ossification.

As the name mentions (endochondral) that means cartilage is involved. Its not directly transform from mesenchyme to the bone, we have something in transitional (in the middle) should occur. Instead of that mesenchyme will form bone, but it's not actually bone (it is similar to the bone in shape, but it's made entirely in **Hyaline cartilage**).

This will be replaced, and we will eventually end up with a bone.




(رح أعبر عن كل صورة منفصلة بكلمة step)

Step 1: This is a long bone, I have Hyaline cartilage, the event of Endochondral ossification begins in the first 3 months of the fetal life (first trimester).

Step 2: first thing that will form is what is called the **Bone collar.**

Now the question is where dose this bone collar come from?

We have cartilage (in the step1) which is have perichondrium on the outside, in the perichondrium specifically on the inner cellular we have mesenchymal stem cells, and they will differentiate into osteoblast instead of cartilage cells, because we have specific pathways (signal this event).

Step2 continuous: so, we have osteoblast which is mean bone, and bone formation occur which is lead to bone collar formation.

Now I have perichondrium, which is eventually will be replaced by periosteum, so we have a bone collar around the cartilage. Now the cartilage in the centre doesn't have a perichondrium around it, and as we know the cartilage relays on the perichondrium for nutrient by the blood vessels supply the cartilage cells by diffusion when they reaches to the perichondrium, but I no longer have perichondrium, I have only periosteum, so the presence of the bone collar eventually lead to final death of the cells in the centre because they be deprived of supply (nutrient), so the final result of this event no more cartilage, I have empty spaces (which was contain cartilage), and the matrix of the cartilage will undergo ossification, ( we have now empty spaces(ghost homes) with calcificated matrix of the previous cartilage), coincides with this (تزامنا مع ذلك )a vascularization increases, blood supply brings with it osteogenic cells which will make residence of the space that was previously occupied by the

chondrocytes,(in other words, they attach to the calcified cartilage) and start producing woven bone.

Step 3: we now have a bone with high vascularization and from outside periosteum, but we still have a cartilage in the two ends of the bone, is this beneficial? Absolutely, we have to preserve this cartilage in the two ends where we have Epiphysis connected to the diaphysis, these two ends we should name them **growth plate** or **Epiphyseal plate**, and the growth of the Epiphyseal plate is the one will actually give the bone the chance to grow, and it will grow and proliferation, but in the same time this cartilage will remove from both ends and increase the bone size.

(بكبر الcartilage, بيجي الbone بزيل الcartilage وبزيد وبكبر)

Step 4: As we said the first sign of ossification or (primary ossification) start around the **first trimester**, and after birth another sign of ossification starts **(secondary sign of ossification)** or **(secondary ossification centers)** and they appear as the starting of the bone formation in the Epiphysis.

Step5: we have removed most cartilage except for the articular and I still have the Epiphysial plate (which is as we mentioned allowed the bone to become longer), but at certain time (18 years old) in average it will be all removed (Epiphysial plate) and this whole structure is bone except the articular surface (as in the step 6)

Now the next points were mentioned in the slides related to **Endochondral ossification:**

1. Takes place within hyalin cartilage shaped as a small version of the bone to be formed.
2. Forms most bones of the body (well-studied in developing long bones).

3. First occurs within a bone collar (osteoblasts that differentiate within the perichondrium (transitioning to periosteum)).

The collar impedes (separate or deprive) diffusion of oxygen/nutrients into the underlying cartilage --local chondrocytes hypertrophy (increase in size) --compress the matrix--- calcification (osteocalcin and alkaline phosphatase)--- death.

4. The hypertrophic chondrocytes eventually die, creating empty spaces within the calcified matrix.

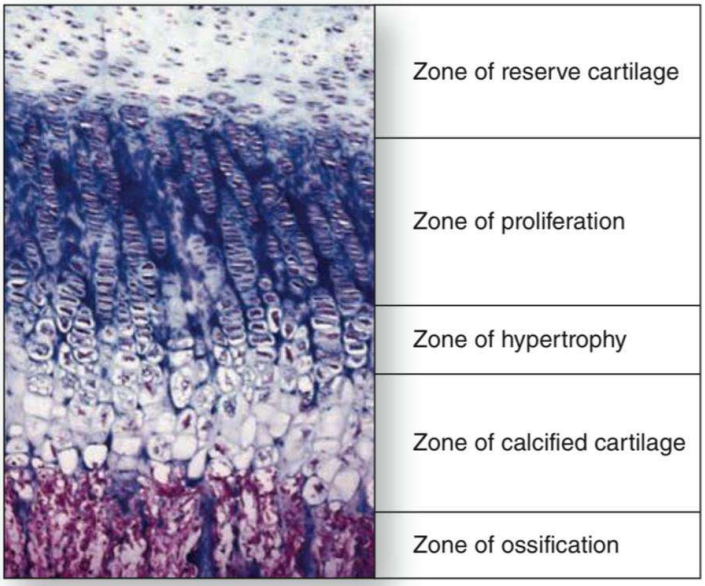
5. **Primary ossification center:** blood vessels from the perichondrium (periosteum) penetrate the bone collar--osteoprogenitor cells--- produce woven bon (first trimester).

6. **Secondary ossification centers:** appear later at the Epiphyses.

   **Cartilage remains**:
   - Articular cartridge breezed through adult life

- epiphyseal cartilage (epiphyseal plate or growth plate): connects each epiphysis to the diaphysis--longitudinal growth.

One step backword, what happen in the epiphysial plate? What are the events happen in it? We will talk about it, but in terms of zones.



**b** Epiphyseal plate

Zone of reserve cartilage:

This is where the future chondrocytes are coming, وأيضا هذا بغذي باقي الzones

Zone of proliferation:

It comes from zone of reserve cartilage.

والخلايا بزيد عددهم بشكل كبير (chondrocytes or chondroblast)

They will release the matrix around them.

They will organize into columns.

In terms of staining, look to the deep basophilia of the cartilage, that's typical hyaline cartilage because its matrix rich with negatively charged GAGs.

Zone of hypertrophy:

The cells will be bigger and swollen, more area for cells less matrix, that will eventually go through calcification (in the next stage).

Increased vascularization which is very important to bone formation to provide the osteoblast with the nutrient they need to lay down the new matrix of the bone

Zone of calcified cartilage:

The cells will go through apoptosis and the matrix between them will be calcified, and we prepare this area for the next stage.

Zone of ossification ما حكت اشي خارج السلايدات عنه

## Proliferative zone:

The cartilage cells divide---enlarge- matrix release.

Become organized into columns.

**Zone of hypertrophy:**

Contains swollen terminally differentiated

chondrocytes.

Increased vascularization.

**Zone of calcified cartilage:**

Chondrocytes about to undergo apoptosis.

Release matrix vesicles and osteocalcin.

**Zone of ossification:**

Bone tissue first appear.

Capillaries and osteoprogenitor cells invade the vacant chondrocytic lacunae.

Osteoblasts settle in a layer over the spicules of calcified cartilage matrix and secrete osteoid

(becomes woven bone).

Woven bone is then remodelled as lamellar bone.

Osteoporosis and osteopetrosis they are opposite to each other, which one is more related to the lighter bone? Osteoporosis.

Whereas osteopetrosis the bone is more dense.

# Osteoporosis هشاشة العظام

- Frequently found in immobilized patients (due to extreme heavy weight or due to specific medical conditions) and in postmenopausal women (females after they no longer have their periods, its all related to the hormones which effect on bone biology)
- The less physical activity you are engaged the more negative impact will be in your bones.

- Is an imbalance in skeletal turnover (I am losing more than I am adding, in other words I lose from bone tissue or from matrix more than the deposition amount, (more resorption less formation),I am loosing the inorganic material particularly calcium) so that bone resorption exceeds bone formation---calcium loss---reduced bone mineral density (BMD).
- Individuals at risk are routinely tested for BMD by dual-energy x-ray absorptiometry (DEXA scans).

(The people with osteoporosis have weaker bone, if they fall, they likely have a high probability to have fractures, so this patient should be managed in the clinic in terms of specific medications they need to take in terms of their diets, what they should eat to make sure that they manage the condition)

# Osteopetrosis

- Genetic disease.
- Characterized by dense, heavy bones ("marble bones").

- The osteoclasts lack ruffled borders and bone resorption is defective.
  (Osteoclast is responsible for resorption, the size of cancellous increases, and the spaces of bone marrow will fill with bone tissue, increase the general density of bone)
- Overgrowth and thickening of bones---obliteration of the marrow cavities--depressing blood cell formation--anaemia and the loss of white blood cells. (less amount of RBC WBC)

## ›› MEDICAL APPLICATION

The network of dendritic processes extending from osteocytes has been called a "mechanostat," monitoring areas within bones where loading has been increased or decreased, and signaling cells to adjust ion levels and maintain the adjacent bone matrix accordingly. **Lack of exercise** (or the weightlessness experienced by astronauts) leads to **decreased bone density**, due in part to the lack of mechanical stimulation of these cells.

The last thing we will take about is the role of the osteocytes and particularly their processes in canaliculi, these processes not only use of them to communicate with the other cells and nutrition for that cell, but also they act as what we called "mechanostat", so it's actually the tool the chondrocytes uses to know what's going on in the bone matrix,(how much I have of pressure on the bone), that's common between people with low physical activity then our mechanostat will signal osteocytes and then will this adjust the level of the mineralization of the matrix, one good example of this is the astronaut, no gravity, they don't walk, they don't move, they don't use much of their muscles( the environment around them is the one that actual move them), and this muscles is attached to the bone and that's why the bone can feel if we moving or no, so this will give same sense as someone not exercising or more, so this lead eventually to decrease bone density because the decrease in mineralization of the bone matrix.

# V2: in page4

We deleted the last paragraph

(Which was: In these pictures a
(ground bone specimen)decalcified and
unstained was put in plastic resin.

We add istead

In the left picture a(ground bone
specimen)decalcified;we know that
since it's rounded cells that lack
canaliculi in between.
But the picture in the right side is
calcified; since it's compact& it has
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