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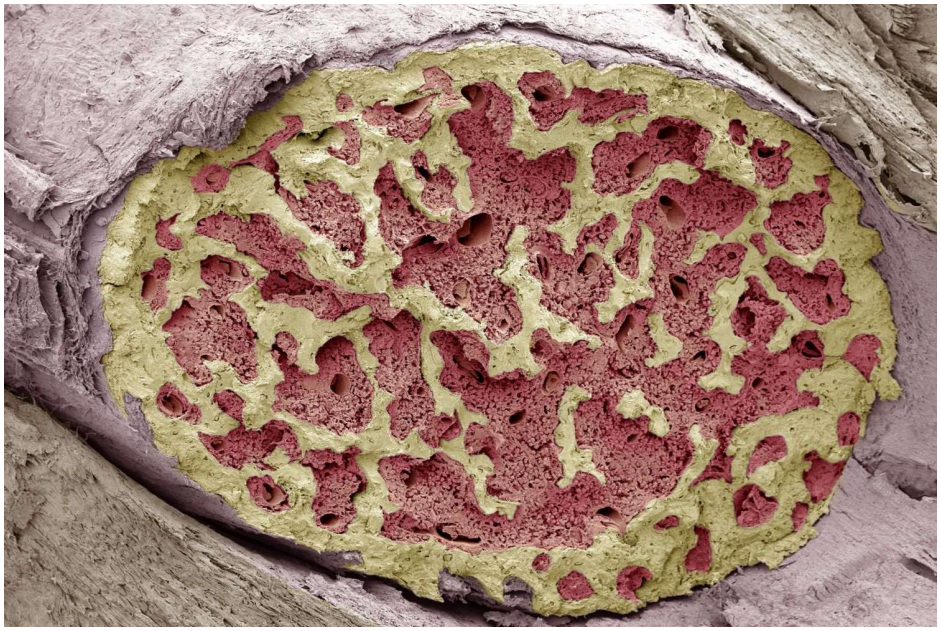
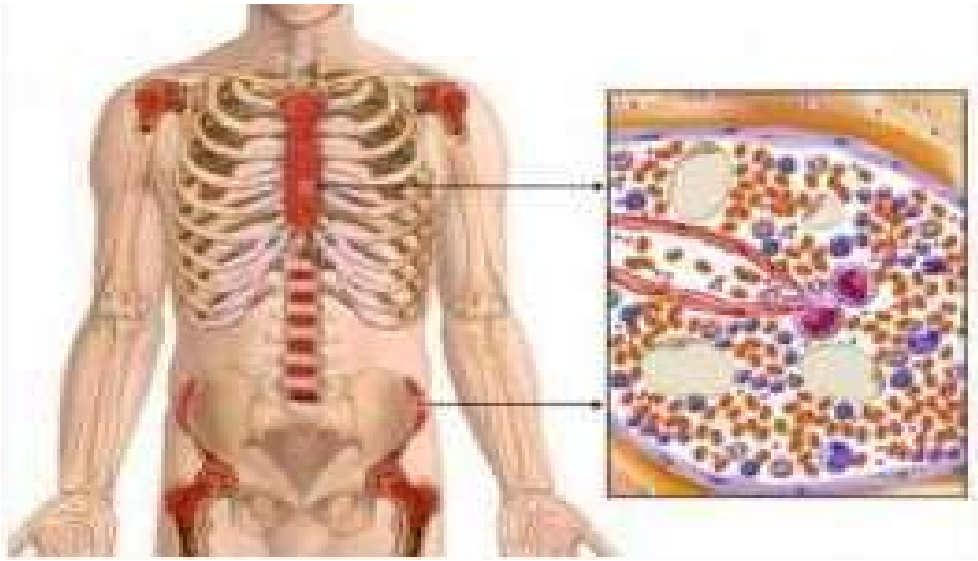
Bone Marrow

- Bone marrow is responsible for the production of the blood cells and contains many different cell types.



- Cylindrical cavities in the middle of the long bones
- Vertebral bones
- Ribs (costa)
- Sternum (breastbone)
- Pelvis (hip bones)
- Located in the spongy bone of the skull



Activity

- Active red bone marrow is present in all bones in the newborn
- At 4-5 years of age, number of blood-making cells decrease and the number of fat cells begins to increase
- Diaphyseal (middle) regions of long bones are completely surrounded by yellow bone marrow, rich in fat cells.
- In the adult, red bone marrow remains in the metaphyseal (tip) regions of the long bones, such as the femur and humerus, and in the axial flat bones.
- When needed, yellow bone marrow can turn into red bone marrow.

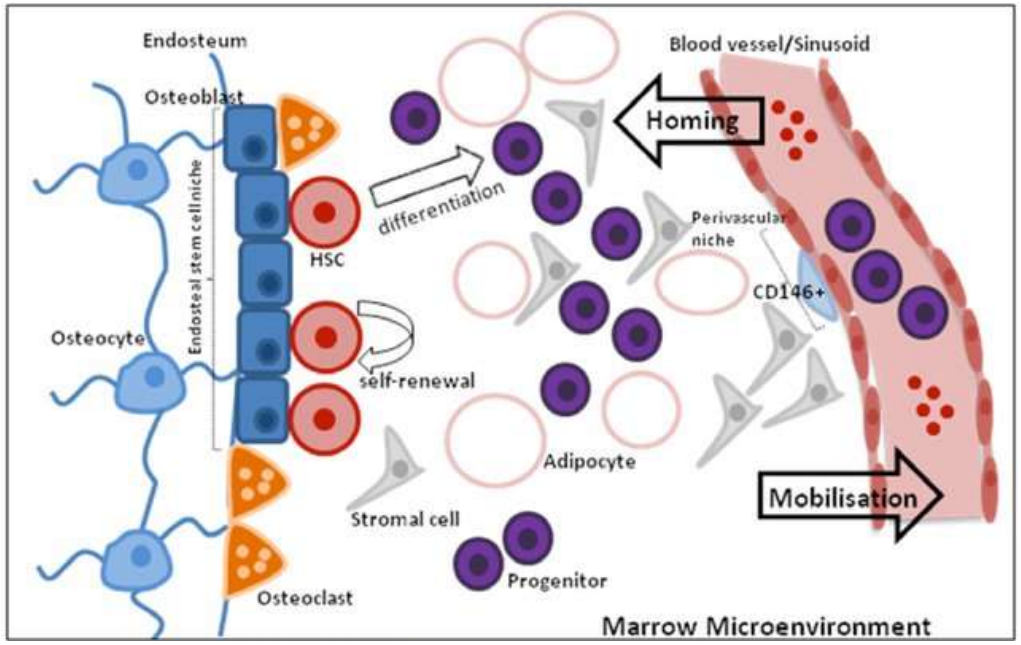
General structure

- Bone-bone marrow (macroenvironment)
- Bone marrow cells, stroma
- Matrix
- Stem cells

(microenvironment)

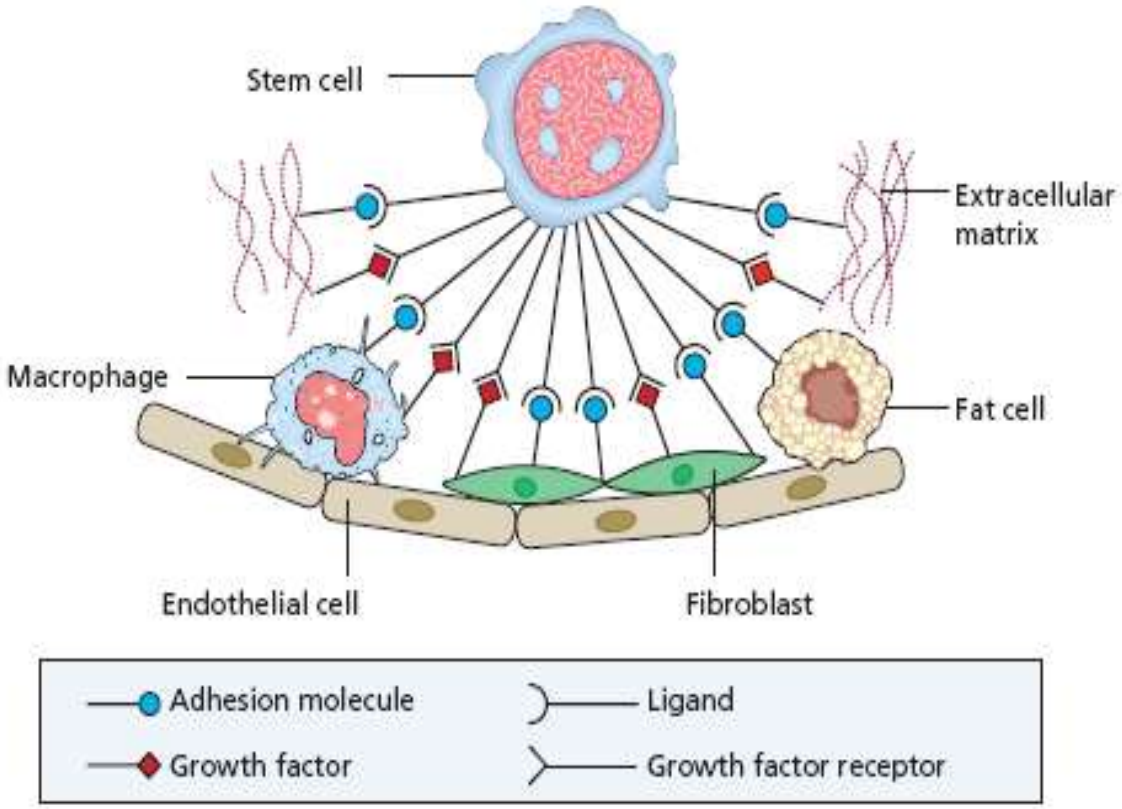
Blood forming unit

- Hosts hematopoietic stem cells
- These cells are irregularly located in the bone marrow, among which «venous sinus networks» or sinusoids perforate the tissue.
- The sinusoid wall consists of an endothelial lining, a discontinuous basement membrane, and an incomplete covering of adventitial cells.
- The endothelium is a simple squamous epithelium.



General structure

- Skeleton of the tissue has **reticular cell network**
- Network of **reticular fibers**
- **Fat cells**
- **Macrophages**



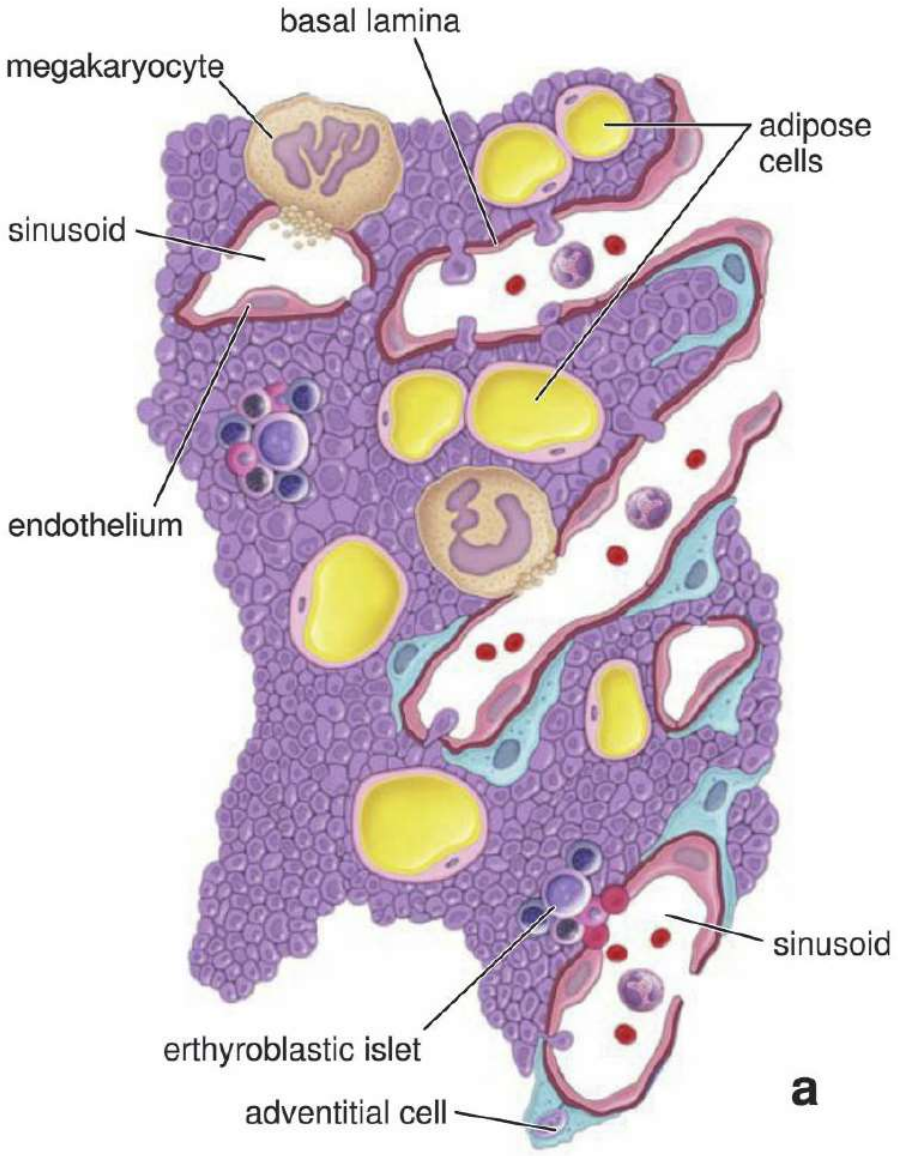
Microenvironment

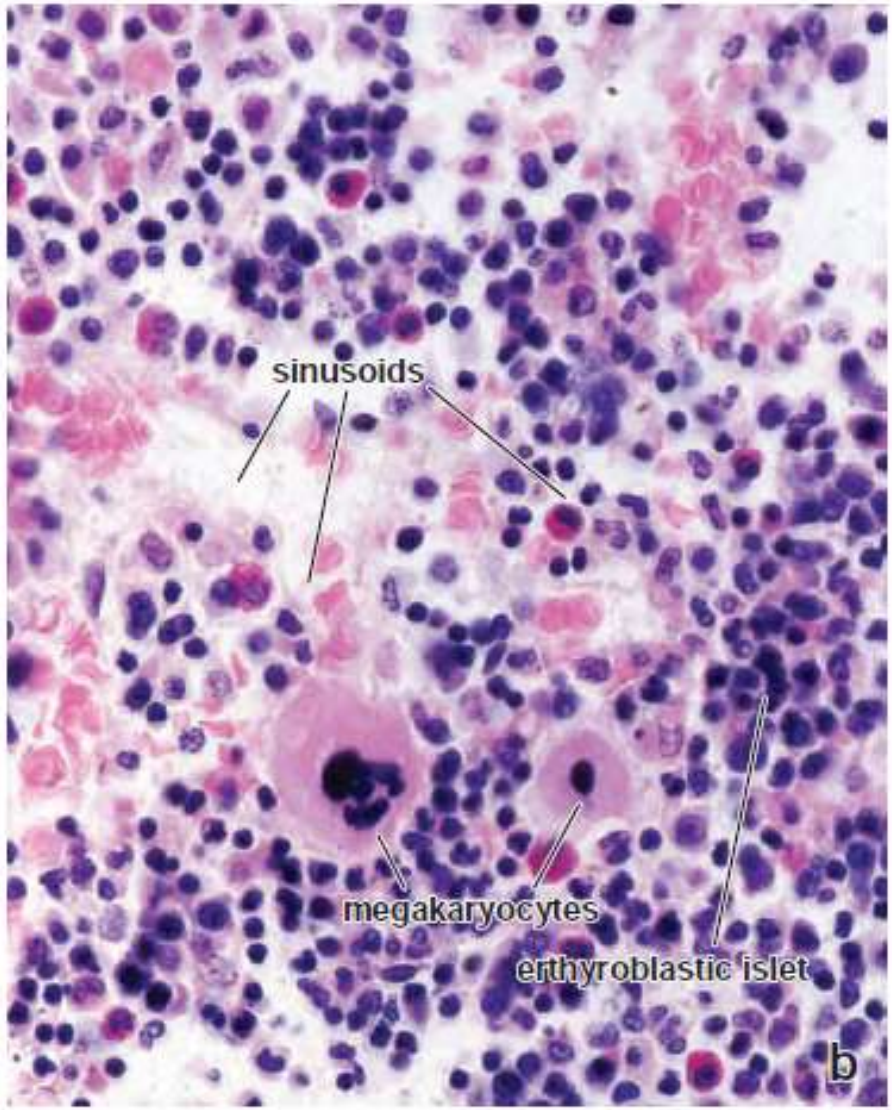
Stroma

- Endothelial cells
- Fibroblasts
- Adventitial cells
- Macrophages
- Adipose cells
- Lymphocytes and plasma cells
- Osteoblasts and osteoclasts

Matrix

- Fibronectin
- Laminin
- Collagene (type I & III)
- Proteoglican
- Hemonectin





Sinusoids are special vascular structures. Lined with endothelium, there are intermittent adventitial (reticular) cells outside the basement membrane.

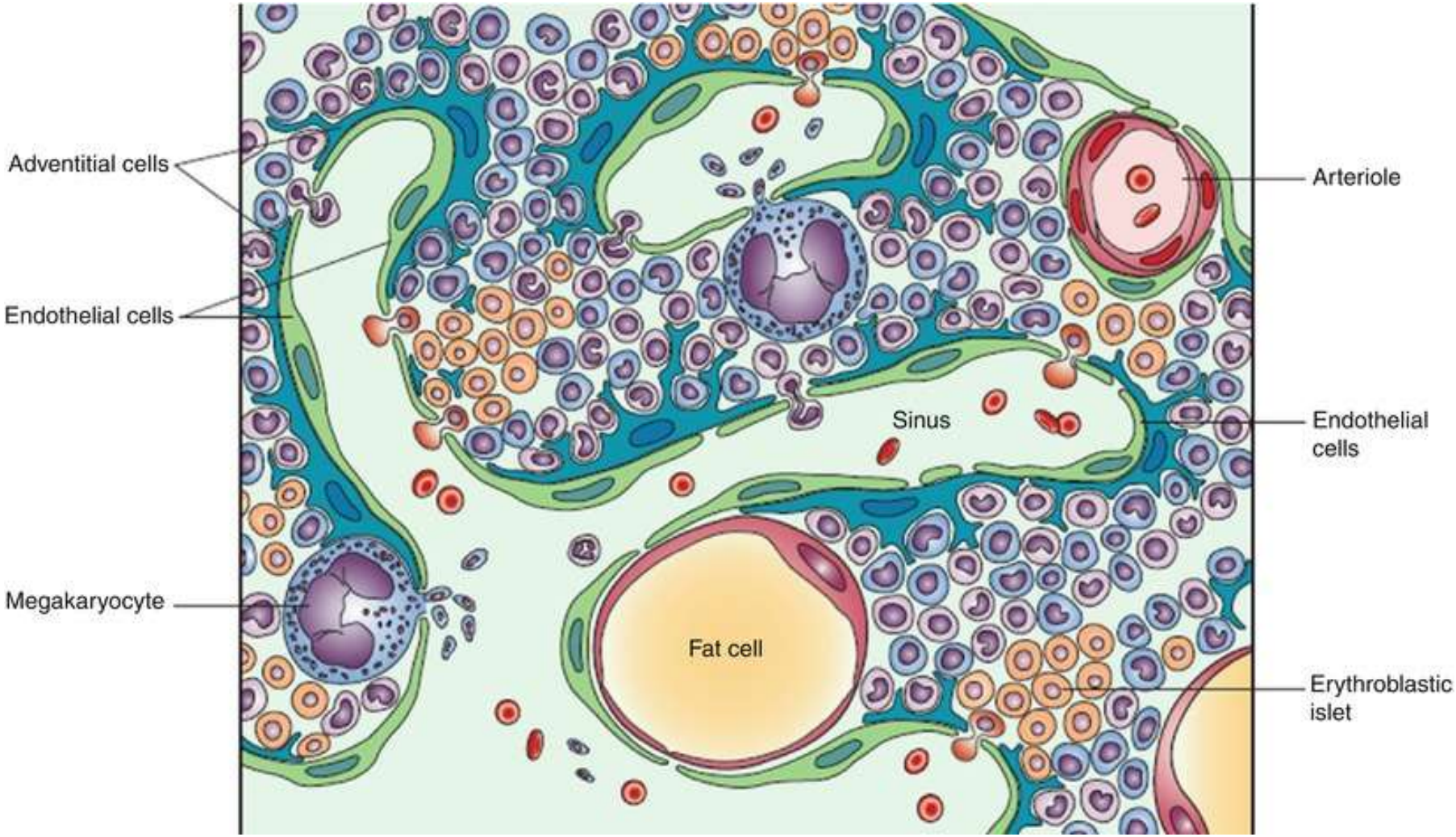
Adventitial (reticular) cells

- They send leaf-like appendages to hematopoietic cell cords and acts as a support during the development of blood cells.
- Responsible for the production of reticular fibers
- It allows the precursor cells to be differentiated into blood cells by the various cytokines that they secrete (colony-stimulating factors, IL-5, IL-7).
- Differentiated or matured cell is replaced with the adventitial cell and approaches the sinusoid and is released into the circulation by connecting with the endothelium.

Adventitial (reticular) cells

- It is similar to fibroblasts of connective tissue and is of mesenchyme origin.
- They are stained pale, difficult to spot between hematopoietic cells
- Unlike fibroblasts, they form cell networks
- Fat cells in the stroma are formed by storing fat in the cytoplasm of these cells.

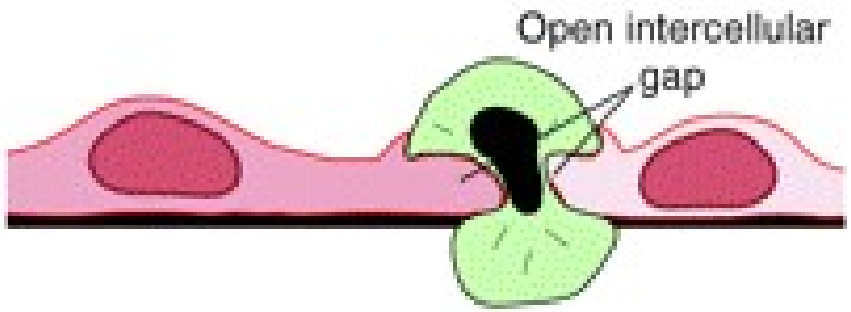
The **sinusoid** wall consists of an **endothelial lining**, a **discontinuous basement membrane**, and an incomplete covering of **adventitial cells**.



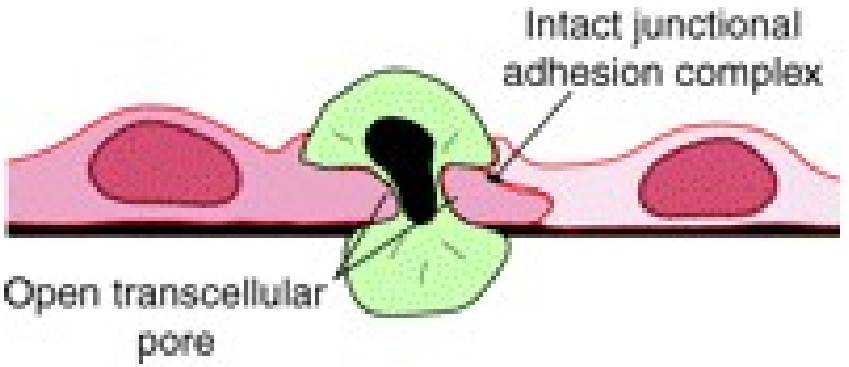
Venous sinuses-Sinusoids

- Lined with squamous endothelial cells, connected by intercellular complexes
- It is a closed circulatory system in the bone marrow. Maturing cells must cross the endothelium and enter the sinusoids
- A maturing cell or a piece of megakaryocyte pushes the endothelial cell membrane, membrane is pressed against the luminal plasma membrane until they fuse, thus forming a transitory opening or aperture.
- This is a trans-cellular transition. (NOT inter-cellular or para-cellular)
- After the transition, the endothelium repairs itself and closes the aperture

C Paracellular diapedesis
(migration between endothelial cells)



D Transcellular diapedesis
(migration through a pore in an individual endothelial cell)



Red Bone Marrow

- Hematopoietic cords with blood cell precursors and megakaryocytes
- These cords also contain macrophages, mast cells, fat cells.
- It is known that cells that look like scattered actually cluster, nest, group
- There is always one macrophage in each nest where erythrocytes are produced.
- While erythrocyte production areas and megakaryocytes are adjacent to the sinusoid wall, granulocytes are created away from the sinusoids, mature granulocytes migrate to the sinusoid wall

Bone marrow contains mainly 3 cell populations

1. **Stem cells**: They are cells that can renew themselves.
   - Stem cells are morphologically indistinguishable from other cells, they can only be recognized by specific cell surface markers.
   - Construction of blood cells in the bone marrow depends on the presence of high potential hematopoietic stem cells (pluripotent stem cell)
2. **Progenitor cells**: It provides the formation of different cell lines.
3. **Mature cells**: It is a mature blood cell and is the cell that participates in the bloodstream.

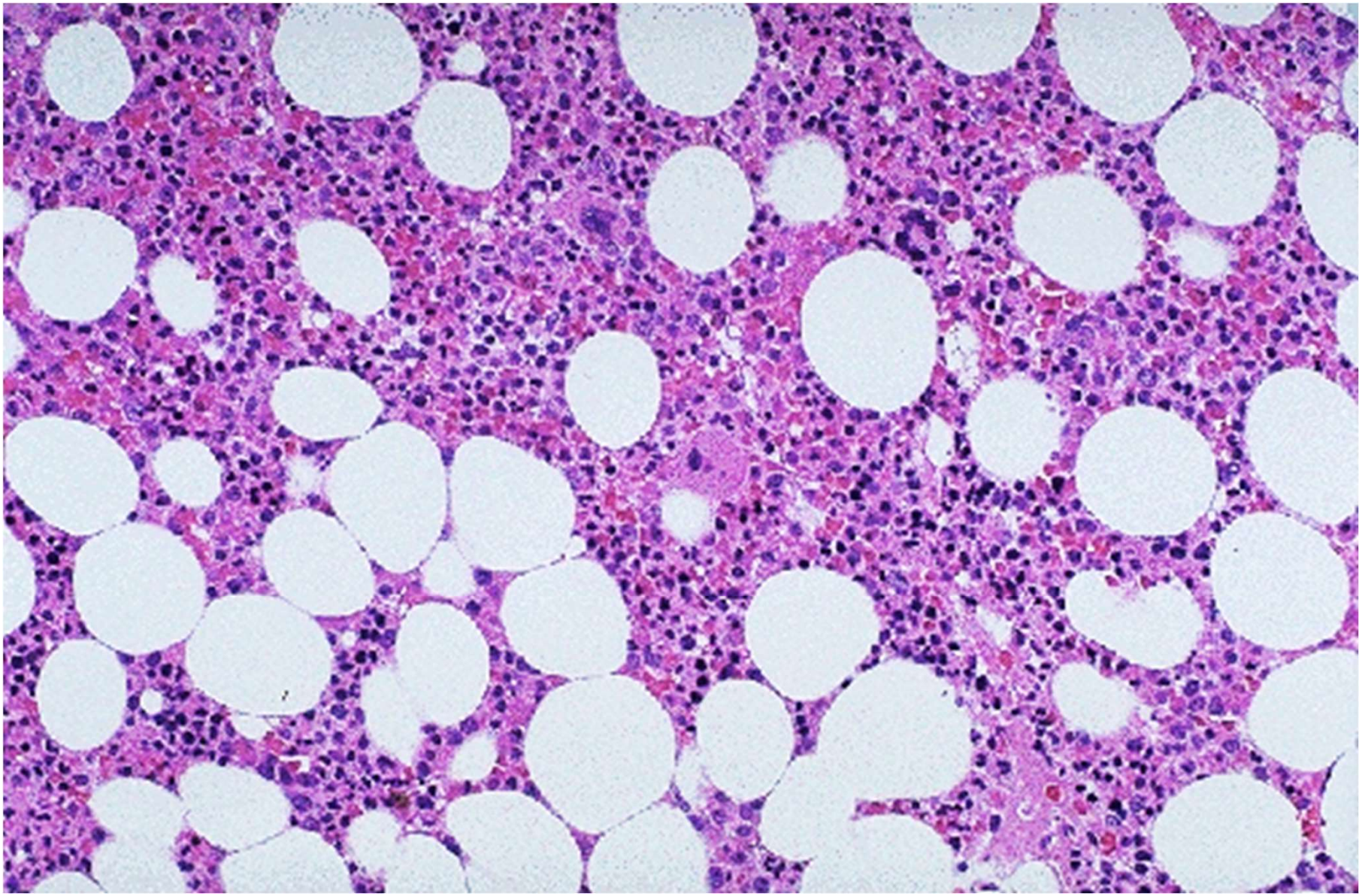
Functions of the red bone marrow

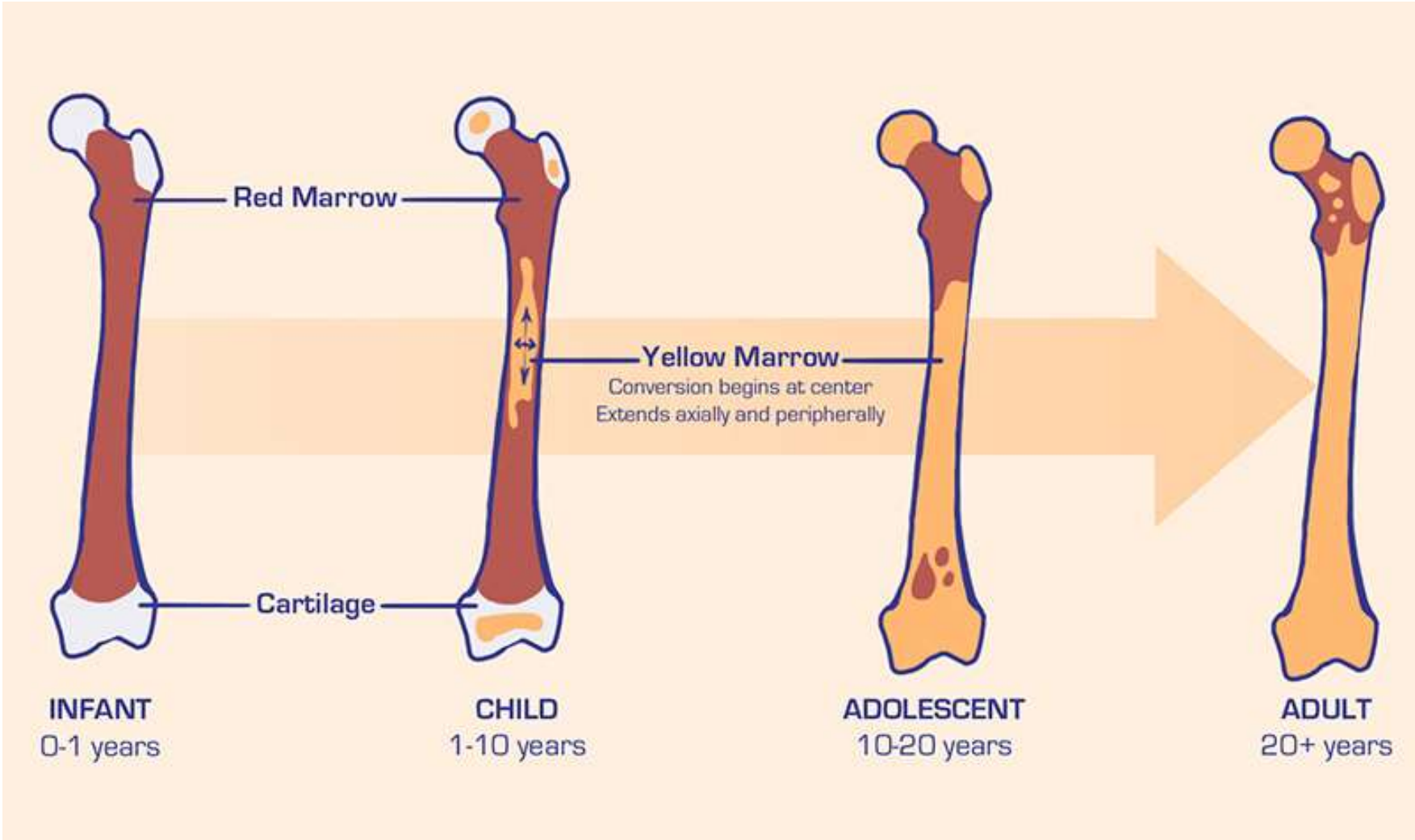
1- Making of blood cells.

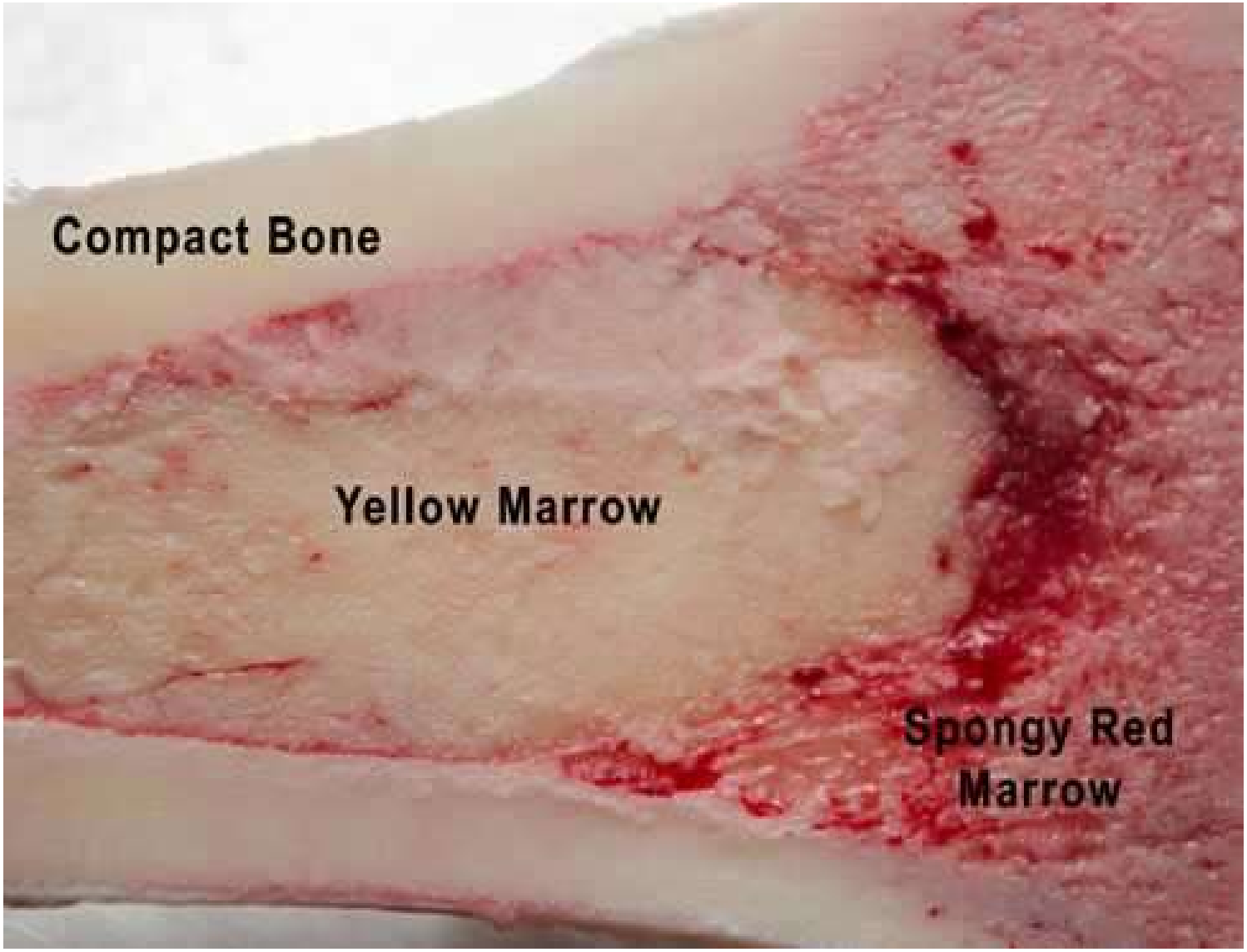
2- Degradation of erythrocytes and storage of iron released as a result of destruction.

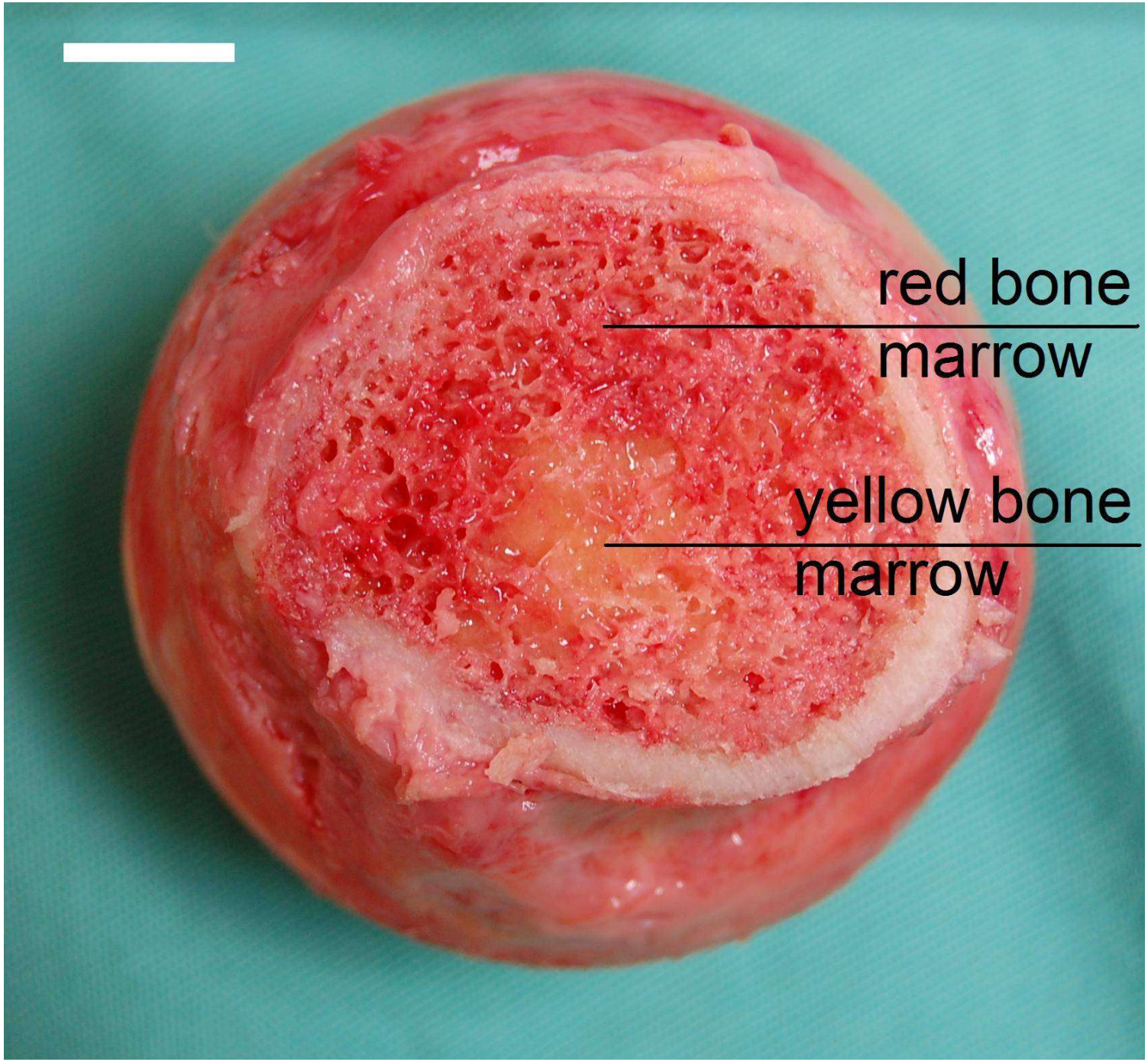
Iron is stored in the cytoplasm of reticular cells and macrophages in the form of ferritin and hemosiderin. Apart from bone marrow, iron is also stored in liver cells, striated muscle fibrils and spleen macrophages.

3- Indifferentiated T and B-lymphocyte production




Red Marrow
Cartilage
Yellow Marrow
Conversion begins at center
Extends axially and peripherally
INFANT
0-1 years
CHILD
1-10 years
ADOLESCENT
10-20 years
ADULT
20+ years


Compact Bone
Yellow Marrow
Spongy Red Marrow


red bone marrow
yellow bone marrow

Homing within the bone

- Hematopoietic stem cells are located in areas close to bone surfaces. This is called endosteal bone marrow-hematopoietic stem cell niche.
- The area near the sinusoids is called vascular bone marrow-hematopoietic stem cell niche.
- Adipose cells can be used as an energy source, as well as undertake the synthesis of growth factors.
- Osteopontin is synthesized by osteoblasts and negatively affects hematopoietic stem cell count.

Yellow bone marrow

- The number of adipose cells increases in the inactive bone marrow and the blood production stops reversibly, this structure is seen in the feature of adipose tissue.
- In adulthood, hematopoiesis has stopped in the diaphyseal region of all long bones and appears covered with fat cells.
- Even in the flat bone marrow with active production, more than half of the tissue is filled with **adipocytes**.

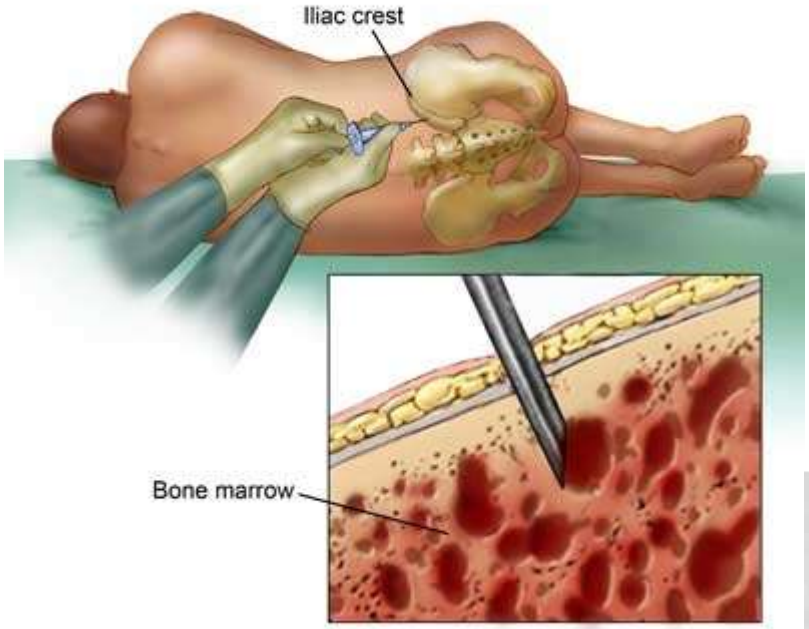
Macroscopically Bone Marrow…

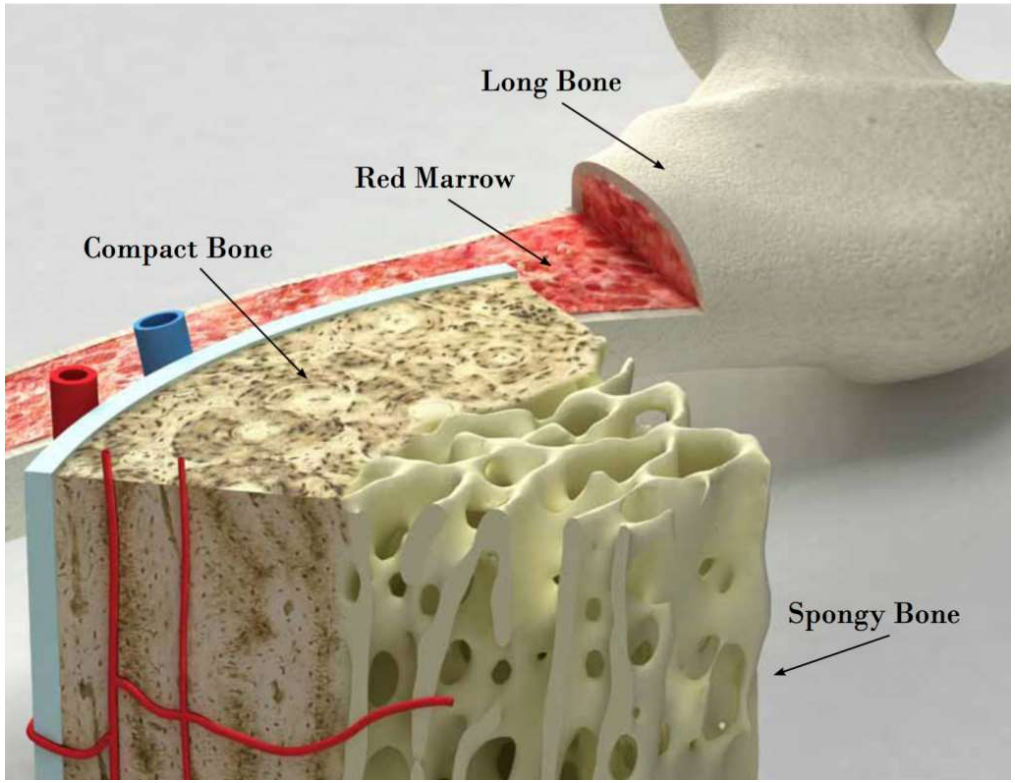
Red BM

- Its red color comes from the large number of erythrocytes and developing erythrocyte series.
- Fetal and newborn bones contain only red BM.
- Formation of blood cells
- Degradation of erythrocytes and storage of iron resulting from destruction
- Indifferentiated T and B lymphocyte production

Yellow BM

- Its yellow color is because of its rich fat content.
- Transformation begins at the age of 5-6
- The adult's diaphyses of the long bones contain yellow BM
- Blood cells are not made in the yellow marrow.
- In heavy bleeding or hypoxia, the yellow marrow turns into a red marrow.
- Spare hematopoetic tissue

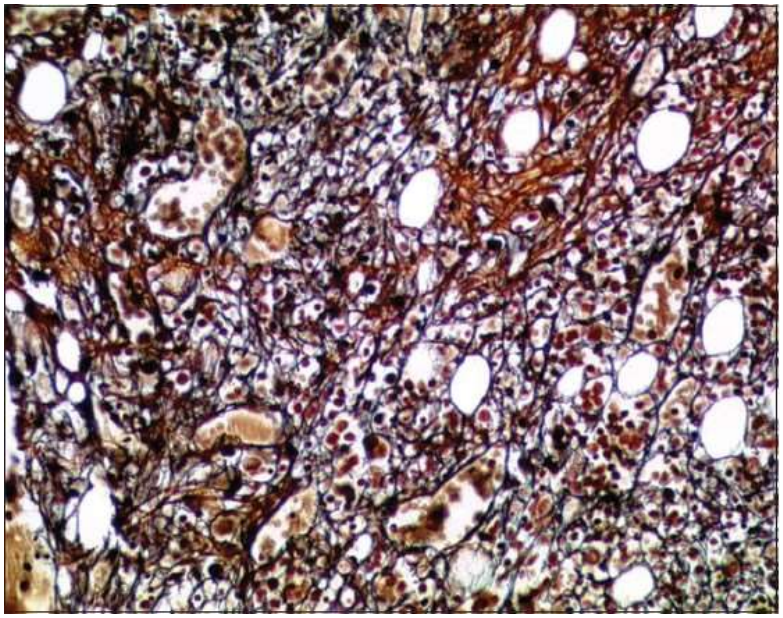

Iliac crest
Bone marrow

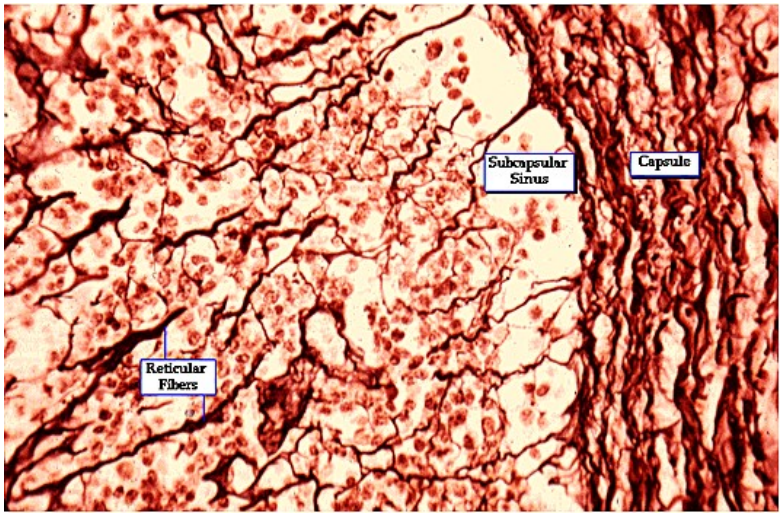

Long Bone
Red Marrow
Compact Bone
Spongy Bone

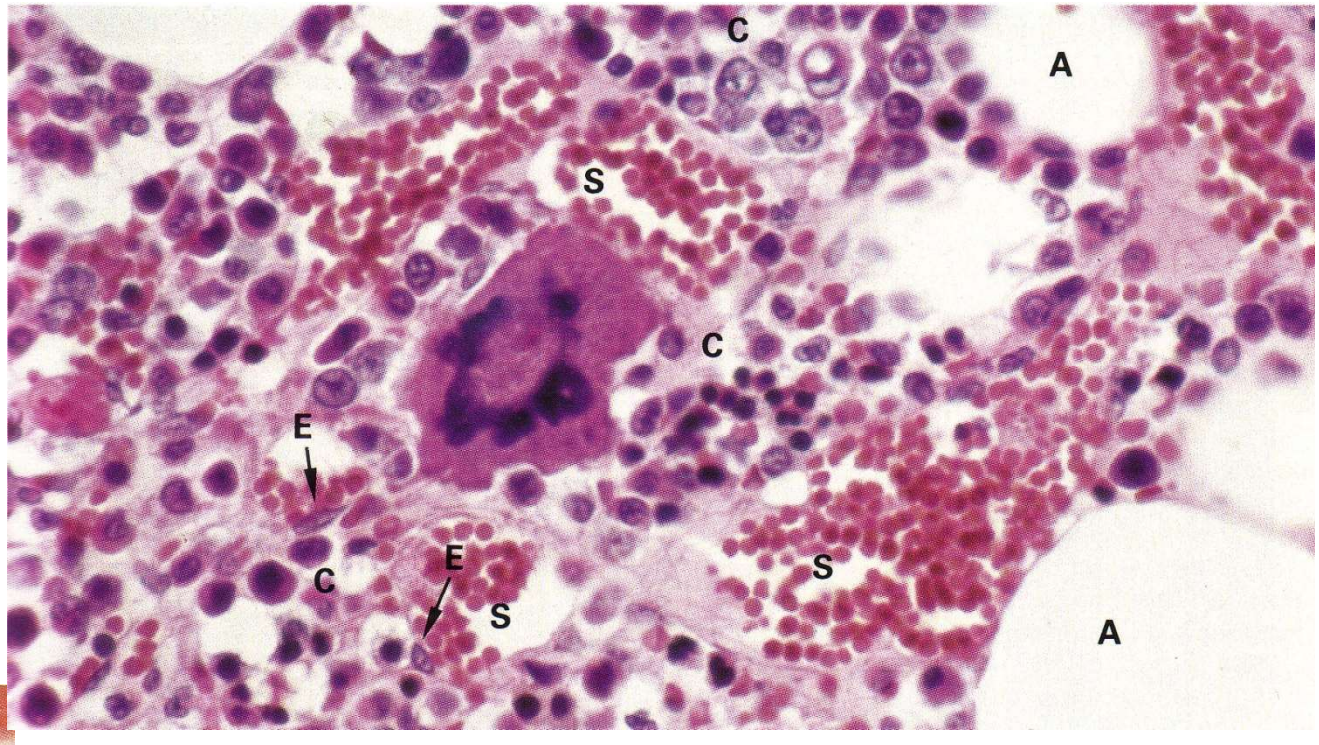
Reticular Connective Tissue

Reticular Connective Tissue

- It is a kind of loose connective tissue in which reticular fibrils are concentrated and forms the skeleton of lymphoid organs (lymphoreticular) and bone marrow (myeloreticular).
- It forms the supporting core of tissues containing various cells.
- Reticular fibrils are of type-III collagen structure and cannot be observed by routine staining methods.
- They have very thin diameters of up to 20 nm, they branch out but do not join together to form thicker fibrils.
- Since they contain large amount of sugar groups (glycosaminoglycans) on them, it is possible to display them specifically with some techniques:
  - silver impregnation method → argyrophilic
  - periodic acid – Schiff (PAS) reaction



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