Bone Marrow and Hematopoiesis (Hemopoiesis)

ASS. Prof.

Dr. Heba El-kaliny

Histology & Cell biology department

Intended learning outcomes (ILOs)

Knowledge :

1. Recognize the structural characteristics of the bone marrow.
2. Define and describe the structure of the different types of bone marrow.

Intellectual skills:

1. Differentiate between different types of bone marrow.
2. Relate the composition of each type of bone marrow to its specific functions.

Bone Marrow (Myeloid Tissue)

- The myeloid tissue is a specialized vascular **connective tissue** rich in cells that are responsible for formation of blood cells.

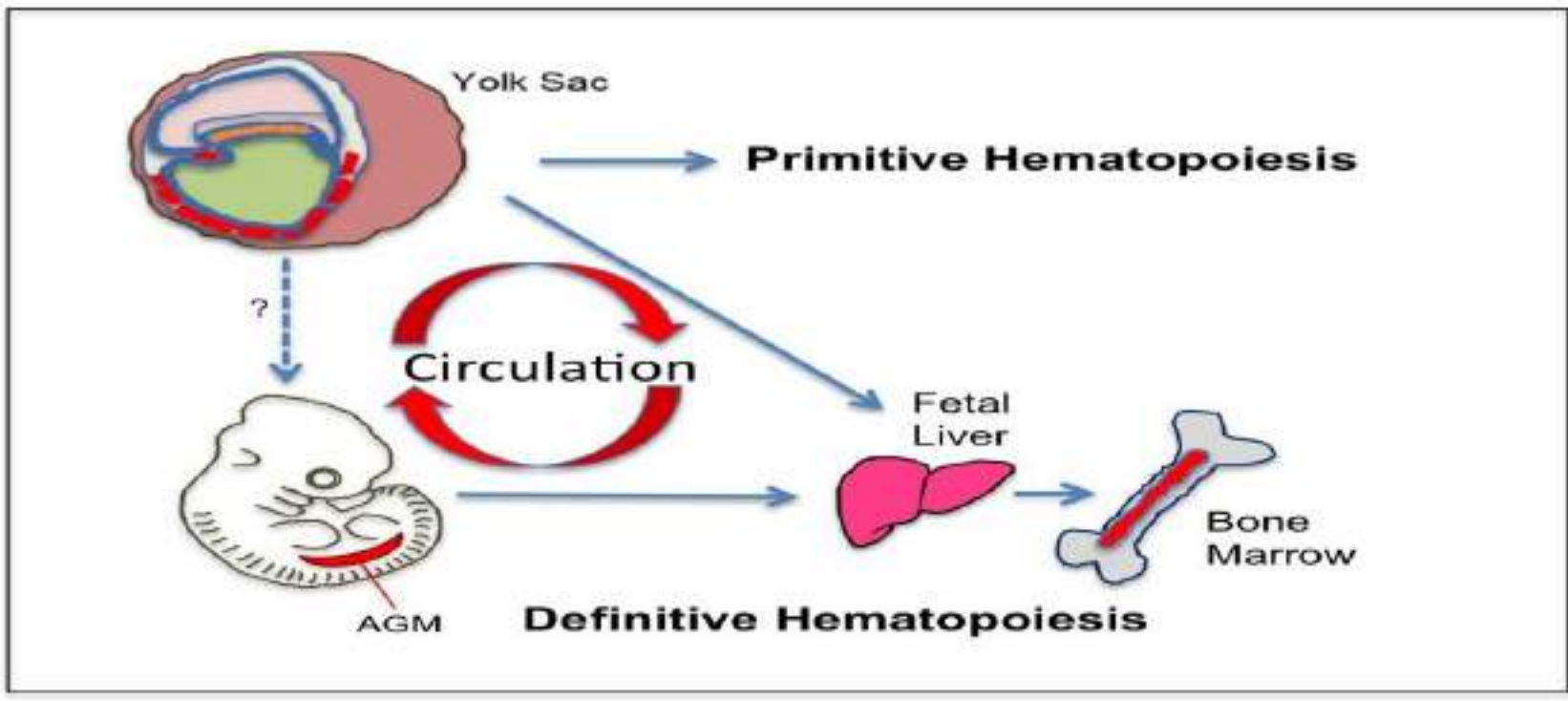
daily formed = daily destroyed elements

Site of hematopoiesis :

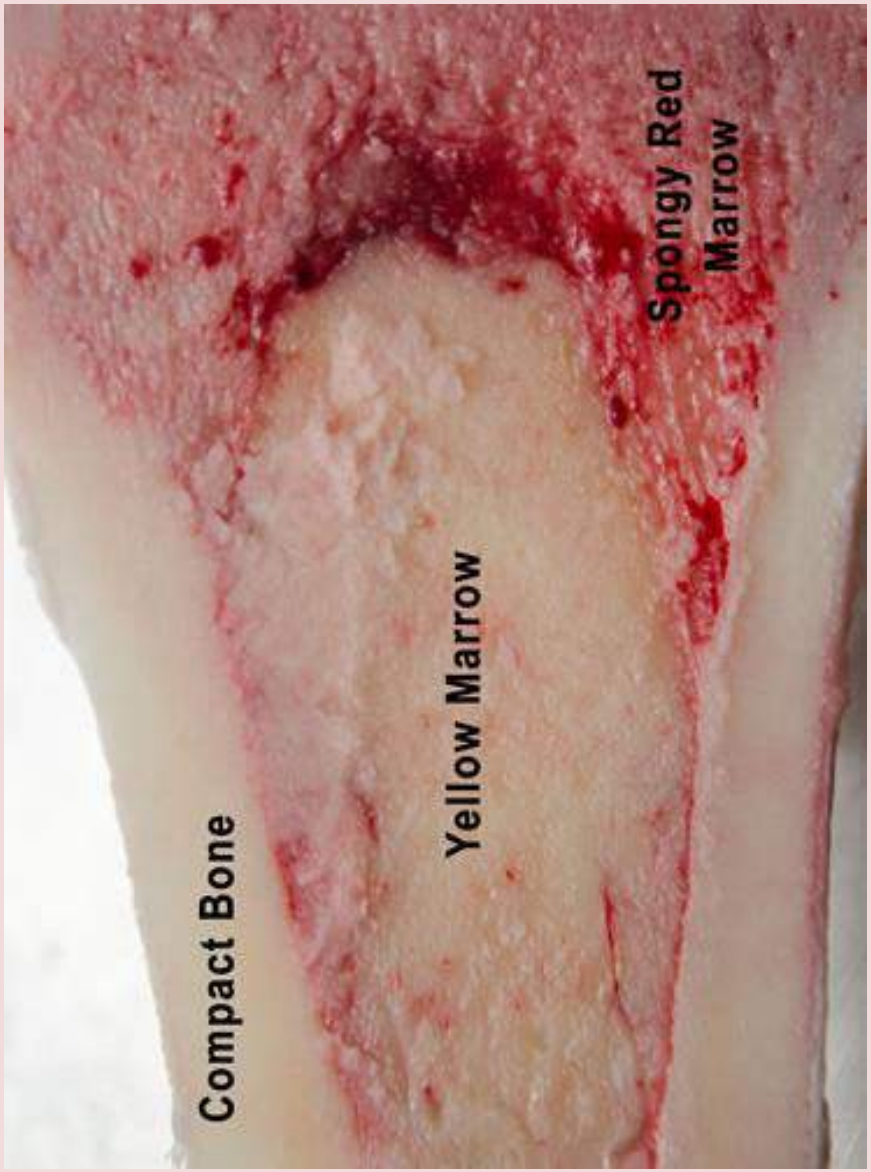
- **Yolk Sac:** very early embryo
- **Liver, Spleen**: NEWBORN
- **BONE**

CHILDHOOD: AXIAL SKELETON & APPENDICULAR SKELETON BOTH HAVE RED (active) MARROW

ADULT: AXIAL SKELETON (RED MARROW), APPENDICULAR SKELETON (YELLOW MARROW)



Types of Bone marrow

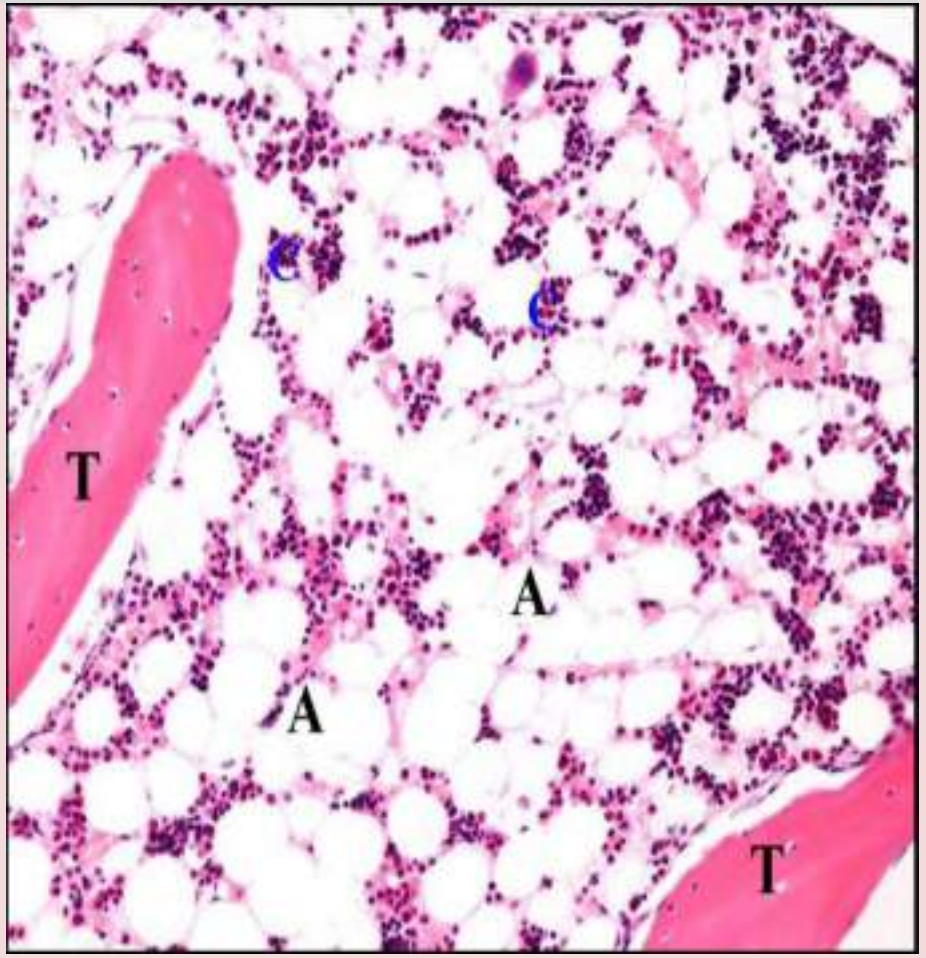


Types of Bone marrow

Red bone marrow	yellow bone marrow
• It is the active bone marrow.	• It is inactive bone marrow.
• It is red in color due to presence of blood and blood forming cells.	• It is yellow in color due to great number of adipose (fat) cells.
• It is found in all bones of the fetus.	• Not present in fetus
• In adults, it occupies the bone marrow spaces of spongy bone.	• It is present in the adult long bones.
• Function: Formation of blood cells	• Function: It does not form blood but stores fat
	• Under certain conditions, such as severe hemorrhage yellow bone marrow becomes active and forms blood cells

Red B.M

Yellow B.M

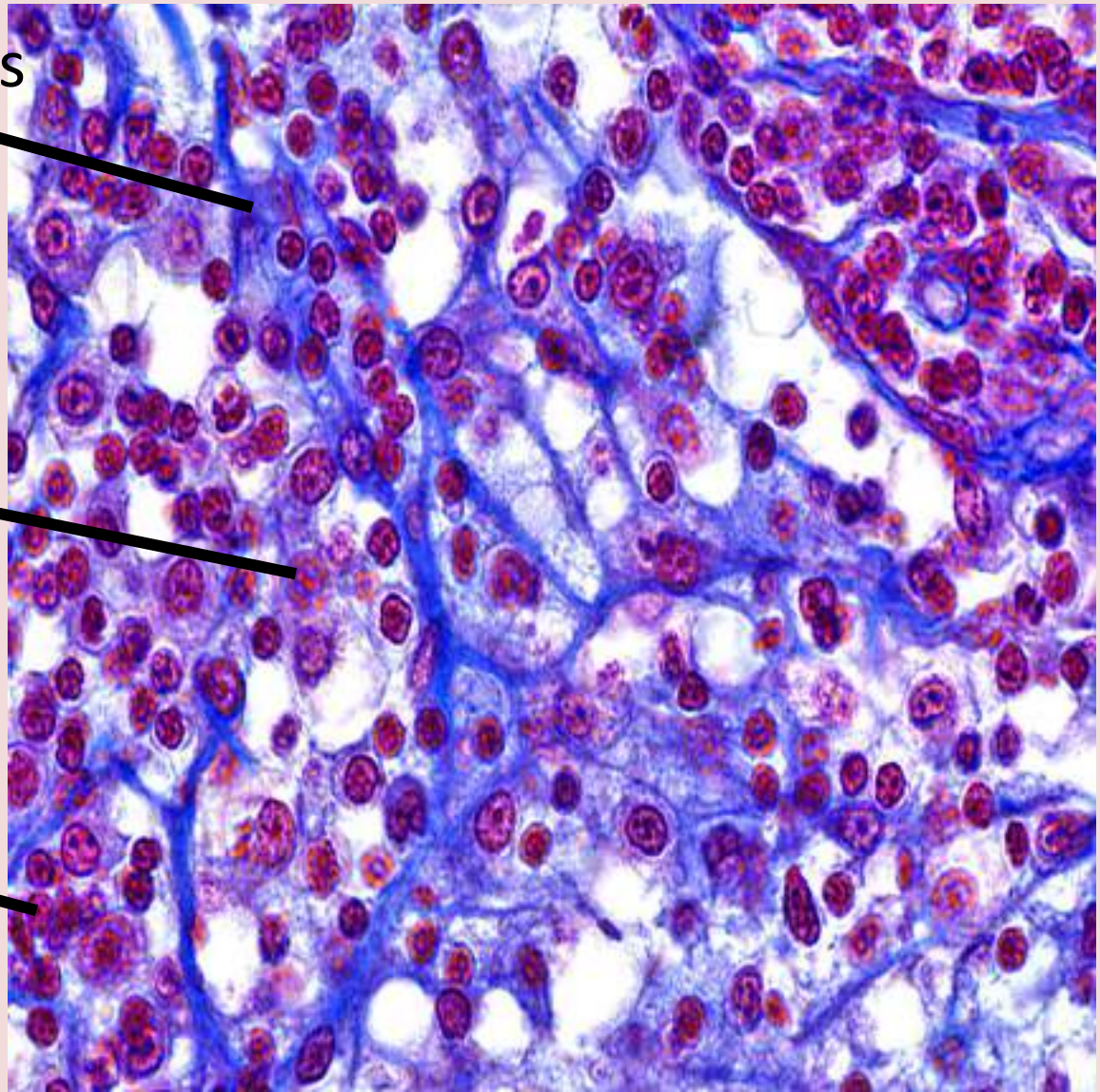


Structure of red bone marrow

1.Stroma:Reticular cells + fibers (network)

2.Capillaries

3.Hematopoietic cords



Structure of red bone marrow

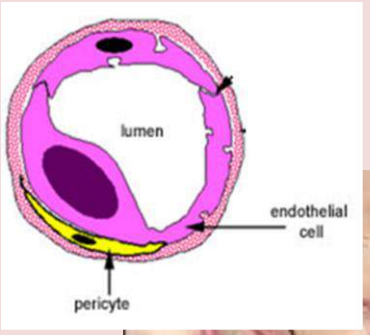
1) Stroma: (C.T)

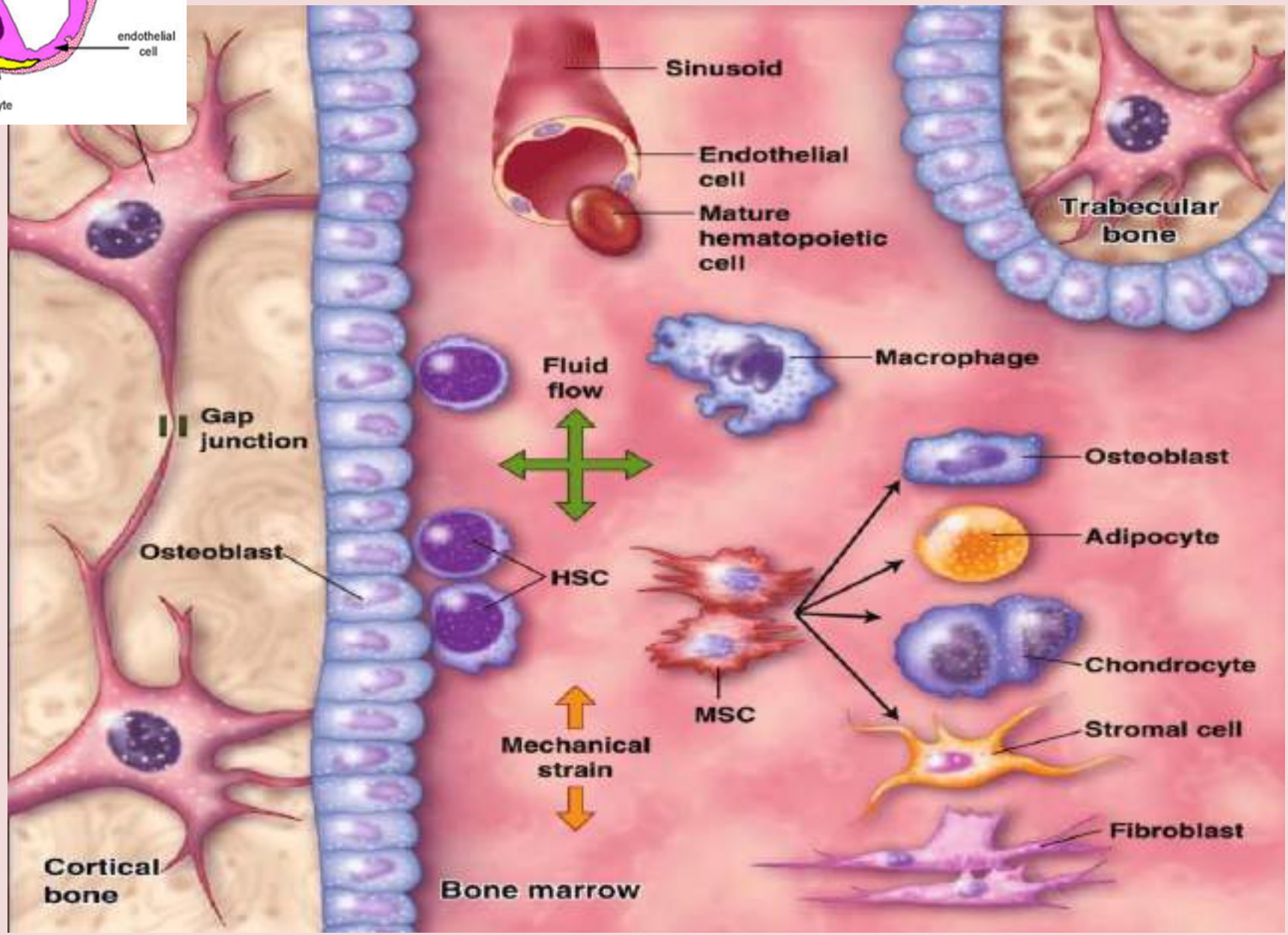
- **Network** formed of reticular fibers + reticular cells.

- **Matrix (fibers + ground subs.): collagen** type I and III, **glycoproteins** as fibronectin, laminin, hemonectin and **proteoglycans**.

- **The cells** of stroma includes; Mesenchymal cells, reticular cells, fibroblasts, macrophages, fat cells, osteogenic cells, endothelial cells and pericytes.

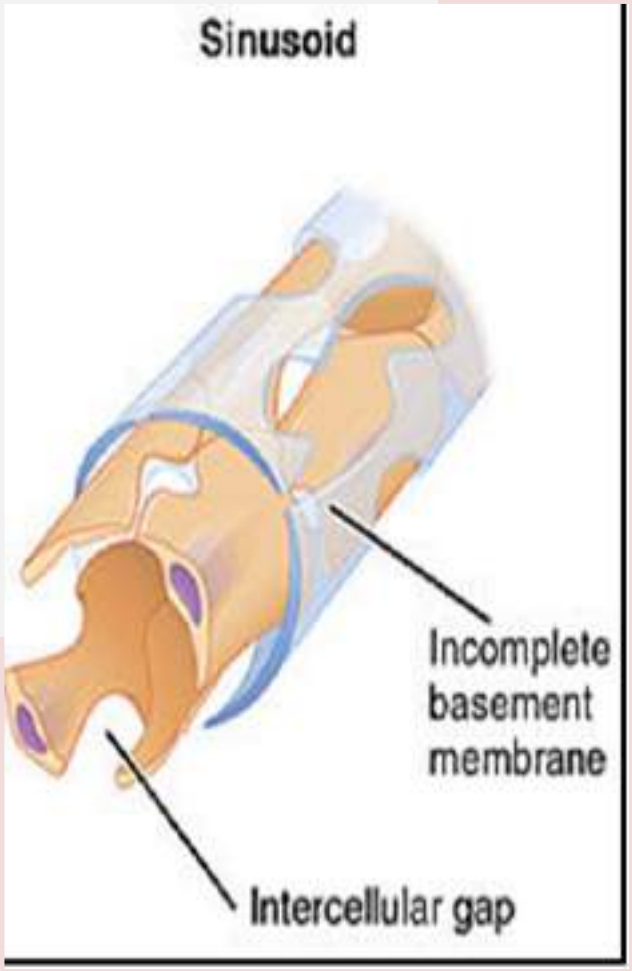
Bone Marrow Stromal cells





2) Sinusoidal capillaries: wide, very thin walled lined with a single layer of fenestrated endothelial cells with discontinuous basement membrane through which transendothelial migration of newly formed blood cells occurred.

3) Hematopoietic cords: developing blood cells



Reticular cells:	They are large branched cells with pale cytoplasm and lightly stained nucleus. - **synthesize** reticular fibers + limited **phagocytic** power.
Fibroblasts:	They form collagen type I, glycoproteins and proteoglycans of the matrix.
Macrophages:	**phagocytosis** of malformed and old RBCs and store iron to be used for formation of new erythrocytes + extruded nuclei of erythrocyte precursors and excess cytoplasm.
Fat cells:	They accumulate fat as a **local fuel** for energy needed for hematopoiesis.
Osteogenic cells:	They are the stem cells of cartilage and bone. They may have a role in **stimulating the stem cells** to form blood cells in red bone marrow.
Endothelial cells and pericytes	are present in the walls of blood sinusoids.

HEMATOPOIESIS
(Formation of blood cells)

I- Pluripotential stem cells

II- Multipotential stem cells → **lymphoid**

→ **myeloid**

III-Progenitor cells (Colony Forming Units, CFU):

IV- Precursor cells (blasts):

V- Mature cells

I- Pluripotential stem cells

- Major type of pluripotent stem cell in the bone marrow that can give rise to all the blood cell types.
- 0.1% of bone marrow cells.

- Small cells, large pale rounded nucleus, basophilic cytoplasm.(ribosomes+ RER)

- ½ Reserve other ½ becomes more differentiated and form multipotential stem cells.

II- Multipotential stem cells

1-Lymphoid → which will develop → lymphocytes.

2-Myeloid → which will develop → myeloid cells → erythrocytes, granulocytes, monocytes & megakaryocytes.

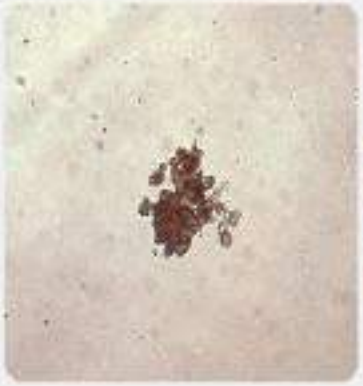
- Form progenitor cells.

III-Progenitor cells (Colony Forming Units)
CFU

- Form colonies of blood cells.
- Initial letter of cell type denote its specific CFU.
  - CFU-E for erythrocytes.
  - CFU-M for monocyte.
- Form precursor cells.
- -unipotential or bipotential stem cells.
- High mitotic activity.
- Self renewing.

- They are common in bone marrow and lymphoid organs.

Hematopoietic Progenitor Classes



CFU-E

- colony-forming unit-erythroid
- produce 1 - 2 cells clusters
- 8 - 200 erythroblasts per colony

BFU-E

- burst-forming unit-erythroid
- > 200 erythroblasts per colony
- single or multiple cell clusters per colony

CFU-GM

- colony-forming unit-granulocyte, macrophage
- colonies with > 40 granulocytes and macrophages

CFU-GEMM

- colony-forming unit-granulocyte, erythroid, macrophage, megakaryocyte
- erythroblasts with ≥ 20 cells from other lineages

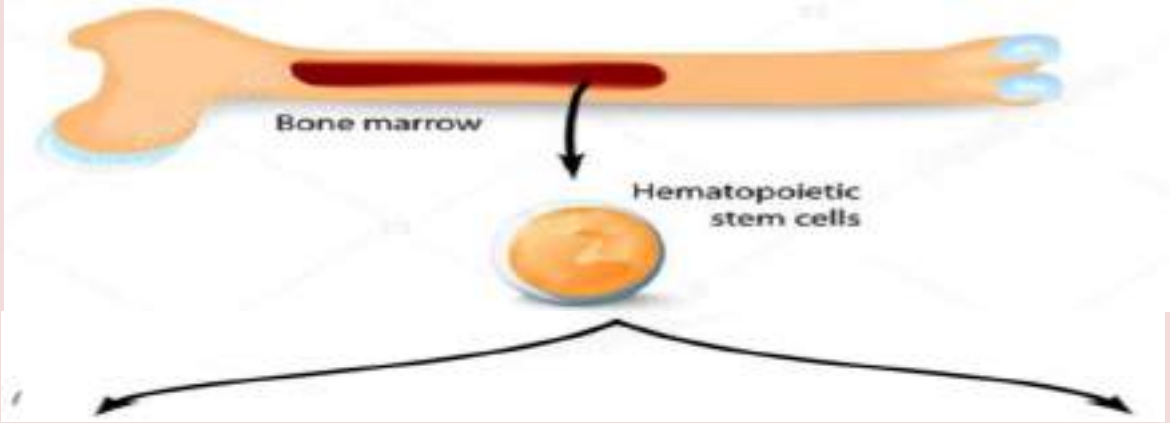
IV- Precursor cells (blasts)

- They are common in bone marrow and lymphatic organs and show the beginning of morphological differentiation.
- Form mature cells.
- **High mitotic activity.**
- Non self renewing.
- They are unipotential cells.

V- Mature cells

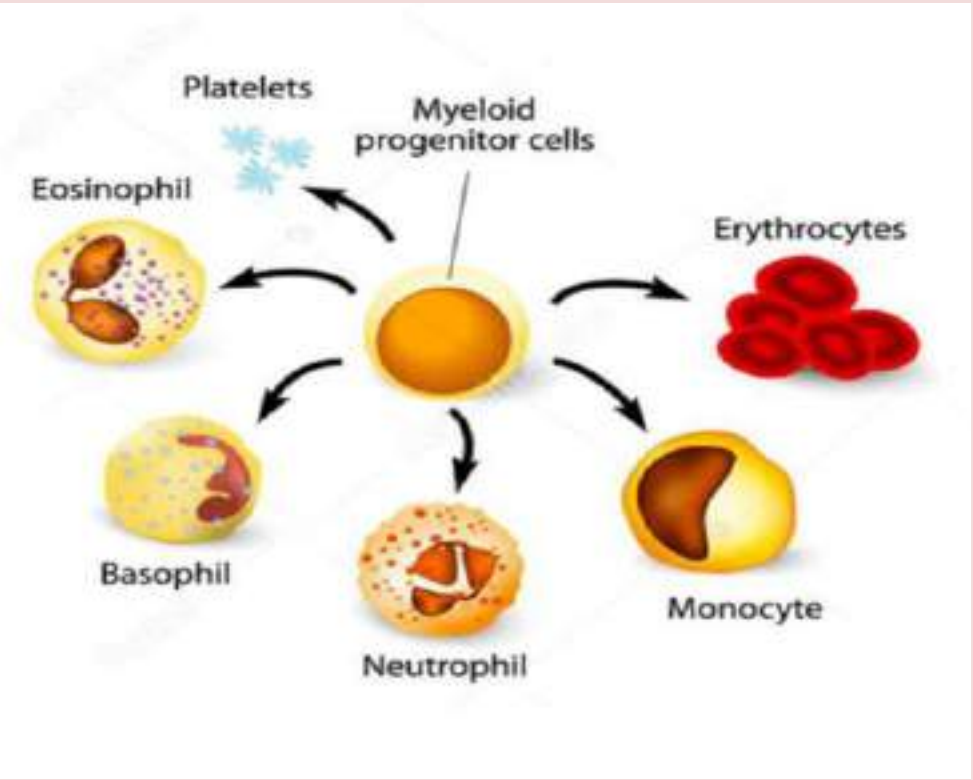
- Clear morphologic differentiation.
- No mitotic activity.

-**They are common in bone marrow and hematopoietic organs**



Myeloid multipotential

Lymphoid multipotential



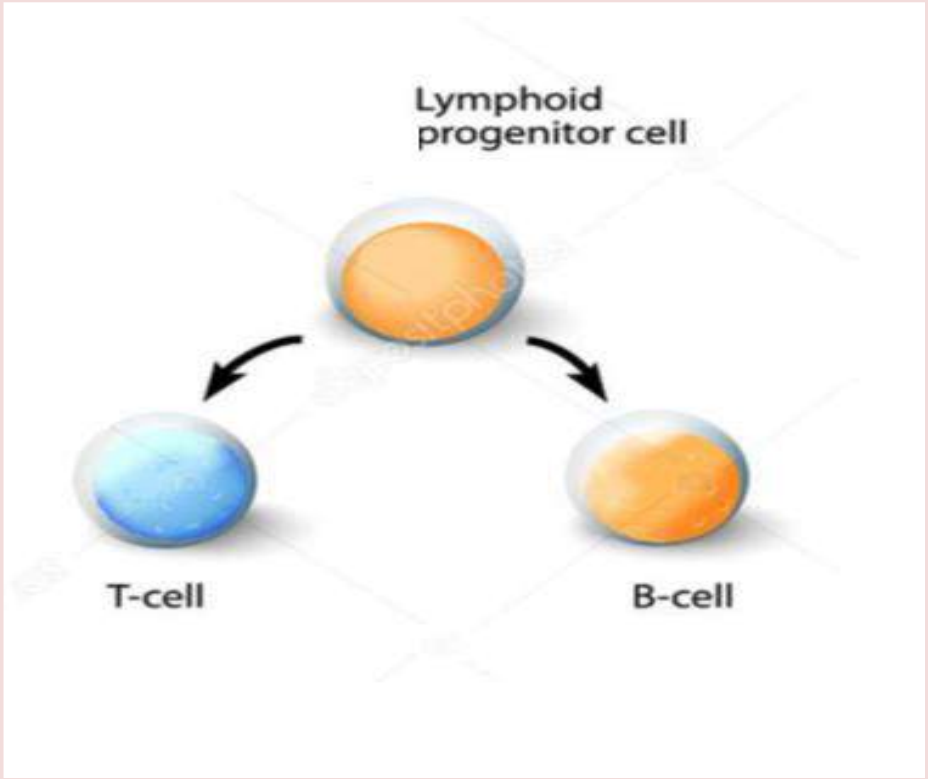
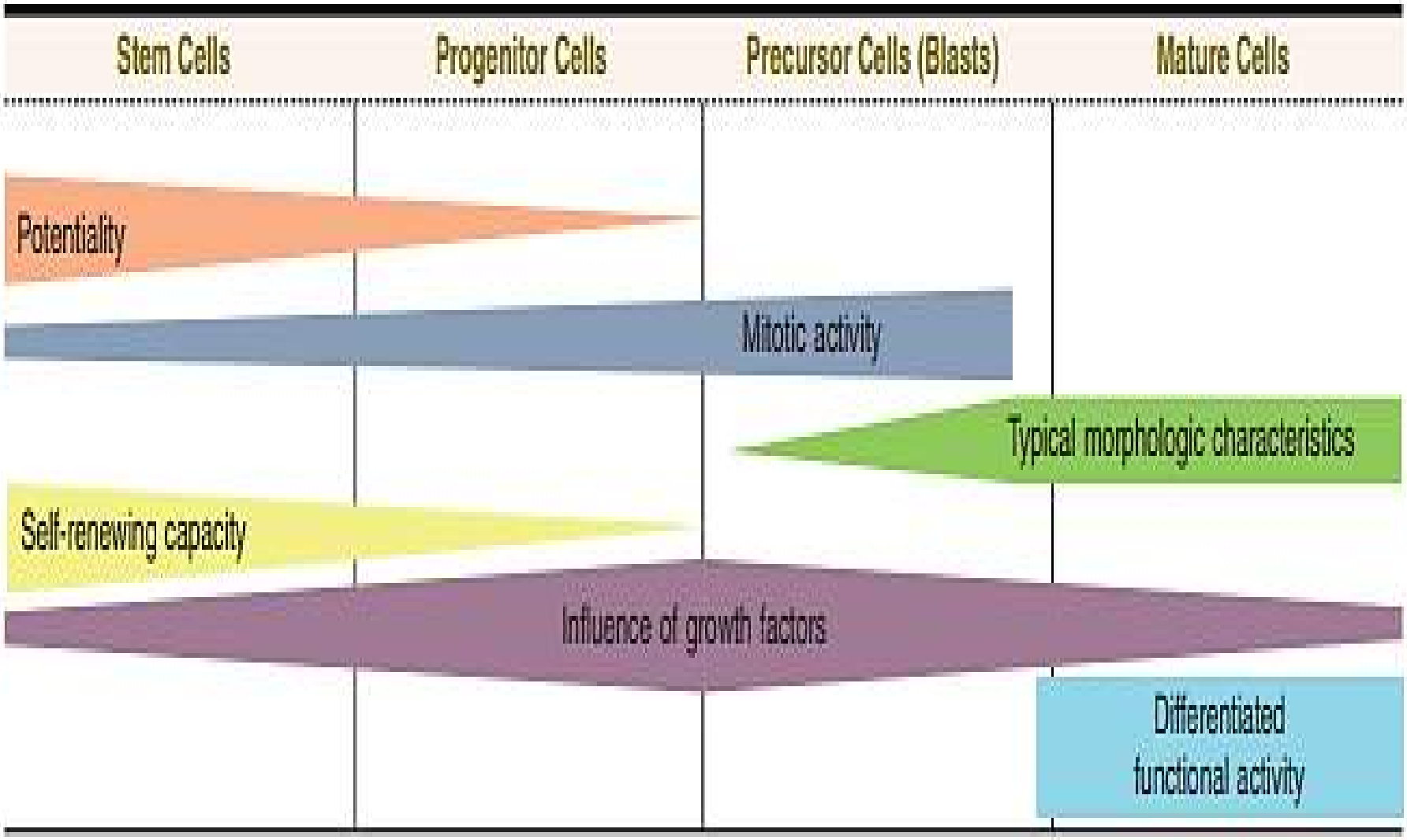
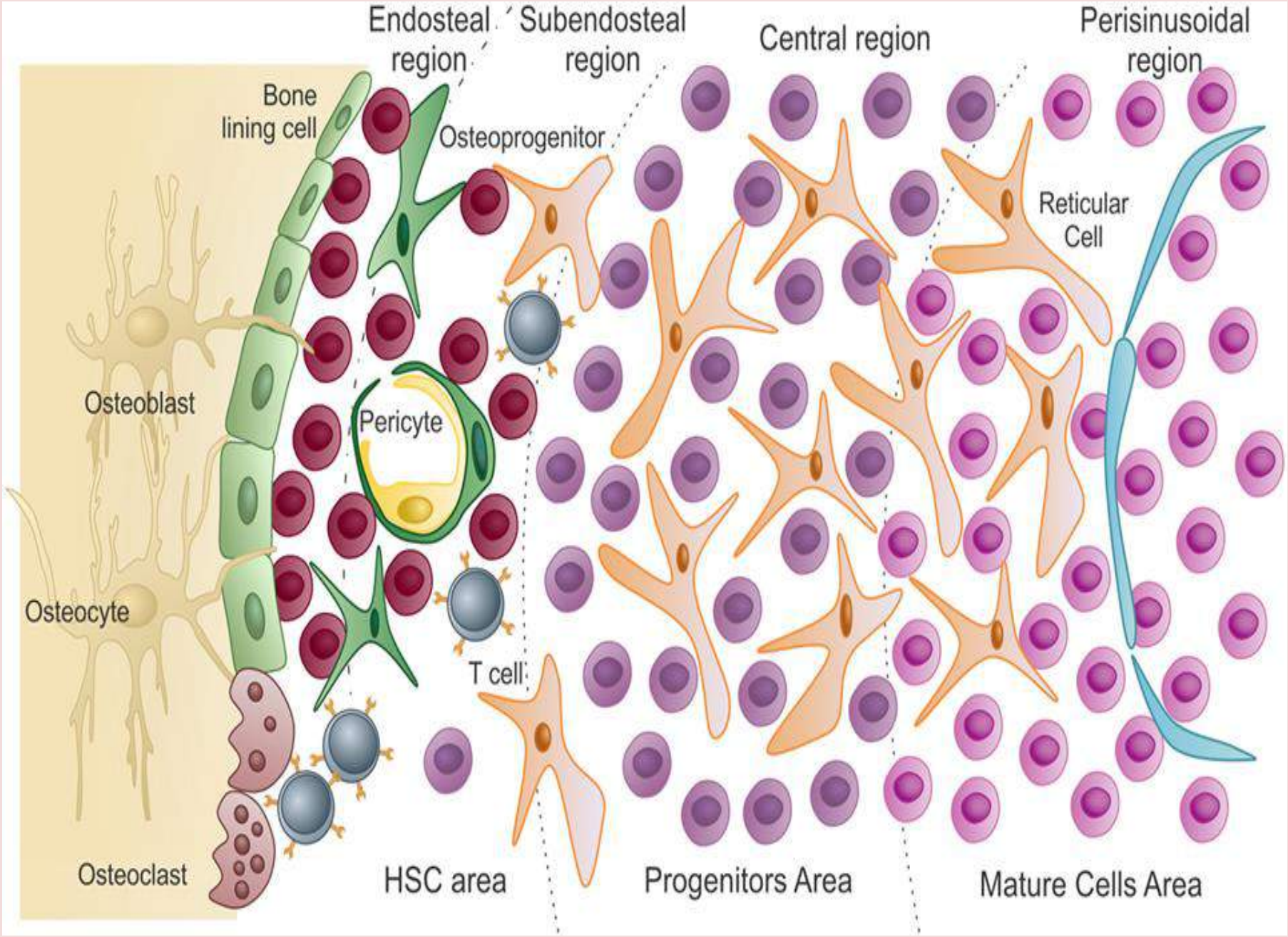


FIGURE 13–3 Major changes in developing hemopoietic cells.




Endosteal region
Subendosteal region
Central region
Perisinusoidal region
Bone lining cell
Osteoprogenitor
Reticular Cell
Osteoblast
Pericyte
Osteocyte
T cell
Osteoclast
HSC area
Progenitors Area
Mature Cells Area

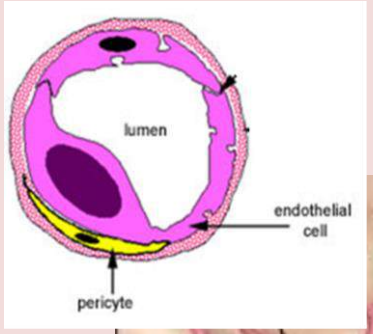
Bone marrow microenvironment

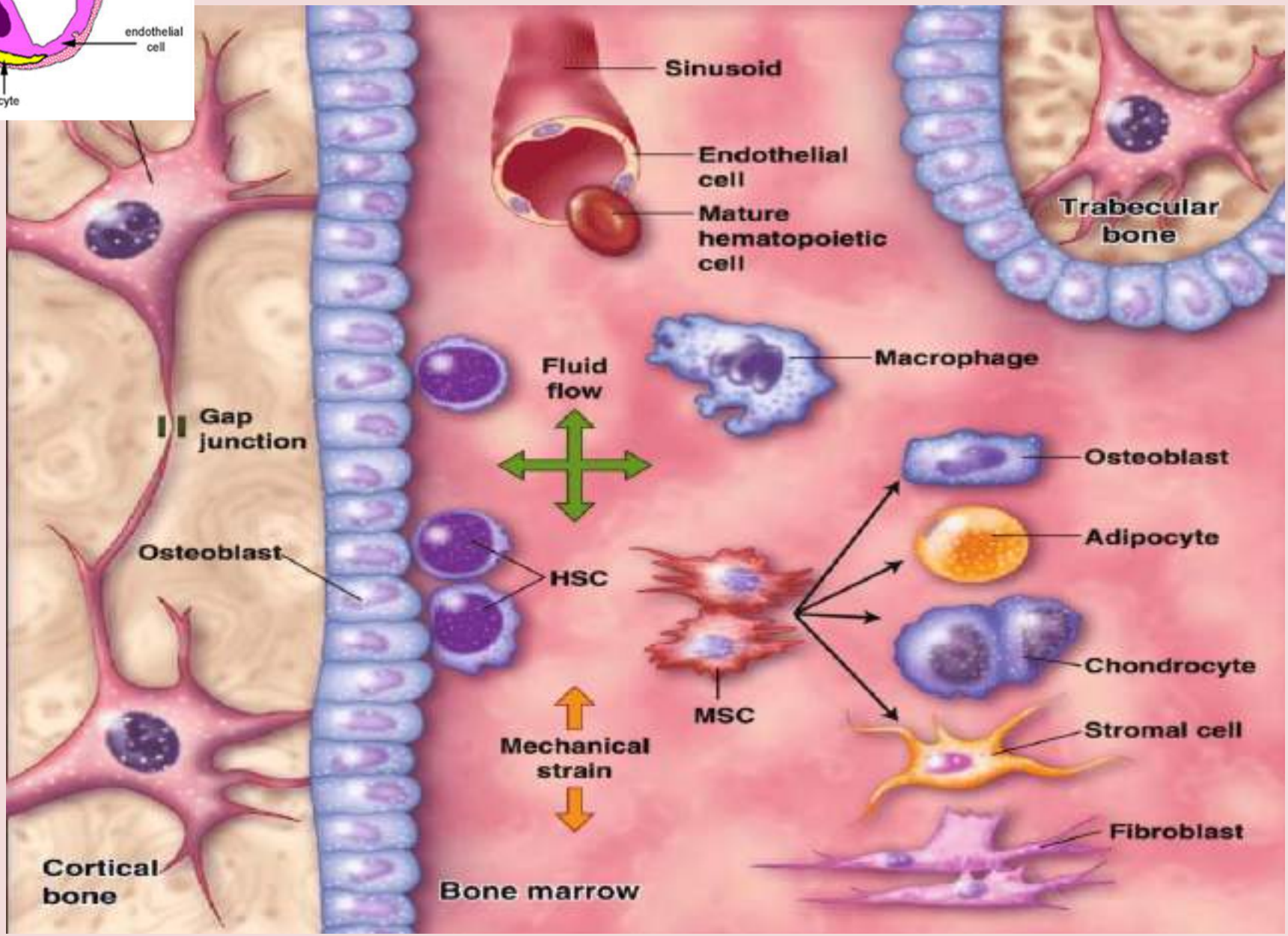
- **HSC area,** which harbors quiescent hematopoietic stem cells and uncommitted progenitors (multipotent), comprises both endosteal and subendosteal niches.

- Committed progenitors and differentiated cells are distributed in the central and perisinusoidal niches, respectively.

- As HSCs exit quiescence to proliferative states, they migrate and colonize and interacting with both endothelial cells and pericytes.

Bone Marrow Stromal cells



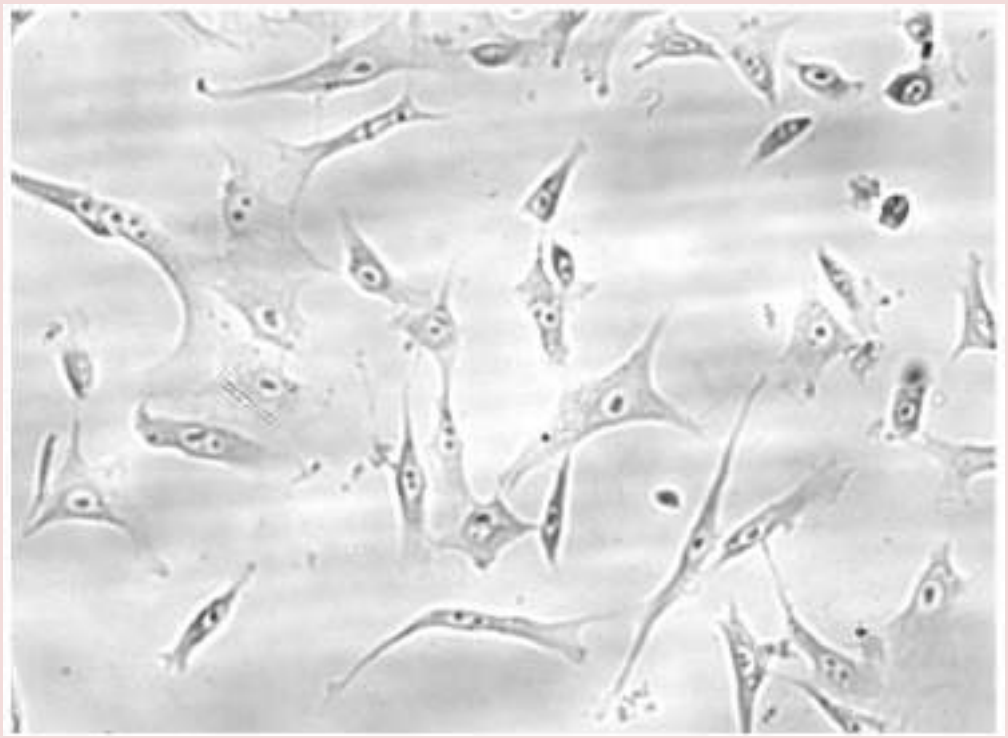


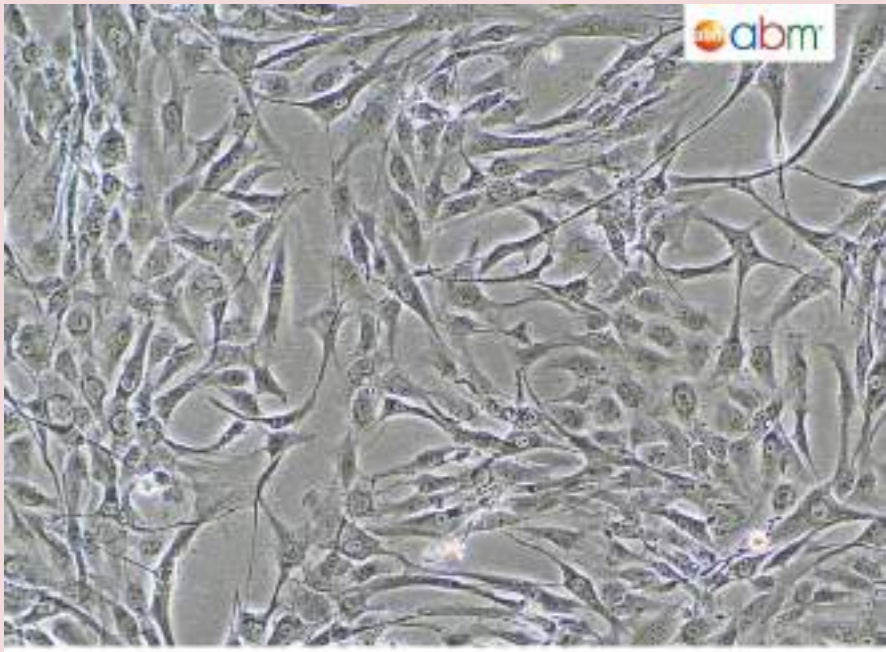
Mesenchymal stem cells

- The bone marrow stroma also contains mesenchymal stem cells (MSCs), also known as **marrow stromal cells.**
- These are multipotent stem cells that can differentiate into a variety of cell types. MSCs have been shown to differentiate, in vitro or in vivo , into osteolasts, chondrocytes, myocytes, marrow adipocytes.
- MSCs constitute less than 0.1% of the total cells. they are heavily used in cell therapy (regenerative medicine) due to their ability to quickly expand in culture conditions while retaining their multilineage potential.

Mesenchymal stem cells

- These cells are typically spindle-shaped, fibroblast-like,





T0520 – Immortalized Human Bone Marrow Mesenchymal Stem Cells - SV40T

Bone marrow barrier

- The blood vessels of the bone marrow constitute a barrier, inhibiting immature blood cells from leaving the marrow. Only mature blood cells contain the membrane proteins, such as **aquaporin and glycophorin**, that are required to attach to and pass the blood vessel endothelium.

Thank you