

Hematopoiesis II

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Erythropoiesis

- Is the process of formation of **Erythrocyte** which occurs through several stages.
- The glycoprotein erythropoietin, a growth factor produced by cells in the kidneys, stimulates production of mRNA for globins, the protein components of hemoglobin, and is essential for the production of erythrocytes.

Erythropoiesis

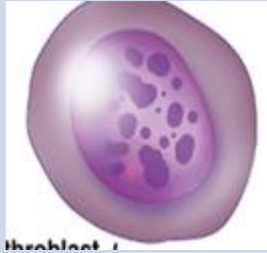
- 1-Pluripotential stem cell  myeloid multipotential
- 2-Erythrocyte colony forming unit (CFU-E) (progenitor)
- 3- Pro-erythroblast
- 4- Basophilic erythroblast
- 5- Polychromatophilic erythroblast
- 6-Orthochromatophilic erythroblast (normoblast)
- 7-Reticulocyte



Erythrocyte

color

Pro-erythroblast

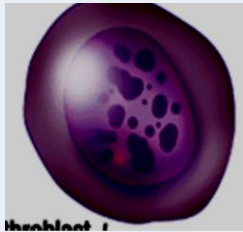


It is a large cell (12-15 μm in diameter)

The **nucleus** is central, pale and contains fine chromatin and two visible nucleoli.

The **cytoplasm** is **basophilic** due to presence of many polyribosomes for synthesis of protein of Hgb.

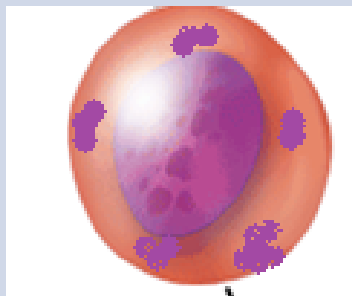
Basophilic erythroblast



The **nucleus** is smaller than that of pro-erythroblast with condensed chromatin.

The **cytoplasm** is deeply **basophilic** due to large number of polysomes and free ribosomes.

Polychromatophilic erythroblast

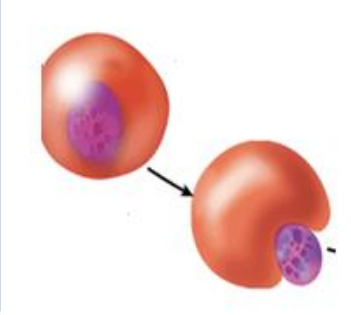


The cell becomes smaller.

The **nucleus** becomes smaller with more condensed chromatin.

The **cytoplasm** shows areas of **acidophilia** due to hemoglobin and others of **basophilia** due to free ribosomes and polysomes.

Orthochromatophilic erythroblast (normoblast)



The size still becomes smaller.

The **nucleus** condensed pyknotic and extruded peripherally.

The **cytoplasm** is markedly and uniformly **acidophilic** as hemoglobin becomes the main constituent.

The cytoplasm also contains ribosomes and polyribosomes.

This cell at last expels its nucleus.

They do not divide.

Reticulocyte

It is **non-nucleated** immature erythrocyte.

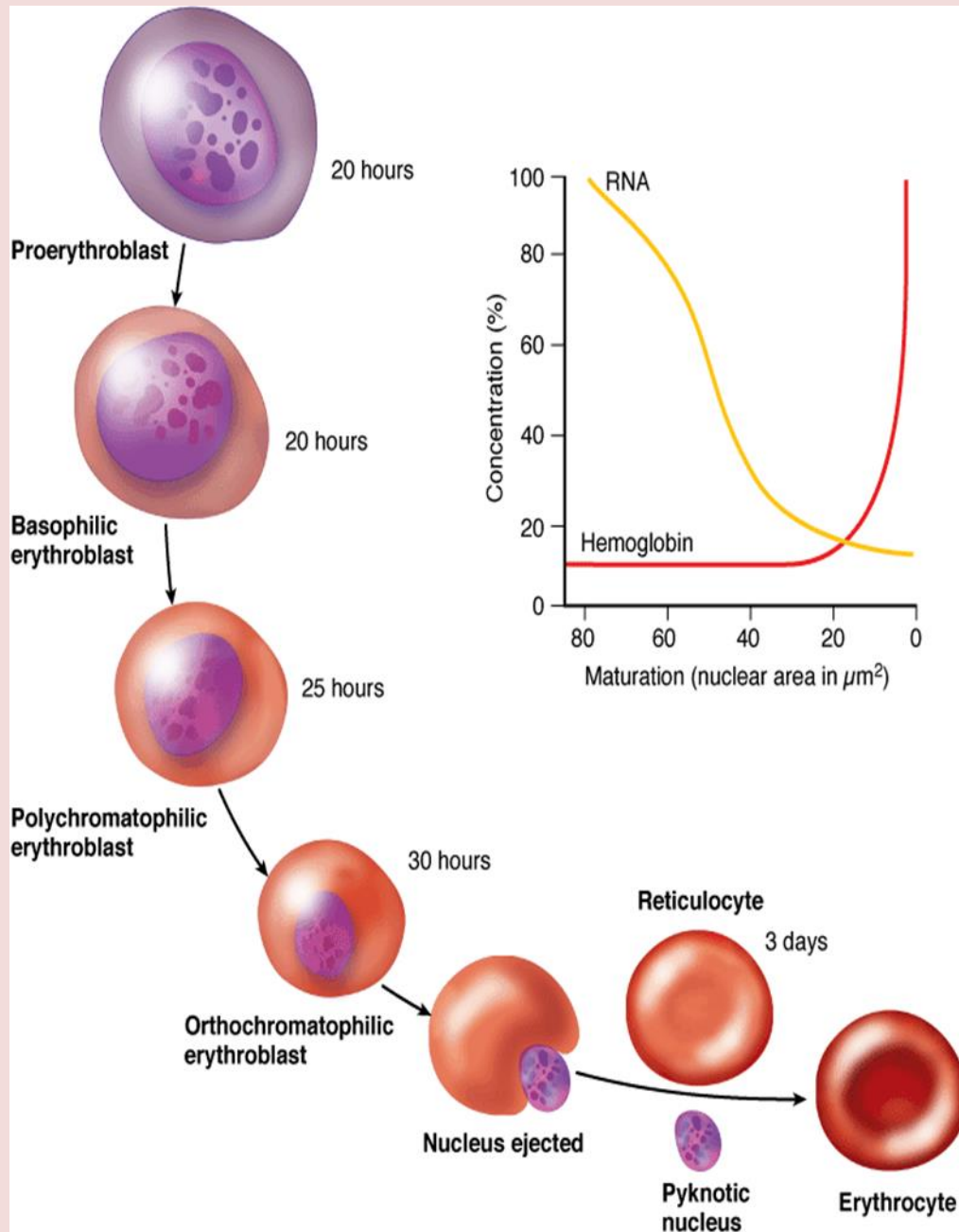
Its cytoplasm is filled with hemoglobin and small amount of polyribosomes.

When stained with **brilliant cresyl blue**, the polyribosomes aggregate to form a **basophilic network** (reticulum).

Reticulocytes pass to the circulation where **99%** of reticulocytes lose their ribosomes and change into mature erythrocytes.

Normally, **1%** of reticulocytes may appear in the peripheral blood.

Changes during erythropoiesis





1) The **cell size** becomes smaller.

2) The **nucleus** becomes smaller, condensed, pyknotic and finally extruded from the cell.

3) Decrease in free **ribosomes** and polysomes (decrease of basophilia) and increase of hemoglobin (increased acidophilia).

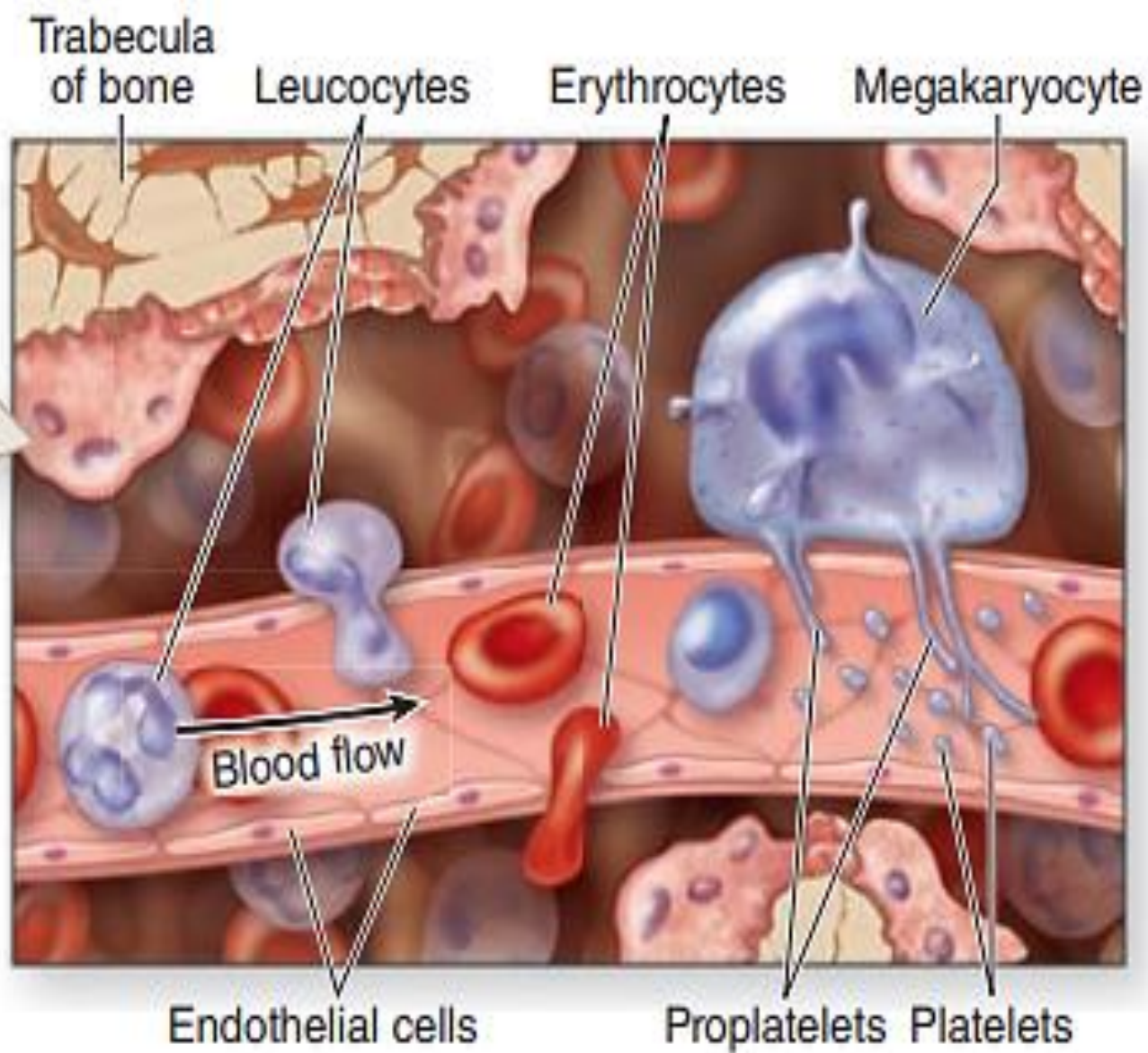
4) **Mitochondria** and other cell organelles gradually disappear.

Megakaryopoiesis

- Pluripotential stem cell  myeloid multipotential stem cells  CFU-Meg
- - **Megakaryoblast:**
 - It is 15-50 um in diameter.
 - It has large **kidney-shaped nucleus** with numerous nucleoli.
 - These cells undergo endomitosis, with repeated rounds of DNA replication not separated by cell divisions, resulting in a nucleus that is highly polyploidy
 - The cytoplasm is intensely **basophilic**

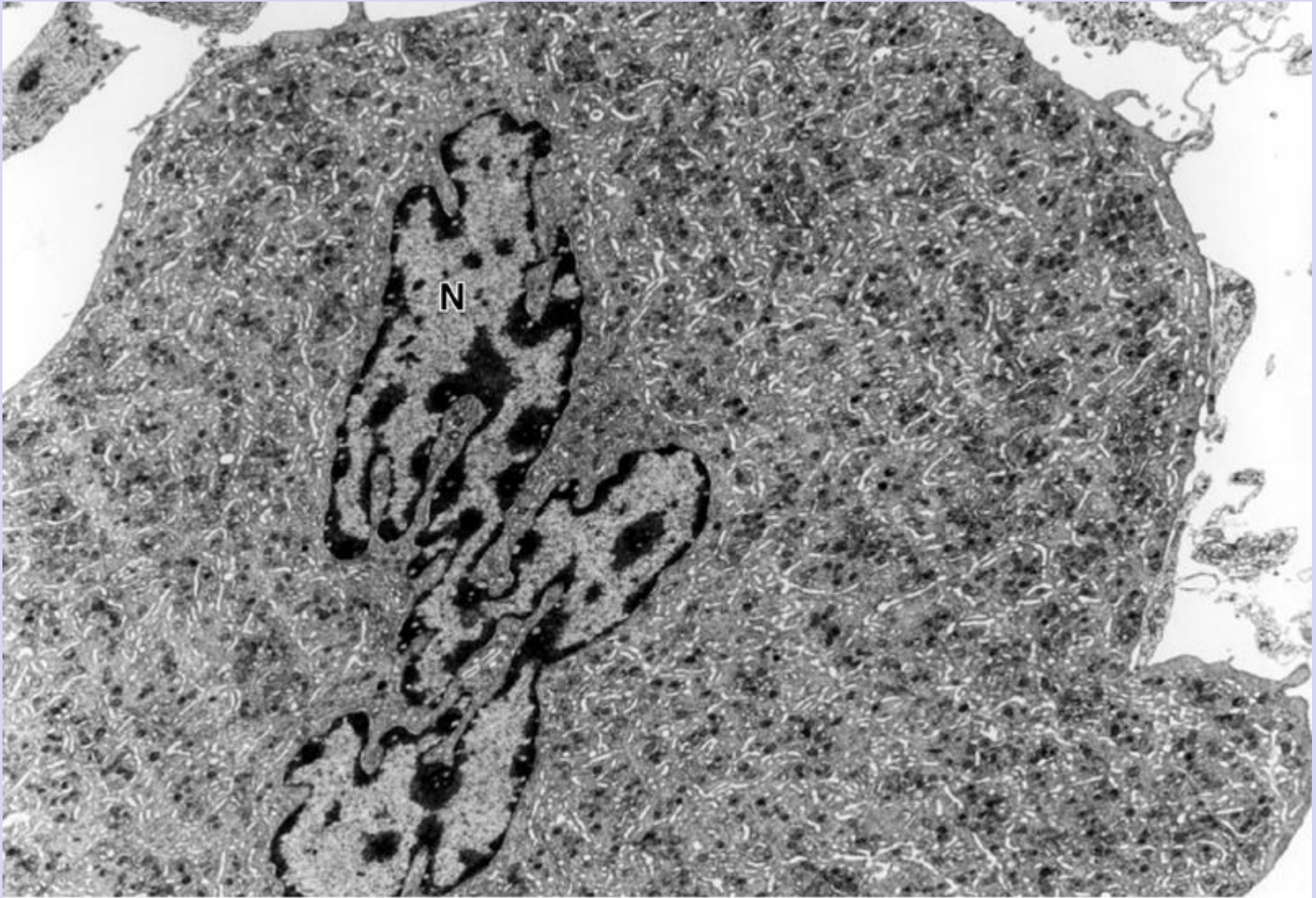
Megakaryocyte:

- It is a **giant cell** up to 150 um in diameter.
- It has an irregular **lobulated nucleus** with coarse chromatin and no visible nucleoli.
- The cytoplasm is **basophilic** and contains azurophilic granules, numerous mitochondria, well developed RER and Golgi apparatus.
- The process of Megakaryopoiesis is driven by thrombopoietin (liver,kidney)



- With maturation of megakaryocytes, they extend several long, wide branching processes called **proplatelets**. These cellular extensions penetrate the sinusoidal endothelium and are exposed in the circulating blood of the sinusoids.
- Numerous **demarcation channels** formed throughout the cytoplasm (fracture lines) for the release of platelets.
- Platelets originate by **fragmentation of cytoplasm** of mature megakaryocytes and the remainder of cells degenerated and phagocytosed by macrophages.

Demarcation membranes seen as tubular lines



Development of Leukocytes

- Development of leukocytes is divided into three processes

1- Granulopoiesis through which the granulocytes (Neutrophil, Eosinophils and Basophils) are formed.

2-Monocytopoiesis through which the monocytes are formed.

3-Lymphopoiesis through which the lymphocytes are formed.

Granulopoiesis

1-Pluripotential stem cell  myeloid multipotential

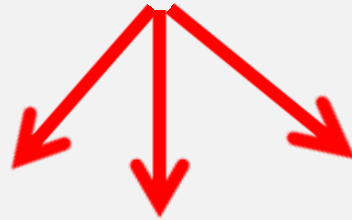
2-Granulocyte colony forming unit (CFU-G)

3- Myeloblast

4- Promyelocyte

5- Myelocyte

6-Metamyelocyte  **Band**

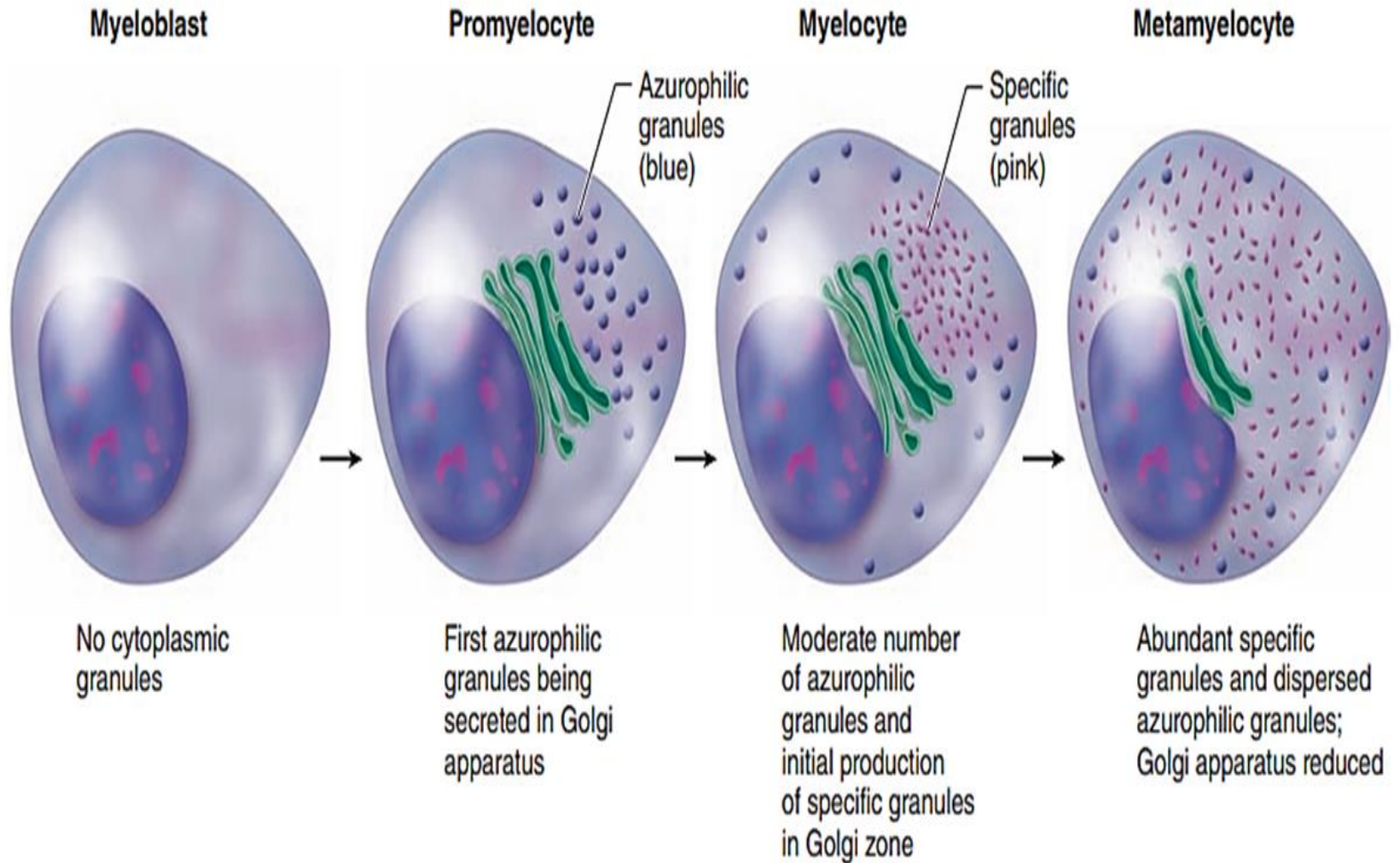


Neutrophils

Basophils

eosinophils

Granulopoiesis




- **The myeloblast** have finely dispersed chromatin, and faint nucleoli.
- **the promyelocyte** is characterized by basophilic cytoplasm and azurophilic granules containing lysosomal enzymes and myeloperoxidase.
- **the myelocyte stage** initial production of specific granules. the first visible sign of this differentiation appears in this stage
- **metamyelocyte stage** gradual increase in number of specific granules which eventually occupy most of the cytoplasm with indentation of nuclei

-These neutrophilic, basophilic, and eosinophilic metamyelocytes mature with further condensations of the nuclei.

-Before its complete maturation, granulocytes pass through an intermediate stage, **the band cell**, in which the nucleus is elongated. May be present in peripheral blood.

- **Mature cells**: (Neutrophils ,Eosinophils ,Basophils)

Development of Monocytes (Monocytopoiesis)

- 1- Pluripotential hematopoietic stem cell  myeloid multipotential stem cells
- 2- Colony forming unit of monocyte (CFU-M)
- 3- Monoblasts: identical to the myeloblast morphologically
- 4- Promonocytes: a large cell with basophilic cytoplasm and a large, slightly indented nucleus
- 5- Monocytes: circulate for three days then enter C.T and become macrophages.

Development of Lymphocytes (Lymphopoiesis)

1-Pluripotential hematopoietic stem cell

2- **Lymphoid multipotential stem cells:** divide into CFU-LyT (thymus) and CFU-LyB (bone marrow).

3-Lymphoblasts

4-Prolymphocytes

5-Mature Lymphocytes (T, B, NK)

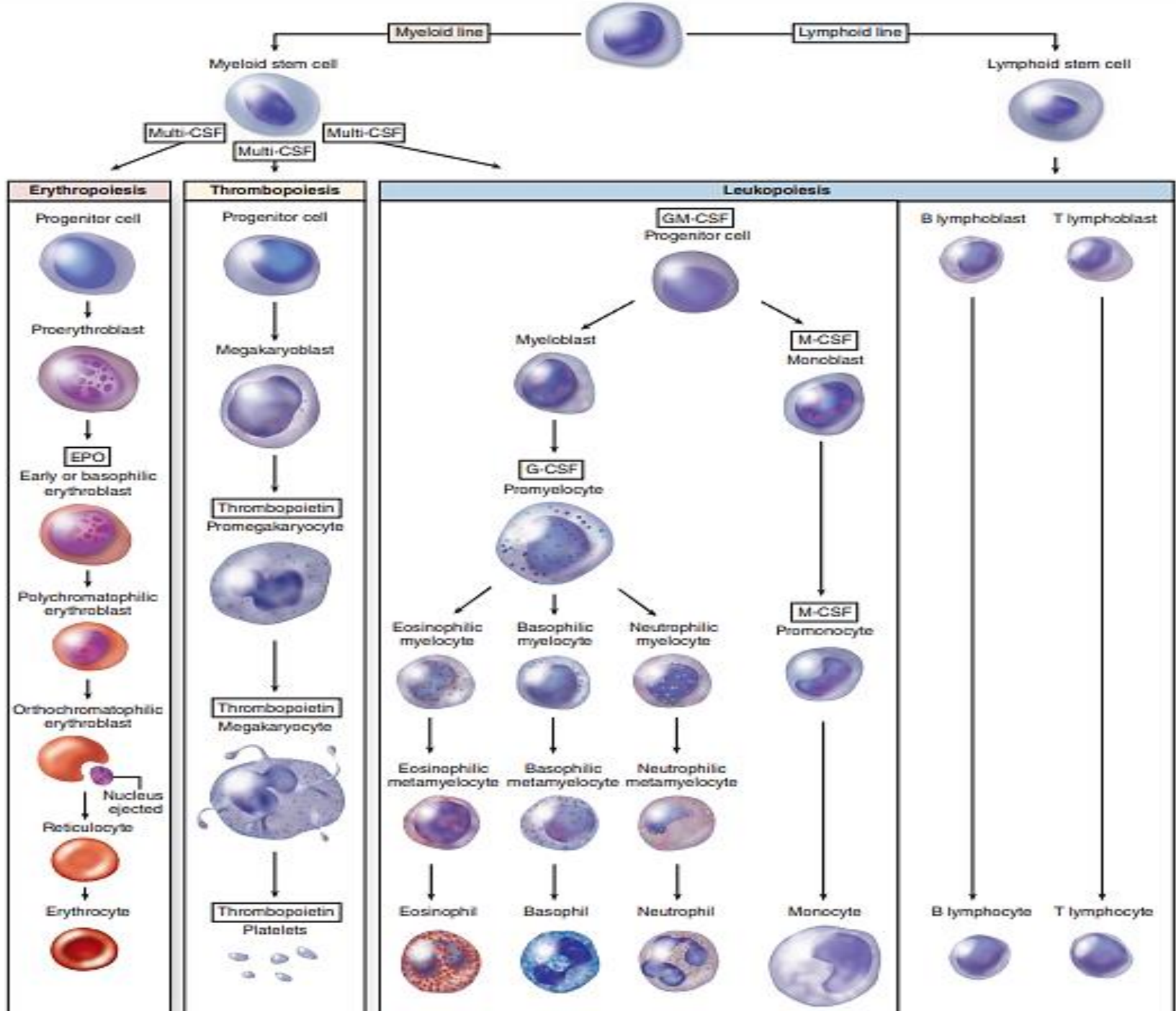
- As lymphocytes develop, their nuclei become smaller, nucleoli become less visible, and the cells decrease in size overall.
- In the bone marrow and in the thymus, these cells synthesize the specific cell surface proteins that characterize B or T lymphocytes, respectively

Major hemopoietic cytokines (growth factors or colony-stimulating factors).

Cytokine	Major Activities and Target Cells ^a	Important Sources
Stem cell factor (SCF)	Mitogen for all hemopoietic progenitor cells	Stromal cells of bone marrow
Erythropoietin (EPO)	Mitogen for all erythroid progenitor and precursor cells, also promoting their differentiation	Peritubular endothelial cells of the kidney; hepatocytes
Thrombopoietin (TPO)	Mitogen for megakaryoblasts and their progenitor cells	Kidney and liver
Granulocyte-macrophage colony-stimulating factor (GM-CSF)	Mitogen for all myeloid progenitor cells	Endothelial cells of bone marrow and T lymphocytes
Granulocyte colony-stimulating factor (G-CSF or filgrastim)	Mitogen for neutrophil precursor cells	Endothelial cells of bone marrow and macrophages
Monocyte colony-stimulating factor (M-CSF)	Mitogen for monocyte precursor cells	Endothelial cells of marrow and macrophages
Interleukin-1 (IL-1)	Regulates activities and cytokine secretion of many leukocytes and other cells	Macrophages and T helper cells

Major hemopoietic cytokines (growth factors or colony-stimulating factors).

Cytokine	Major Activities and Target Cells ^a	Important Sources
Interleukin-2 (IL-2)	Mitogen for activated T and B cells; promotes differentiation of NK cells	T helper cells
Interleukin-3 (IL-3)	Mitogen for all granulocyte and megakaryocyte progenitor cells	T helper cells
Interleukin-4 (IL-4)	Promotes development of basophils and mast cells and B-lymphocyte activation	T helper cells
Interleukin-5 (IL-5) or eosinophil differentiation factor (EDF)	Promotes development and activation of eosinophils	T helper cells
Interleukin-6 (IL-6)	Mitogen for many leukocytes; promotes activation of B cells and regulatory T cells	Macrophages, neutrophils, local endothelial cells
Interleukin-7 (IL-7)	Major mitogen for all lymphoid stem cells	Stromal cells of bone marrow



Thank you