Hematopoiesis

Lecture Objectives

- Name organs responsible for hematopoiesis in the fetus.
- List the developmental stages of hematopoiesis both prenatally and postnatally.
- Outline the major steps of post-natal development of blood formed elements (erythropoiesis, granulopoiesis, monocytopoiesis and megakaryopoiesis.
- Identify characteristic features of these cells.

Formation of Blood Cells

- Negative feedback systems regulate the total number of RBCs and platelets in circulation
- Abundance of WBC types based of response to invading pathogens or foreign antigens
- Hemopoiesis or hematopoiesis
- Red bone marrow primary site
- Pluripotent stem cells have the ability to develop into many different types of cells

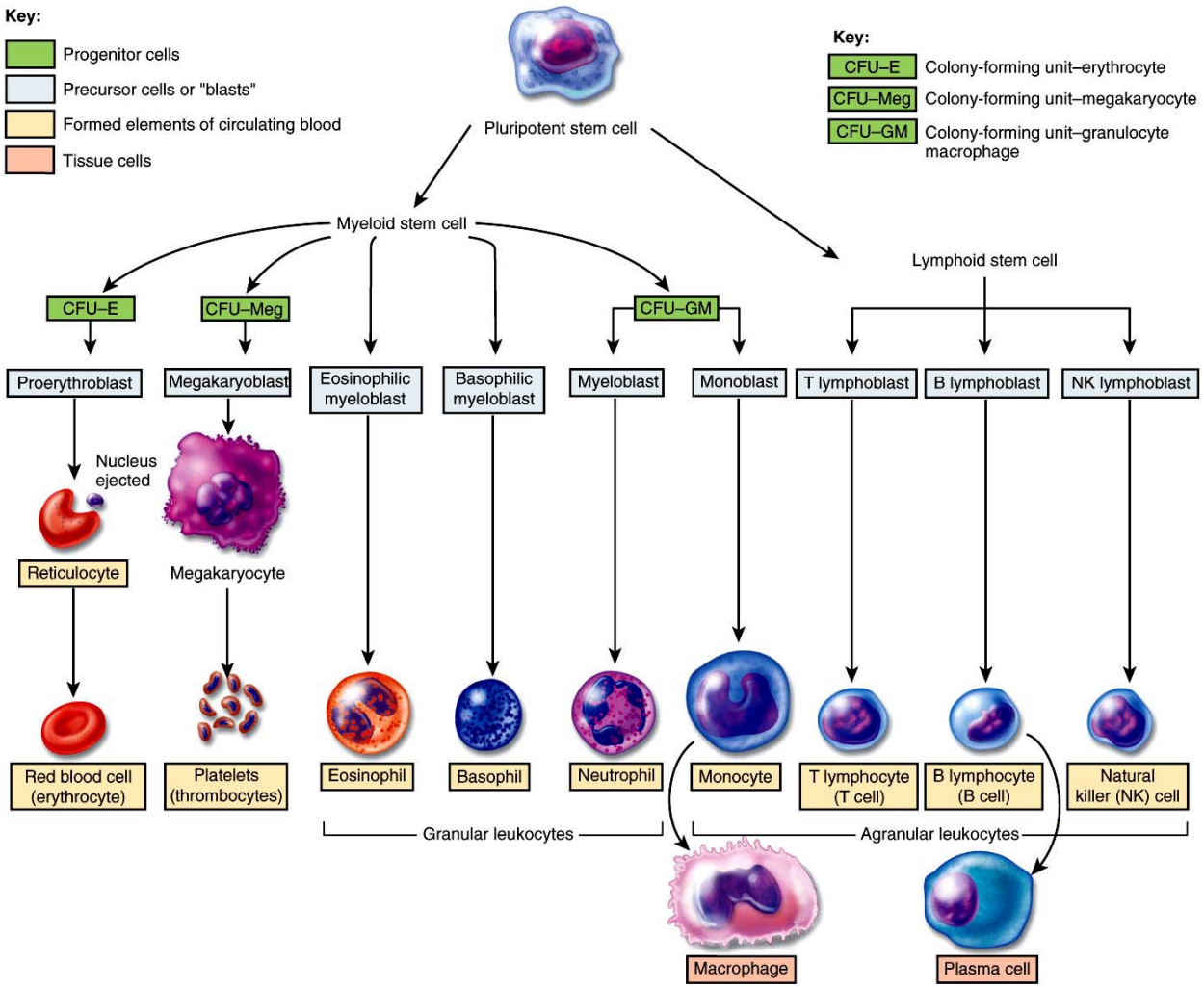


Figure 19.03 Tortora - PAP 12/e

Formation of Blood Cells

- Stem cells in bone marrow
  - Reproduce themselves
  - Proliferate and differentiate
- Cells enter blood stream through sinusoids
- Formed elements do not divide once they leave red bone marrow
  - Exception is lymphocytes

Formation of Blood Cells

- Pluripotent stem cells produce
  - Myeloid stem cells
    - Give rise to red blood cells, platelets, monocytes, neutrophils, eosinophils and basophils
  - Lymphoid stem cells give rise to
    - Lymphocytes
- Hemopoietic growth factors regulate differentiation and proliferation
  - Erythropoietin – RBCs
  - Thrombopoietin – platelets
  - Colony-stimulating factors (CSFs) and interleukins – WBCs

Bone Marrow

- Bone marrow found in the medullary canals of long bones and cavities of cancellous bone
- Tow types:
  - Red bone marrow, color due to blood and blood forming cells
  - Yellow bone marrow, color due to great number of adipose cells
- In newborns all bone marrow is red

Red Bone Marrow

- Functions
  - Production of blood cells
  - Destruction of worn-out RBCs
  - Storage (in macrophages) of iron derived from breakdown of hemoglobin

Red Bone Marrow

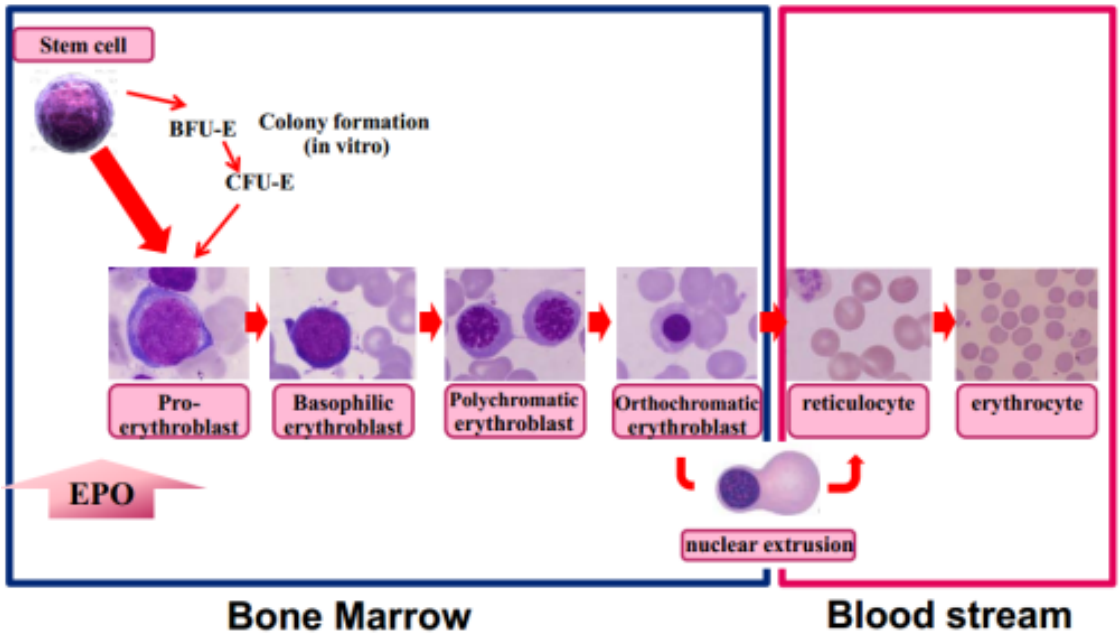
- Structure
  - Stroma
    - Meshwork of reticular cells in delicate web of reticular fibers
    - Collagen type I and III
    - Fibronectin, laminin, and hemonectin
      - Interact with cell receptors to bind cells to stroma
  - Hematopoietic cords
    - Hematopoietic cells
  - Sinusoidal capillaries
    - Reinforced by external discontinuous layer of reticular cells and a loose net of reticular fibers

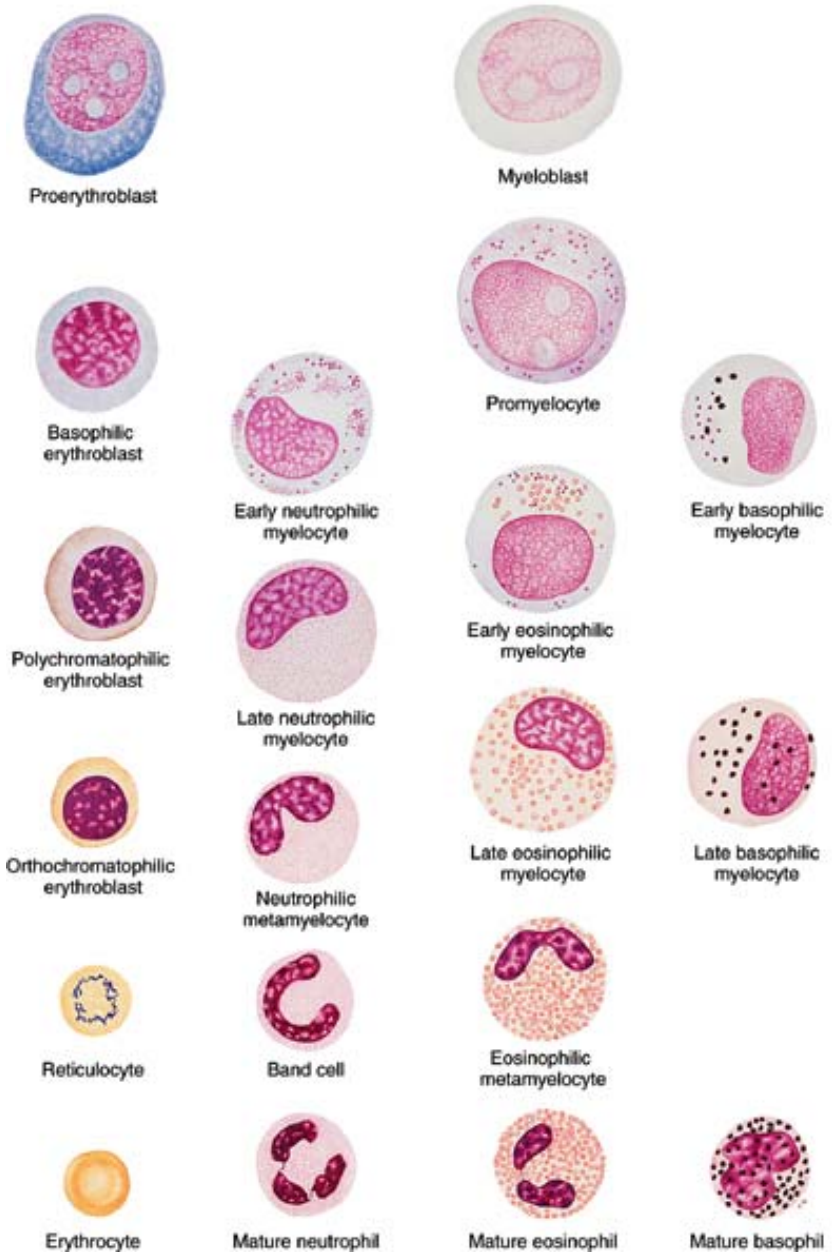
Maturation of Erythrocytes

- The basic process of maturation is synthesis of hemoglobin and formation of enucleated, biconcave erythrocyte
- Changes during maturation
  - Decrease in cell volume
  - Nucleoli diminish in size until invisible in scope
  - Nuclear diameter decrease and chromatin become denser until nucleus have a pyknotic appearance and finally extruded
  - Decrease number of polyribosomes (basophilia decrease) with increase in hemoglobin (acidophilic)
  - Cell organelles gradually disappear
- Development of erythrocyte from the first cell of the series until released to blood take 7 days

Differentiation of Erythrocytes

- Proerythroblast
  - First recognizable cell in the series
  - Large cell with loose chromatin and visible nucleoli
  - Its cytoplasm is basophilic
- Basophilic erythroblast
  - Strongly basophilic cytoplasm
  - Condensed nucleus that has no visible nucleolus
- Polychromatophilic erythroblast
  - Decrease polyribosomes and increase hemoglobin
  - Staining causes several colors to appear
- Orthochromatophilic erythroblast
  - Nucleus continue to condense
  - No basophilia is evident and uniformly acidophilic cytoplasm
- Reticulocyte
  - Nucleus is expelled and engulfed by macrophages
  - Small number of polyribosomes



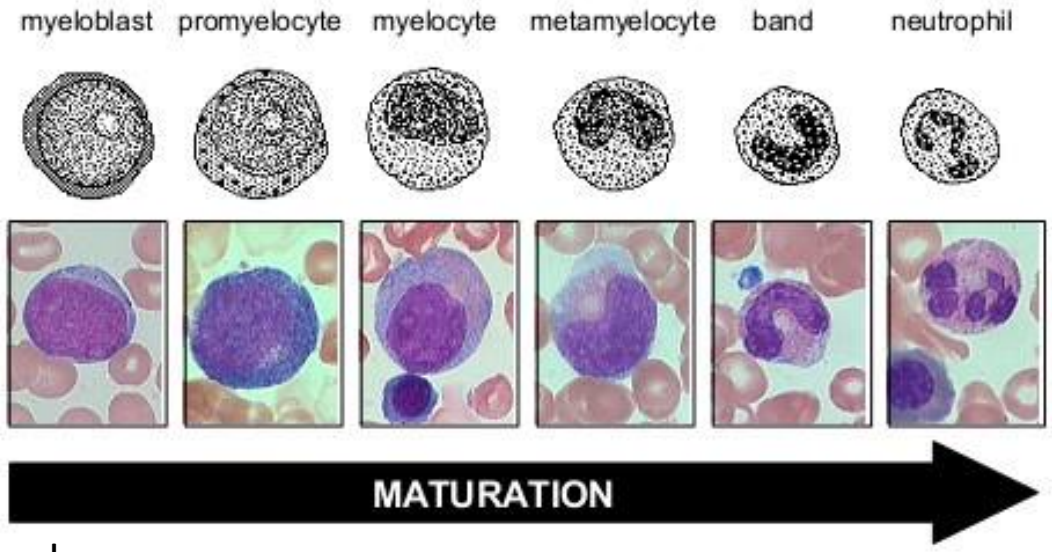

Proerythroblast
Basophilic erythroblast
Polychromatophilic erythroblast
Orthochromatophilic erythroblast
Reticulocyte
Erythrocyte
Early neutrophilic myelocyte
Late neutrophilic myelocyte
Neutrophilic metamyelocyte
Band cell
Mature neutrophil
Myeloblast
Promyelocyte
Early eosinophilic myelocyte
Late eosinophilic myelocyte
Eosinophilic metamyelocyte
Mature eosinophil
Early basophilic myelocyte
Late basophilic myelocyte
Mature basophil

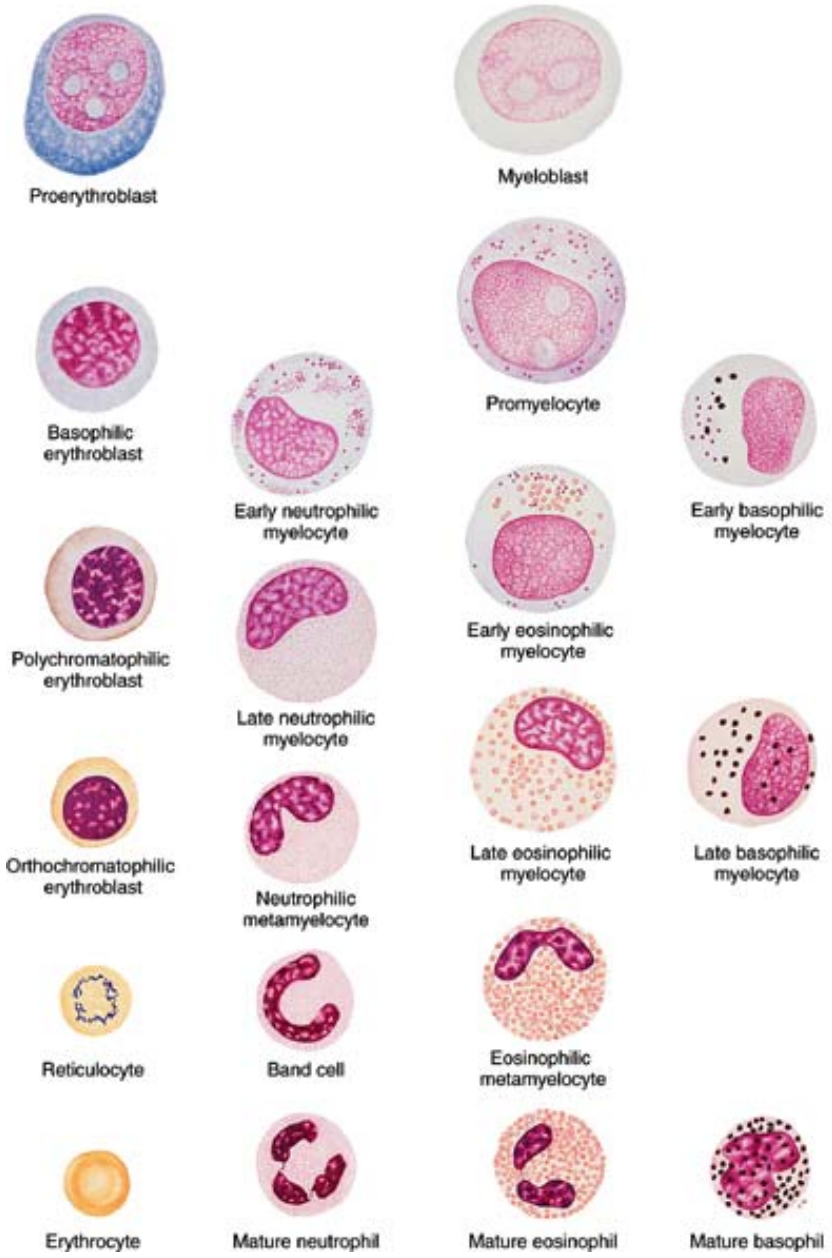
Granulopoiesis

- Maturation process involves synthesis of protein that are backed in granules
- First stage results in the development of the azurophilic granules that contain enzymes of lysosomal system
  - Stain with basic dyes
- In the second stage results in the development of the specific granules
  - several types of proteins are backed in these granules depending on the type of the granulocytes

Maturation of Granulocytes

- Myeloblast is the most immature recognizable cell in the myeloid series
  - Dispersed chromatin with visible nucleoli
- Promyelocyte
  - Basophilic cytoplasm and azurophilic granules
  - Give rise to the three known types of granulocytes
- Myelocyte
  - Specific granules appear and increase
- Nutrophilic, basophilic and eosinophilic myelocyte
  - Further condensation of nucleus
  - Considerable increase in their specific granules
- Neutrophilic granulocyte before maturation passes through an intermediate stage where nucleus has curved rod shape (band cell)

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Maturation of Lymphocytes & Monocytes

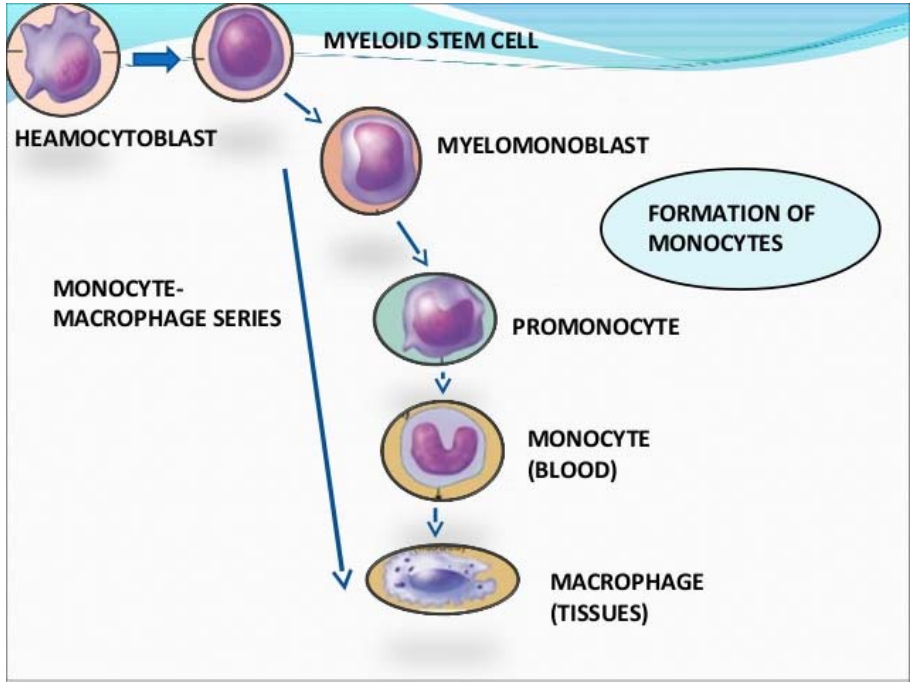
- Precursor cells do not contain specific cytoplasmic granules or nuclear lobulation
- Lymphocytes and monocytes are distinguished on the basis of size, chromatin structure and the presence of nucleoli
- As lymphocyte mature
  - Chromatin becomes more compact
  - Nucleoli become less visible
  - Cell decrease in size

Lymphocytes

- Circulating lymphocytes originate in lymphoid organs
- Lymphocyte progenitor cells originate in the bone marrow
- Lymphoblast
  - First identifiable progenitor of lymphoid cells
  - Large cells
- Polymorphocytes
  - Smaller and more condensed chromatin

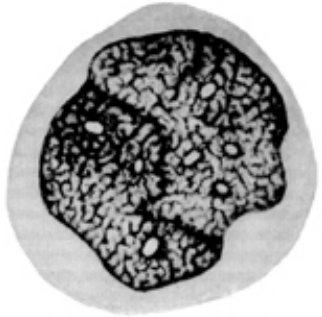
Monocytes

- Monoblast
  - Committed progenitor cell that looks like myeloblast
- Promonocyte
  - Large cell (up to 18 µm in diameter)
  - Basophilic cytoplasm
  - Slightly indented nucleus
  - Chromatin is lacy and visible nucleoli
  - Divide twice leading to monocytes
- Fine azurophilic granules can be seen in the blood monocyte
- Mature monocyte circulate blood for 8 h, then enter the CT and mature into macrophages, which function for several months



Origin of Platelets

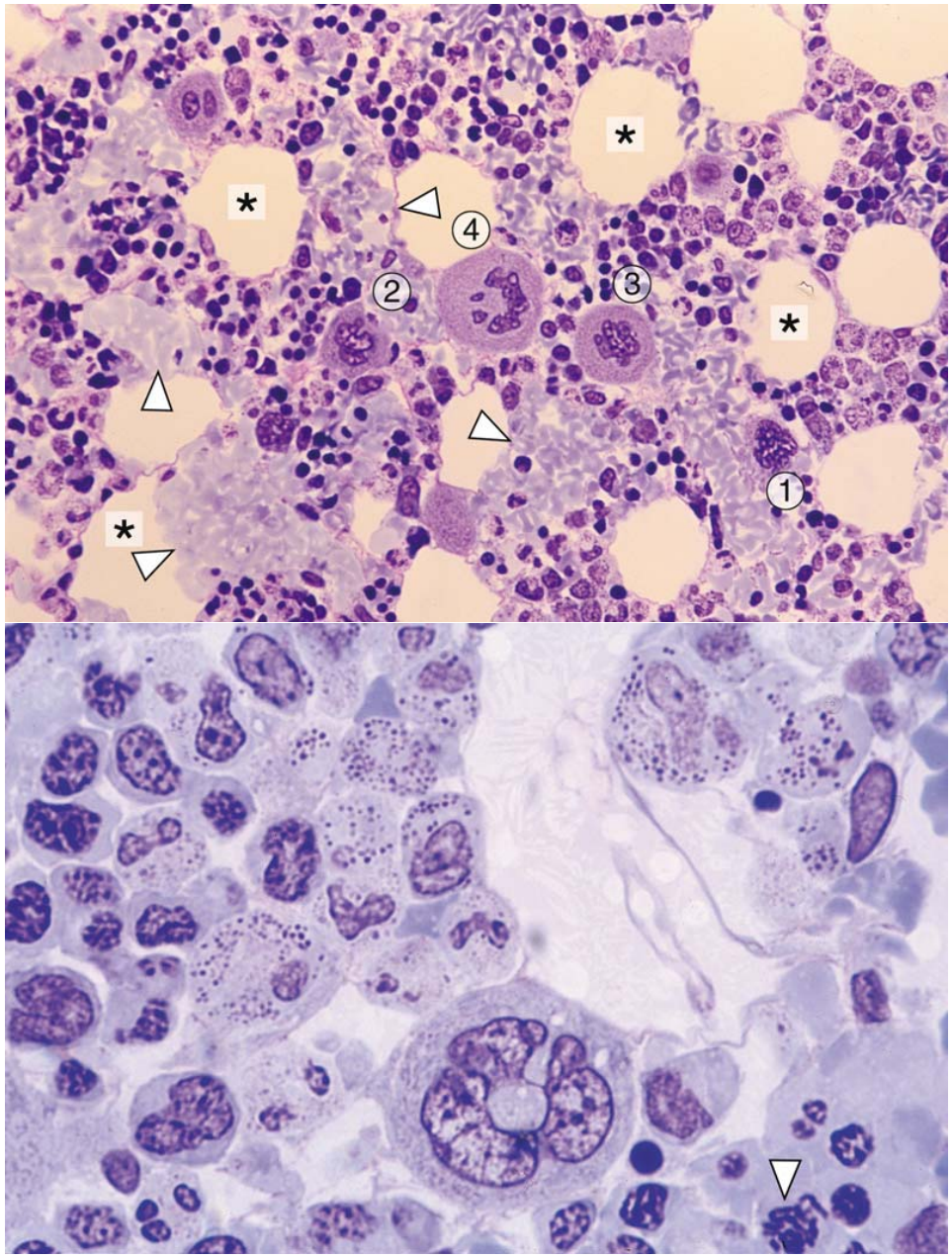
- Megakaryoblasts
  - 15-50 µm in diameter
  - Large ovoid or kidney-shaped nucleus with numerous nucleoli
  - Cytoplasm is homogenous and intensely basophilic
- Megakaryocytes
  - Giant cell, 35-150 µm in diameter
  - Irregularly lobulated nucleus
  - Coarse chromatin, no visible nucleoli
  - Cytoplasm contain well developed organelles



Megakaryoblast

Megakaryocyte

Platelets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