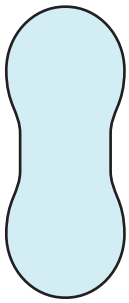
Endochondral Ossification

A Pictorial Guide of

Long Bone Formation

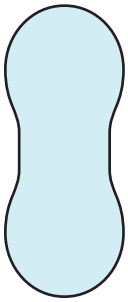
To Accompany Lecture



By Noel Ways

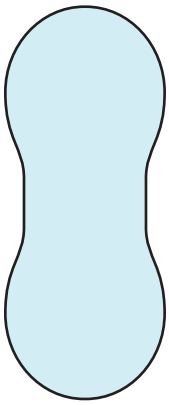
The Cartilage Model

Long bone formation begins with development of a hyaline cartilage "model" of the future bone.

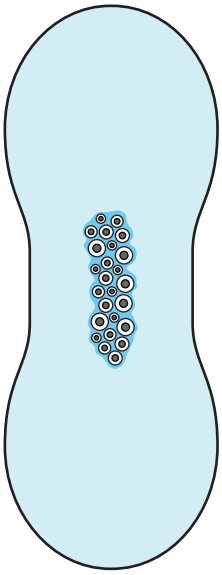


Characteristics of hyaline cartilage:

- Avascular
- Surrounded by a perichondrium
- Receives nutrition by simple diffusion through the perichondrium from the surrounding vascular tissues.
- Cartilage growth occurs appositionally and interstitially.

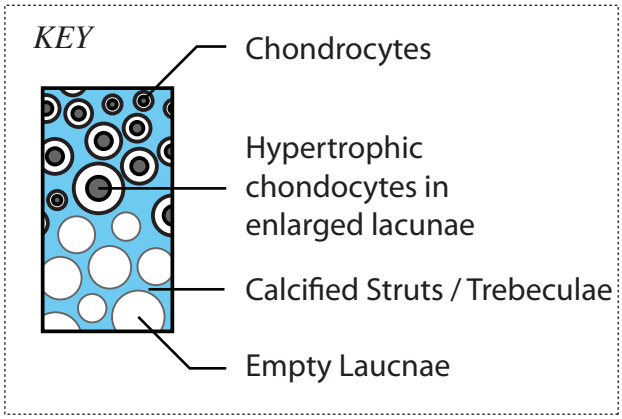


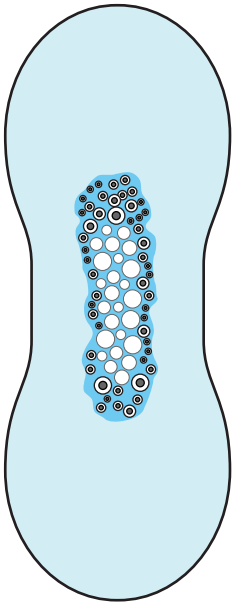
Cartilage growth during this time is rapid, occurring both appositionally as fibroblasts within the perichondrium give rise to chondrocytes which secrete new matrix. Interstitial growth occurs within the matrix as chondrocytes divide and produce new matrix.



Initial Calcification

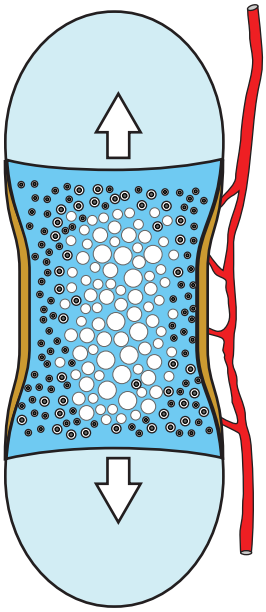
As the cartilage enlarges, chondrocytes within the center of the matrix become further from the source of nutrients, making life support difficult. Chondrocytes respond by enlarging, and as they do, their lacunae likewise enlarge. Another consequence of this process is matrix calcification. This further impedes nutrient passage. Eventually, nutrient deprivation leads to chondrocyte death, leaving behind their empty lacunae, now surrounded by calcified matrix.





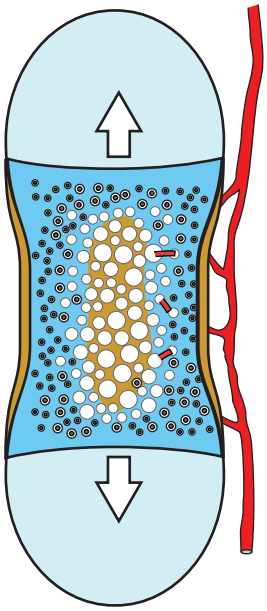
Calcified matrix, and bone tissue: Know the difference

- *Calcified Matrix:* matrix where calcium salt deposits have formed. This is not bone tissue as it is not formed nor maintained by cells and it is not under significant homeostatic control.
- *Osseous (Bone) Tissue:* osteoblast activity results in matrix secretion followed by calcification. This calcified matrix will be maintained through time as osteoblasts differentiate into osteocytes. Osseous tissue is a living and dynamic tissue under control of precise homeostatic regulatory mechanisms.



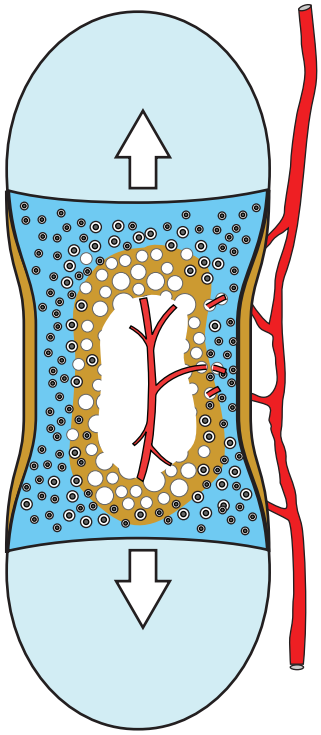
Vacularization

Blood supply develops along cartilage perimeter, and at this time the perichondrium is converted into the periostium. Therefore, the fibroblasts function as osteoprogenitor cells and promote appositional bone growth. Here, osteoprogenitor cells give rise to osteoblasts, which secrete a matrix that spontaneously ossifies. This tubular structure is called the periosteal collar . Appositional growth will continue on the deep surface of the periostium. As this collar of bone continues to grow lateral expansion of hyaline cartilage begins to be impeded, forcing cartilage growth to be longitudinal, only.



Primary Ossification Center

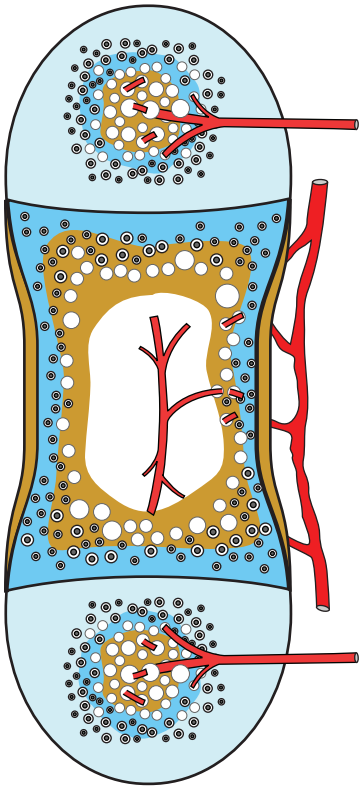
Blood vessels now penetrate the bone, and begin to grow through the “empty” lacunae. This blood supply allows osteoprogenetor cells to enter the developing bone. Osteroprogenitor cells give rise to osteoblasts which produce bone tissue around the calcified matrix surrounding the empty lacunae. This results in the production of the plate-like trabeculae.



Medullary Cavity

Simultaneously, osteoclasts migrate into the matrix and begin to reabsorb calcified matrix and bone tissue. The collective action of both osteoblasts and osteoclasts results in the establishment of the primary ossification center.

Continued osteoclast activity forms the medullary cavity, which continues to enlarge while the osteoblasts simultaneously produce new osseous tissue. At this time bone formation proceeds at the same rate as bone reabsorption. As the primary ossification center expands, growing closer to the periosteal collar, all the calcified matrix and cartilage will be transformed into osseous tissue, and the primary ossification center and the periosteal collar will have fused.



Secondary Ossification Centers

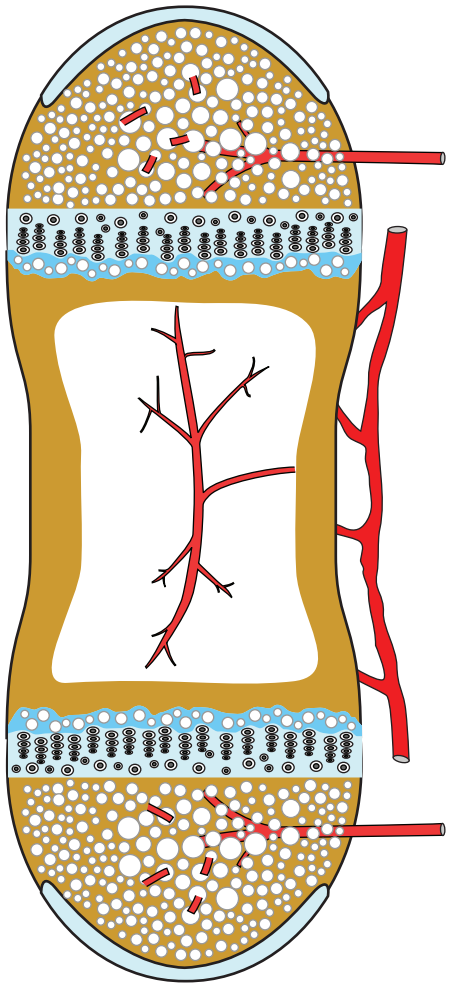
The conversion process from calcified matrix to osseous tissue continues with an ever expanding medullary cavity.

As this continues, blood vessels penetrate the proximal and distal epiphyses establishing two secondary ossification centers. There is now a "repeat performance" where cartilage degrades and osteroprogenitor cells give rise to osteoblasts which lay down the trebecular (or spongy) bone. Osteoclasts will also help in forming the spaces between the trabeculae, however a medullary-like cavity does not form.

Growth Plate and Articular Cartilage Formation

As endochondral ossification continues, all cartilage tissue is replaced with osseous tissue except for two regions:

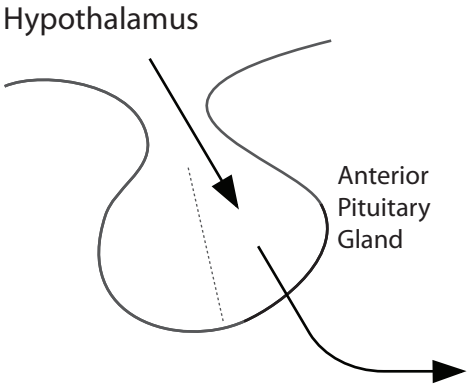
- First, where the bone is to articulate to another bone, the cartilage will now serve as the articular cartilage.
- Second, between the diaphysis and the two epiphysis, there is a disk of hyaline cartilage called the growth plate or the epiphyseal plate. It is this region where significant longitudinal growth will occur up through puberty.



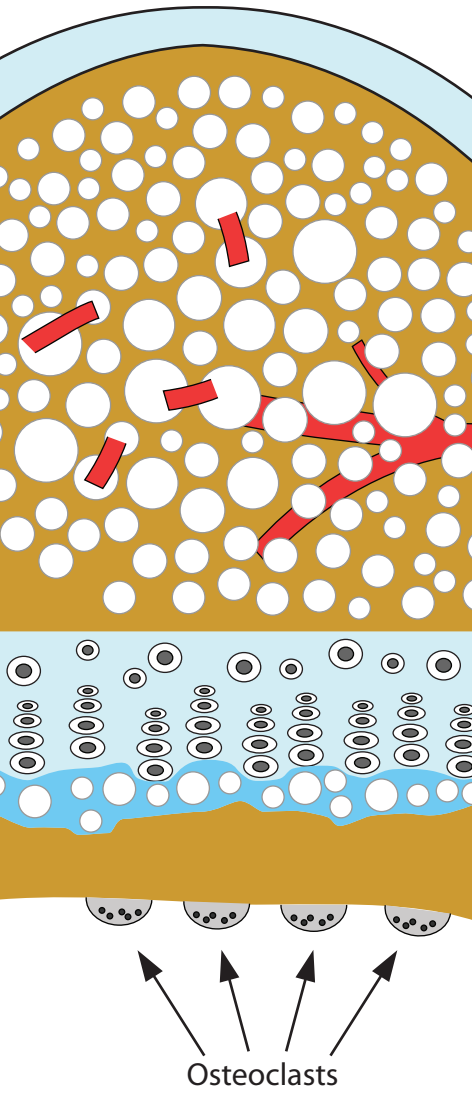
Growth Plate Maintenance and Proliferation

Continued bone growth depends upon continued stimulation of the growth plate which is maintained by the presence of human growth hormone, secreted by the hypothalamus. Human growth hormone stimulates the proliferation of chondrocytes. As new cartilaginous matrix is secreted, the epiphyses are moved further apart. Older chondrocytes die and in this region bone formation continues in similar fashion as described previously.

Simultaneously, osteoclasts reabsorb old bony matrix and enlarge the medullary cavity.



Human Growth Hormone



Articular Cartilage

Bone

Resting Cartilage (Mature cartilage adheres growth plate to epiphysis)

Zone of Proliferation (Area of interstitial growth)

Zone of Hypertrophy and matrix calcification (Region where chondrocytes enlarge and apoptose)

Osseous Tissue

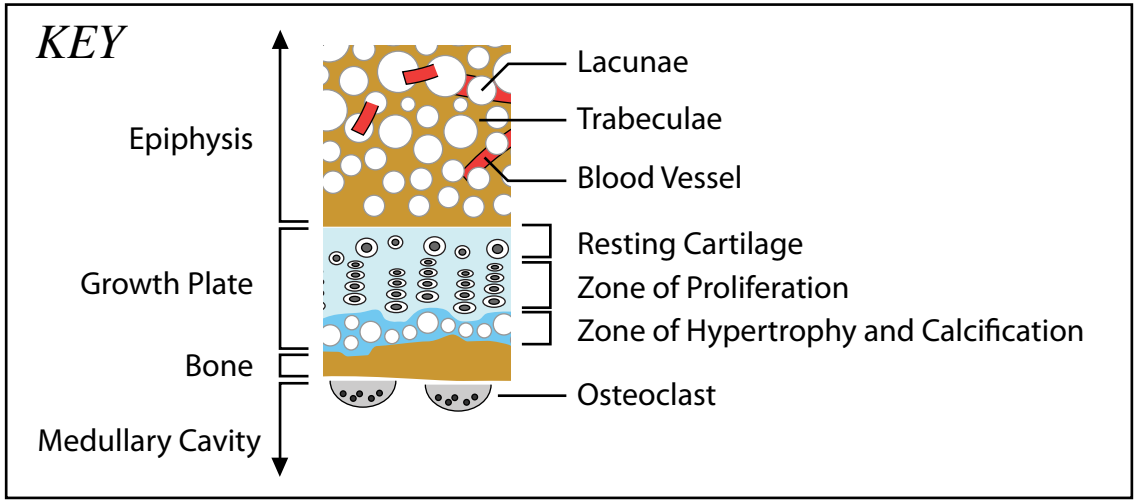
Growth Plate

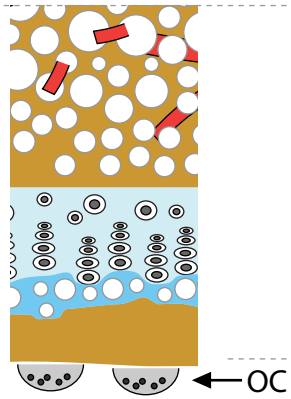
Medullary Cavity - osteoclasts reabsorb calcified matrix which is subsequently replace with osseous tissue by osteoblast activity.

Osteoclasts

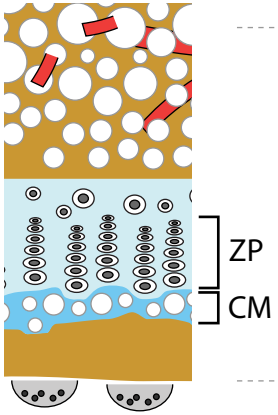
Growth Plate Activity

Note that all steps shown occur simultaneously and at the same relative rates.

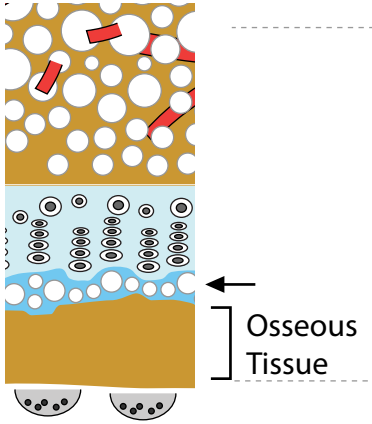




1. Starting point. All zones involved with bone growth are present as well as osteoclasts (OC) within the medullary cavity.

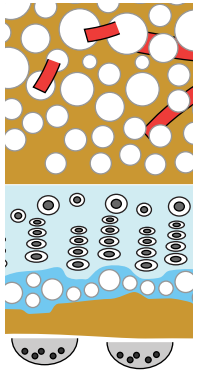


2. Zone of proliferation (ZP) exhibits interstitial growth. The epiphysis is pushed further away from the medullary cavity and diaphysis as this growth continues.



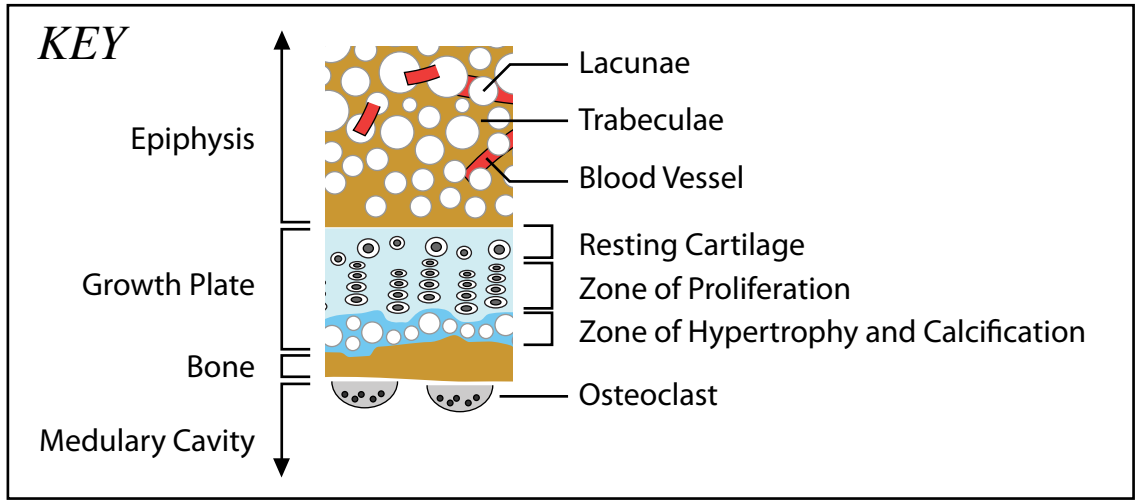
3. Older chondrocytes enlarge (←) and make new cartilage matrix. This is then followed by chondrocyte apoptosis and matrix calcification.

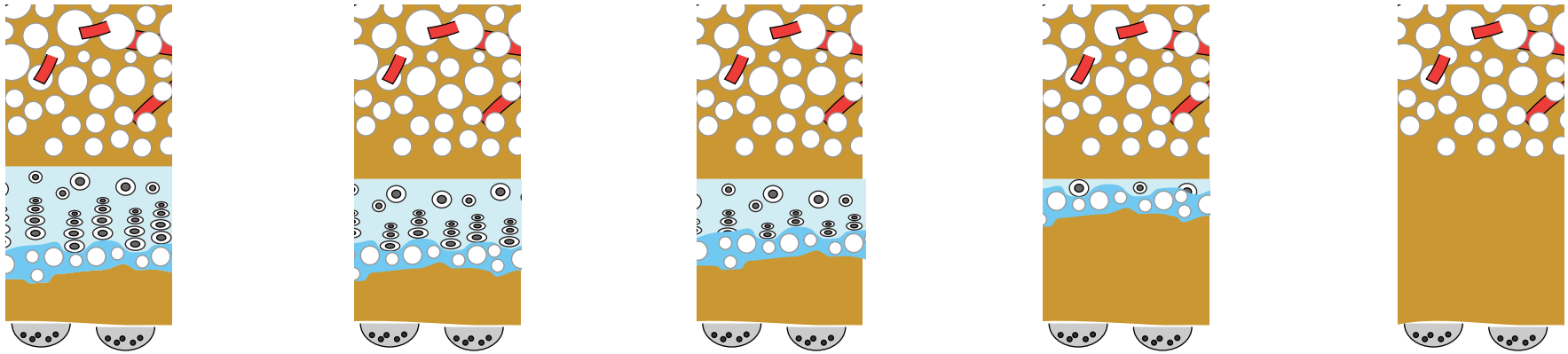
Note osseous tissue has expanded due to osteoblast migration and activity with new matrix



4. Osteoclast activity now reabsorbs calcified matrix and bone, enlarging the medullary cavity.

Puberty and Beyond





With the onset of puberty, hormonal changes result in altered rates in the processes involved in bone formation. In particular, bone tissue formation exceeds the rate of cartilage proliferation. This results in the gradual disappearance of the growth plate. Once all growths plate have ossified, the individuals stature is set and growth in hight will not again occur.