Lec 06 : Leukopoiesis II

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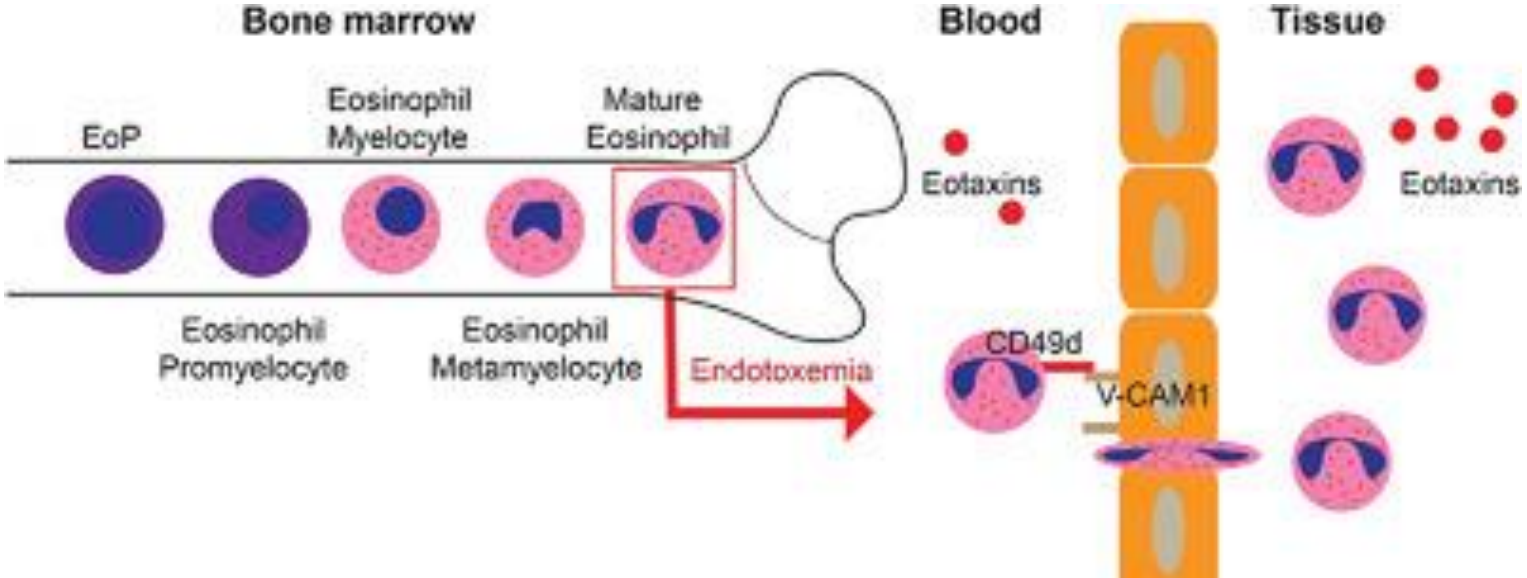
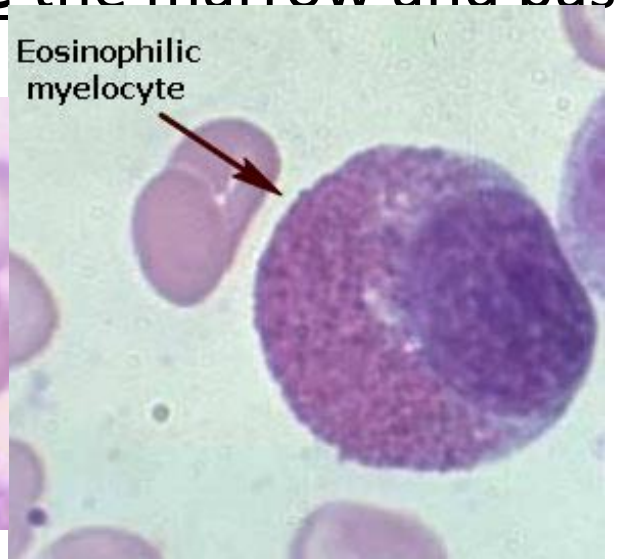
Eosinophil Maturation

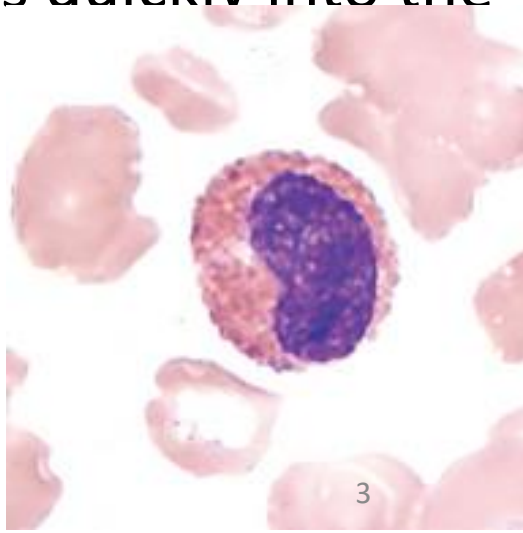
- **Close relative** of the **PMN** whose **secondary granules** stain **orange-red** with **Romanowsky-based stains**
- Development of **PSCs** into eosinophils requires **IL-3, IL-5 and GM-CSF** and is inhibited by the presence of **interferon**
- **CFU-GEMM** to **CFU-Eo** to **myeloblast**
- **Myeloblast** to **promyelocyte** which is indistinguishable from other **promyelocytes**



Eosinophil Maturation

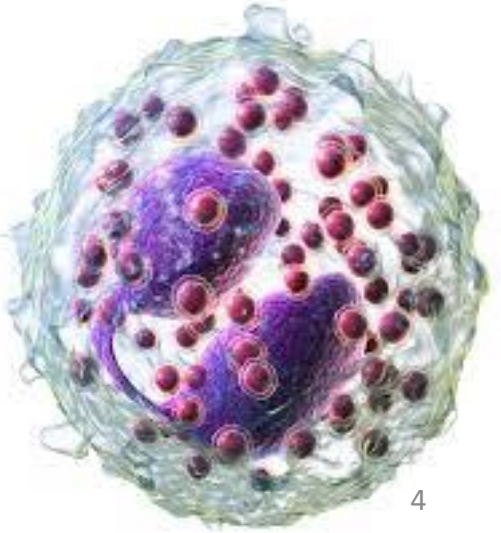
- **Myelocyte** becomes distinguishable from neutrophilic line due to **presence of large, round granules containing major basic** protein, which in turn is **responsible** for the staining qualities of the **eosinophilic granules**.
- Eosinophils spend less than **1 week in the PB**
- Large storage capacity of Eos in **BM** allow rapid deployment, on demand
- When **stimulated**, **leave** the marrow and pass quickly into the **tissues**





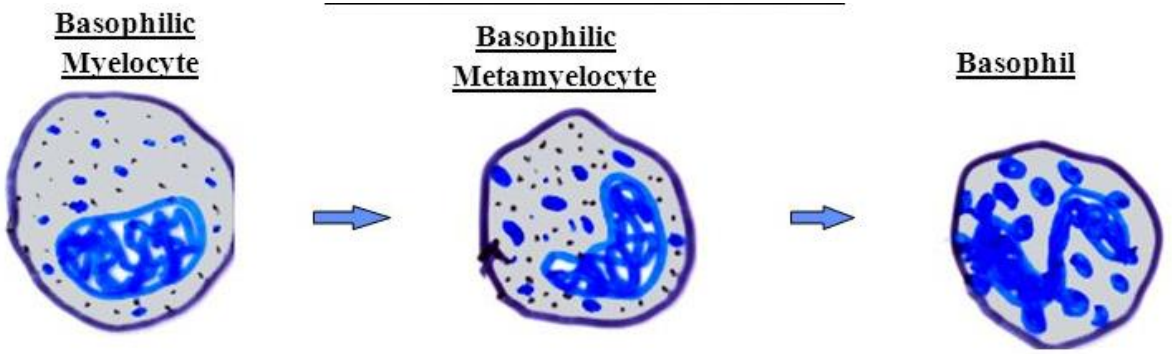
Eosinophil Maturation

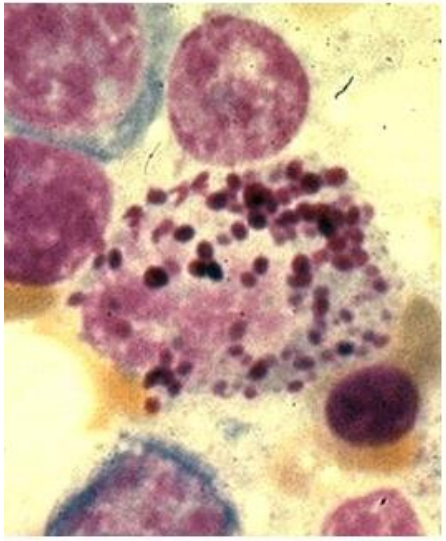
- Actively **motile**, using same **migration** paths as neutrophils
- **Short transit times in PB** cause **variability** in Eo numbers in the WBC differential
- Less than 5% of **circulating** WBCs
- **Allergic** response may **increase** numbers o Eos
- Mature Eos may be in **band form** or **bilobed** while nuclei with higher lobe counts are seldom seen
- **Slightly larger than PMN at 12-17 um**

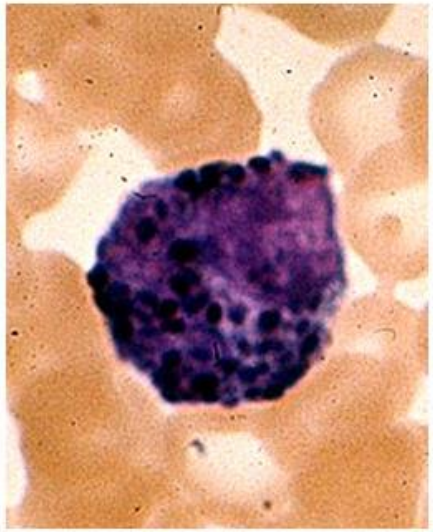


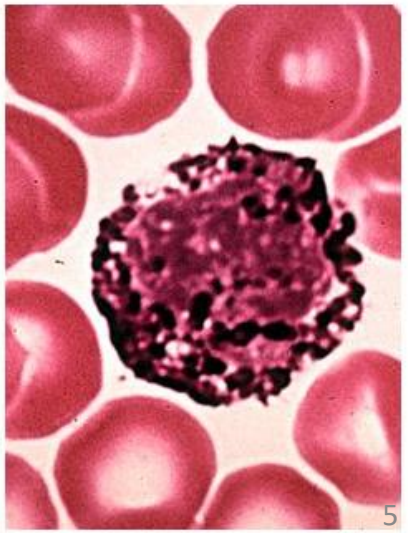
Basophil Maturation

- Characterized by presence of large purple granules
- **Granules** are **irregularly shaped**, unevenly distributed and deep purple to black when stained with **Romanowsky stains**
- **Maturation** from **stem cell** to **mature** Basophil is not well defined, but thought to **parallel** that of the Eo



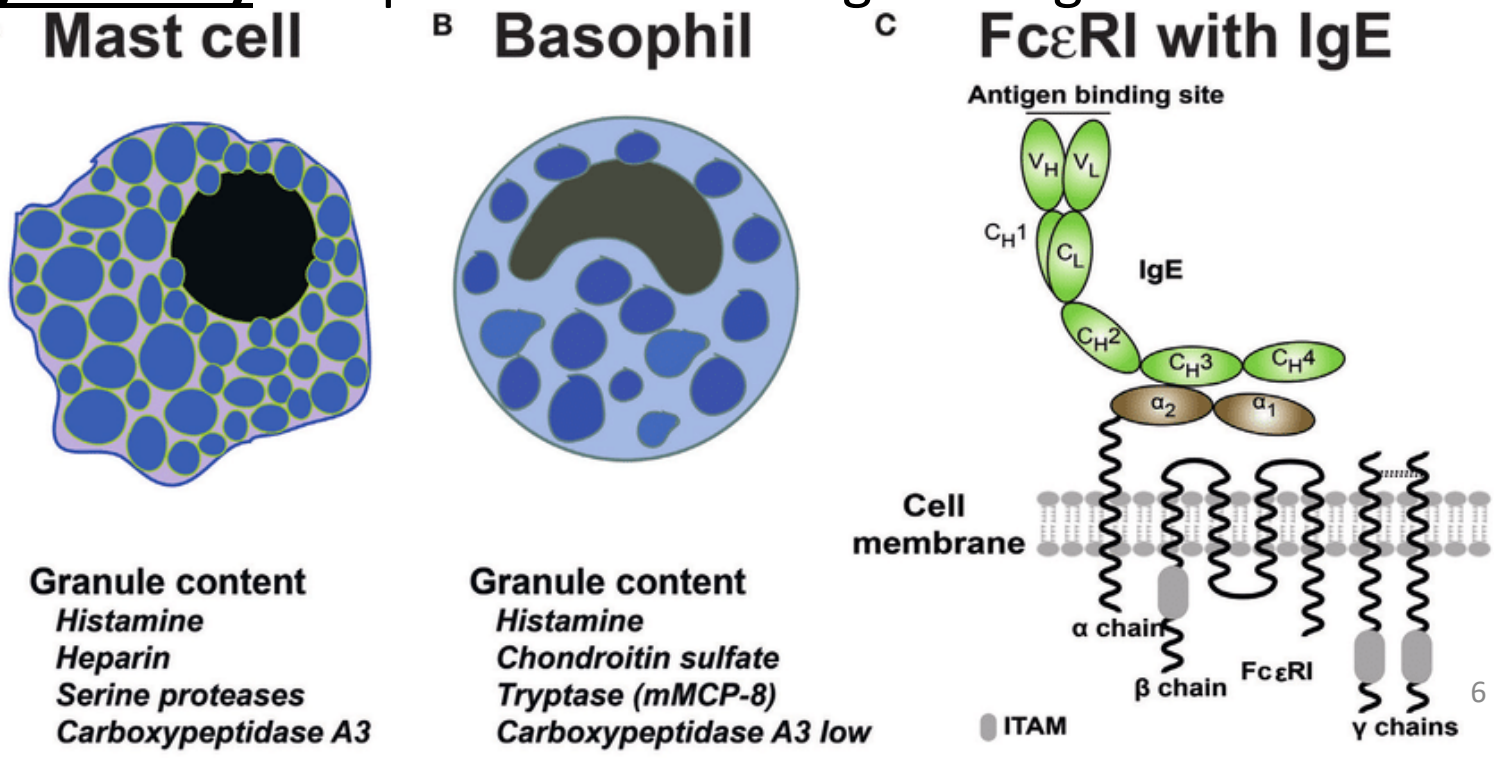






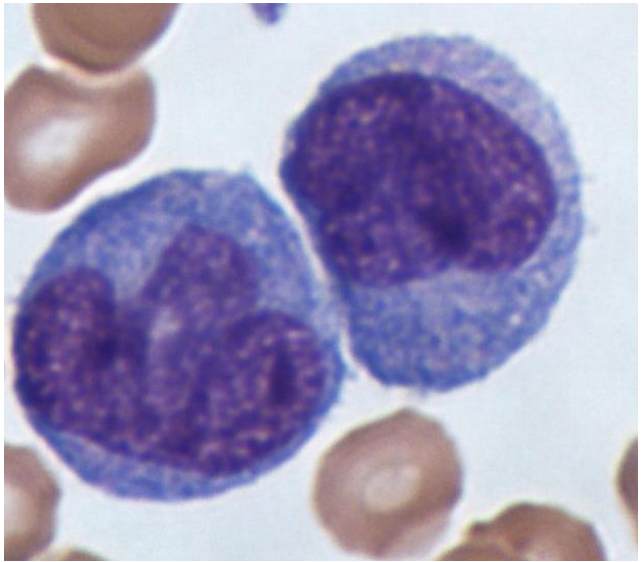
Basophil Maturation

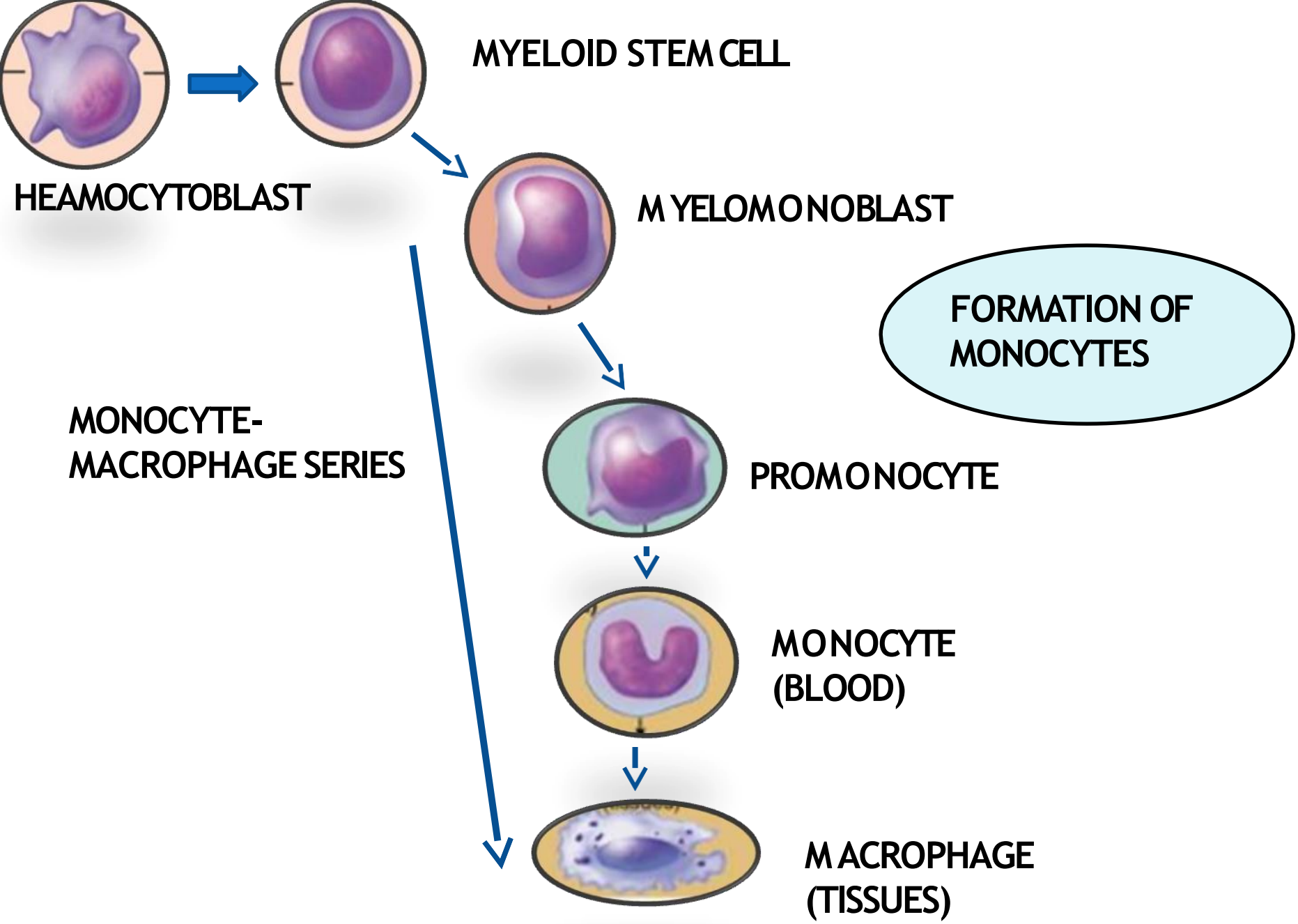
- As with Eos, Basos can be classified as **myelocytes**, **metamyelocytes**, **bands** and **PMN** cells on the basis of nuclear development
- As with Eos, mature cells with **more than 2 nuclear lobes** are not usually seen
- The least common cell in the **PB**, at less than 1% of circulating WBCs
- Have **high-affinity** receptors for the Fc region of IgE



Monocyte/Macrophage Maturation

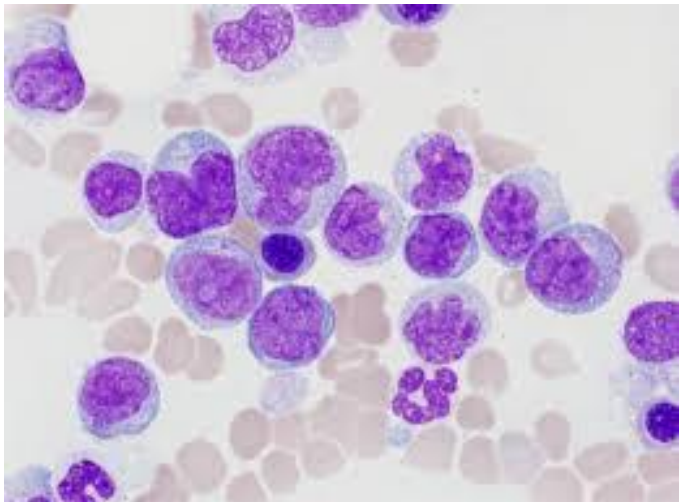
- **Monocyte/Macrophage** cells mature from **monoblast** to **promonocyte** to blood monocyte to **free** and **fixed macrophages**, but the mechanism of commitment is not well understood.
- **Granular** content **vary** considerably with more than **50 secretory** compounds having been identified.
- **PB** monocytes demonstrate morphologic variability
- **Aggressive motility** and **adherence** may distort the **monocytes** during PB smear preparation

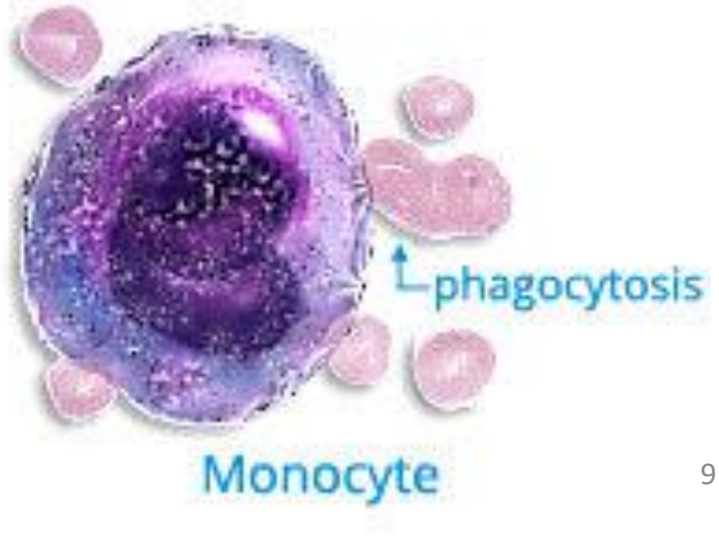



MYELOID STEM CELL
HEAMOCYTOBLAST
MYELOMONOBLAST
FORMATION OF MONOCYTES
MONOCYTE-MACROPHAGE SERIES
PROMONOCYTE
MONOCYTE (BLOOD)
MACROPHAGE (TISSUES)

Monocyte/Macrophage Maturation

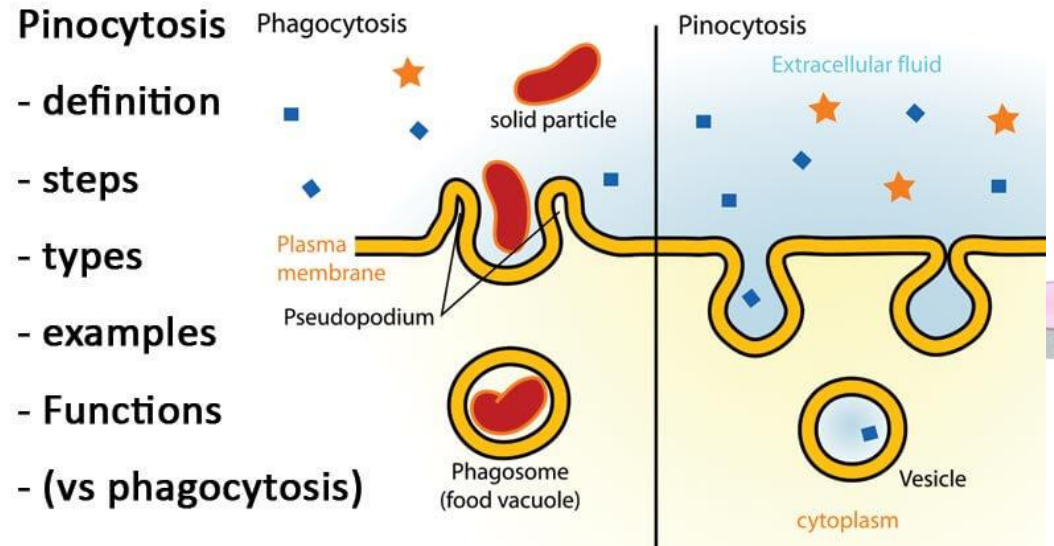
- **Monocyte nucleus** is indented or curved with chromatin that is lacy with small clumps
- Typically the **largest cell** in the **PB**
- **Cytoplasm** is filled with **minute granules** that produce a **cloudy appearance**
- Cytoplasmic **membrane** may be **irregular**, **pseudopods** and **phagocytic** vacuoles may be evident
- Described as a **transitional cell** because it leaves the **BM** to enter the **PB** and then leaves to enter tissues in response to **chemotactic factors**

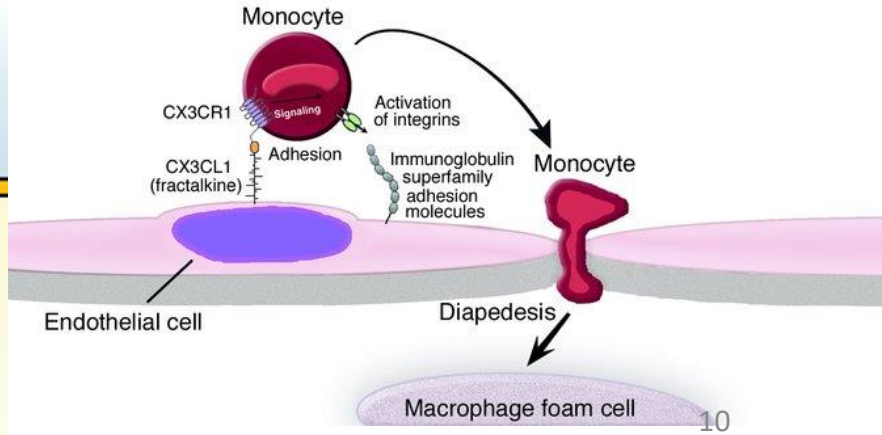




Monocyte/Macrophage Maturation

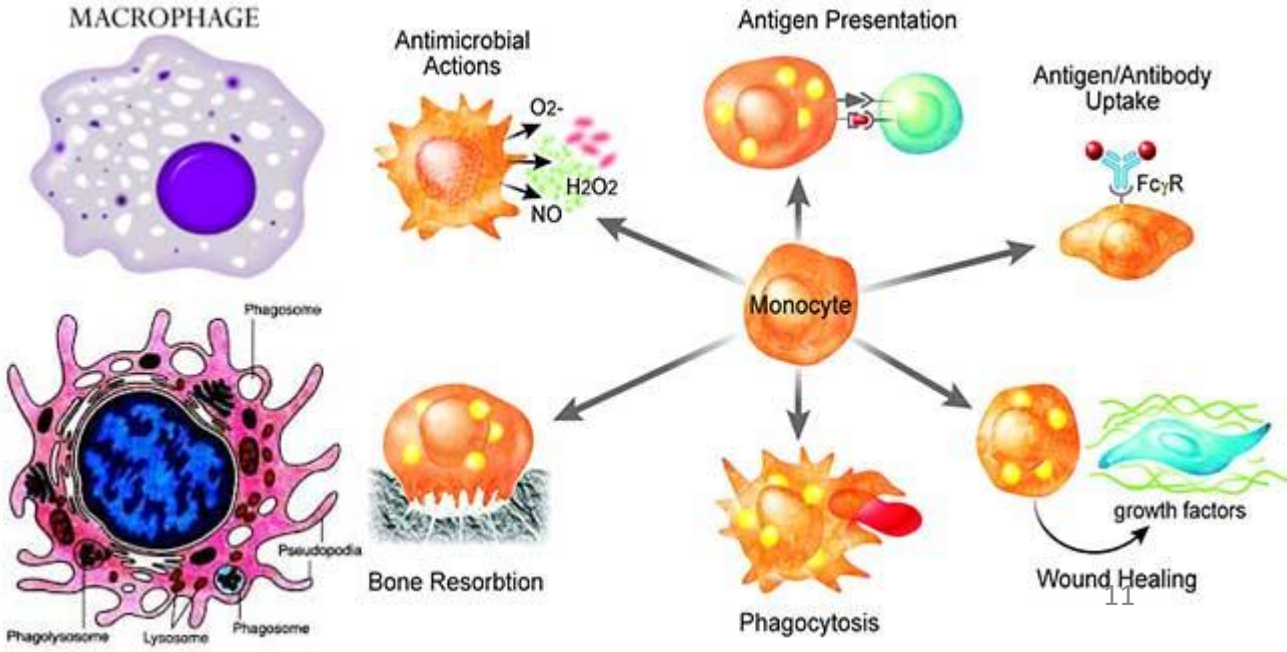
- Makes up les than **15%** of PB WBC differential
- Highly **motile** and tend to **marginate** along vessel walls with a strong tendency to **adhere** to surfaces
- May be stimulated to undergo **diapedesis** and become **free macrophages** with increased **phagocytic** activity
- Macrophages are **large**, **actively phagocytic** cells with a size of **15-85 um** .
- **Pleomorphic** in shape, **frequently** with **pseudopods**
- Function is **phagocytosis**
- Material **ingested** is highly variable
- **Pinocytosis** also occurs with items less than 2 um in size





Monocyte/Macrophage Maturation

- Multistep process of **recognition/ attachment**, **ingestion**, **intracellular kill**, **digestion/degradation**, and **exocytosis** occurs in both **phagocytosis** and **pinocytosis**.
- **Monocytes kill** any recognizable non-self agents including **dead** or **dying** cells, **bacteria**, **fungi viruses**.
- Play a role in processing **antigens** for **lymphocyte recognition** and **stimulation** of lymphocyte transformation.
- May function as **anti-tumor** agents by **phagocytic** action of **nonself** cells via **elaboration** of tumor necrosis factor and stimulation of lymphocyte activity



Monocyte/Macrophage Maturation

- **Macrophages** are in 2 categories

1. **Free** — found in varying concentrations all sites of **inflammation** and **repair**, **alveolar spaces** and **peritoneal** and **synovial fluids**

2. **Fixed** — found in specific concentrations in specific sites such as the nervous system (**microglial cells**), **liver** (**Kupffer** cells), **spleen**, **bone marrow** and **lymph nodes**

- Macrophages are large, **15-80** um, have abundant cytoplasm filled with **granules** a often have multiple **vacuoles**
- **Nucleus** is round to reniform and may contain **1 or 2** nucleoli

Lymphopoiesis

- Lymphoid progenitor > T or B cell
- T cell in thymus
- B cell in adult bone marrow
- Null cells (natural killer cell NK) in bone marrow – unknown maturation sequence
- T, B, Null cells **morphologically identical**
- **Distinguished functionally** and **by immunological markers**
- **In thymus and bone marrow lymphocytes differentiate, proliferate and mature into fully functional immune cells**
- In **secondary lymphoid organs** – **lymphocytes** interact with **antigen-presenting** cells (APC), phagocytes and macrophages in an active immune response
  - Secondary organs = lymph nodes, spleen, mucosal tissues (tonsils, Peyer's patch)

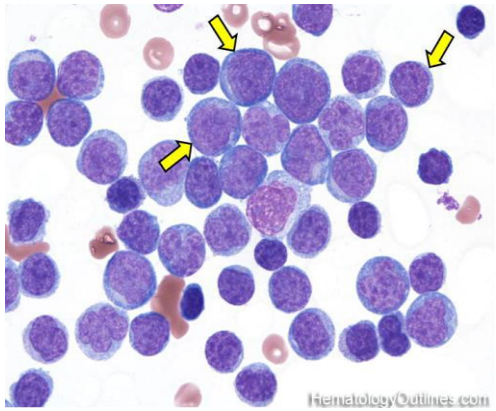
Lymphopoiesis

- T-lymphocytes, which undergo maturation in the **thymus** = 75% of lymphocytes
- **T-lymphocytes** possess distinct cell surface antigens (CD3)
  - Play a central role in **cell-mediated immunity**
  - T helper cells, cytotoxic T cells, memory T cells, regulatory T cells, natural killer T cells
- **B-lymphocytes** produce the **antibodies** after antigen exposure
  - Become **plasma** cells.
  - B-lymphocytes comprise **25%** of all lymphocytes.
- **NK cells** – large granular lymphocytes - **~5%** of blood and **splenic lymphocytes**
  - Play important role in **innate immune response** to **infections** and some **tumors**

Lymphopoiesis

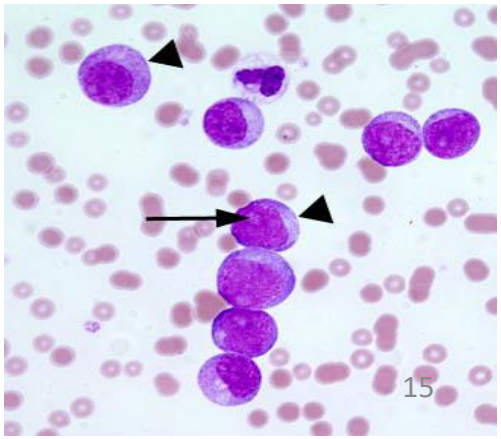
Lymphoblast

- Large round nucleus, small basophilic cytoplasm N:C = 7:1 to 4:1
- Nuclear chromatin – thin, loose evenly stained strands, not clumped
- Nucleoli – 1-2
- 10-20 µm

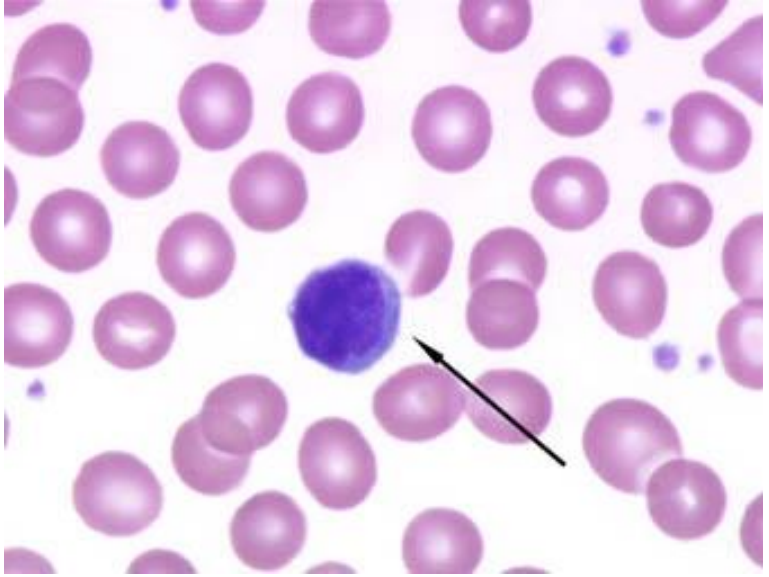


Prolymphocyte

- Intermediate chromatin pattern with clumping
- 9-18 µm
- N:C = 5:1 to 3:1
- Nucleoli – 0-1
- Slightly different from lymphoblast

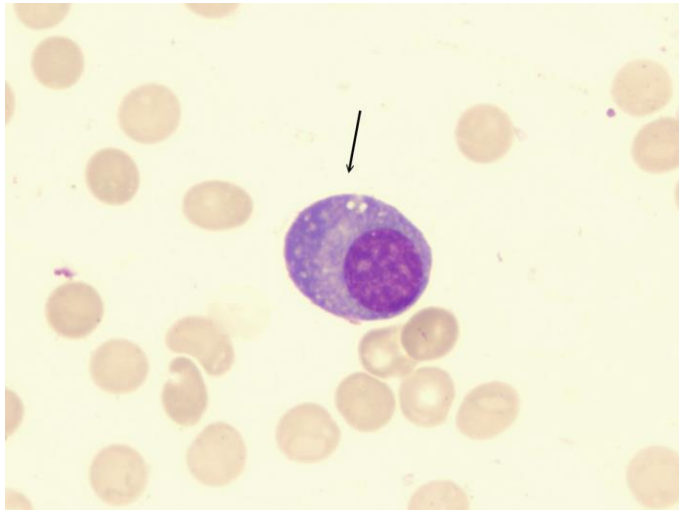


Lymphopoiesis



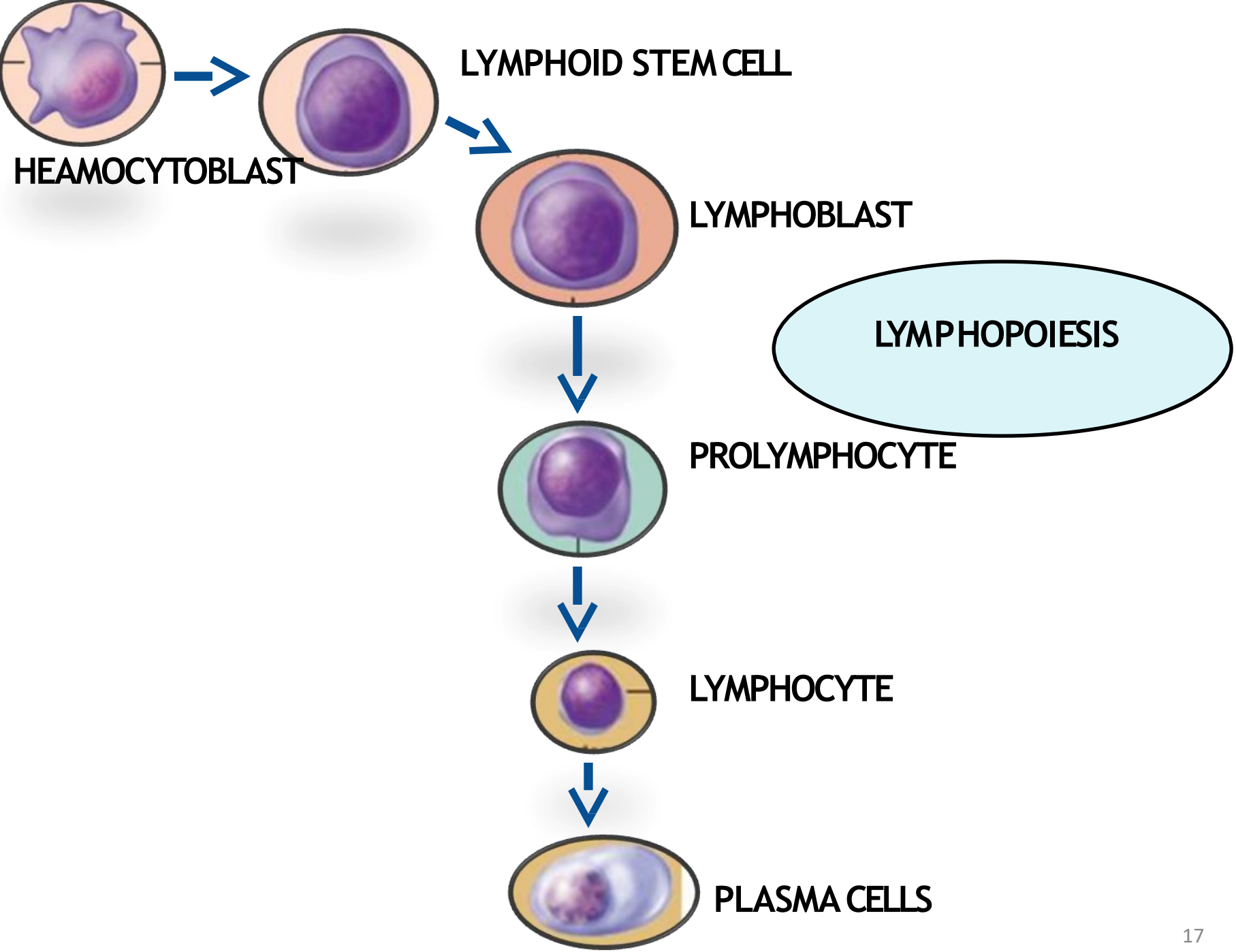
Plasmablasts

- Similar to other blast cells
- N:C – 5:1 to 4:1
- Cytoplasm – blue
- 16-25 µm



Plasmacytes

- End stage of B-lymphocyte lineage
- **Not seen in normal PB, 1% in BM**
- 10-20 µm
- Round, oval, slightly irregular margins
- **Cytoplasm** deep blue with perinuclear clear zone
- **Secretory** vesicles at cell periphery
- **Nucleus** – eccentrically placed


HEAMOCYTOBLAST
LYMPHOID STEM CELL
LYMPHOBLAST
LYMPHOPOIESIS
PROLYMPHOCYTE
LYMPHOCYTE
PLASMA CELLS

Lymphocytes — Immunologic Differentiation

- Lymphocytes may be classified by **immunologic** function

- **B Cells**
- 1. Possess cytoplasmic **IG** concentrations and **IgM**
- 2. Some **membrane receptors** are apparent
- 3. The fully committed **B lymphocyte** is the **plasma cell**
- 4. Demonstrate **class I and class II** human leukocyte antigens (HLA-A, HLA-B, HLA-C and HLA-D, HLA-DR)

Lymphocytes—Immunologic Differentiation

- **T Cells**

1. The primitive T cell, CFU-L, travel' thymus

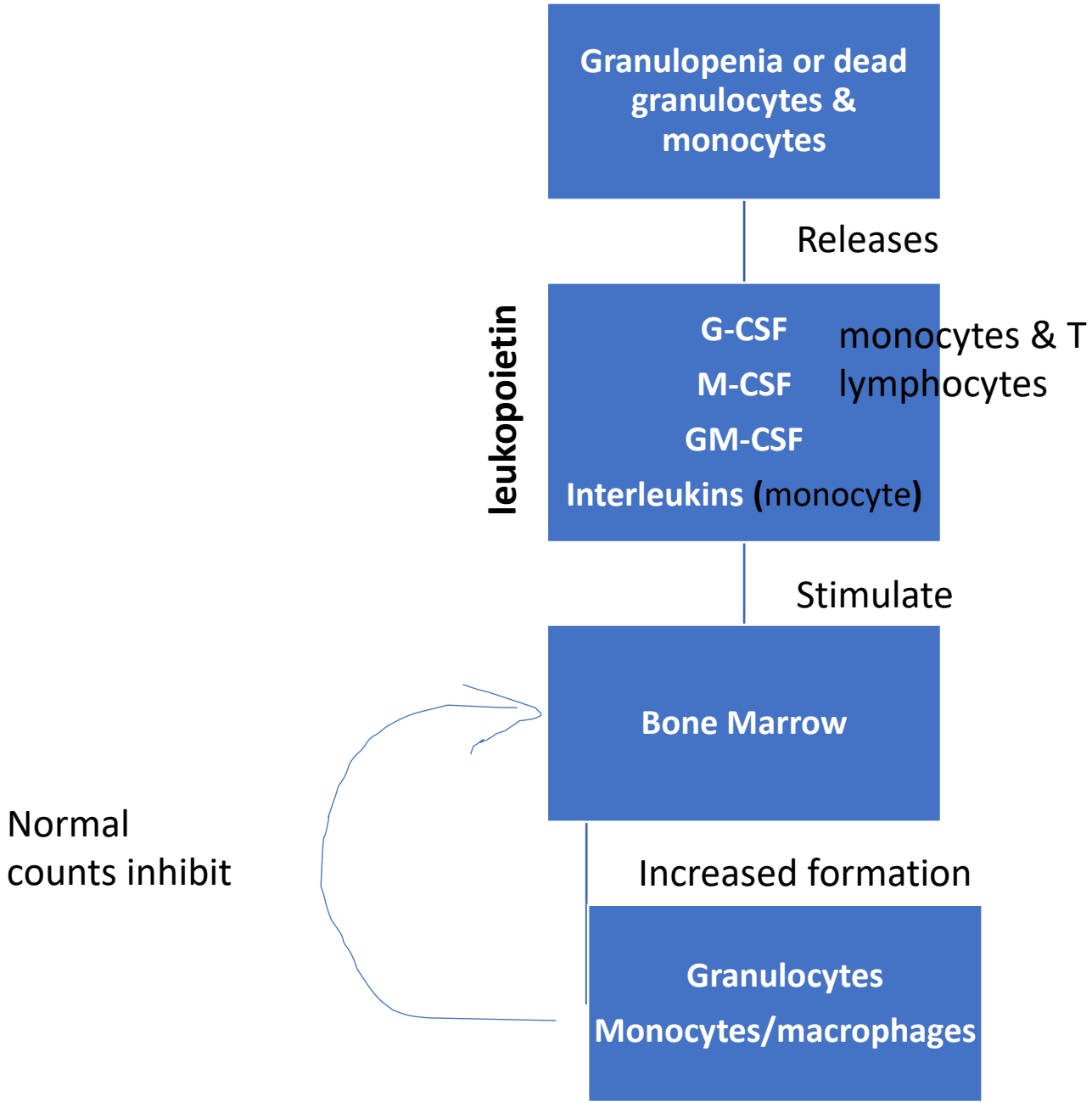
2. Acquires a transferrin receptor that is specific to proliferation

3. Mature T cells lose all precursor markers an have an active helper or suppressor function

4. T cells are further differentiated through presence or absence of HLA-D antigens

5. T cells possess HLA-A, HLA-B and HLA-C class I antigens

Regulation of leucopoiesis



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