Hematopoiesis II

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Erythropoiesis

formation Process

- 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.

GF hormone

Erythropoiesis

blast → cyte

1-Pluripotential stem cell → myeloid multipotential

2-Erythrocyte colony forming unit (CFU-E) (progenitor)

3- Pro-erythroblast

blue

4- Basophilic erythroblast

multi- color

5- Polychromatophilic erythroblast

1 - color

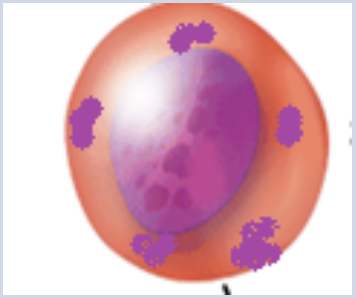
6-Orthochromatophilic erythroblast (normoblast)

color

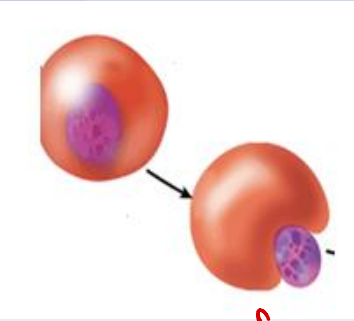
7-Reticulocyte

↓

Erythrocyte

Pro-erythroblast 	*note: cell smaller / nucleus smaller & condense / darker It is a large cell (12-15 um in diameter) The 1 nucleus is central, pale and contains fine chromatin and two visible nucleoli. The 2 cytoplasm is **basophilic** due to presence of 3 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)

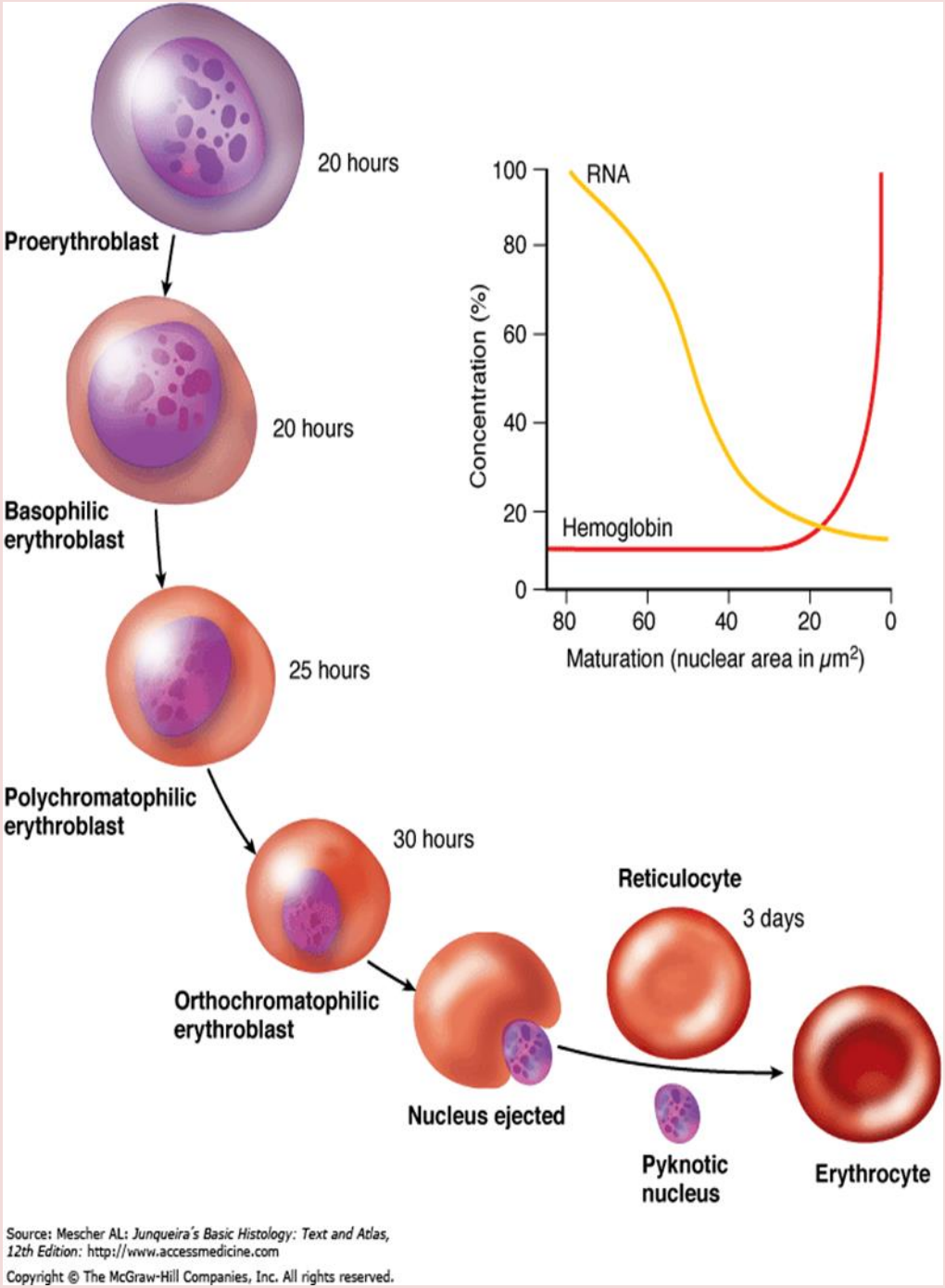


The size still becomes smaller.
The nucleus condensed pyknotic and extruded peripherally.
The cytoplasm is markedly and uniformly **acidophilic** as hemoglobin becomes the main constituent.
The cytoplasm also contains ribosomes and polyribosomes.
This cell at last expels its nucleus.
They do not divide.

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.



Source: Mescher AL: *Junqueira's Basic Histology: Text and Atlas, 12th Edition:* http://www.accessmedicine.com

1)The cell size becomes smaller.

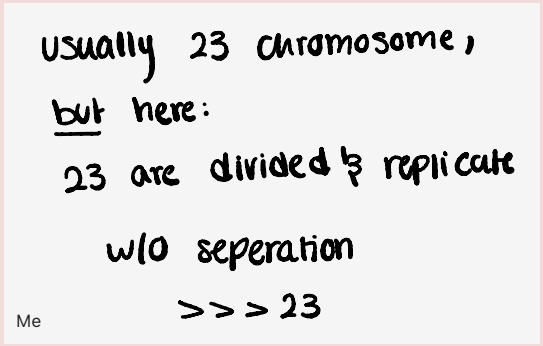
2)The nucleus becomes smaller, condensed, pyknotic and finally extruded from the cell.

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

4)Mitochondria and other cell organelles gradually disappear.

Big nucleus Megakaryopoiesis

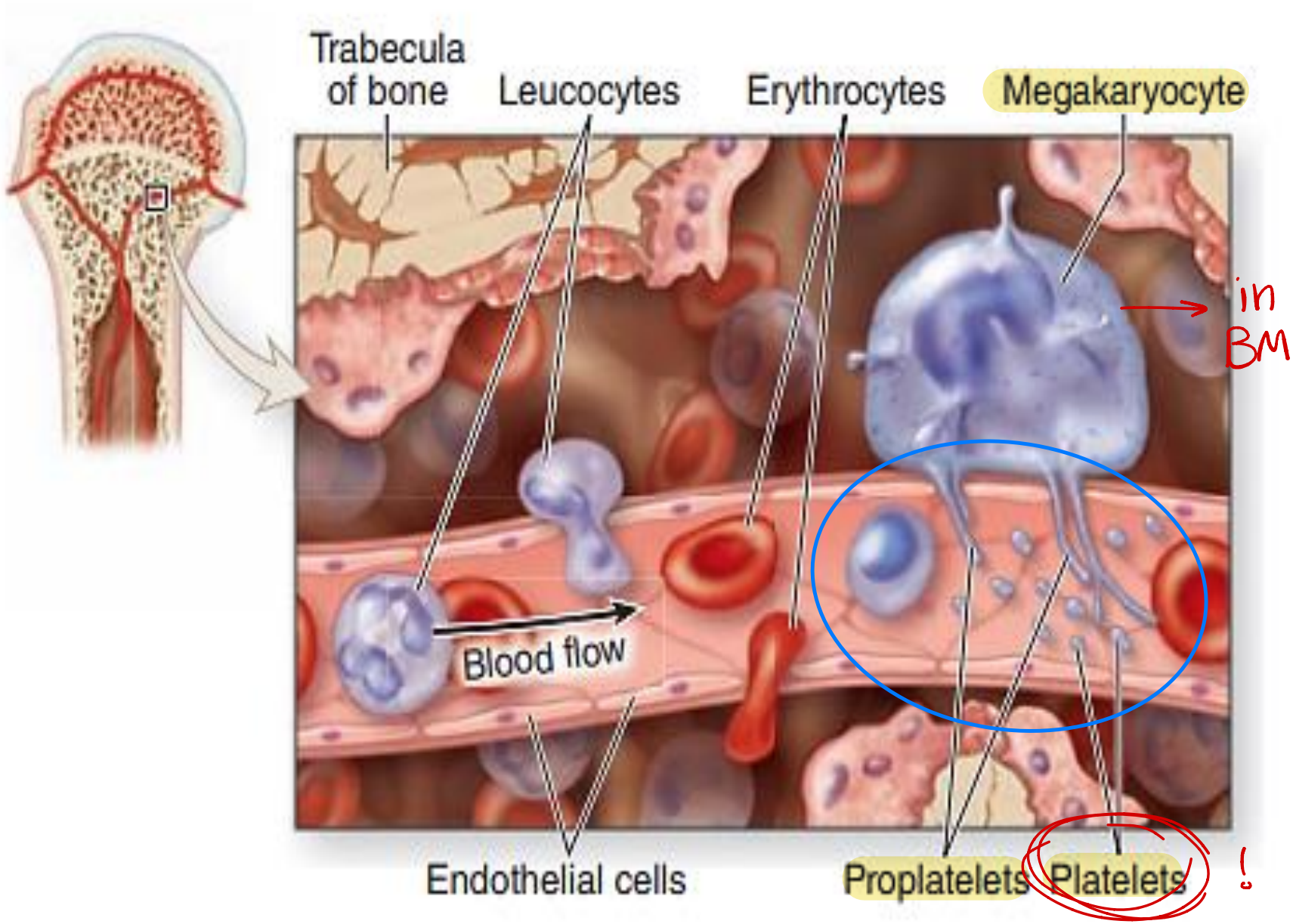
- **Pluripotential stem cell ⟶ myeloid multipotential stem cells ⟶ CFU-Meg**



- **- Megakaryoblast:**
  - It is 15-50 um in diameter.
  - It has large kidney-shaped nucleus with numerous nucleoli.
  - polyploidy nucleus [multiple sets of haploid number (23 chromosomes). endomitosis (multiple nuclear divisions without separation)
  - The cytoplasm is intensely basophilic

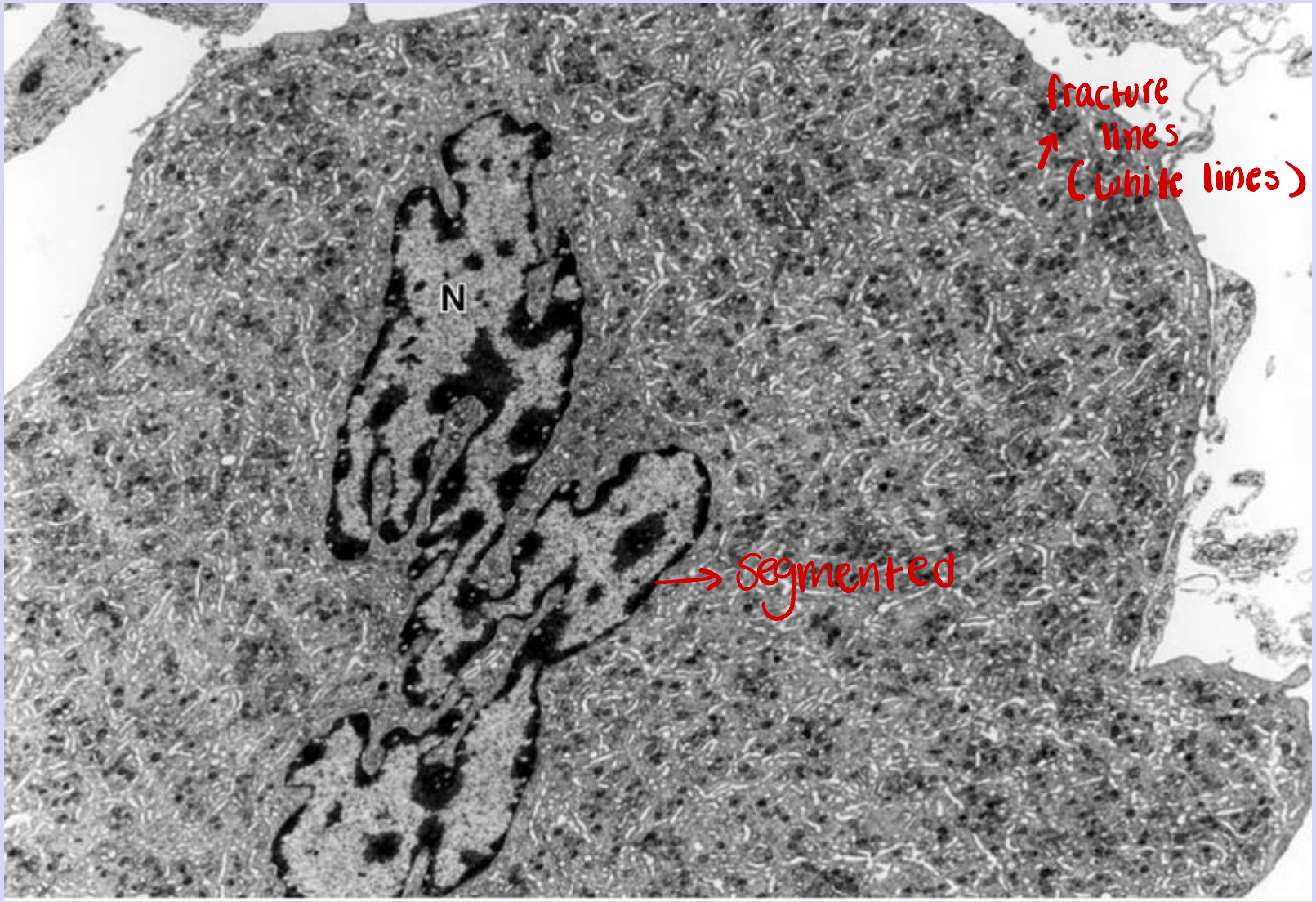
Megakaryocyte:

- It is a giant cell up to 150 um in diameter.
- It has an irregular lobulated nucleus with coarse chromatin.
- The cytoplasm is basophilic and contains azurophillic granules, numerous mitochondria, well developed RER and Golgi apparatus.
- The process of Megakaryopoiesis is driven by thrombopoietin (liver,kidney)


Trabecula of bone
Leucocytes
Erythrocytes
Megakaryocyte
in BM
Blood flow
Endothelial cells
Proplatelets
Platelets
!

- 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

the growth factors are called granulocyte colony-stimulating factors (G-CSFs) and cytokines

+ cytokines

1-Pluripotential stem cell ⟶ myeloid multipotential

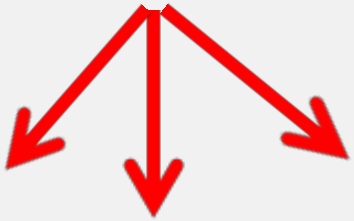
2-Granulocyte colony forming unit (CFU-G) ← progenitor

3- Myeloblast

4- Promyelocyte

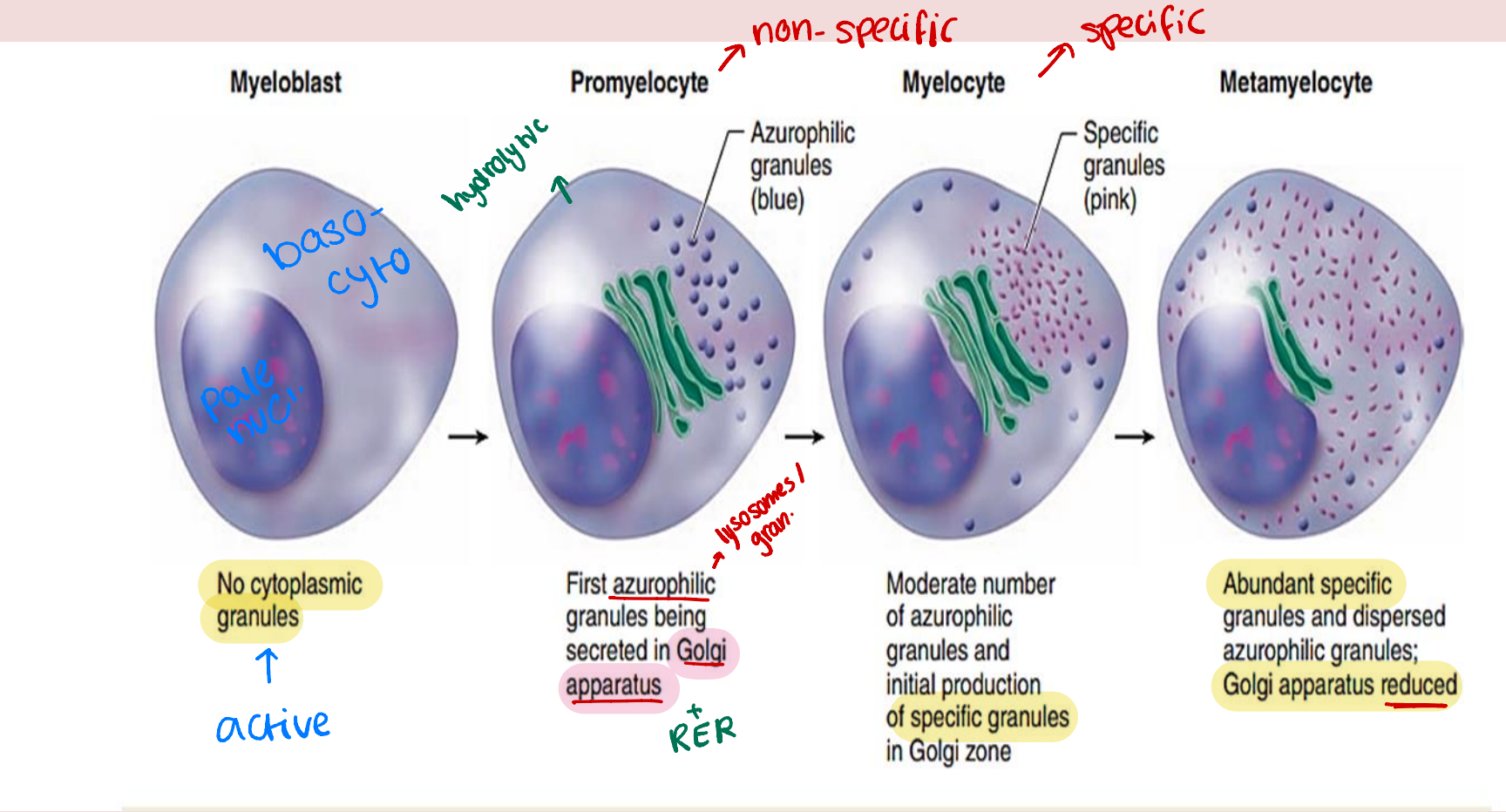
5- Myelocyte

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
- **metamyelocyte stage** gradual increase in number of specific granules which eventually occupy most of the cytoplasm with indentation of nuclei

RER

each myelocyte alone
eosino neutro baso
start to have seperate pathway

NOT lost (imp) → active cells

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

all nuclei are band diff but hold granules

-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.

+ specific granules to each

w/ immune stim, diff into:

- **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) (M-CSF)

macrophage

3- Monoblasts: identical to the myeloblast morphologically

use lysosomes from RER to phagocyte

4- Promonocytes: a large cell with basophilic cytoplasm and a large, slightly indented nucleus

RER = baso

5- Monocytes: circulate for three days then enter C.T and become macrophages.

mature

Development of Lymphocytes (Lymphopoiesis)

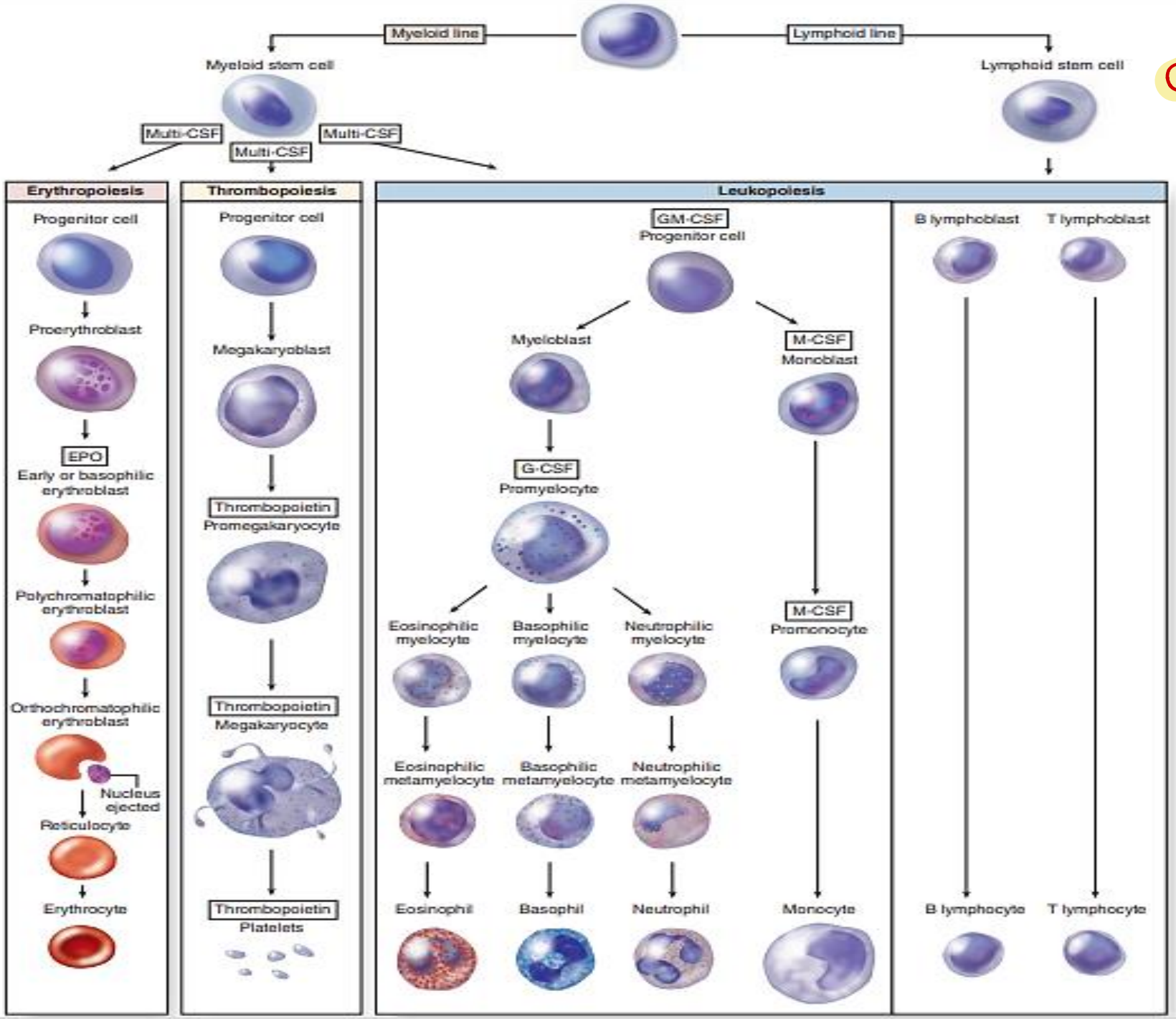
1-Pluripotential hematopoietic stem cell

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


Myeloid line
Lymphoid line
Myeloid stem cell
Lymphoid stem cell
Multi-CSF
Multi-CSF
Multi-CSF
Erythropoiesis
Progenitor cell
Proerythroblast
EPO
Early or basophilic erythroblast
Polychromatophilic erythroblast
Orthochromatophilic erythroblast
Nucleus ejected
Reticulocyte
Erythrocyte
Thrombopoiesis
Progenitor cell
Megakaryoblast
Thrombopoietin
Promegakaryocyte
Thrombopoietin
Megakaryocyte
Thrombopoietin
Platelets
Leukopoiesis
GM-CSF
Progenitor cell
Myeloblast
M-CSF
Monoblast
G-CSF
Promyelocyte
M-CSF
Promonocyte
Eosinophilic myelocyte
Basophilic myelocyte
Neutrophilic myelocyte
Eosinophilic metamyelocyte
Basophilic metamyelocyte
Neutrophilic metamyelocyte
Eosinophil
Basophil
Neutrophil
Monocyte
B lymphoblast
T lymphoblast
B lymphocyte
T lymphocyte