Stage of hematopoiesis, normal peripheral blood smear and bone marrow aspiration smear

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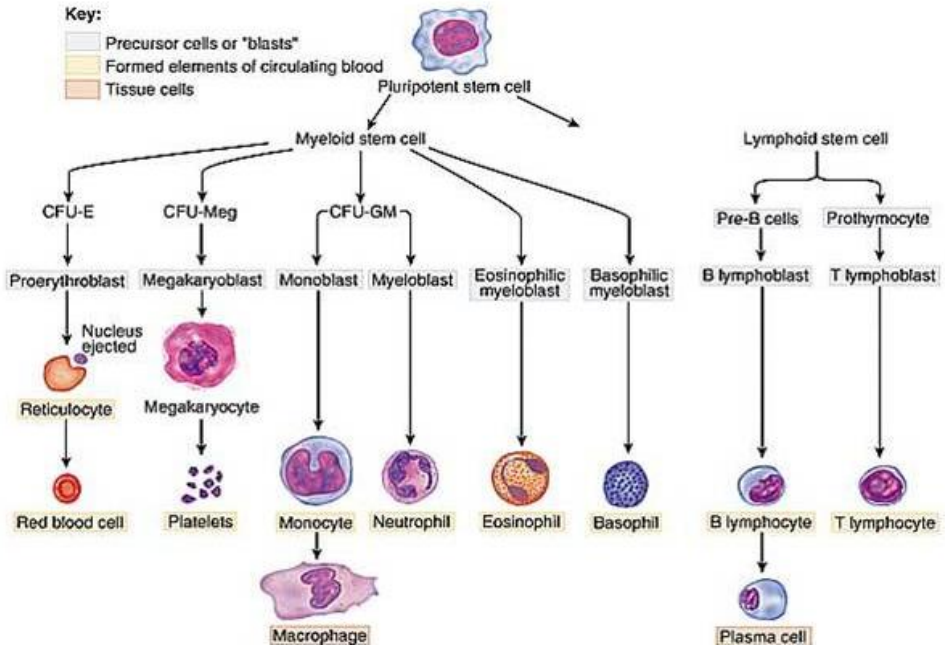
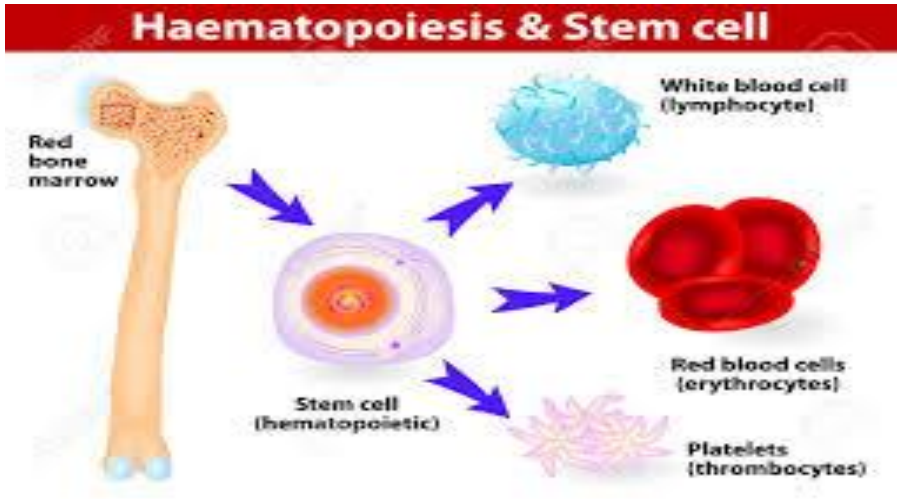
Hematopoiesis

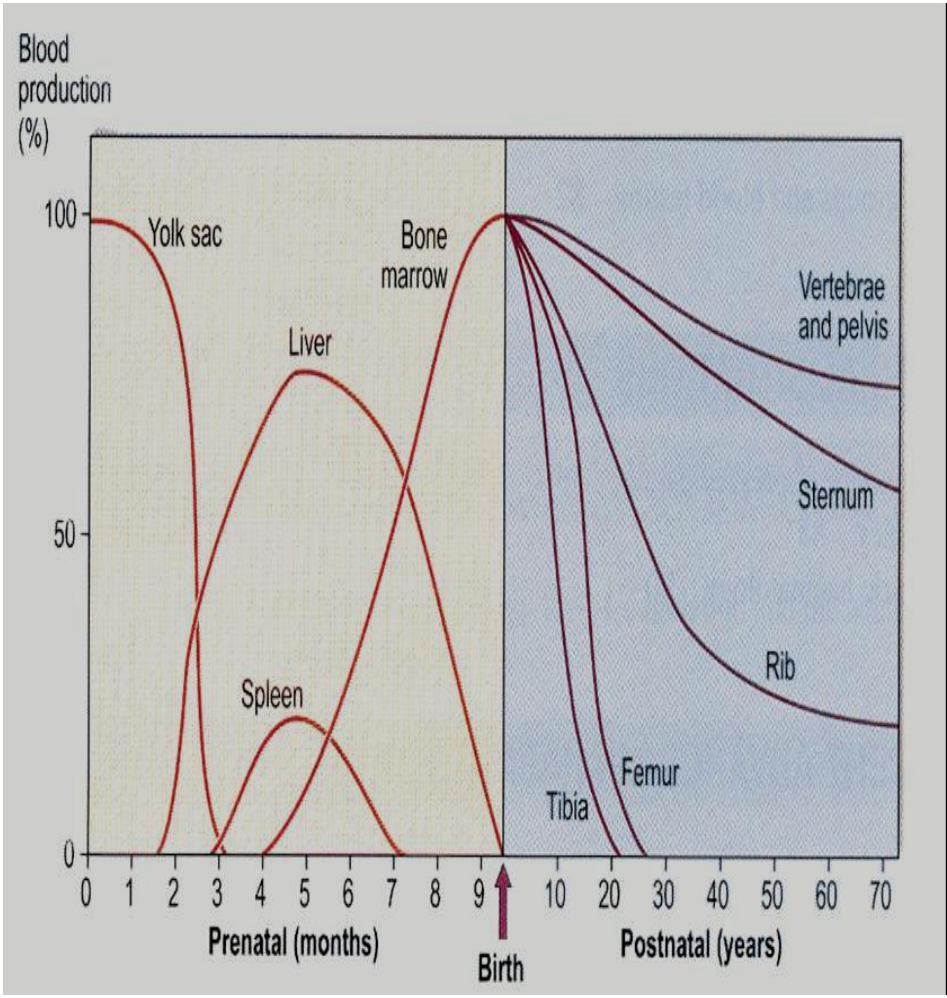
- Stem cells
  - Self renewal
  - Plasticity
- Progenitor cells
  - Developmentally-restricted cells
- Mature cells
  - Mature cell production takes place from the more developmentally-restricted progenitors





Sites of Hematopoiesis

- Yolk sac
  - –Embryonic stem cells - mesenchymal cells in yolk sac
- Liver and spleen
  - –After 12 weeks, fetal liver and spleen become the main site
- Bone marrow
  - –From week 20, bone marrow starts to become important and by the time of birth it is the main hematopoietic organ



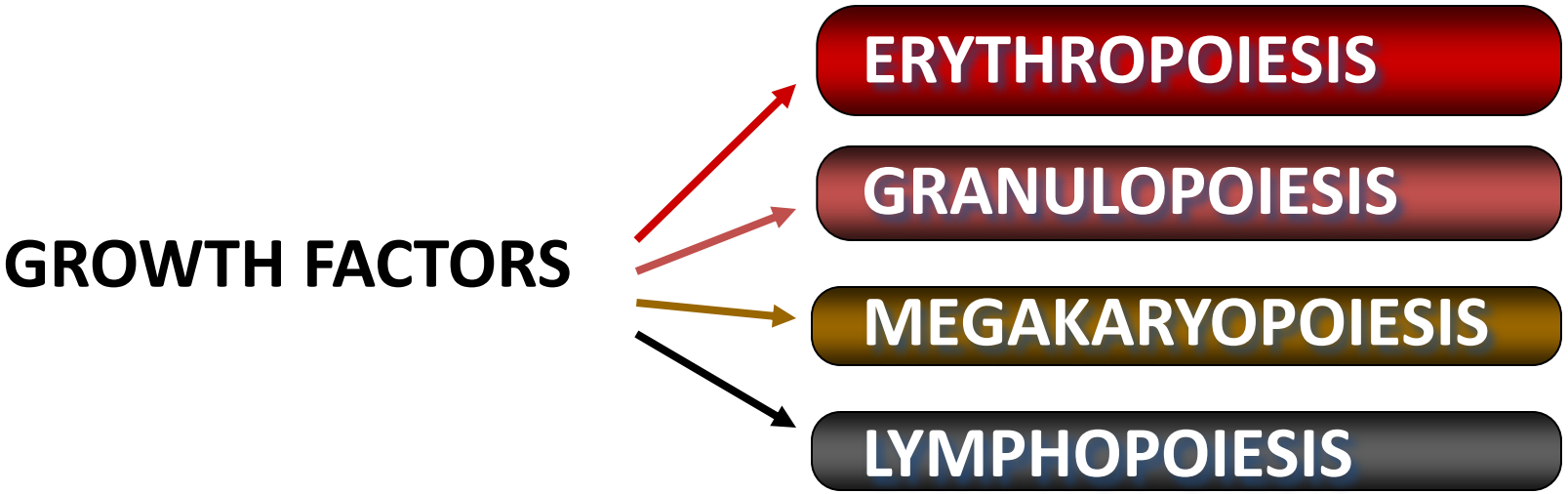
Hematopoietic growth factors

- These factors have the capacity to stimulate the proliferation of their target progenitor cells when used as a sole source of stimulation.
  - **G-CSF = Granulocyte- colony stimulating factor**
  - **GM-CSF = Granulocyte Macrophage- colony stimulating factor**
  - **M-CSF = Macrophage- colony stimulating factor**
  - **Erythropoietin = Erythropoiesis stimulating hormone**
  - **Thrombopoietin= Stimulates megakaryopoiesis**
- The hematopoietic growth factors are glycoprotein hormones that **regulate the proliferation and differentiation** of hematopoietic progenitor cells and **the function** of mature blood cells.

Hematopoietic growth factors

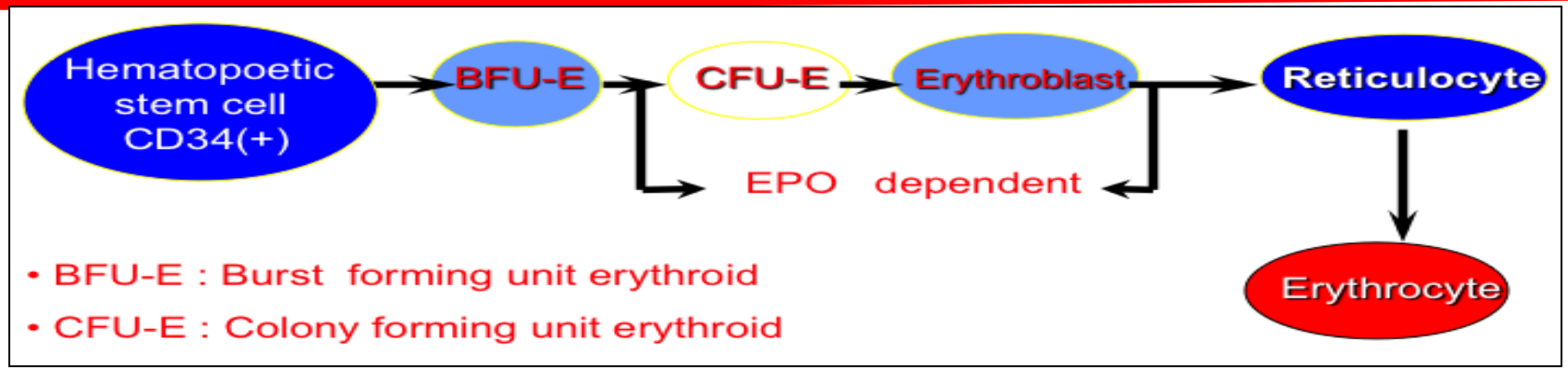
- Cytokines
  - IL 1 (Interleukin 1), IL-3, IL-4, IL-5, IL-6, IL-9, IL-11
  - TGF-β
  - SCF (Stem cell factor, also known as kit-ligand)

Hematopoiesis



Generation of each specific lineage of mature blood cells **is regulated by** a **specific** set of hematopoietic **growth factors**.

Hematopoietic growth factors-Erythropoiesis

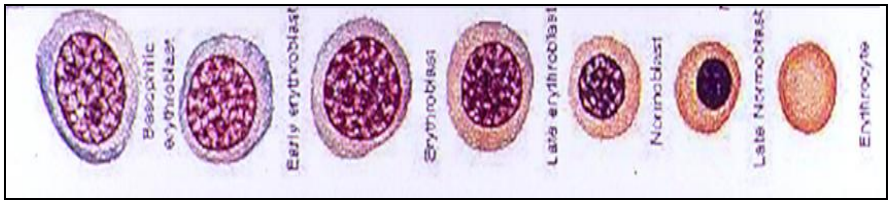


- Erythropoietin-independent stage:
  - GM-CSF
  - SCF

marrow stromal cells
IL-3 (activated T-cells)

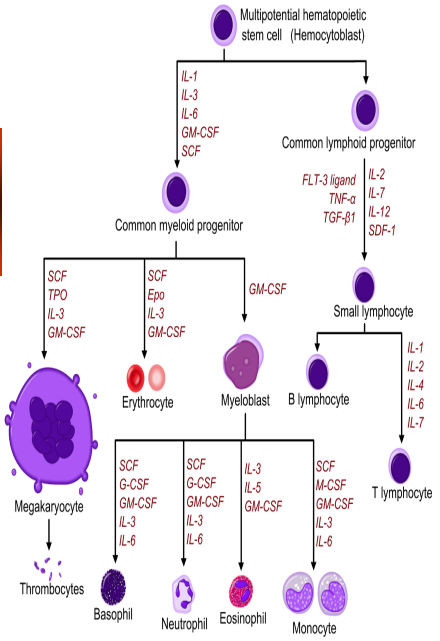
- Erythropoietin-dependent stage:
  - Erythropoietin

hypoxia (liver, kidney)



Hematopoietic growth factors-Granulopoiesis

- Early phase: GM-CSF SCF IL-3
- Neutropoiesis: G-CSF
- Monopoiesis: M-CSF
- Eosinopoiesis: IL-5 IL-3 GM-CSF
- Basopoiesis, Mastpoiesis: SCF IL-3



Hematopoietic growth factors-Megakaryopoiesis

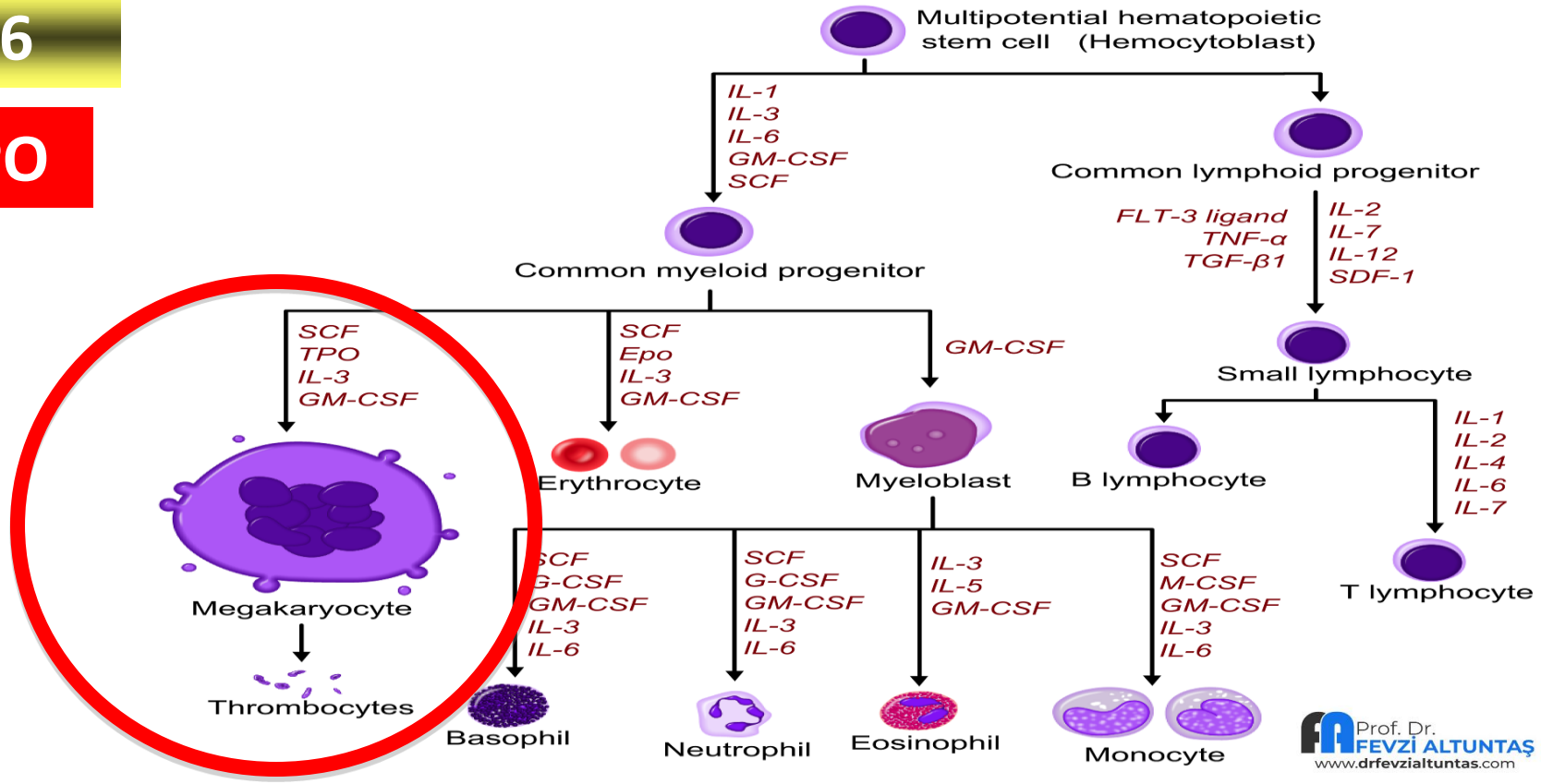
IL-3 **GM-CSF**

SCF

IL-6

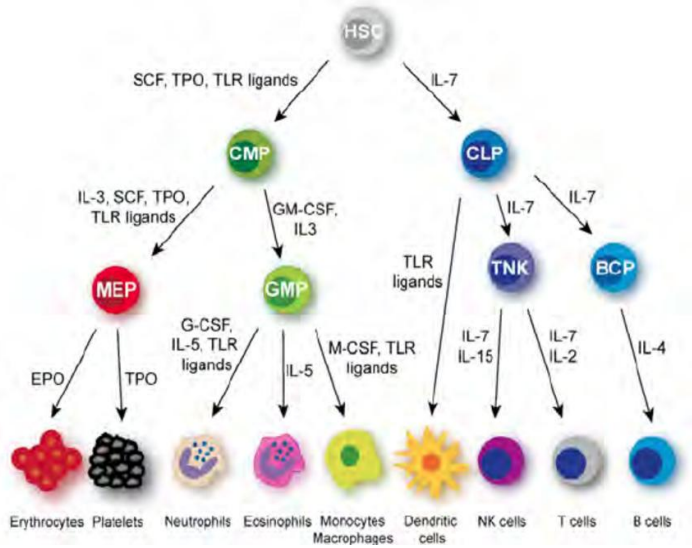
TPO

may also play a role



Hematopoietic growth factors-Lymphopoiesis

- B-cells:
  - initial stage: IL-7 SCF
  - later stage: Fcg rec IL-4 IL-6
  - final proliferation and Antibody secretion: IL-6 GM-CSF
- T-cells:
  - CD8 cells: IL-2 Ag
  - CD4 cells: TCR/CD3 CD28



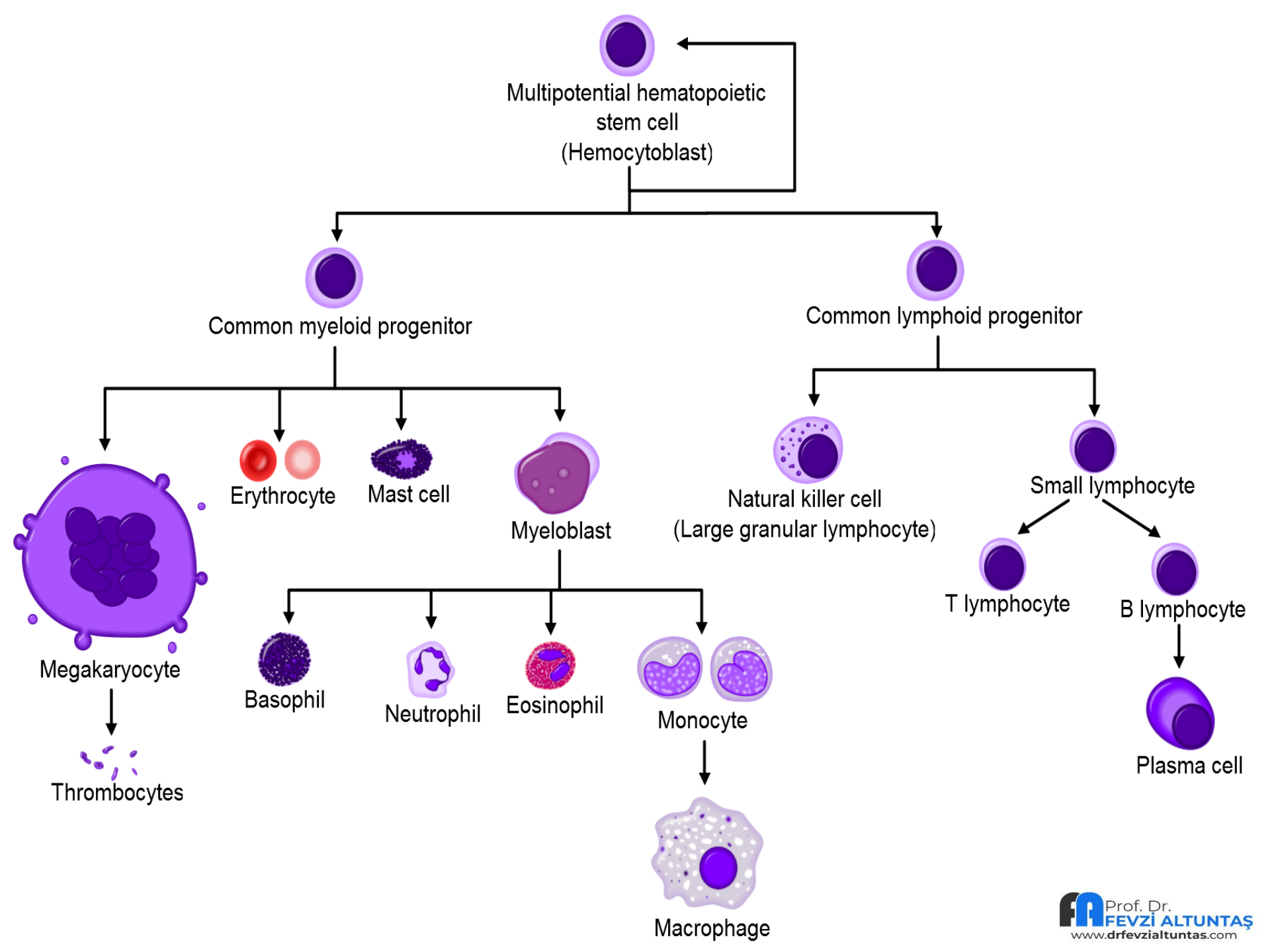
Hematopoiesis

Stem Cell

Proliferative potential

Differentiation

Mature cells

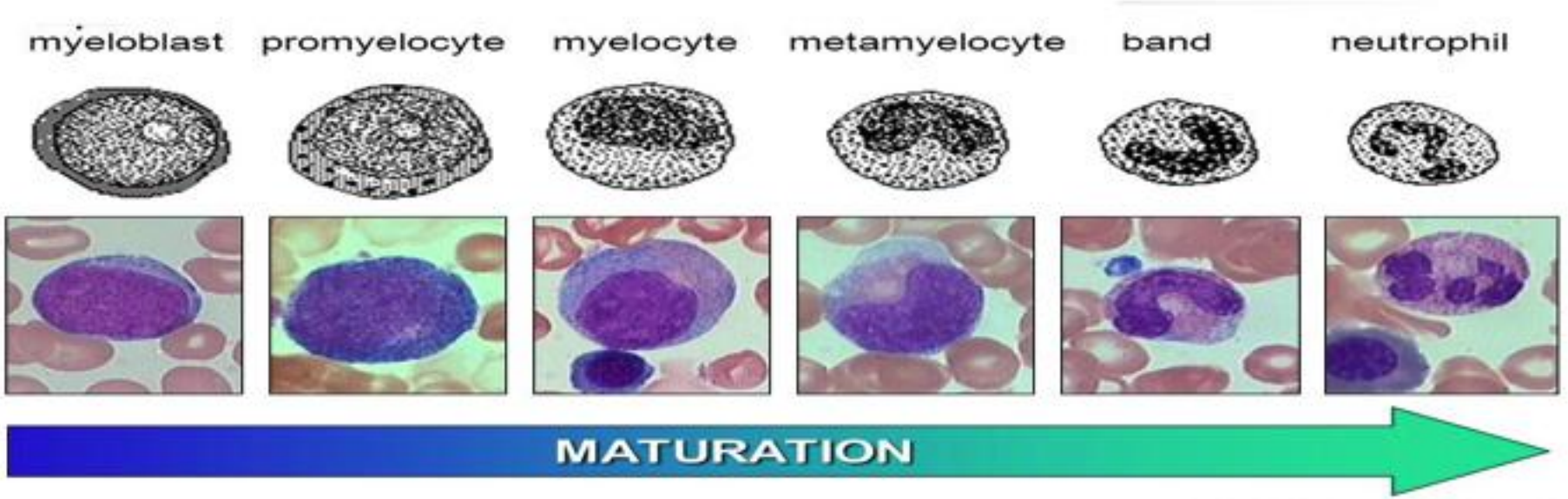


GRANULOPOIESIS

Myeloblast→ promyelocyte→myelocyte

→ metamyelocyte → band form →

mature neutrophil.



Myeloblast

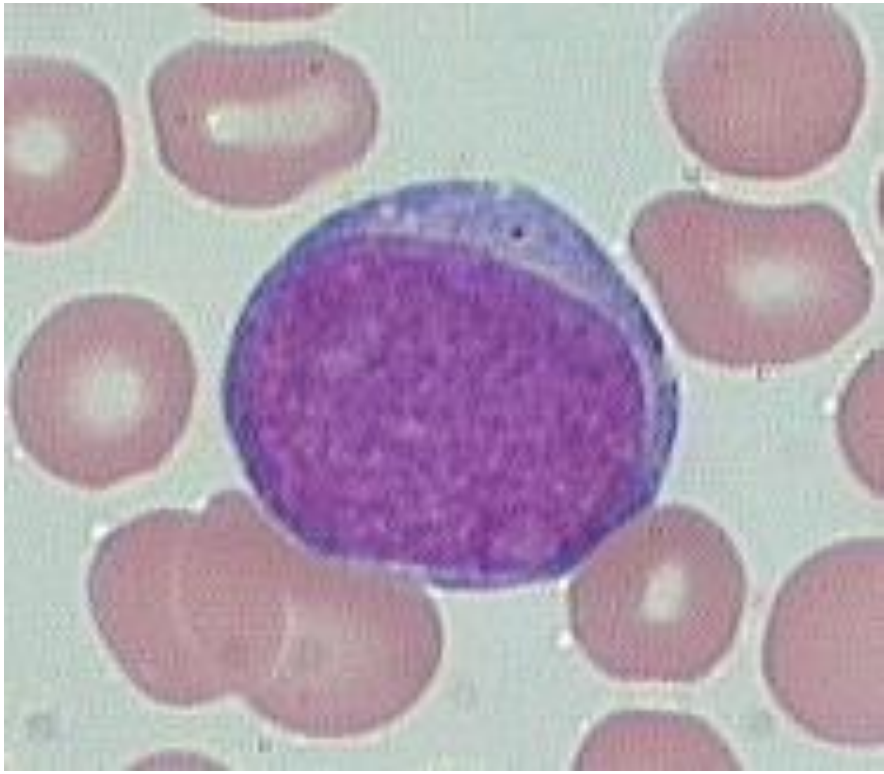
- Cell division: +
- ~2% of nucleated cells in BM
- Size: 8-13 mm diameter
- Cytoplasm:

  basophilic (many free ribosomes) granules
- Nucleus:

  undifferentiated

  round to ovoid

  coarse nucleoli --> **sieve-like appearance**



≥20% myeloblast=Acute Myeloid Leukemia (AML)

Promyelocyte

- undergo cell division (+)
- ~5% of nucleated cells in BM
- Size: 20 mm diameter
- Cytoplasm:

  deep blue **azurophilic granules**

  abundant rER, free ribosome

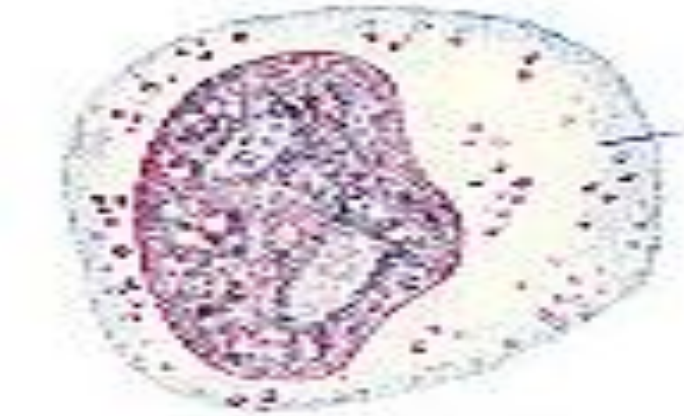
  numerous mitochondria

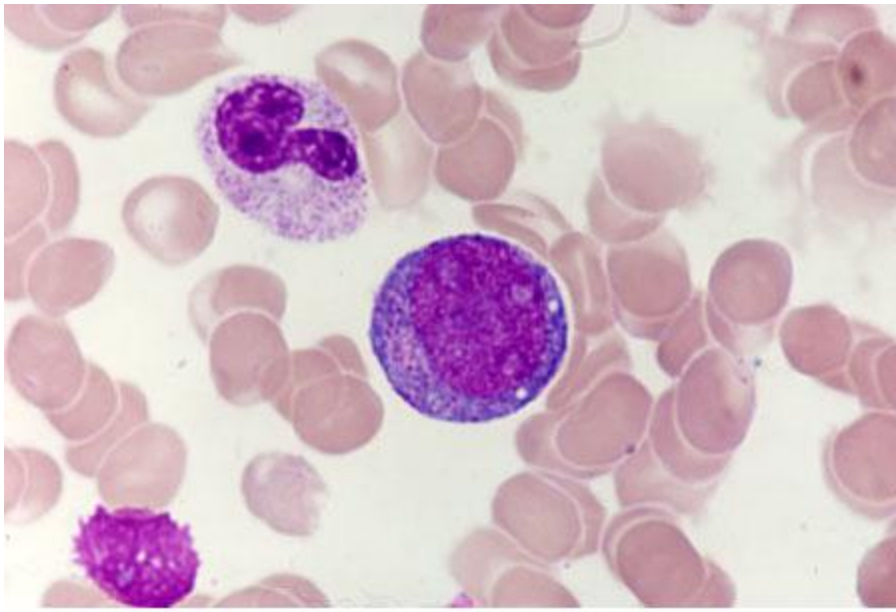
  well developed Golgi
- Nucleus:

  round to ovoid

  occasionally indented

  prominent nucleoli





Source: Lichtman MA, Shafer MS, Felgar RE, Wang N:
Lichtman's Atlas of Hematology: http://www.accessmedicine.com

Myelocyte

- **cell division: +**
- 5-20% of nucleated cells in BM
- cytoplasm:

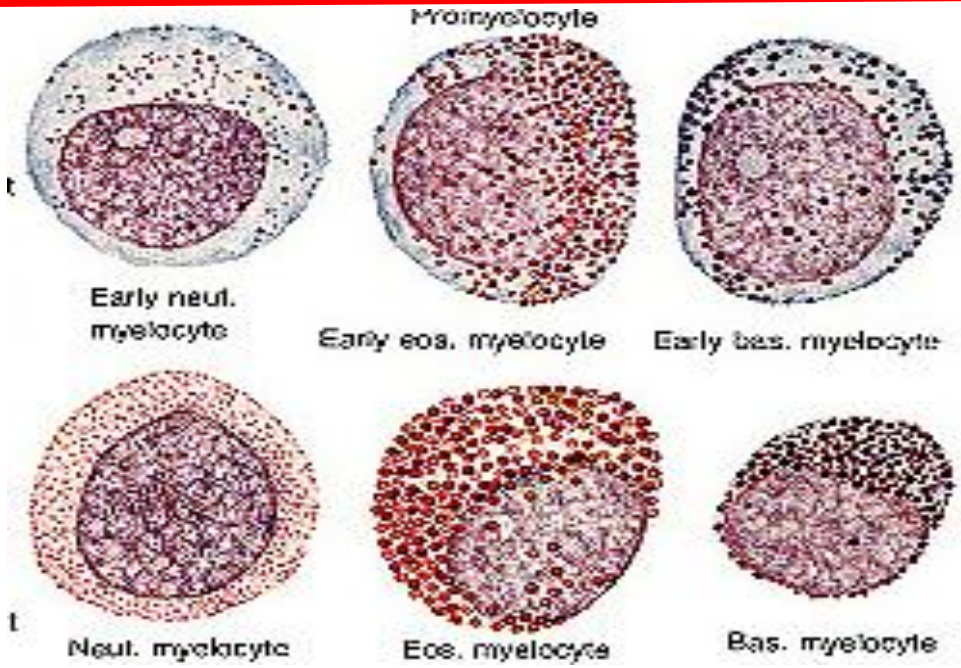
  specific granules

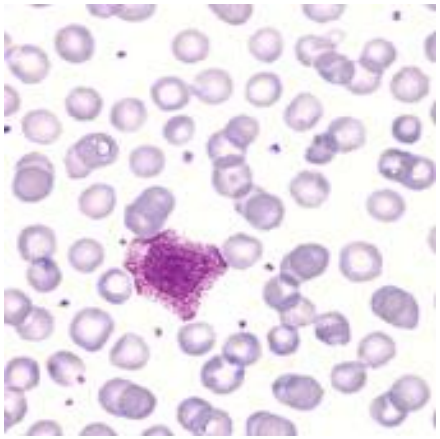
  decreased in basophilia
- nucleus:

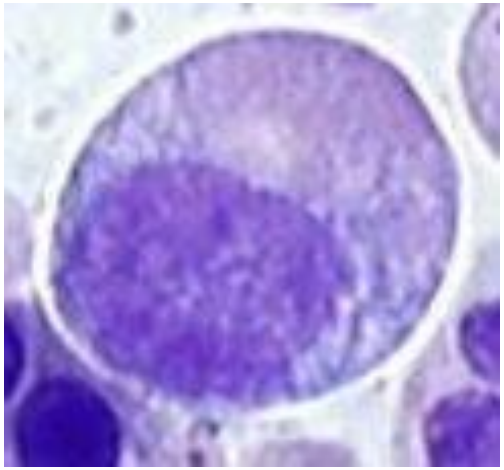
  <u>ovoid</u> irregular shape

  disappearing of nucleoli

  dense and compact chromatin







Metamyelocyte

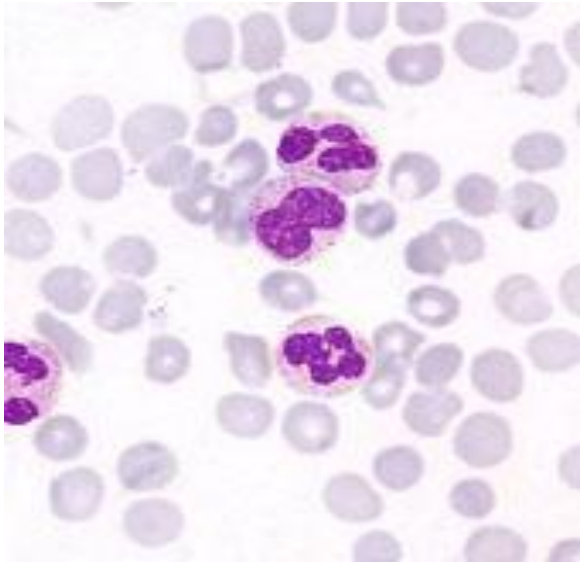
- **no more cell division**
- ~22% of nucleated cells in BM
- size: 10-18 mm diameter (slightly larger than mature PMN)
- cytoplasm: prominent secondary granules
- nucleus:

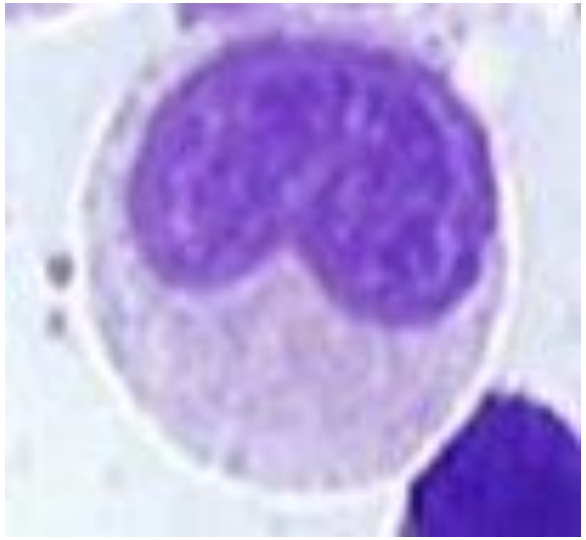
  slightly indented,

  kidney-shaped

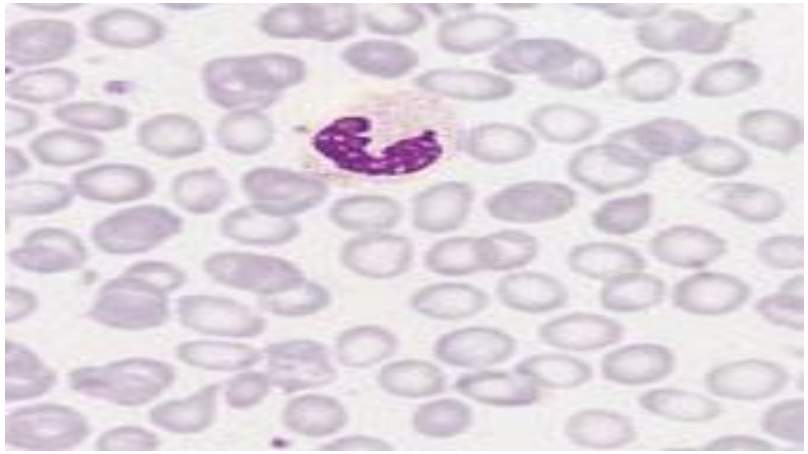
  dense chromatin

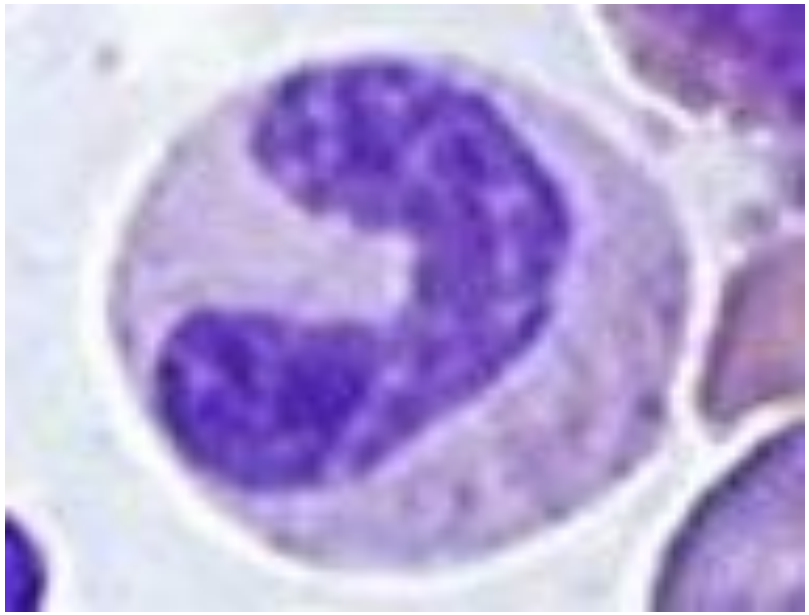
  no nucleolus





Band Neutrophils

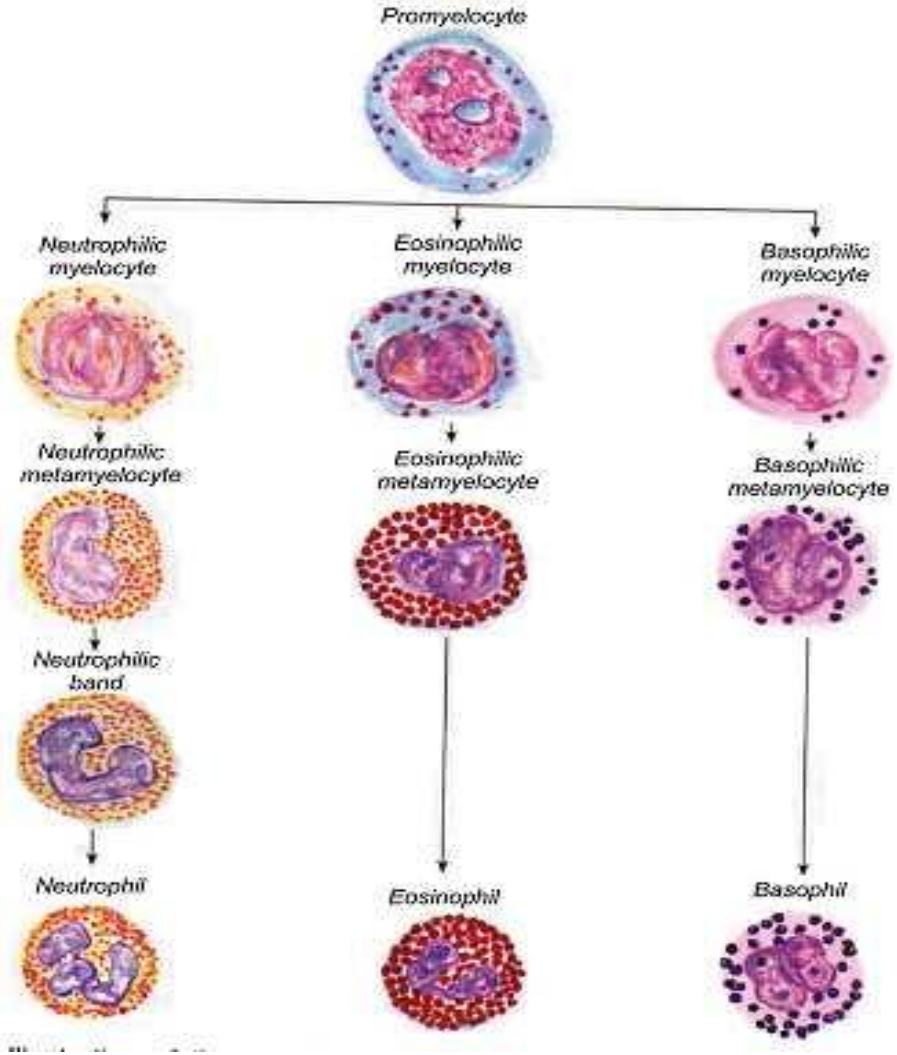




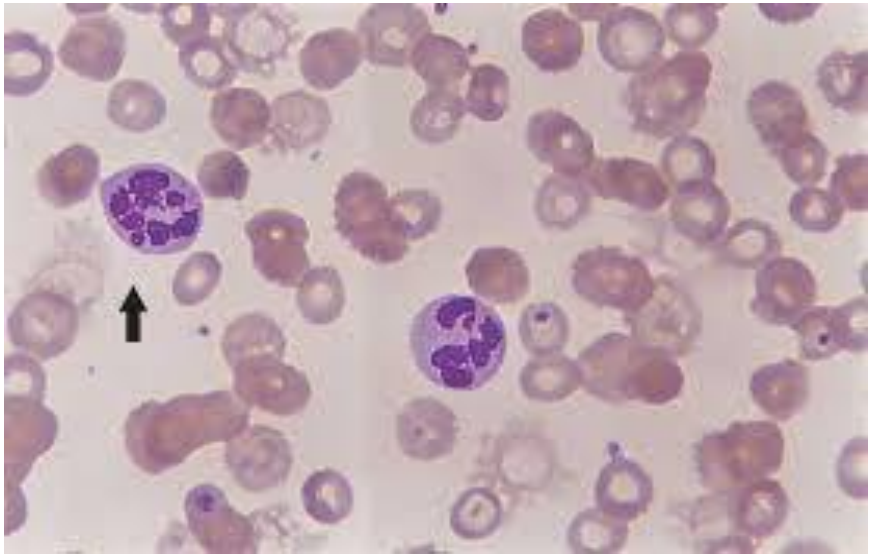
- There are smaller numbers of cells of neutrophil lineage with non-segmented nuclei.
- They are referred to as neutrophil band cells or band forms.
- They are less mature than segmented neutrophils.
- An increased number of band cells is referred to as a'**left shift**'.

Granulocytes

- There are three types of granulocyte named according to their staining characteristics in blood films.
  - Neutrophils
  - Eosinophils
  - Basophils

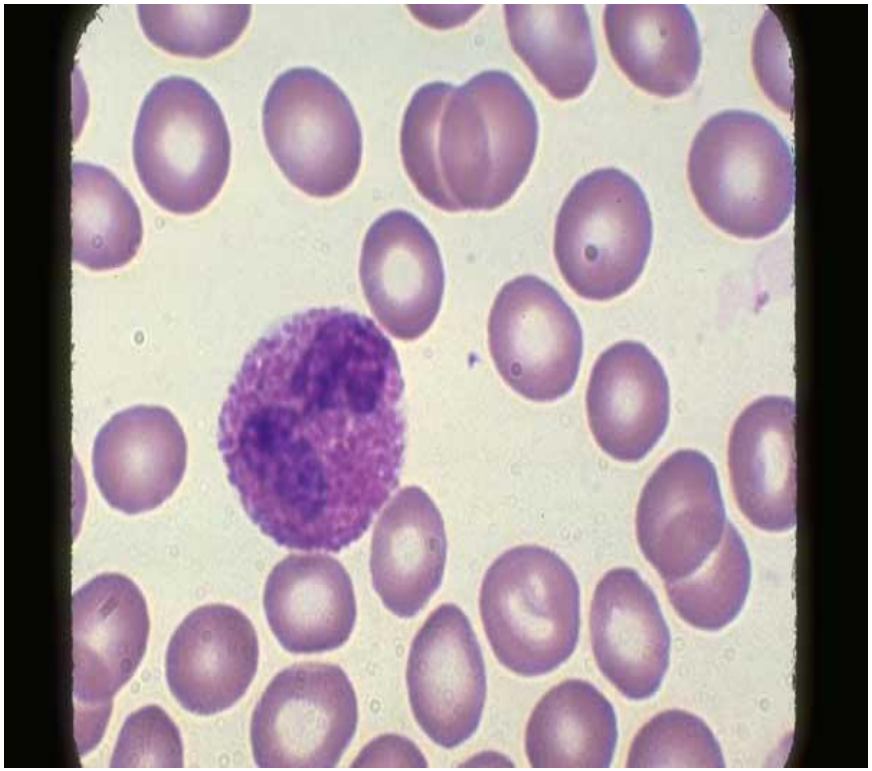


Neutrophils



- Neutrophil
  - –2-5 lobe nucleus
    - •>**5 lobes= hypersegmentation**
  - –Primary or secondary granules
    - •Pink (azurophilic granules)
    - •Grey-blue granules
  - –Life 6-10 hours
- The neutrophils in the circulating blood are mainly mature segmented neutrophils.
- **involved in acute infections with bacteria.**

Eosinophil



•One eosinophil.

• **Orange colour granules**.

• **Bi-lobed nucleus**.

•Coarser & more deeply **red staining** granules

• Rarely more than two lobes of nucleus

• **Special role in allergy, inflammation & parasite infection**.

Basophil

- Occasionally seen
- Dark cytoplasmic granules
- Role in **hypersensitivity** response
- Give rise to **mast cells**
- **involved in parasitic infections and allergies**

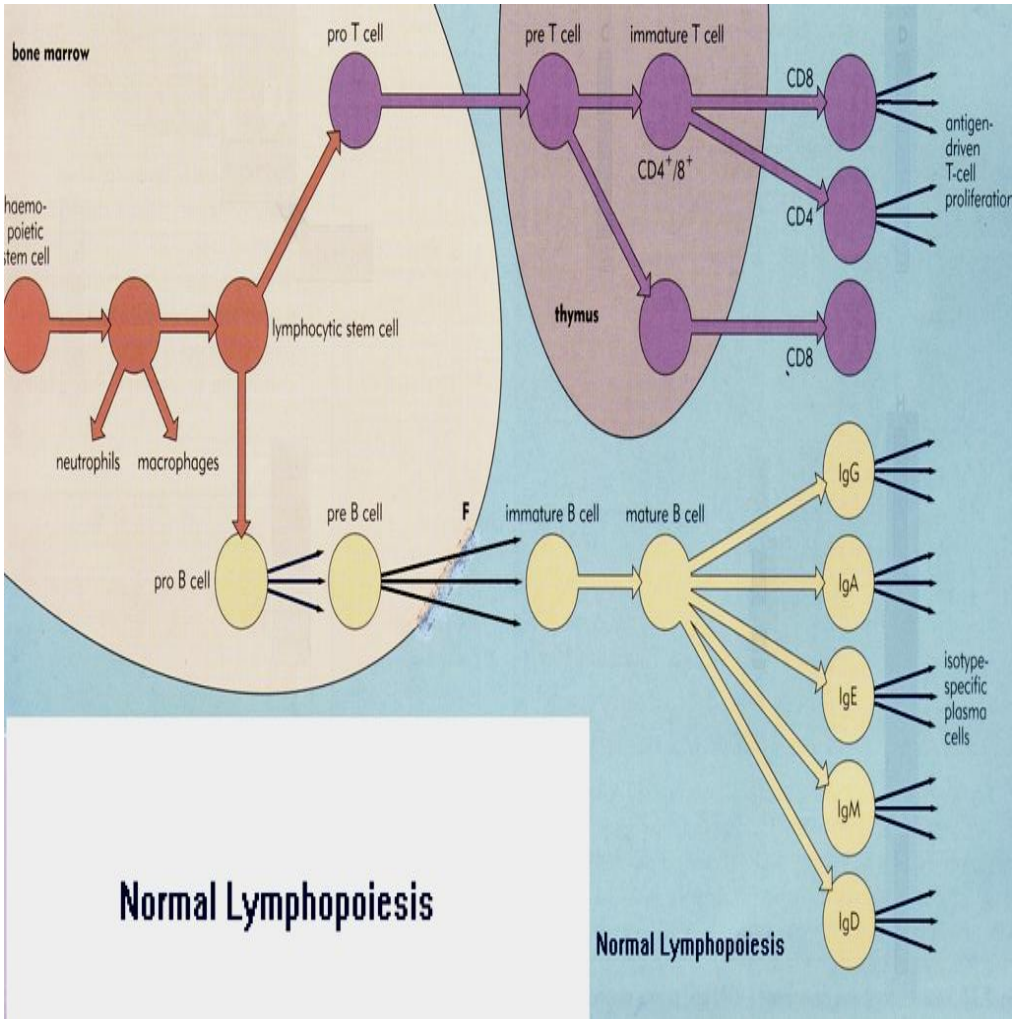
•One mature basophil.

• **Blackish granules overlying the nucleus.**

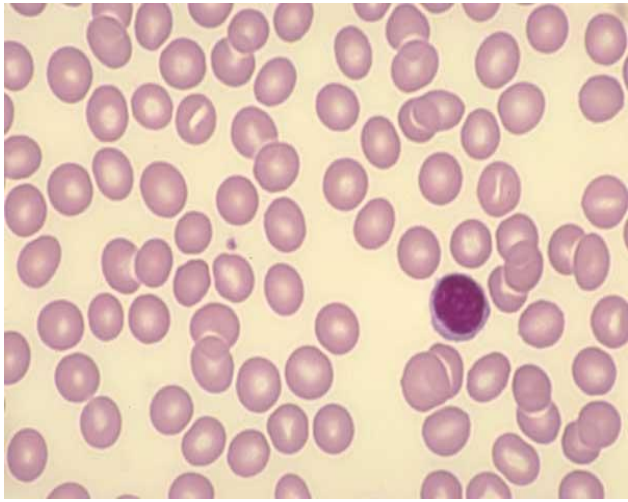
LYMPHOPOIESIS

Lymphopoiesis

- **Primary lymphoid organs**
  - Bone marrow
    - produce all blood cells.
  - Thymus
    - an organ which lymphocyte precursor cells mature
- **Secondary lymphoid organs**
    - Lymph nodes
    - Spleen
    - Lymphoid tissues (MALT)



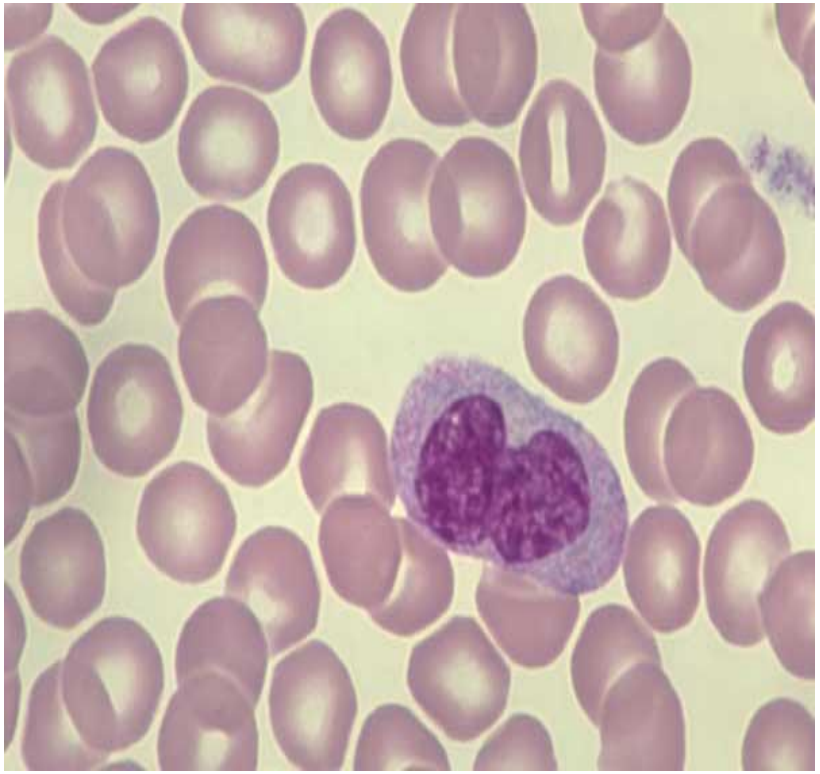
Lymphocytes



- immunologically competent cells
- **the smallest WBC**
- have large condensed nucleus, with a scanty bluish cytoplasm.
- divided into T-cells and B-cells
  - – B cells are responsible for **humoral-type immune response.**
    - **•produce antibodies** and “memory cells”
  - – T lymphocytes are responsible for **cellular-type immune response.**
- **•involved in many types of infection, especially viruses**

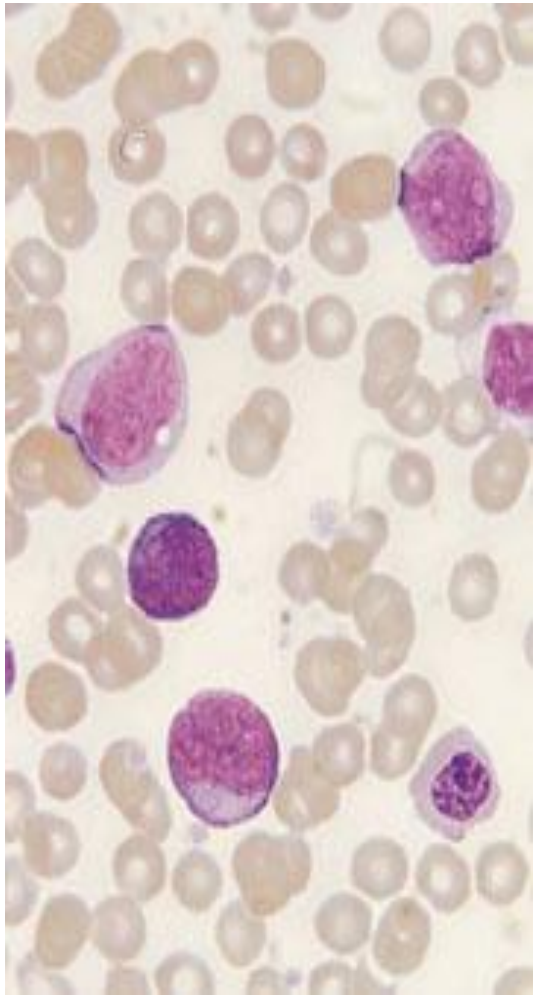
Monocytes

- **The largest WBC**
- Larger than lymphocyte
- The nucleus is slightly indented.
- Oval or indented nucleus
- The cytoplasm is abundant, sky blue in color.
- Some have vacuoles in the cytoplasm.
- Migrate into tissue: then, called as **macrophages**
- involved in **bacterial and parasitic infections** (**phagocyte**)



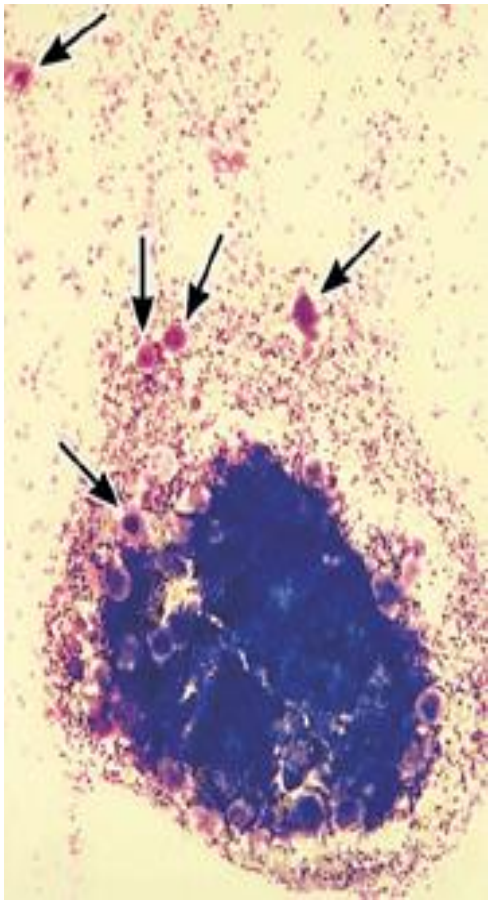
MEGAKARYOPOIESIS

Megakaryoblasts



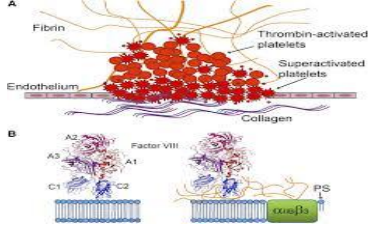
- Megakaryoblasts are the precursors of the megakaryocytes.
- They may show cytoplasmic blebbing.

Megakaryocytes

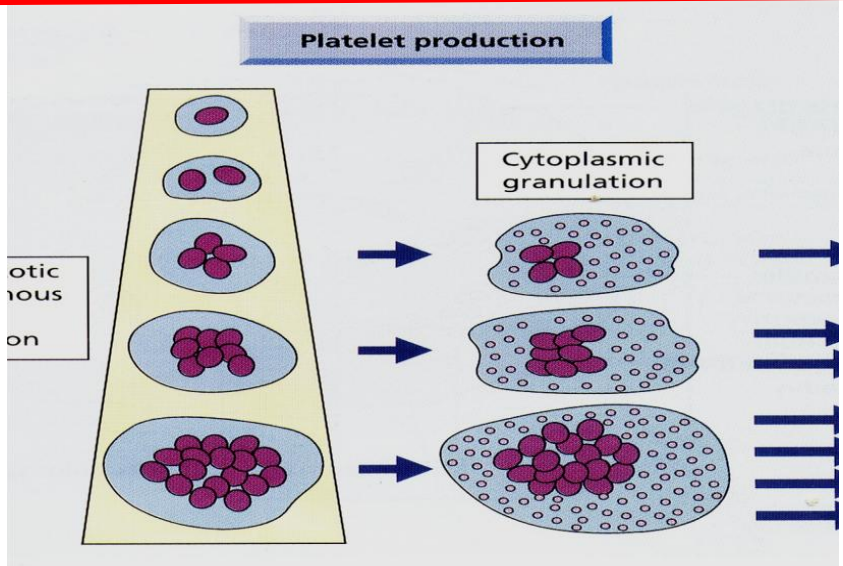


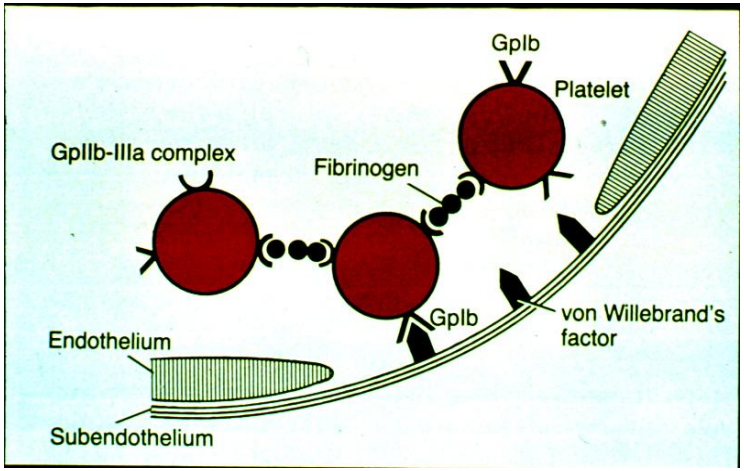
- Most megakaryocytes are large cells which can be identified with low power.
- **The largest hematopoietic cell in BM**
- Their numbers are very variable in normal bone marrow films.
  - –Increase in patients with ITP.
- This image shows increased megakaryocyte numbers.

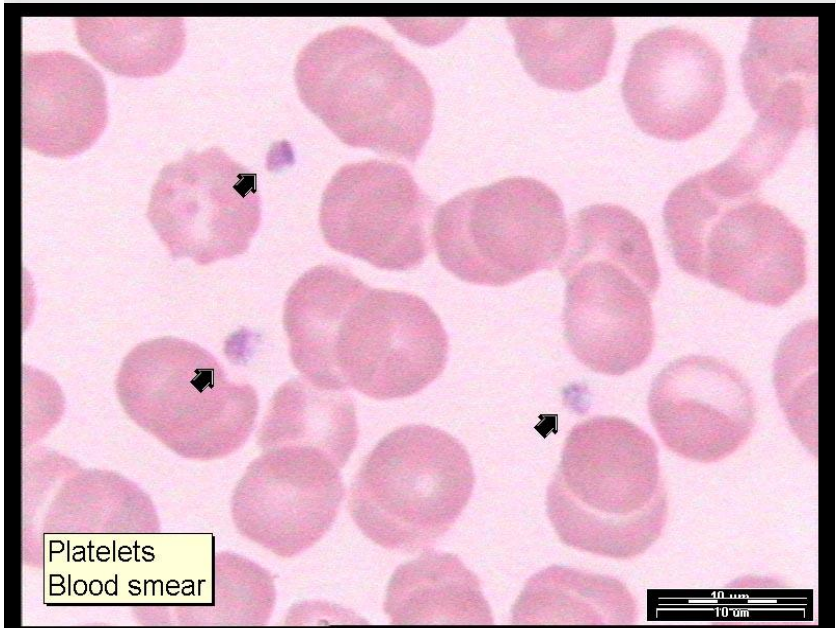
Platelets



- They are broken off from a megakaryocyte
- Primary function is to aid in **blood clotting**
  - Platelets play a major role in **primary hemostasis (adhesion and aggregation)**
- Life span **7-10 days**
- Their clotting function is permanently **inhibited by aspirin**

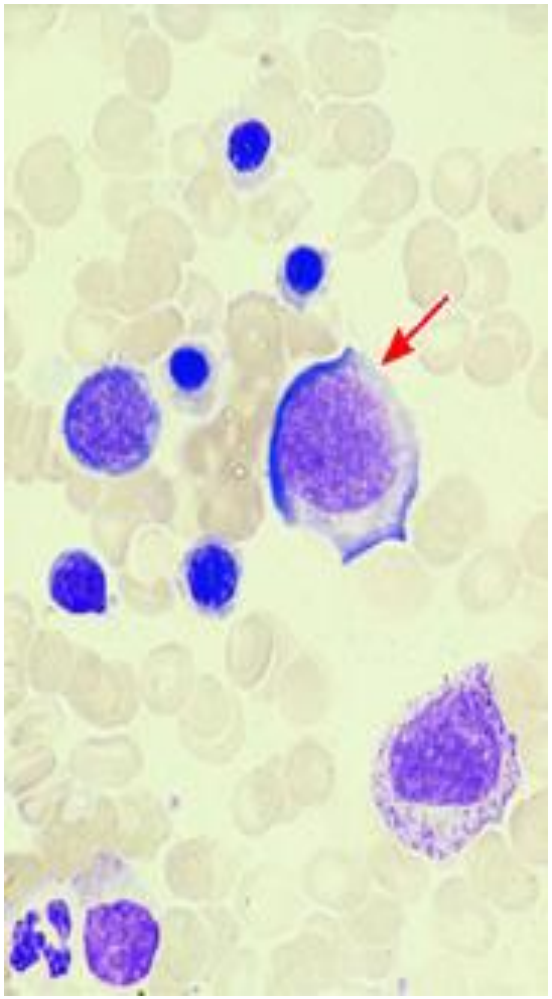






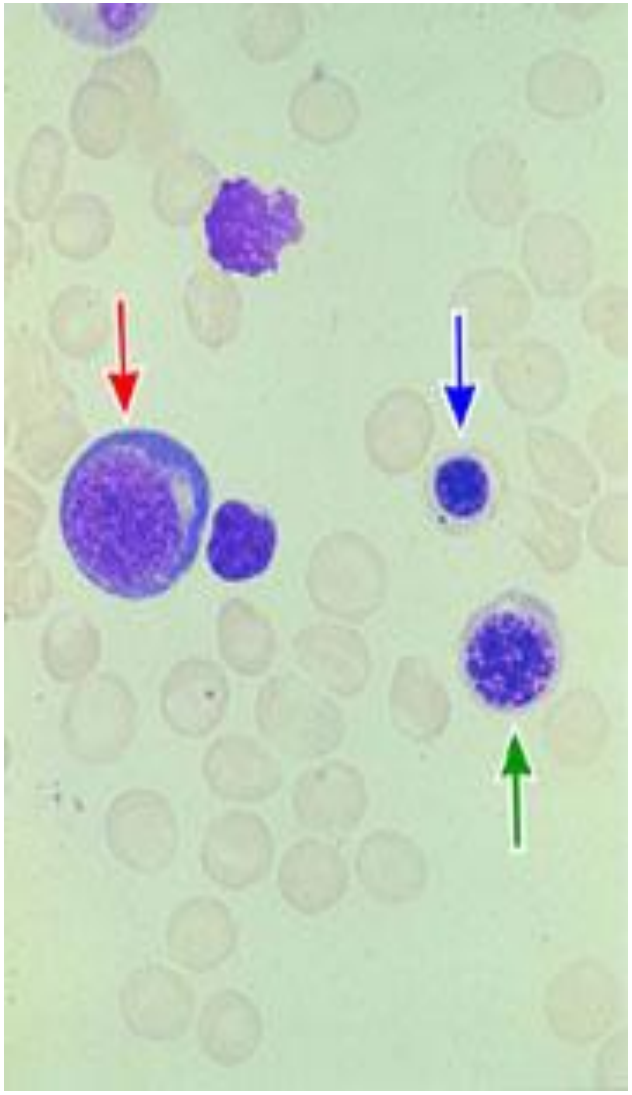
ERYTHROPOIESIS

Proerythroblast



- Normal proerythroblast in the bone marrow.
- This is a large cell with a round nucleus and a finely stippled chromatin pattern.
- Nucleoli are sometimes apparent.
- The cytoplasm is moderately to strongly basophilic.
- There may be a paler staining area of cytoplasm surrounding the nucleus.

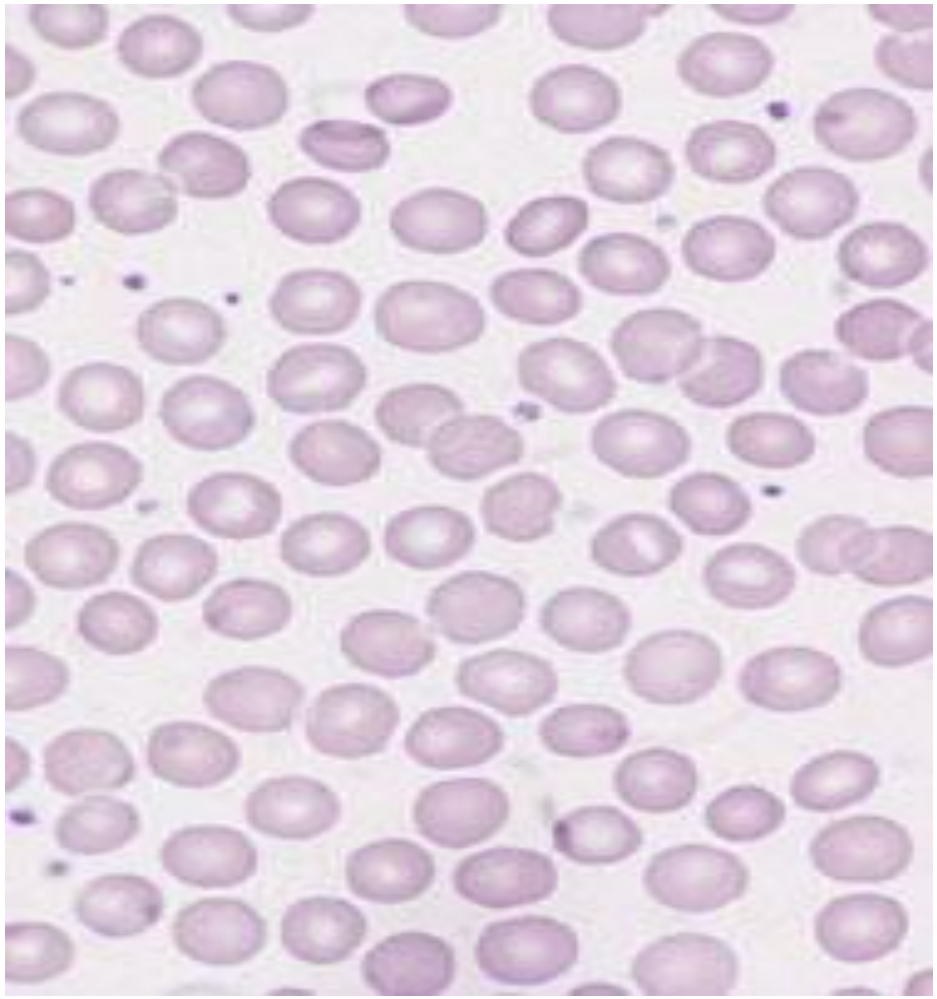
Erythroblasts



- The early erythroblast [red arrow] is similar to a proerythroblast but is smaller and no longer has visible nucleoli.
- The intermediate erythroblast [green arrow] and the late erythroblast [blue arrow] show a progressive reduction in cell size, reduction in cytoplasmic basophilia and increase in chromatin clumping.
- The cytoplasm of the late erythroblast may have a pink tinge attributable to Hb.

Erythrocytes (RBC)

- **Transport oxygen** via hemoglobin from lungs to peripheral tissues and organs
- Lifespan – **120 days**
- **Non nucleated cell**
- **Biconcave** disc
- Production regulated by **EPO**
- Needs iron, vit B12, folate & other elements for development



Descriptive Terms Used on Peripheral Smears

- Anisocytosis:
  - marked **variation in RBC sizes** (visual counterpart of increased RDW)
- Hypochromia:
  - RBCs are **paler** than normal because they contain less hemoglobin (visual counterpart of decreased MCH)
- Microcytosis:
  - increased number of **small RBCs** (visual counterpart of decreased MCV)
- Macrocytosis:
  - increased number of **large RBCs** (visual counterpart of increased MCV)
- Poikilocytosis:
  - marked **variation in the shape** of RBCs

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