

White Blood Cells

(production,....., migration)

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Leukocytes

- ▶ White blood cells are a part of immune system
- ▶ Protect the body from infectious microorganisms
- ▶ Function outside the bloodstream
- ▶ Are colorless but can appear as a very light purple to pink color under microscope
- ▶ Have a round shape with a distinct center membrane (nucleus)
- ▶ Account 1% of blood



Neutrophil



Eosinophil

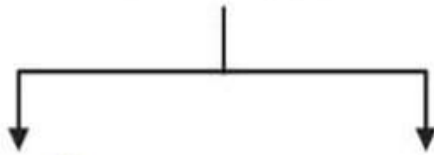


Basophil

Types of Leukocytes (White Blood Cells)



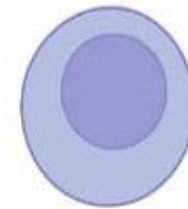
Monocyte



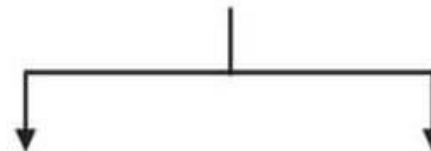
Dendritic cell



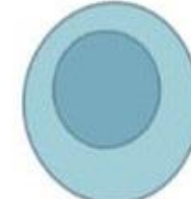
Macrophage



Lymphocyte



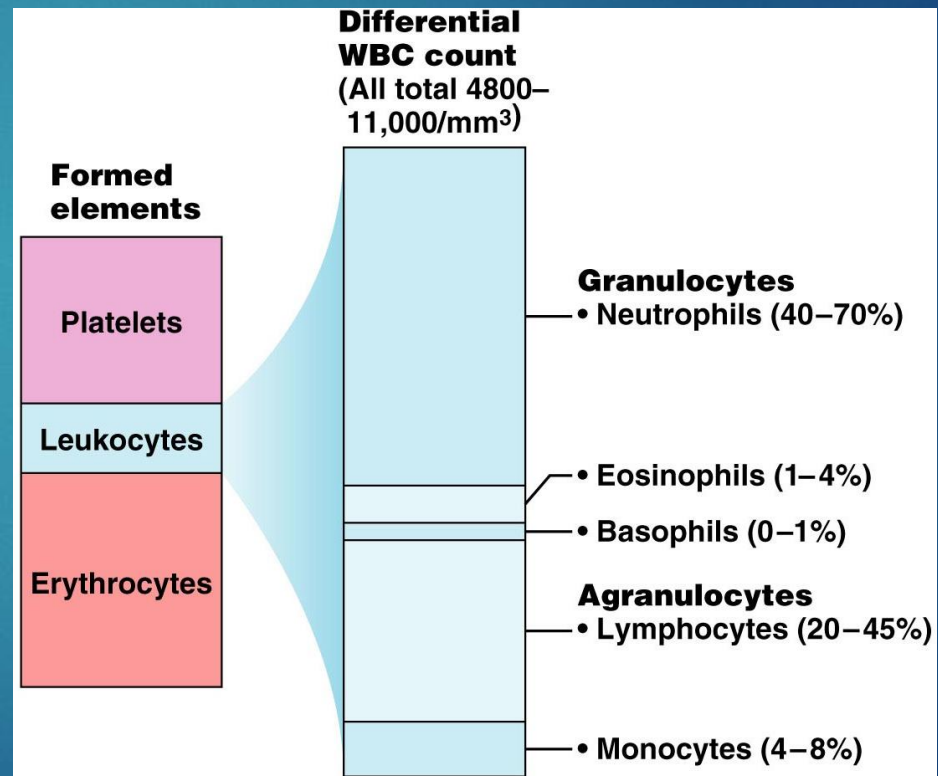
T cell



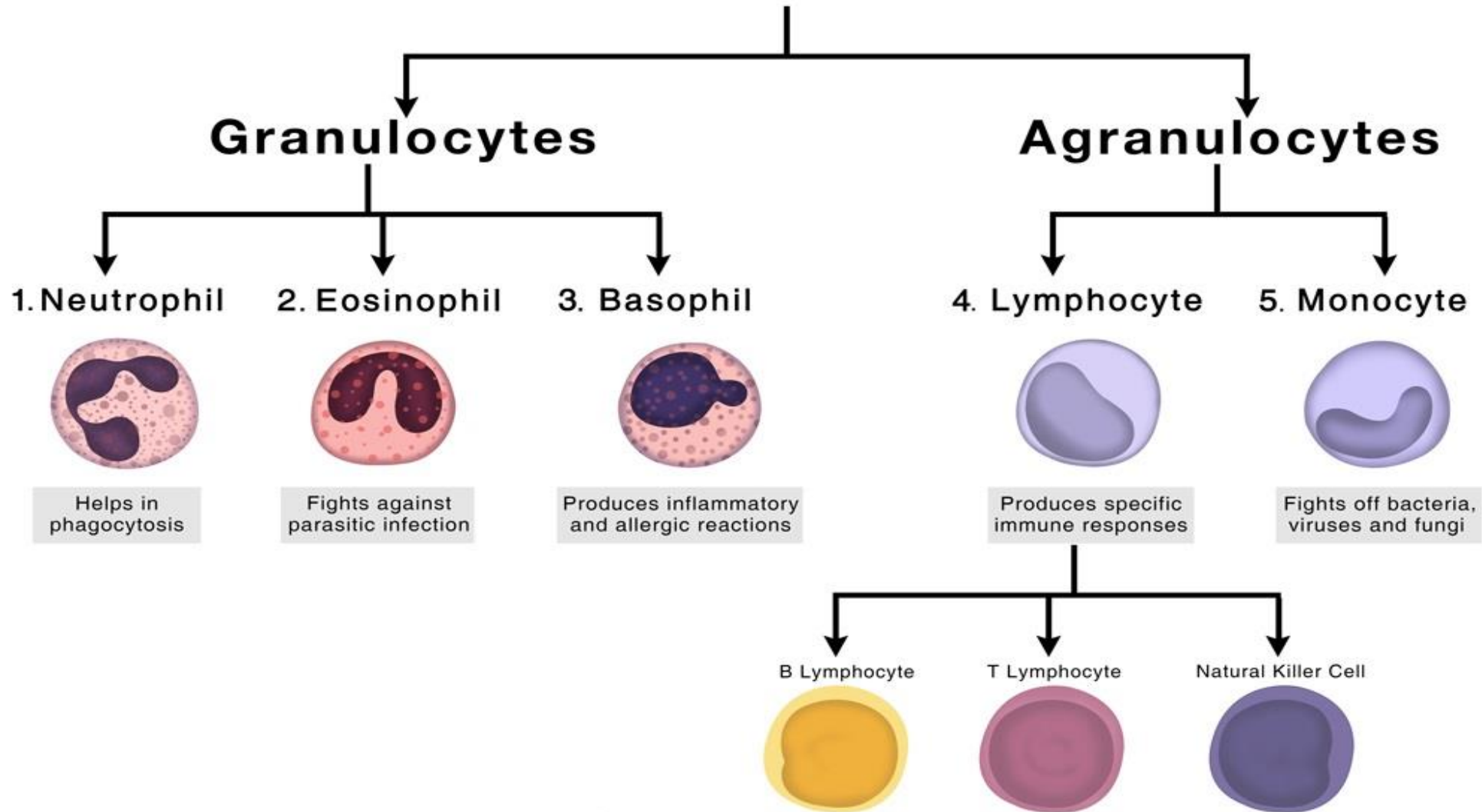
B cell

Another classification of WBCs

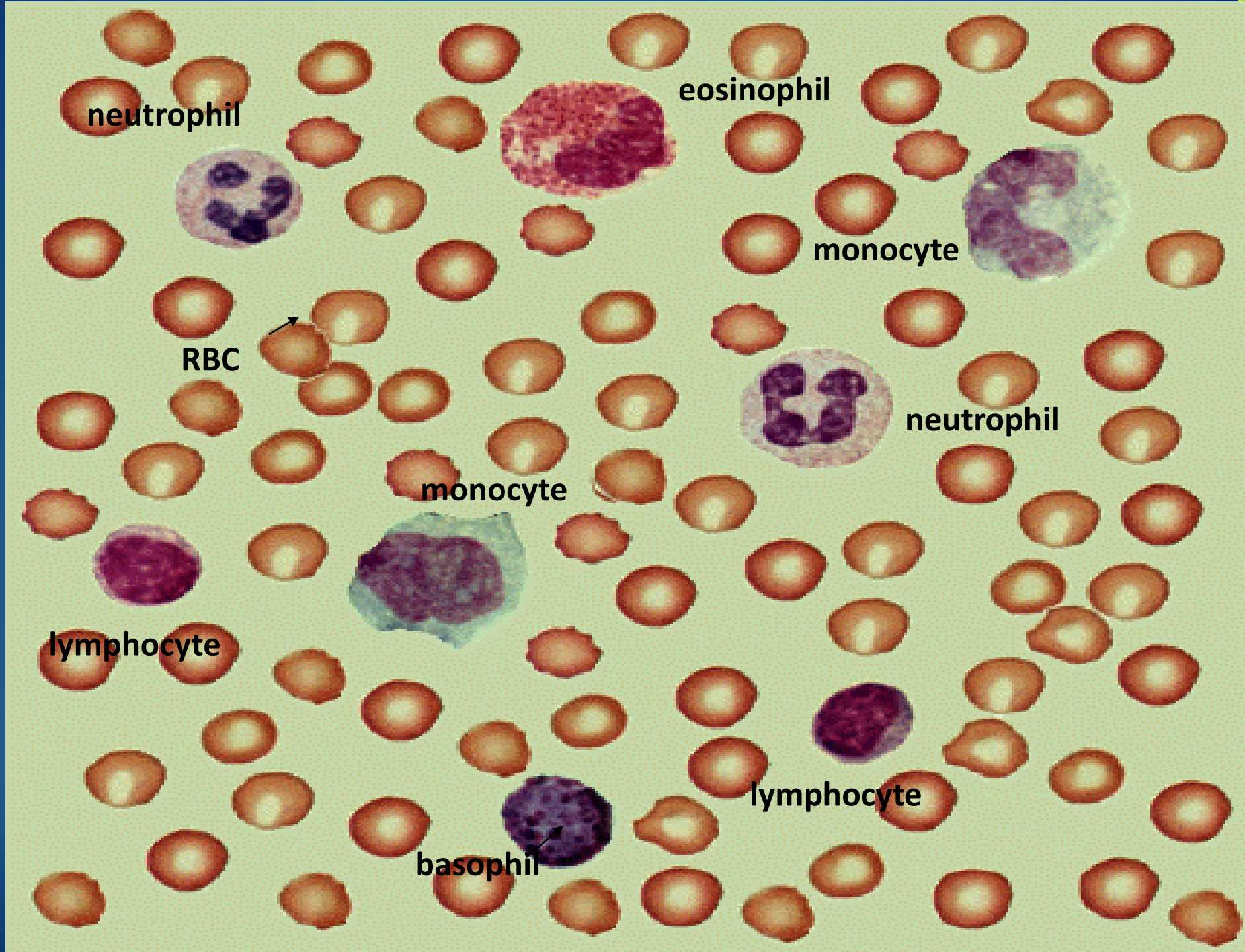
- ▶ Two types of leukocytes
 - Granulocytes
 - Agranulocytes



TYPES OF WHITE BLOOD CELLS



Type Of White Blood Cells	% By Volume Of WBC	Description	Function
Neutrophils	60 – 70 %	Nucleus has many interconnected lobes; blue granules	Phagocytize and destroy bacteria; most numerous WBC
Eosinophils	2 – 4 %	Nucleus has bilobed nuclei; red or yellow granules containing digestive enzymes	Play a role in ending allergic reactions
Basophils	< 1 %	Bilobed nuclei hidden by large purple granules full of chemical mediators of inflammation	Function in inflammation; similar in function to mast cells
Lymphocytes (B Cells and T Cells)	20 – 25 %	Dense, purple staining, round nucleus; little cytoplasm	the most important cells of the immune system; effective in fighting infectious organisms; act against a specific foreign molecule (antigen)
Monocytes	4 – 8 %	Largest leukocyte; kidney shaped nucleus	Transform into macrophages; phagocytic cells



neutrophil

eosinophil

monocyte

RBC

neutrophil

monocyte

lymphocyte

lymphocyte

basophil

Circulating WBC

- ▶ Total (**WBC**) & differential are measured in automated counter
- ▶ WBC in each microliter (ml;mm³) is reported
- ▶ WBC reflects the **circulating** pool of myeloid & lymphoid cells
- ▶ **Relative proportion** of each type of WBC is indicated by a percentage
- ▶ **Absolute number** is the percentage of each type of WBC multiplied by the total WBC

Production of WBCs

- ▶ Leukopoiesis
- ▶ the production of white blood cells
- ▶ Their formation occurs in the soft tissue inside the bone (bone marrow)
- ▶ stimulated by chemical messengers

Chemical messengers

- ▶ Are glycoproteins
- ▶ Act either as paracrine or hormones
- ▶ fall into two families of hematopoietic factors:
 1. Interlukins
 2. Colony Stimulating Factors (CSF)

Hematopoietic factors

- ▶ released by supporting cells of the red bone marrow
- ▶ mature WBCs
- ▶ prompt the white blood cell precursors to divide and mature
- ▶ enhance the protective potency of mature leukocytes

Leukopoiesis

- ▶ is the process of formation of leukocytes (white blood cells)
- ▶ from stem cells in haematopoietic organs.
- ▶ Leukocytes develop from either
 1. multipotential myeloid stem cells (CFU-GEMM)
 2. multipotential lymphoid stem cells (CFU-L)

Leukocytes developing from

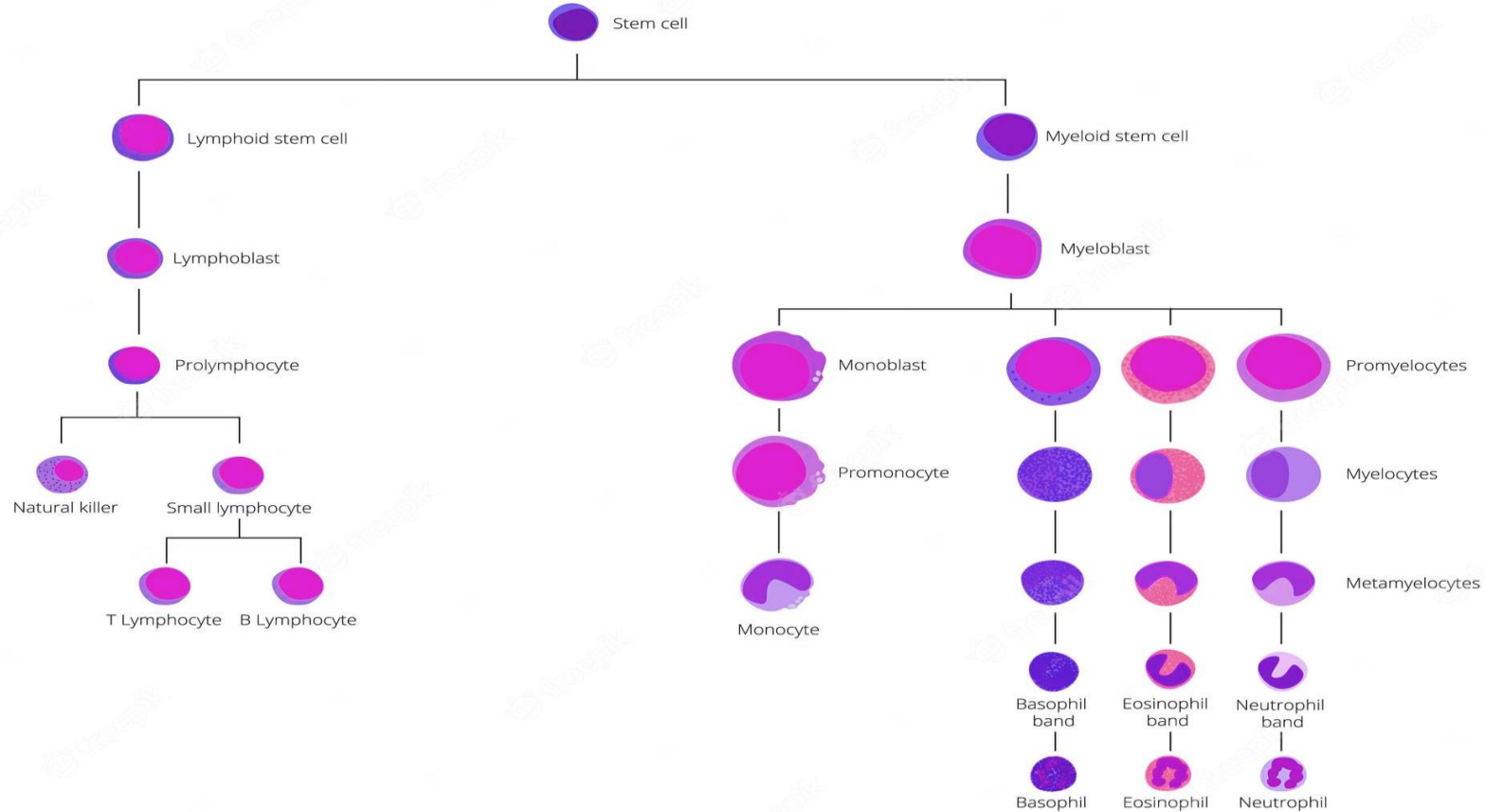
► CFU-GEMM's are:

granulocytes (neutrophils, basophils and eosinophils) or monocytes.

► CFU-Ls are:

lymphocytes (T & B cells, dendritic and NK cells).

Leukopoiesis



The site of production

- ▶ All WBCs, except monocytes, develop fully in bone marrow
- ▶ Monocytes as directed by specific colony stimulating factors (CSFs) produced by Macrophages and T cells
- ▶ two types of WBCs (lymphocytes) grow in the thymus gland (T-cell) and lymph nodes and spleen (B-cell)
- ▶ WBCs originate from cells that morph into the other cells in the body (stem cells) with soft tissue of your bones (bone marrow)

Types of CSF & Types of cells

- ▶ M-CSF: stimulates monocyte production
- ▶ G-CSF: stimulates production of granulocytes
(neutrophils, eosinophils, and basophils)
- ▶ GM-CSF: stimulates granulocyte and monocyte
- ▶ Multi-CSF: accelerates production of granulocytes, monocytes, platelets, and RBCs

Life Span of WBCs

► Formed & stored until needed

- Granulocytes:

- Survive in blood 4-8 hours
- Survive in tissue 1-2 days

- Monocytes:

- Spend 10-14 hours in blood
- Then deposit in tissue = tissue macrophages which survive for months

- Lymphocytes:

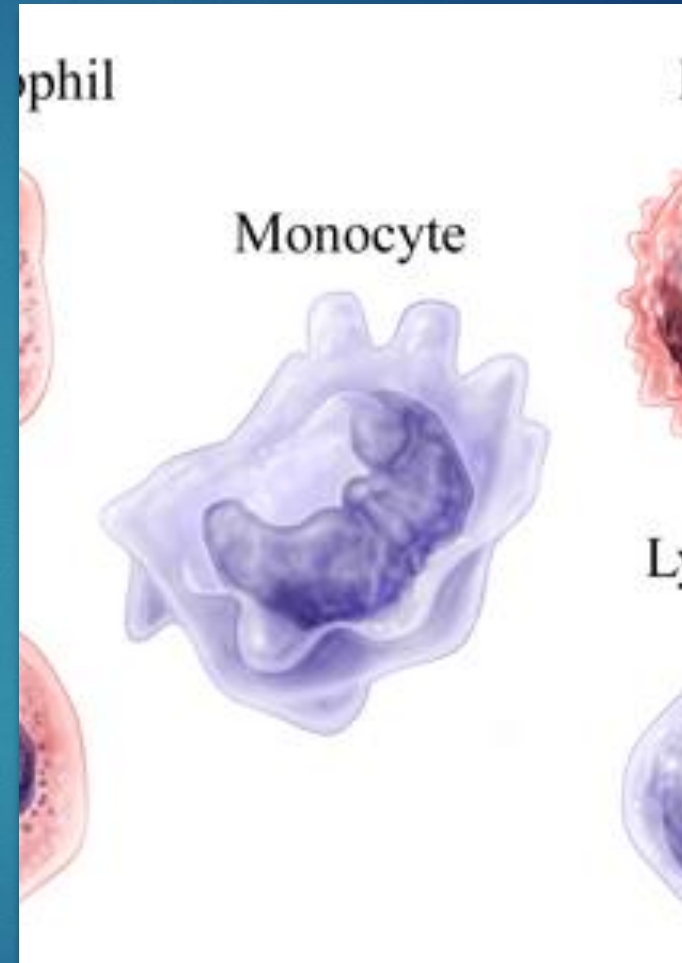
- stored in lymph tissue / pass in & out of blood
- Survive weeks to months

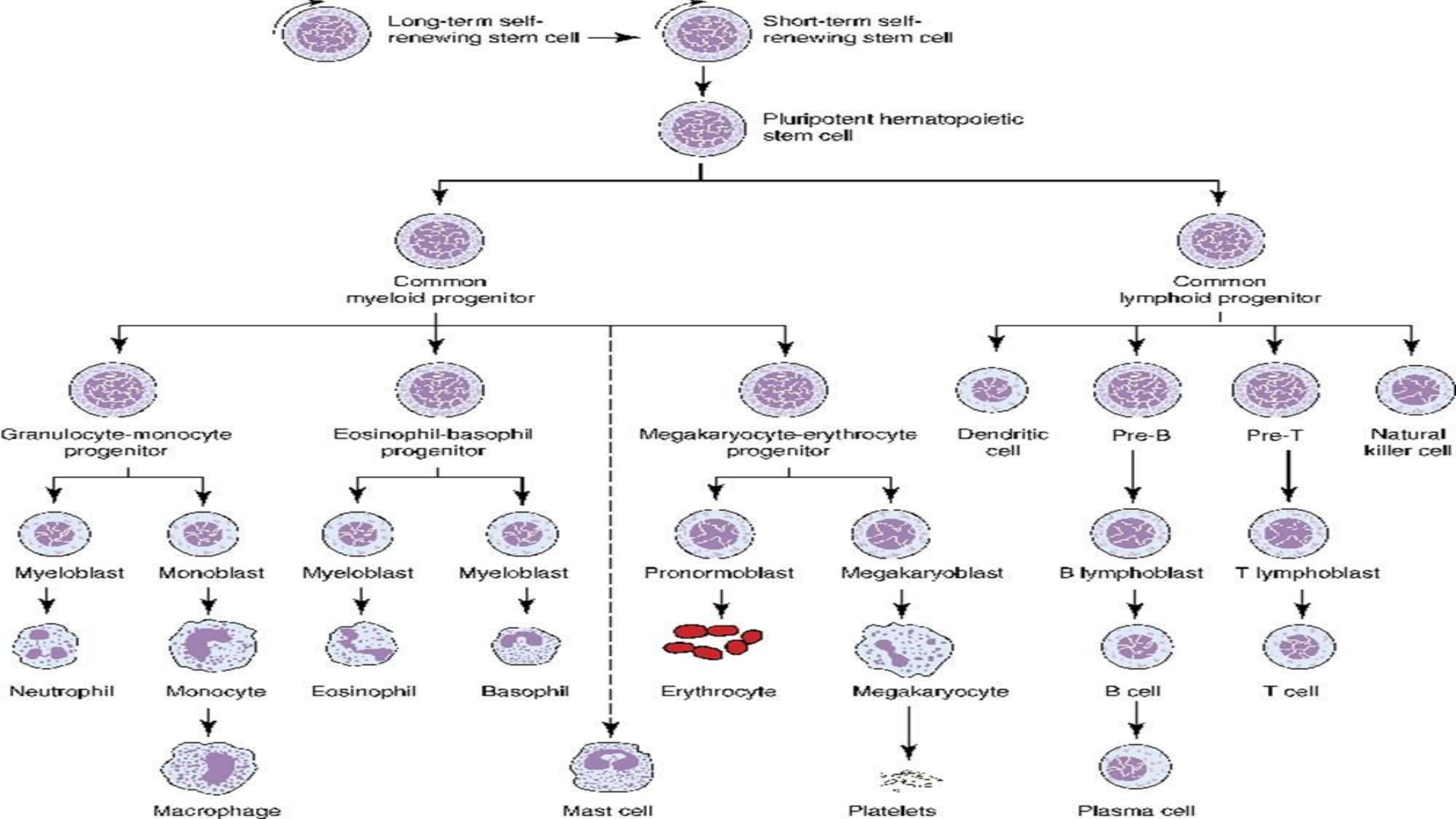
Haematopoietic stem cells

- ▶ reside in the bone marrow and have the unique ability to give rise to all mature blood cell types through differentiation into other progenitor cells.
- ▶ HSCs are self-renewing.
- ▶ When they proliferate, at least some daughter cells remain HSCs, so the pool of stem cells does not become depleted over time.
- ▶ The daughters are the myeloid and lymphoid progenitor cells, which cannot self renew but differentiate into various myeloid leukocytes and lymphocytes respectively.

Two categories

The two major forms of leukopoiesis are myelopoiesis and lymphopoiesis



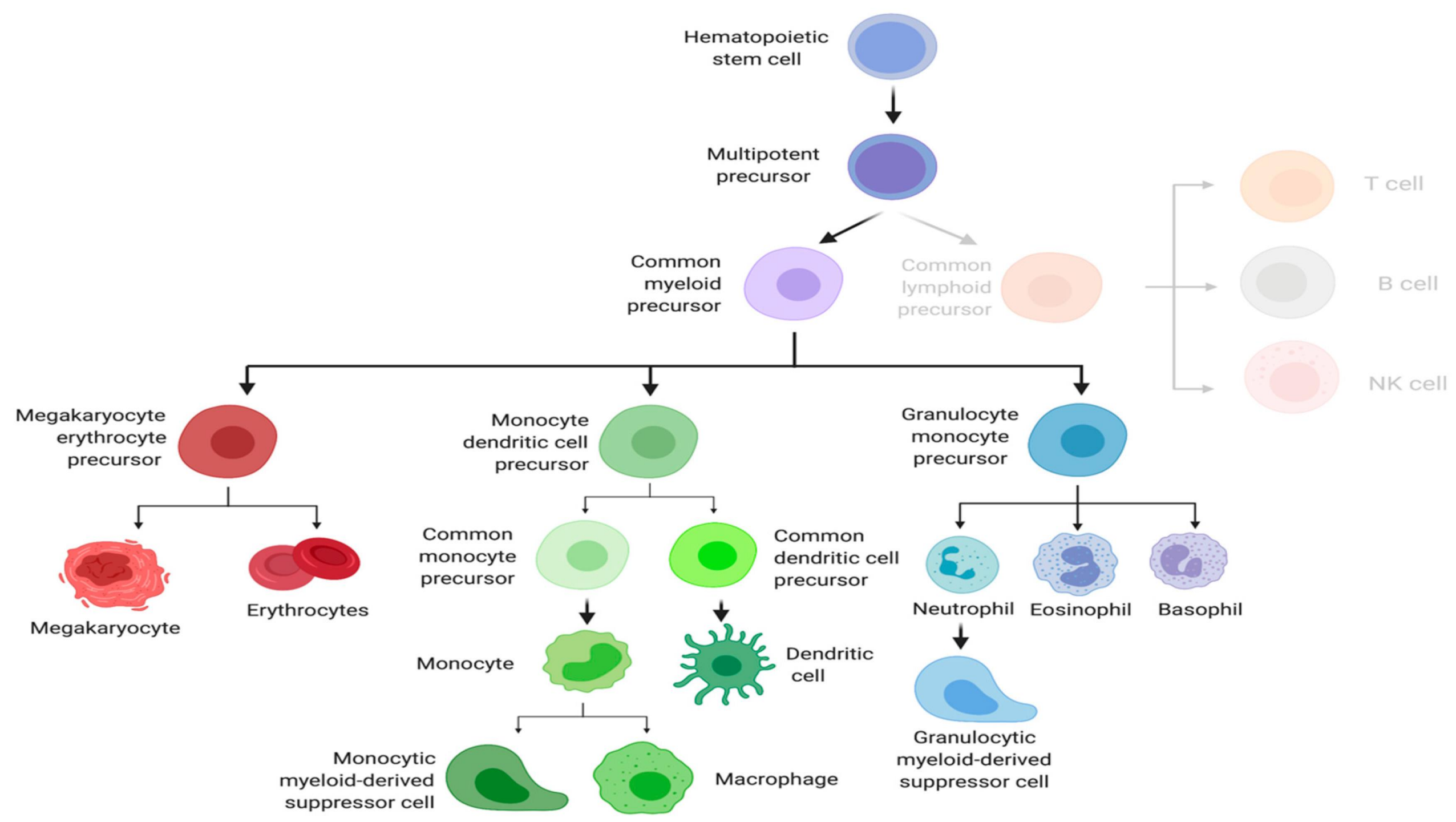


Myelopoiesis

- ▶ involves a series of maturational steps
- ▶ from HSCs to common myeloid progenitor cells
- ▶ through terminal differentiation leading to the formation of
- ▶ granulocytes, including basophils, neutrophils, eosinophils, and monocytes.

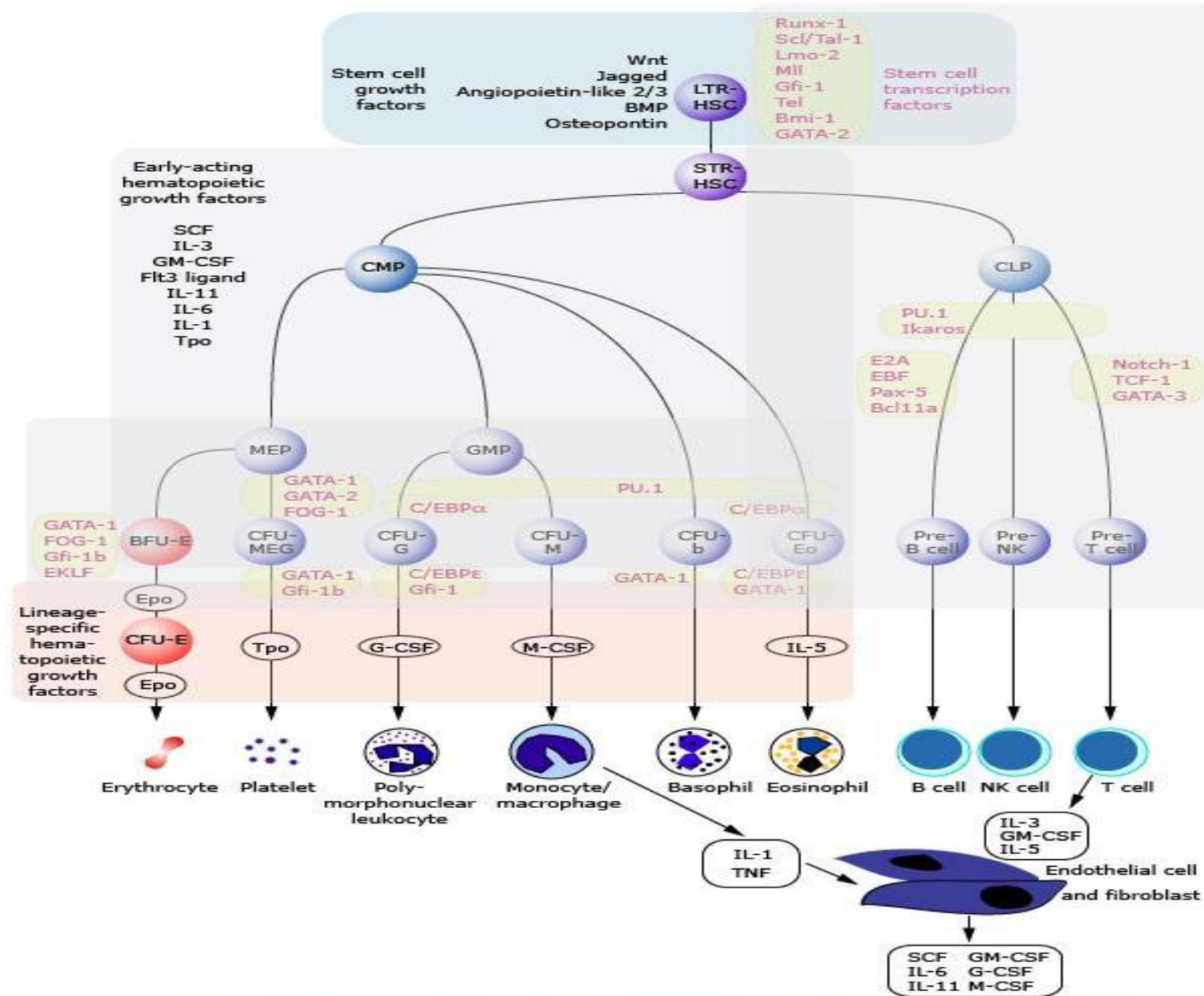
Regulation of myelopoiesis

- ▶ Granulocytes and monocytes are produced in the bone marrow
- ▶ In the complex highly regulated and dynamic process that requires both specific hematopoietic growth factors and appropriate bone marrow micro environment



Maturation in myelopoiesis

- ▶ is controlled by expression transcription factors with the expression of adhesion and hematopoietic growth factor receptors.
- ▶ The most prominent cells producing hematopoietic growth factors include T lymphocytes, monocytes/macrophages, and other mesodermal cells, such as fibroblasts and endothelial cells.



Lymphopoiesis

- ▶ From lymph (Latin, water)
- ▶ the production of new lymphocytes, including B lymphocytes, T lymphocytes, and natural killer (NK) cells.
- ▶ B lymphocytes also known as antibodies are key effectors of humoral immunity.
- ▶ T lymphocytes, effectors of cell-mediated immunity
- ▶ bind antigens prepared by antigen-presenting cells
- ▶ NK cells kill a variety of infected and tumor cells in the absence of prior exposure or priming.
- ▶ Main growth factors for B lymphocytes, T lymphocytes, and NK cells are IL-4, IL-2, and IL-15, respectively.

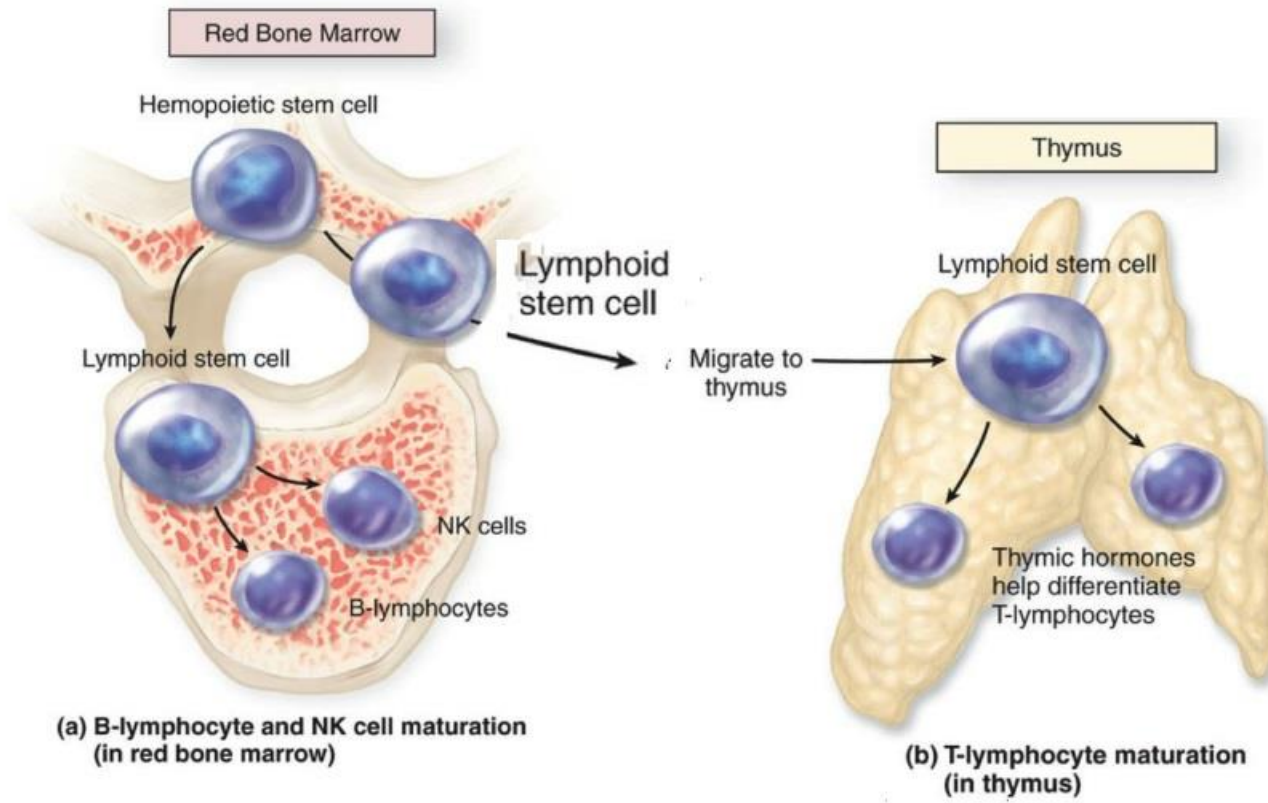
Lymphocytes' development

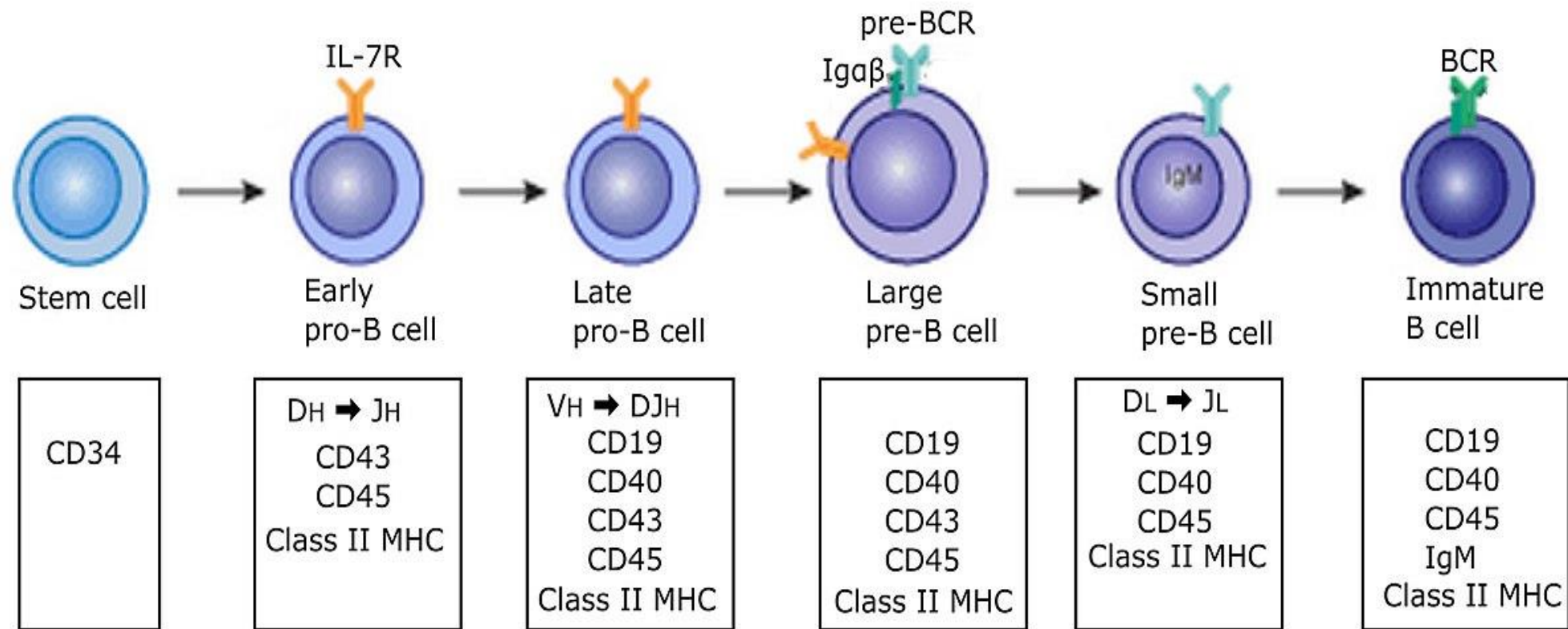
- ▶ derived from HSCs within the bone marrow.
- ▶ B lymphocyte development occurs in two phases:
 1. first in an antigen-independent phase in the bone marrow
 2. then in an antigen-dependent phase in peripheral lymphoid tissues (such as spleen, lymph nodes, and mucosa-associated lymphoid tissue [MALT]).
- ▶ T lymphocyte progenitors migrate from the bone marrow to the thymus, where they undergo differentiation, selection, and maturation processes before migrating to the peripheral lymphoid tissue as effector cells.

T & B lymphocytes

Lymphopoiesis

Lymphopoiesis is the generation of mature lymphocytes



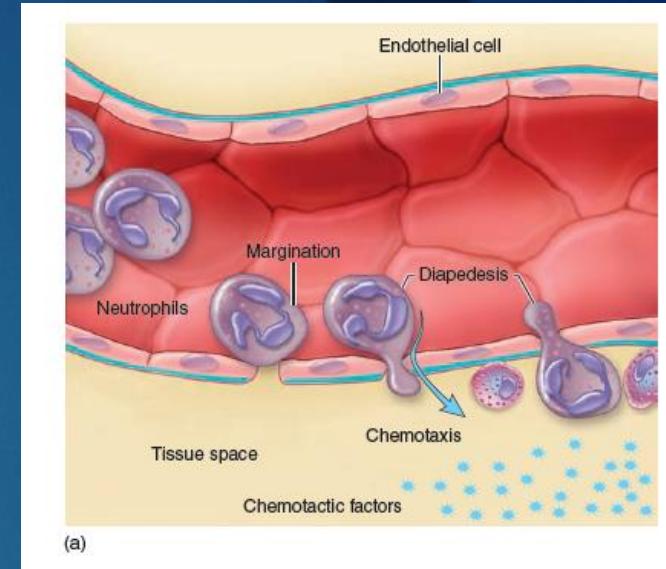


Movement of leukocytes

- ▶ Getting leukocytes to the site of injury or infection
- ▶ series of adhesion events between leukocytes and endothelium
- ▶ leukocytes leave the bloodstream only at the inflammatory site

How?

- ▶ In a sequence of adhesive steps:
 1. leukocytes attach to the vessel wall,
 2. locomote along the wall to the endothelial borders,
 3. traverse the endothelium and the subendothelial basement membrane
 4. migrate through the interstitial tissue

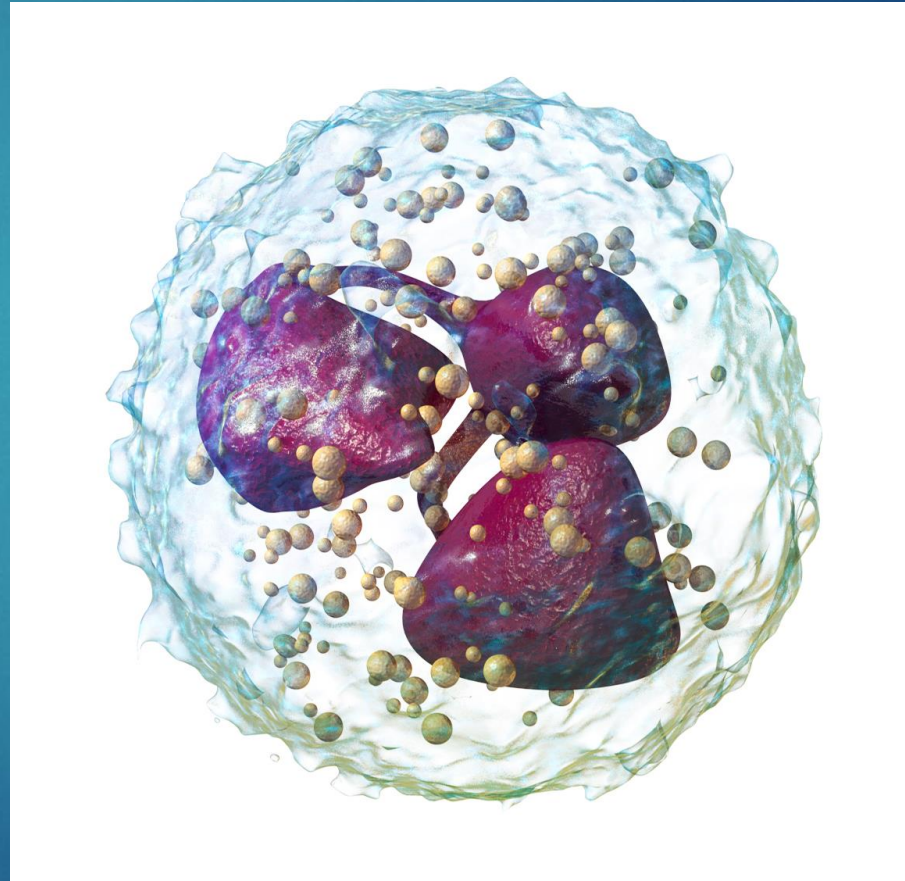


Points of leukocyte's migration

- ▶ Leukocyte migration through the body is not random.
- ▶ is dependent on the inflammatory stimulus, the time point during inflammation, and the localization of the inflammation.
- ▶ mediated by the sequential interaction of different adhesion and signaling molecules on leukocytes and endothelial cells lining the vessel wall.

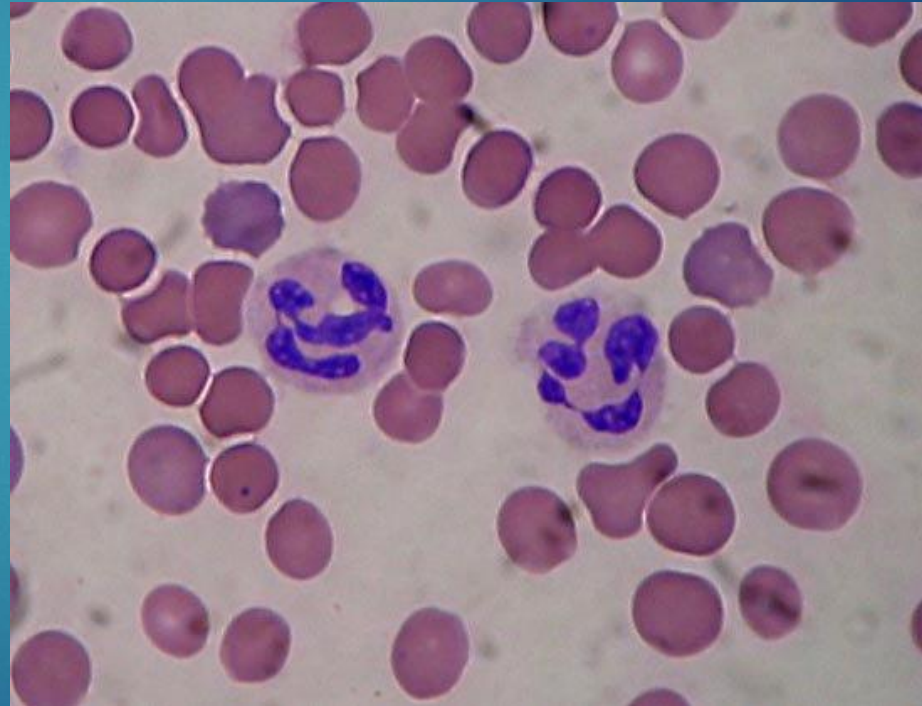
Neutrophils

- ▶ Plays a critical role in host defense
- ▶ The most circulating leukocyte in blood stream
- ▶ Act by phagocytizing and digesting microorganisms



Structure of Neutrophils

- ▶ known as granulocytes
- ▶ The granules typically stain pink or purple-blue following treatment with a dye
- ▶ with a diameter between 9 and 15 μm
- ▶ The nucleus consists of two to five lobes joined together by hair like filaments.
- ▶ Neutrophils move with amoeboid motion.



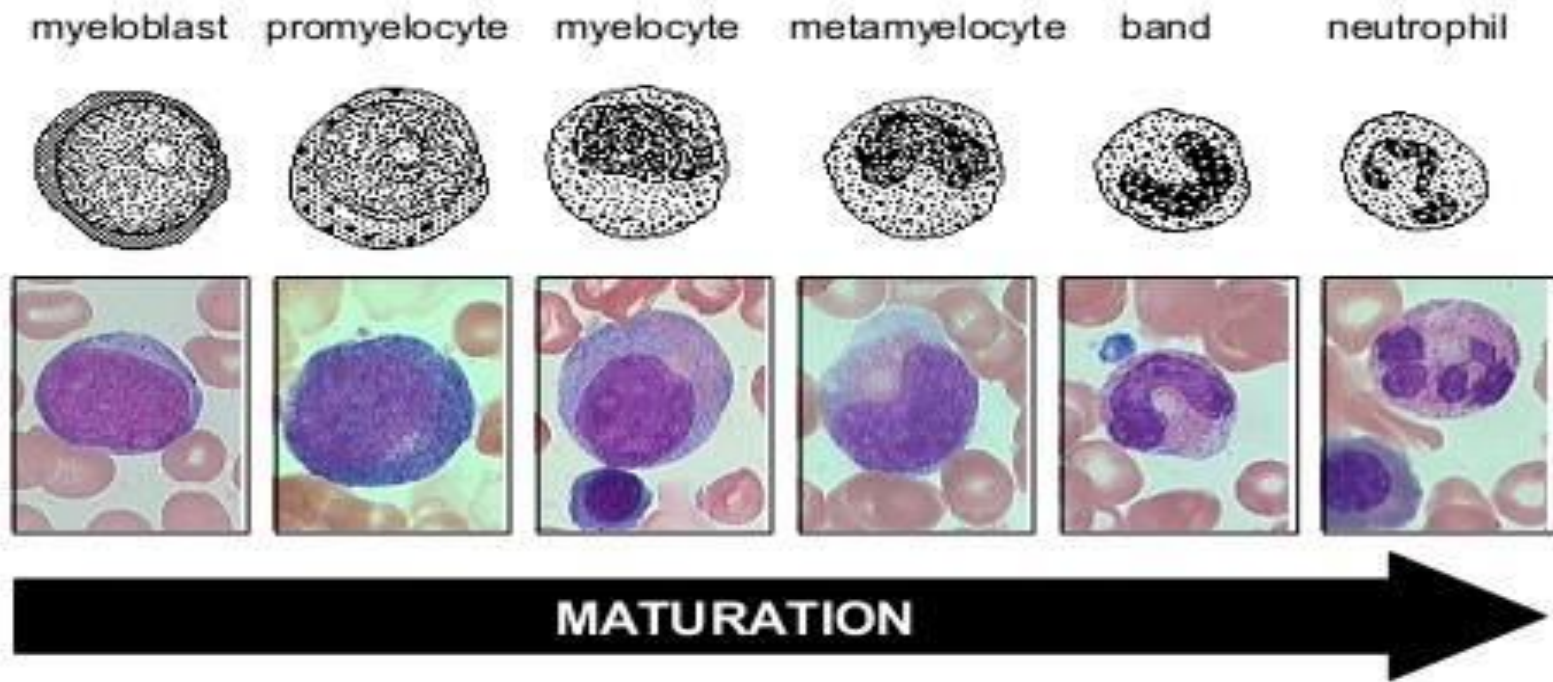
Neutrophils

- ▶ Synthesis and secretion of cytokins, pyrogens and other cellular mediators as well as digestion of senescent cells and debris
- ▶ Circulate
- ▶ Chemotactic signals
- ▶ Adhesion to the vascular endothelial
- ▶ Diapedesis into tissue
- ▶ Migration to the site of microbial

Neutrophils' life span

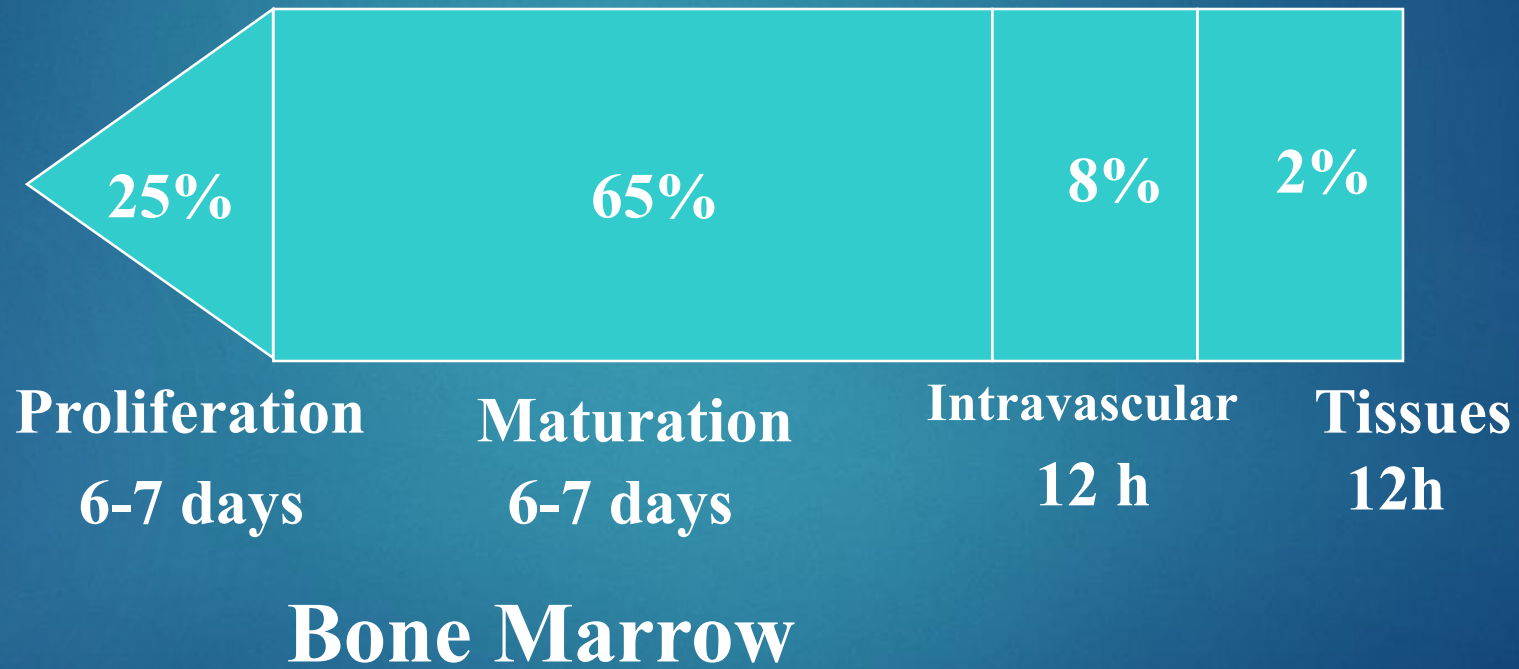
- ▶ Is traditionally divided into the bone marrow, circulation and tissue phases
- ▶ Approximately 14 days in the bone marrow
- ▶ Half life of 6 to 10 hours in blood stream

Neutrophil maturation



Neutrophil Maturation

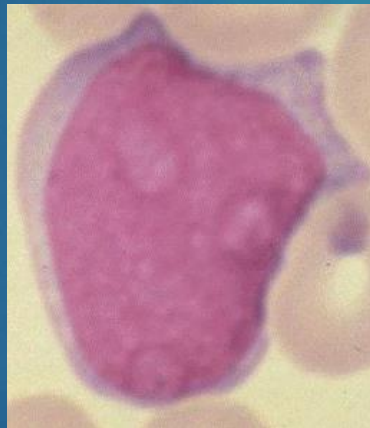
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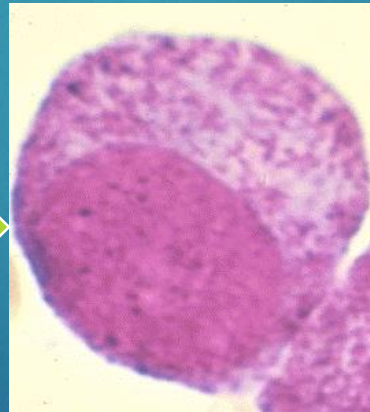
Neutrophil Maturation - Proliferative Phase

Proliferation

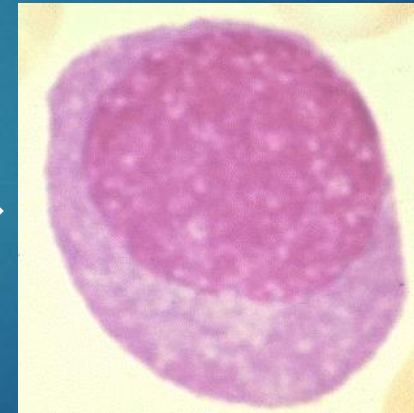
25 %



Myeloblast



Promyelocyte

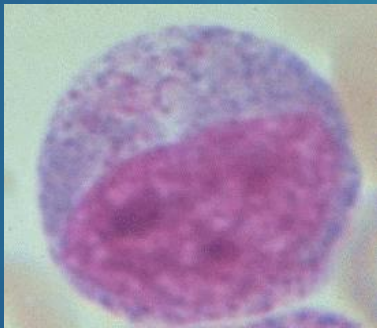


Myelocyte

Neutrophil - Maturation Phase

65 % of myeloid cells

Maturation 6-7 days



Metamyelocyte



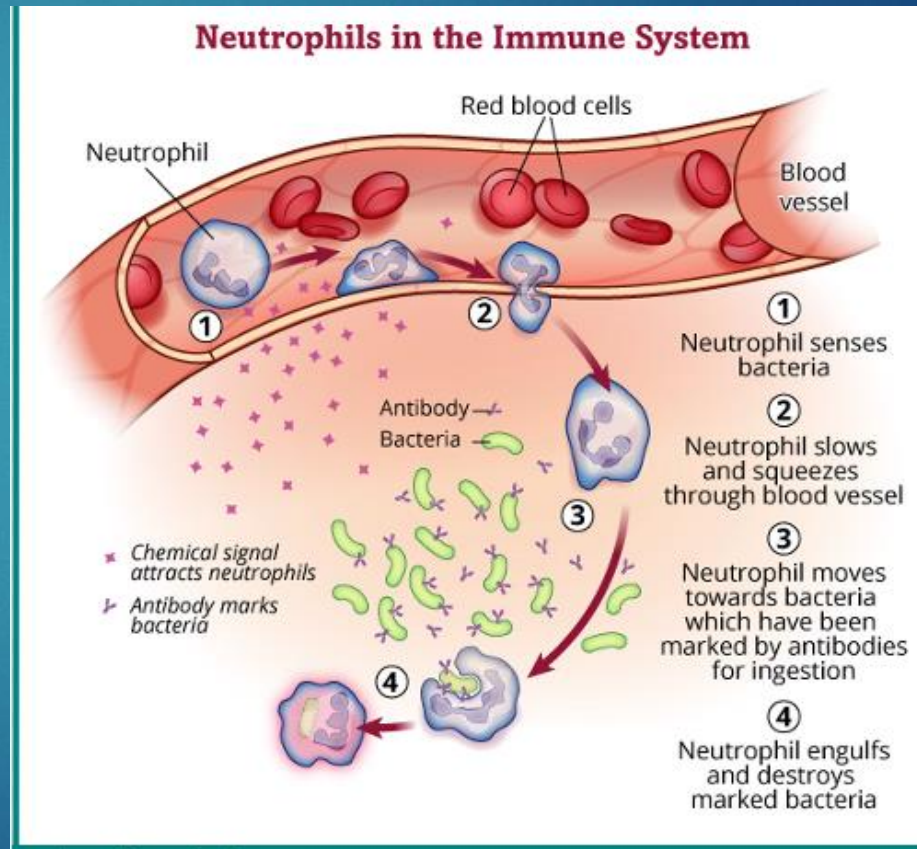
Band



Neutrophil

Neutrophils & Infection

- ▶ By chemotactic agents
- ▶ Migrate to the site of infection
- ▶ Associate with increase of neutrophils' production
- ▶ Release PMN from the B.M



Neutrophils & Macrophages

- Destroy invading microorganisms via **phagocytosis**
- Enter tissue spaces via **diapedesis**
- Move through tissues spaces by **ameboid like** motions

Chemotaxis of Neutrophils & Macrophages

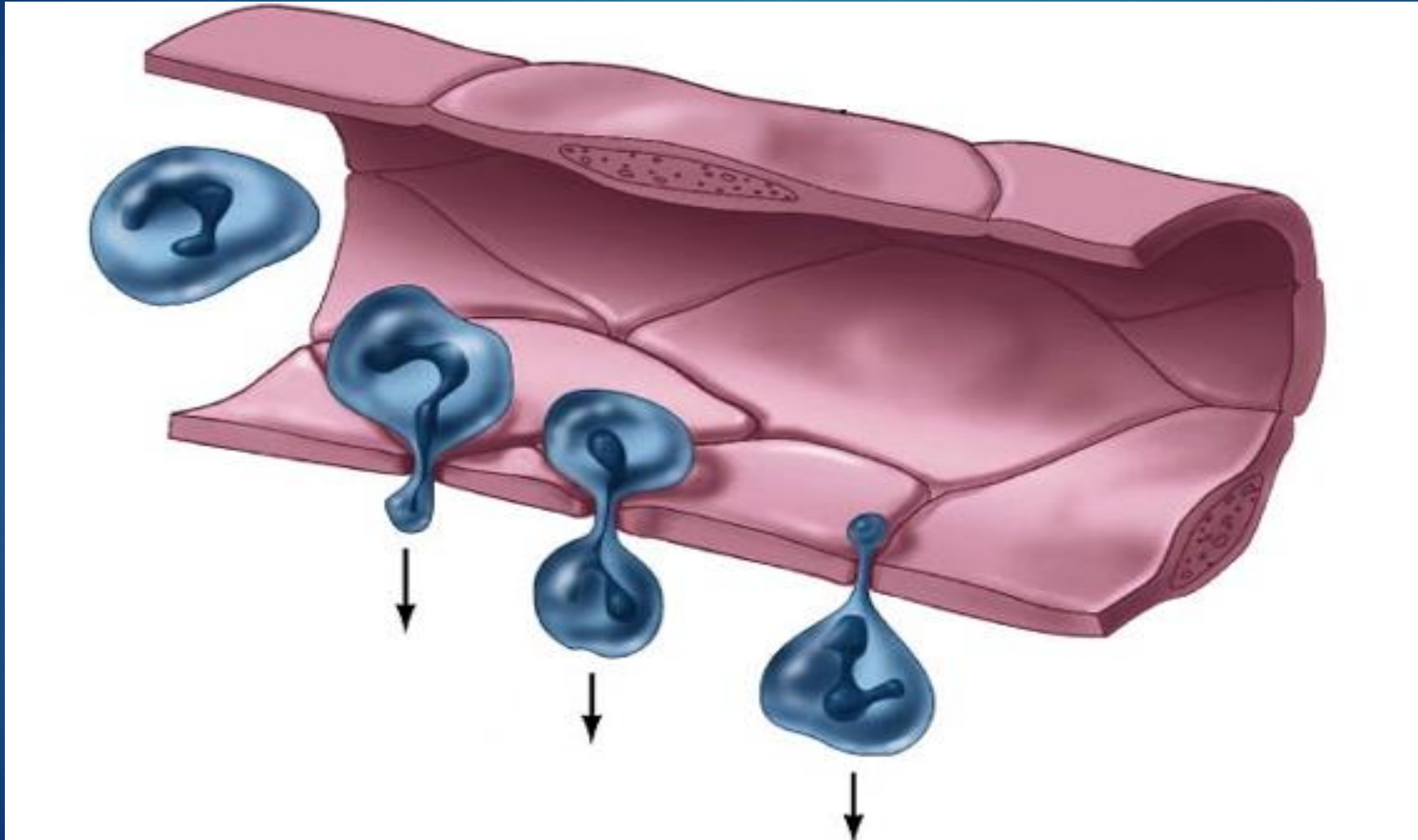
- Chemical substances attract neutrophils & macrophages to a site of injury /inflammation
 - Bacterial & viral toxins
 - Cytokines
 - Complement proteins
 - Clotting proteins
- Associated with increased capillary membrane permeability to facilitate movement of the WBCs from the blood into tissue spaces

Neutrophil & Macrophage Responses During Inflammation

- **First line** , tissue macrophages at site of insult begin phagocytosis
- **Second line** , neutrophils move via chemotaxis & infiltrate the site
- **Within hours**, excessive numbers of neutrophils enter blood from the marrow (neutrophilia ... “left shift”)
- When **bone marrow is hyper-active**, immature forms of WBCs or “bands” may enter blood

Diapedesis

Leukocyte Squeezing Through Capillary Wall



Neutrophil kinetics

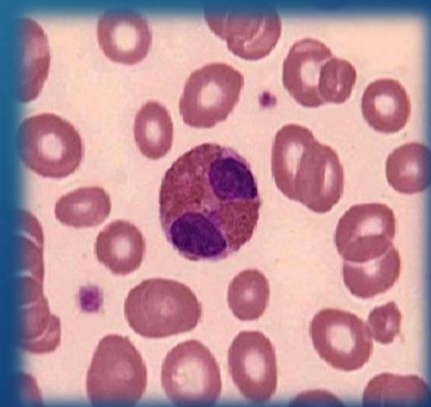
	Transit time range (hr)	Total cells ($\times 10^9$ /Kg)
Marrow mitotic compartment		
Myeloblast	23	0.14
Promyeloblast	26 – 78	0.51
Myelocyte	17 – 1266	1.95
Postmitotic marrow maturation & storage compartments		
Metamyelocyte	8 – 108	2.7
Band	12 – 96	3.6
Neutrophils	0 – 120	2.5
Total marrow storage		8.8
Vascular compartments		
Circulating neutrophils	4 – 10	0.3
Marginated neutrophils	4 – 10	0.4
Total blood neutrophils		
Tissue compartments	0 – 3 days	Not known
Neutrophil turnover rate	1.6×10^6 /Kg/day	

Effective cytokines in differentiation of neutrophils and monocytes

- ▶ IL-3
- ▶ IL-6
- ▶ GM-CSF
- ▶ M-CSF
- ▶ G-CSF

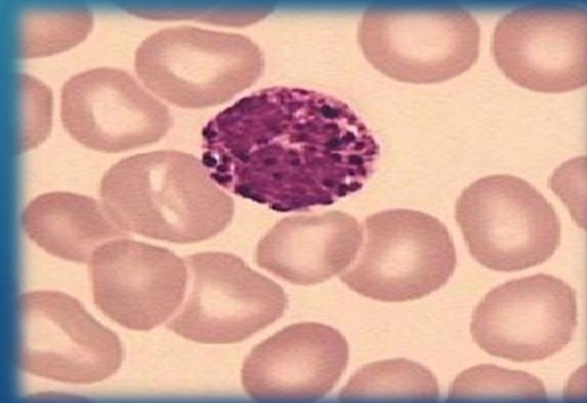
Eosinophil

- Normal mean eosinophil count in the circulating blood is 400/mm³.
- ▶ Most of the eosinophils reside in the connective tissue located in the gut, respiratory tract & urogenital tract.
- ▶ Their number & activation increase as a response to antigens,
- A response is characterized by;
 - ▶ immediate hypersensitivity reaction, mediated by IgE
 - ▶ or delayed hypersensitivity reaction, mediated by T-lymphocytes
- ▶ *Mild eosinophilia: 400–1,500/mm³*
 - *Moderate eosinophilia: 1,500–5,000/mm³*
 - *Severe eosinophilia: greater than 5,000/mm³.*



Basophils

- Contribute to allergic responses to antigens Release histamine and heparin
- Also release bradykinin, serotonin, slow releasing substance of anaphylaxis
- Local vascular reactions (**vasodilation & capillary leak** with erythema & edema)
- IgE type antibodies become attached to basophils (and mast cells) as part of the trigger for an allergic response

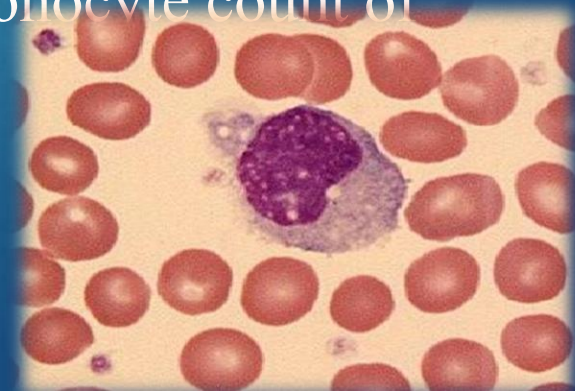


Monocyte

- ▶ first 2 weeks of life, the absolute monocyte count is greater than 1000 cells/iL

With increasing age there is a gradual decline in the monocyte count until it reaches a plateau of 400 cells/iL in adulthood.

- ▶ Monocytosis may therefore be defined as a total monocyte count of greater than 500 cells/iL



Thank
you!!!
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