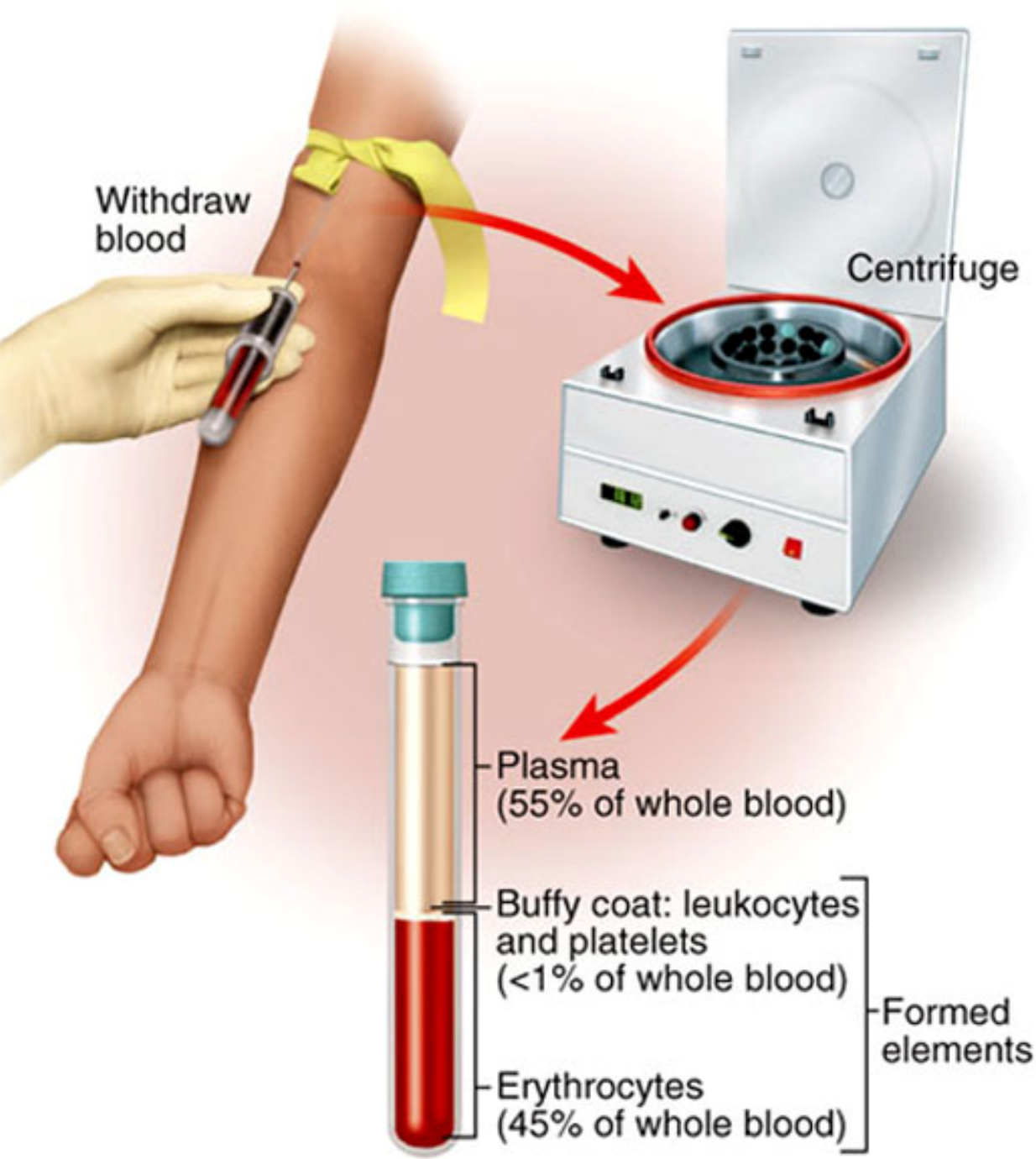
# Hematology

## Hematocrit: Packed Cell Determination

## &

## The Histology of Blood




# Determining Hematocrit

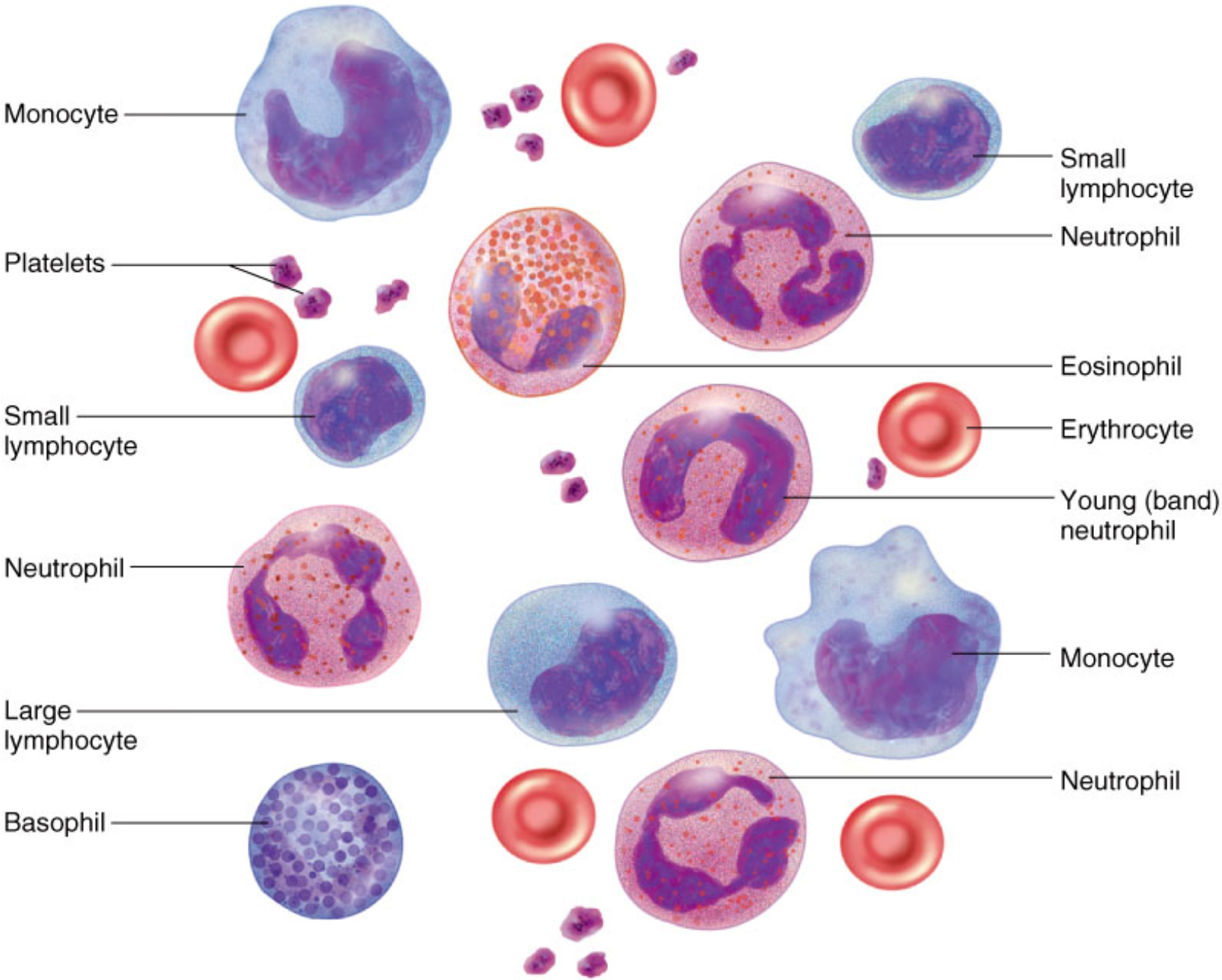
The inside lining of syringe and the test tube must be treated with an anti-coagulant (e.g. heparin) to prevent hemostasis.

Without heparin, platlets are “activated” and start a cascading enzymatic reaction which converts a soluble protein (fibrinogen) into an insoluble protein (fibrin).

See next slide.


Note: This is called the platelet plug

# The Formed Elements of Blood



# Formed Elements

**Formed elements are cells and cell fragments**

- **Red blood corpuscles (RBC)**
  - **Not cells because a mature RBC does not have a nucleus**
- **White blood cells**
- **Platelets**

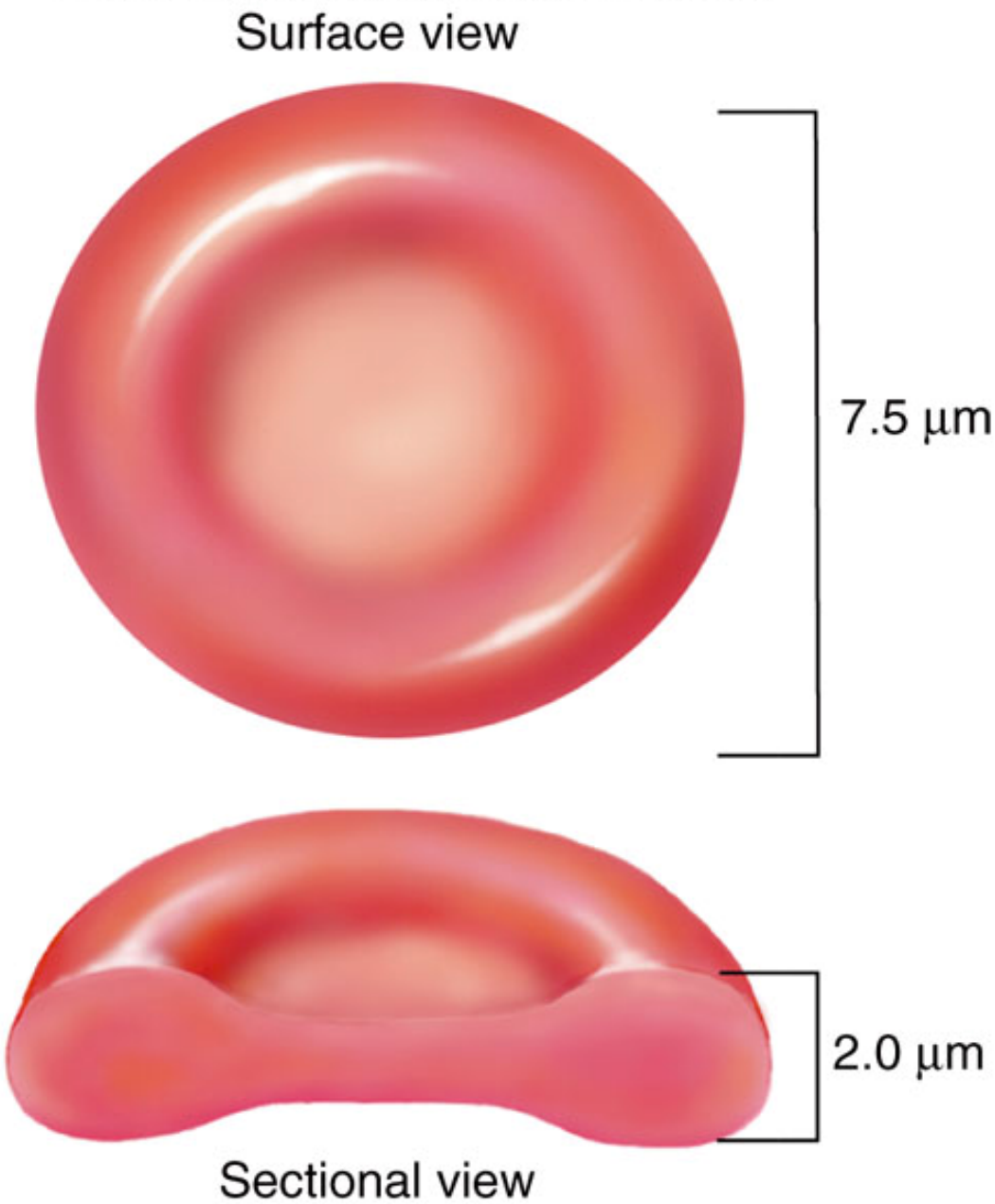
**Formed Elements Classified**

- **Erythocytes (RBCs)**
- **Platelets**
- **Leukocytes (white blood cells / WBCs)**
  - **Granulocytes (i.e. The Nebs)**
    - **Neutrophils**
    - **Eosinophils**
    - **Basophils**
  - **Agranulocytes**
    - **Lymphocytes**
    - **Monocytes**

## TABLE 18.1 General Properties of Blood*

| Characteristic | Average Value for Healthy Adult |
|---|---|
| Mean fraction of body weight | 8% |
| Volume in adult body | Female: 4–5 L; male: 5–6 L |
| Volume/body weight | 80–85 mL/kg |
| Mean temperature | 38°C (100.4°F) |
| pH | 7.35–7.45 |
| Viscosity (relative to water) | Whole blood: 4.5–5.5; plasma: 2.0 |
| Osmolarity | 280–296 mOsm/L |
| Mean salinity (mainly NaCl) | 0.9% |
| Hematocrit (packed cell volume) | Female: 37–48%<br>Male: 45–52% |
| Hemoglobin | Female: 12–16 g/dL<br>Male: 13–18 g/dL |
| Mean RBC count | Female: 4.2–5.4 million/μL<br>Male: 4.6–6.2 million/μL |
| Platelet count | 130,000–360,000/μL |
| Total WBC count | 5,000–10,000/μL |

*Values vary slightly depending on the testing methods used.




# Mature Erythrocytes (RBCs)

Biconcave disc

No nucleus

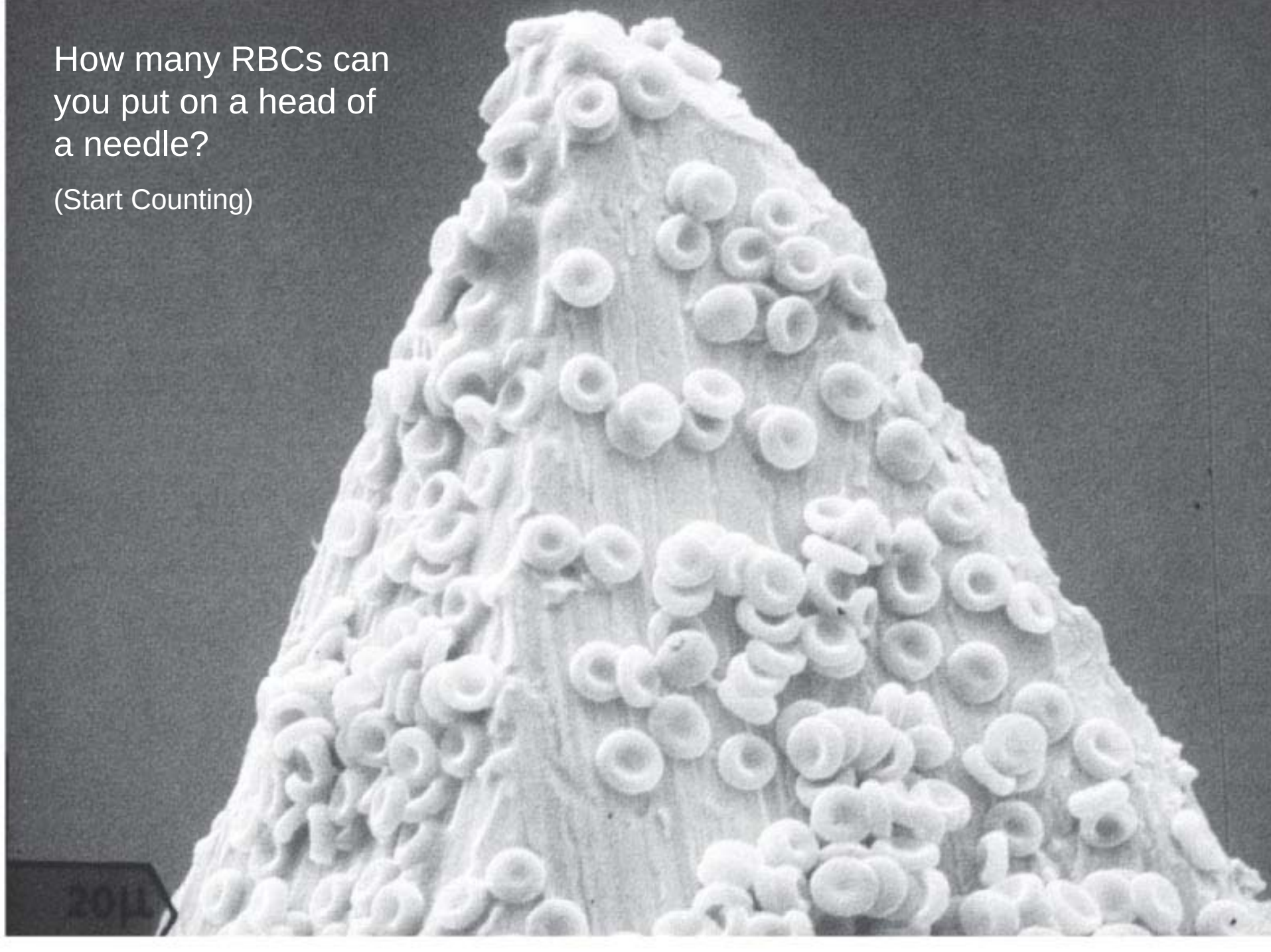
Packed full of hemoglobin

Flexible membrane

**2.5 million RBCs / sec**

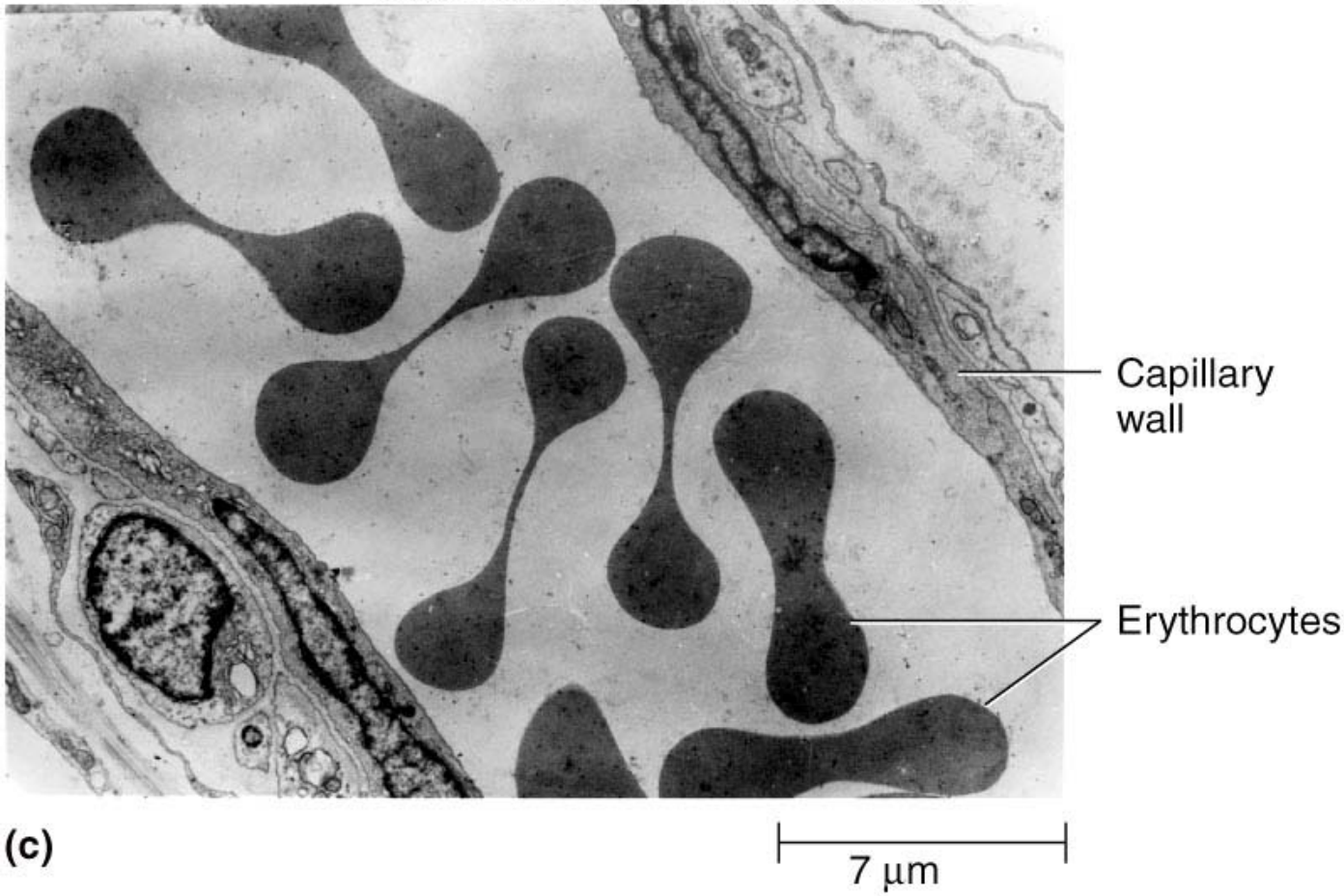
**Development takes 3-5 days. As RBC matures in marrow, reduction in cell size, increase in cell number, synthesis of hemoglobin and loss of nucleus**

**Reticulocystes are immature RBCs released into the blood, the "reticulo" is the left over endoplasmic reticulum which will eventually be discarded.**


How many RBCs can you put on a head of a needle?
(Start Counting)

# Erythrocytes



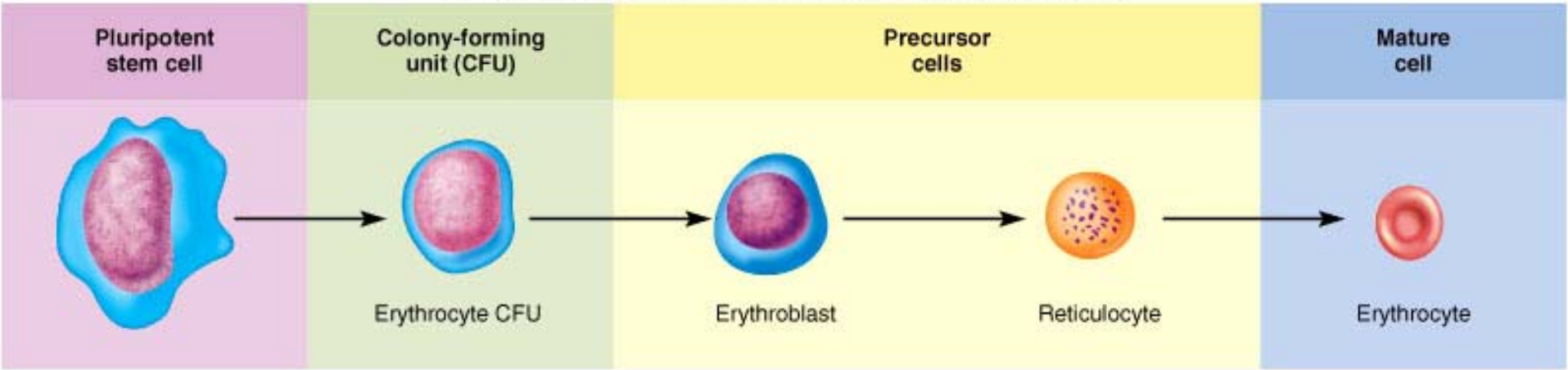



- RBCs must line up single file to pass through capillaries.
- Sickled cells become inflexible, distorted, and cause “log jams” at biforcations.


When oxygen is removed from Hb the protein within cell distorts the plasma membrane. Inflexible corpuscles “jam up” in small capillaries which then causes ischemia, pain, and eventually necrosis.

# Erythrocyte Production

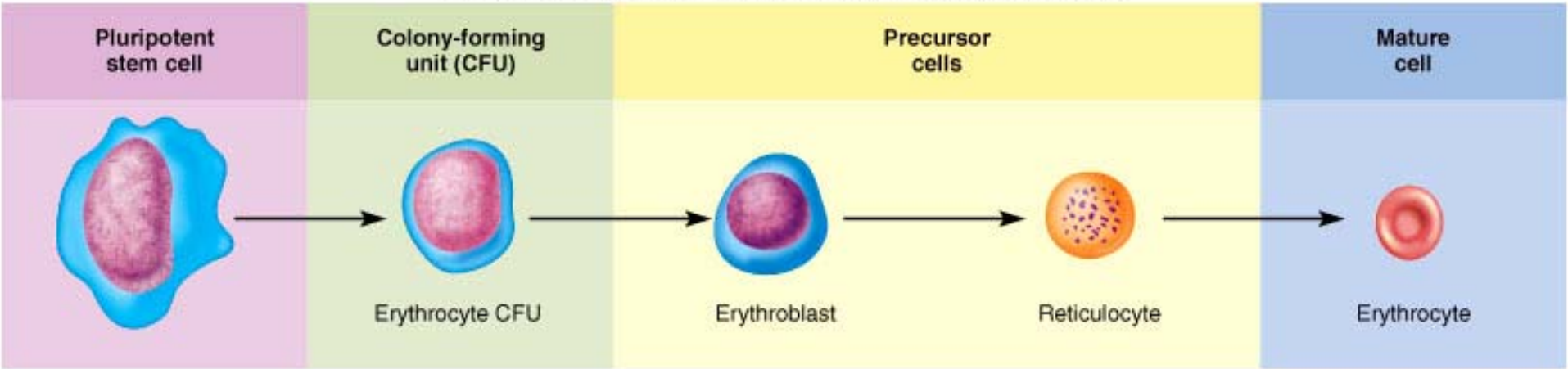





- **First committed cell - erythrocyte colony forming unit**
  - **ECFs have receptors for erythropoietin (EPO)**
  - **Erythropoietin secreted from kidneys (also liver / secondary source)**

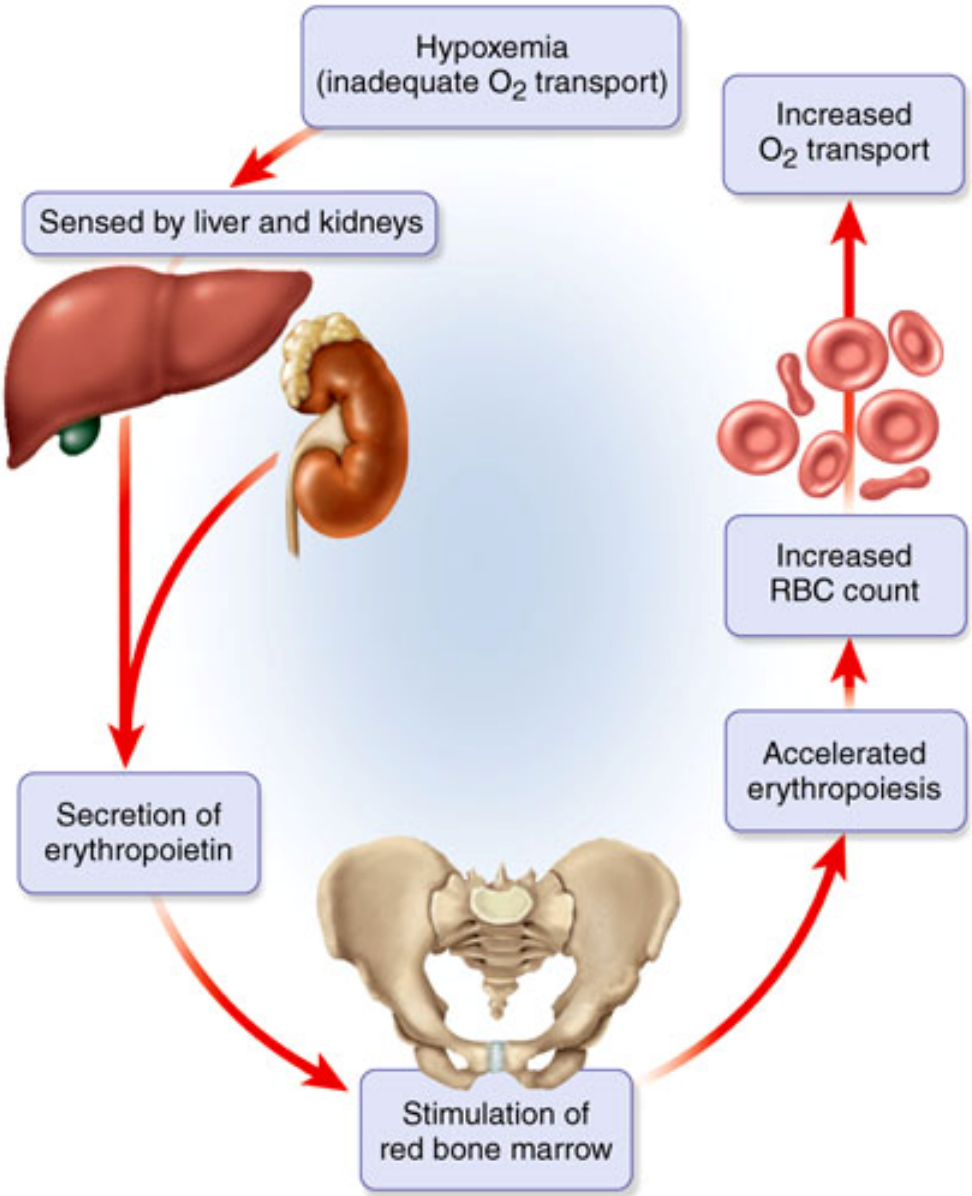
# Erythrocyte Production






- **Erythroblasts multiply and synthesize hemoglobin**
- **Discard nucleus to form a reticulocyte**
  - **named for fine network of endoplasmic reticulum**
  - **0.5 to 1.5% of circulating RBCs**

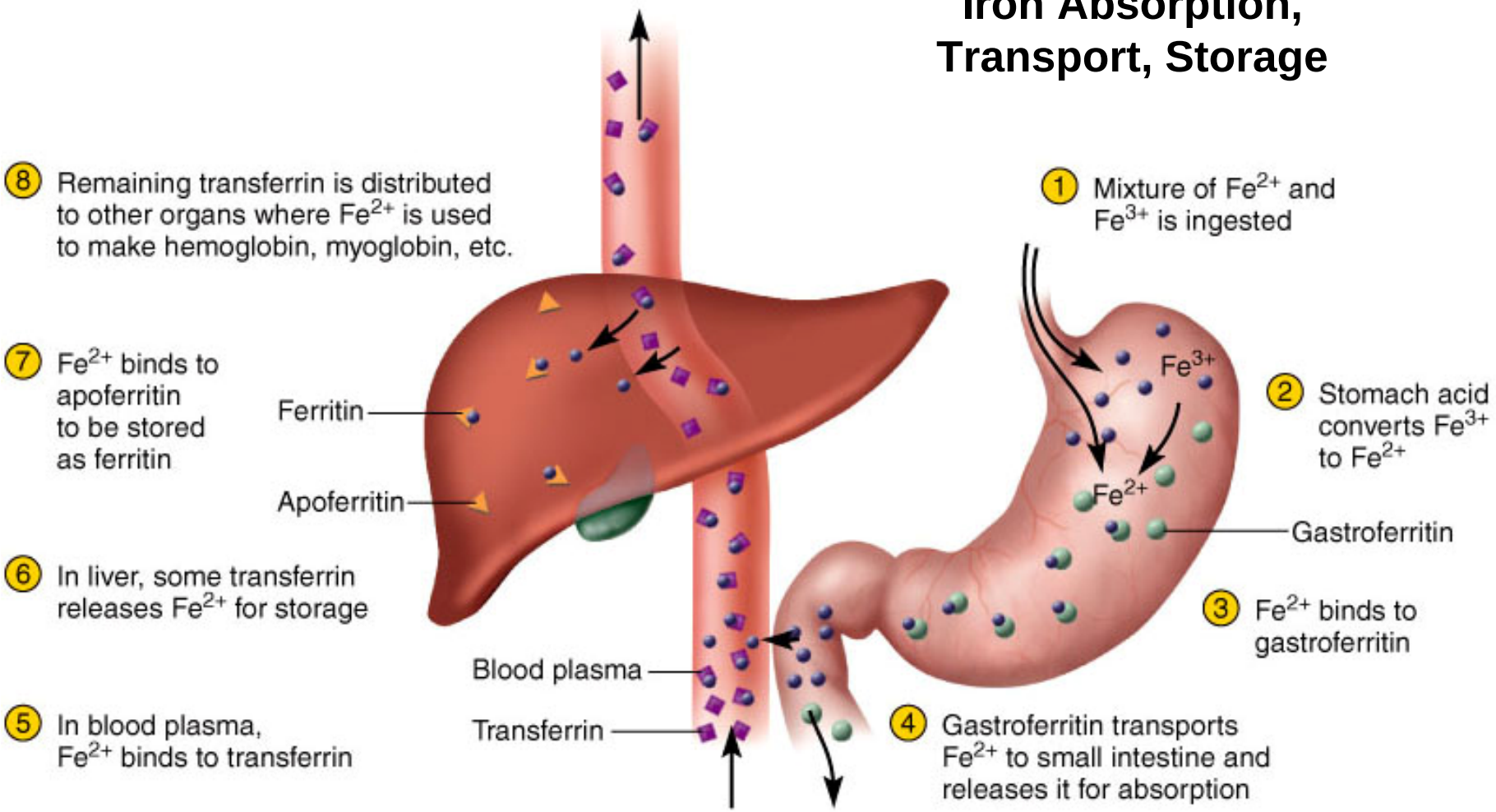
# Erythrocyte Homeostasis



# Nutritional Needs for Erythropoiesis

- **Iron - key nutritional requirement**
  - **lost daily through urine, feces, and bleeding**
    - **men 0.9 mg/day and women 1.7 mg/day**
  - **low absorption requires consumption of 5-20 mg/day**
    - **dietary iron: ferric ($Fe^{3+}$) and ferrous ($Fe^{2+}$)**
      - **stomach acid converts $Fe^{3+}$ to absorbable $Fe^{2+}$**
      - **gastroferritin binds $Fe^{2+}$ and transports it to intestine**
      - **absorbed into blood and binds to transferrin for transport**
        - » **bone marrow for hemoglobin, muscle for myoglobin and all cells use for cytochromes in mitochondria**
    - **liver apoferritin binds to create ferritin for storage**

# Iron Absorption, Transport, Storage

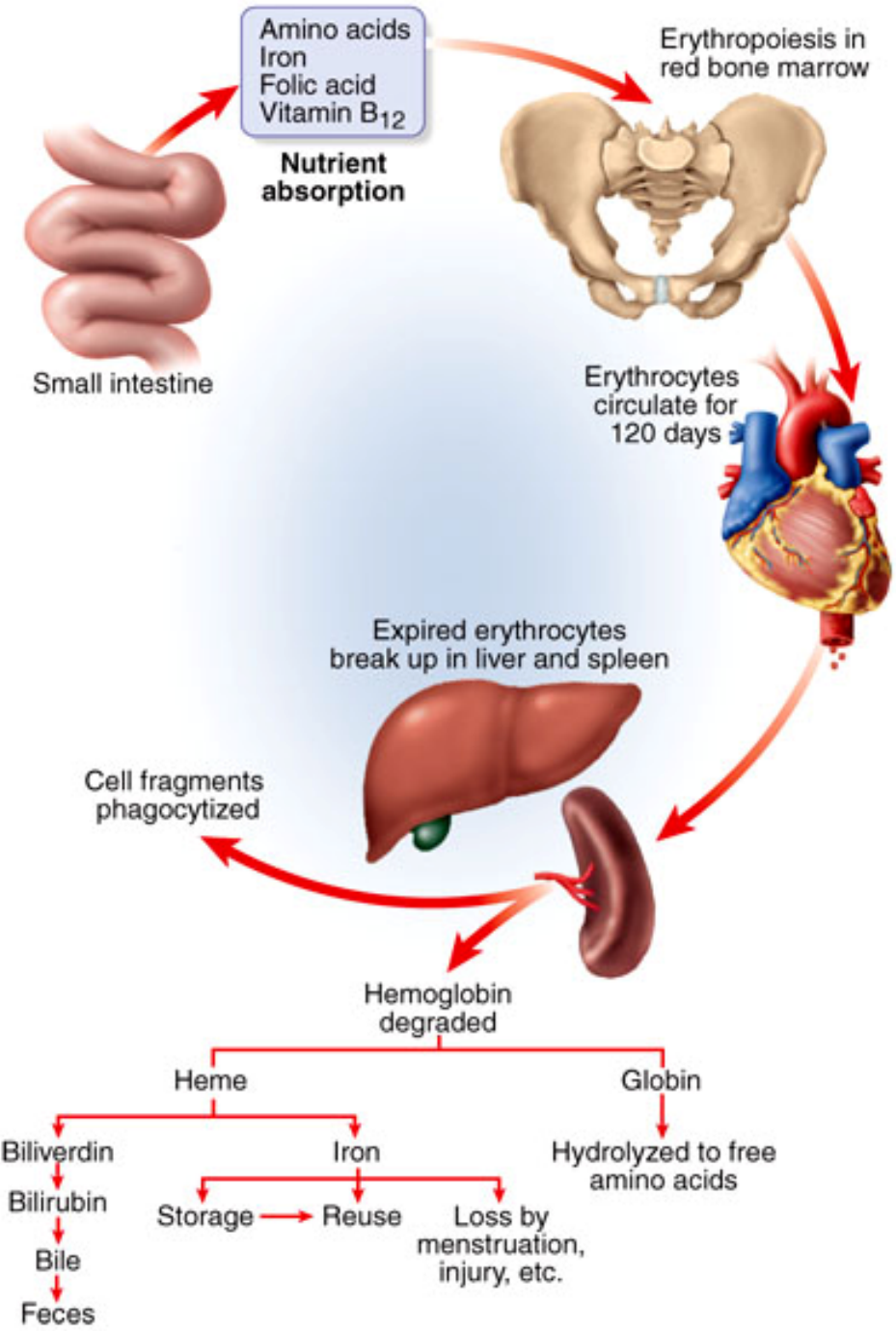



Dietary Iron: ferric (Fe3+) / ferrous (Fe2+)
Stomach acid converts ferric to ferrous, the only form of iron that can be absorbed.

# Erythrocytes Recycle/Disposal

- RBCs lyse in narrow channels in spleen

- Macrophages in spleen
  - digest membrane bits
  - separate heme from globin
    - globins hydrolyzed into amino acids
    - iron removed from heme
      - heme pigment converted to biliverdin (green)
      - biliverdin converted to bilirubin (yellow)
      - released into blood plasma (kidneys - yellow urine)
      - liver secretes into heme-product in bile duct as a bile acid
        - » concentrated in gall bladder
        - » released into small intestine
        - » bacteria create urobilinogen (brown feces)

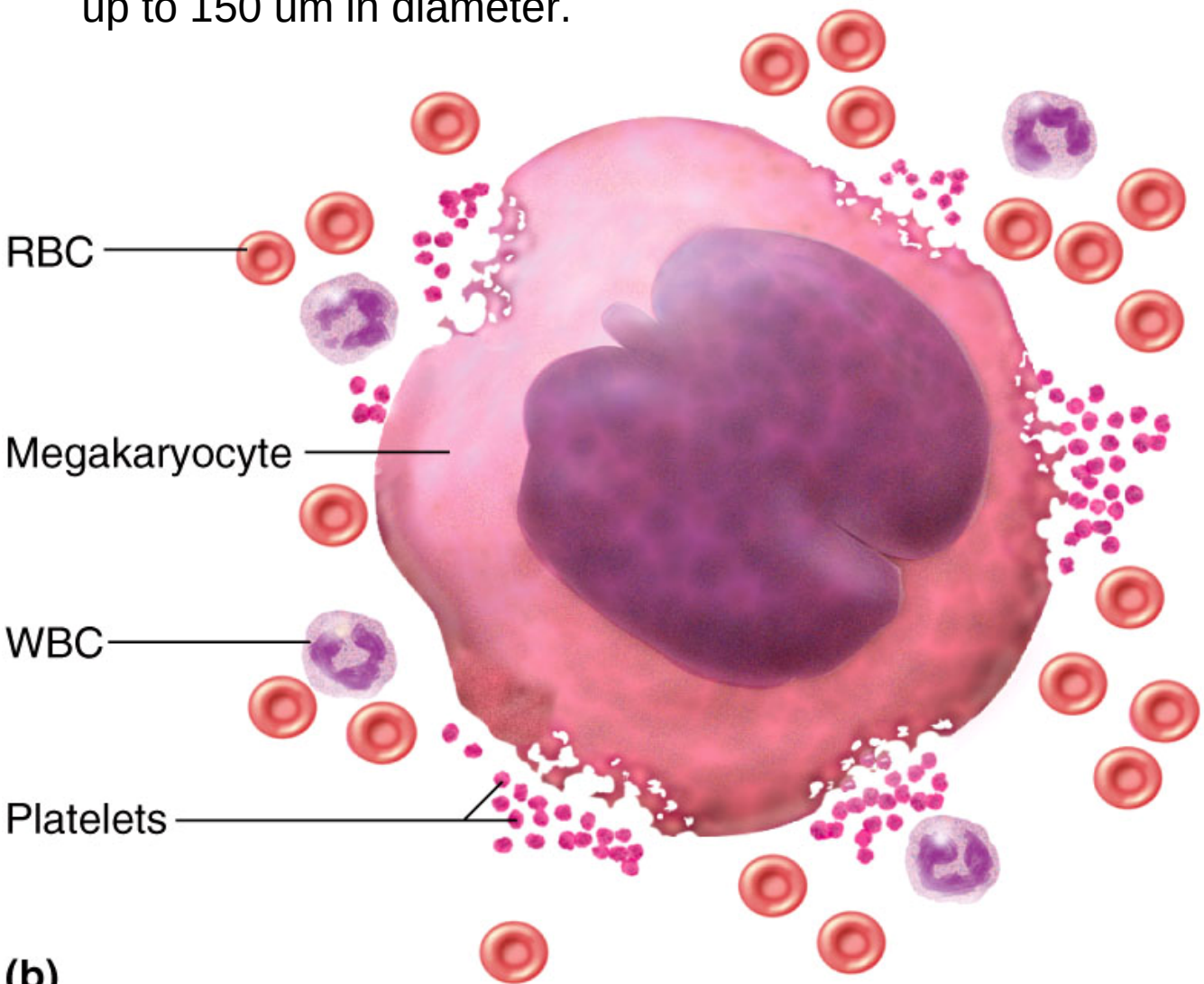



# Erythrocytes Life Cycle

## Recycle & Disposal

# Megakaryocytes: The Mothership of Platelets

The megakaryocyte can be up to 150 um in diameter.




Megakaryocytes live in the bone marrow.

Platelets are “pinched” off of the megakaryocyte’s plasma membrane.

Platelets second most abundant formed element

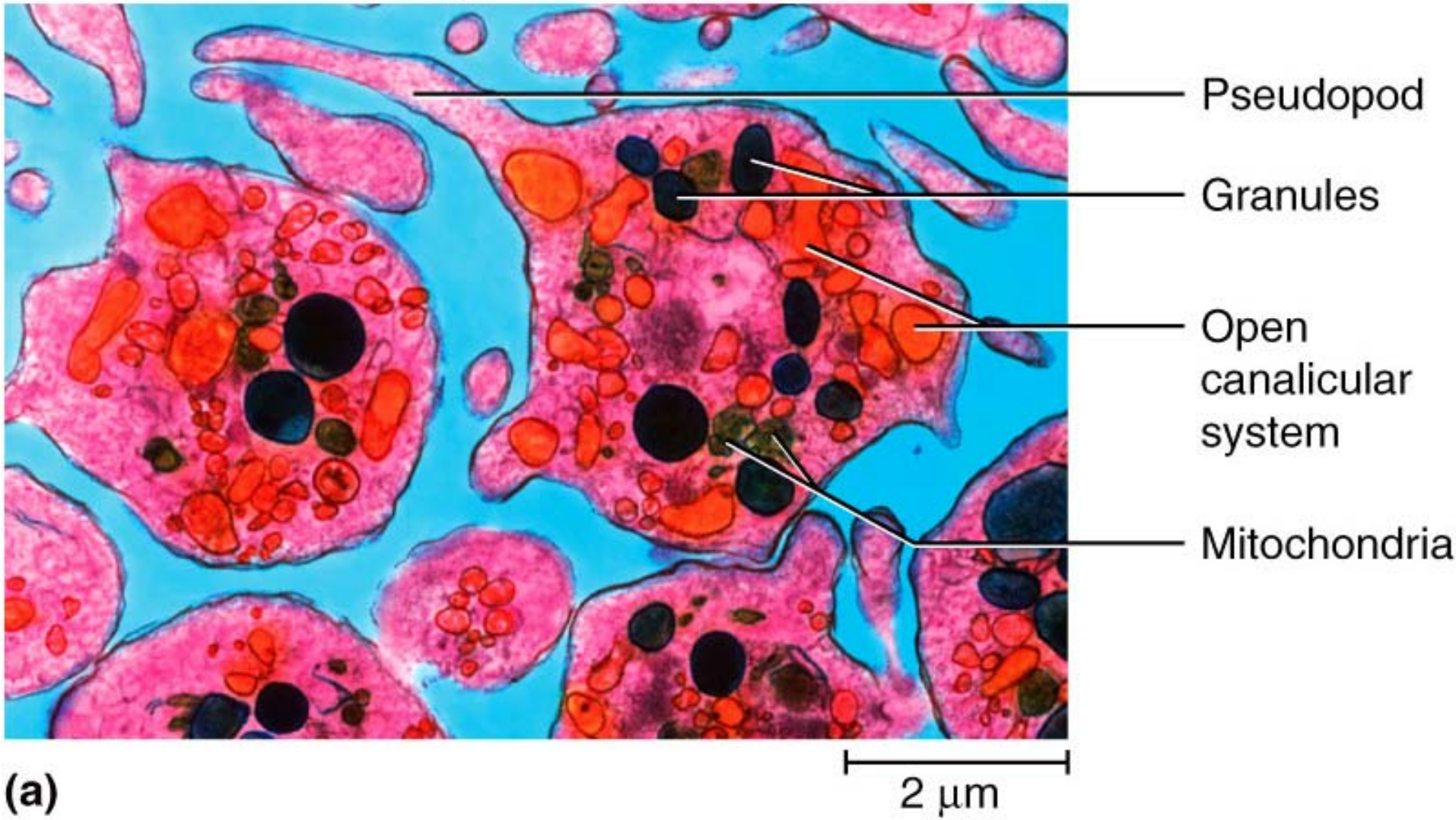
Very small (2 um)

Average 250,000 per microliter.

25% to 40% stored in spleen and released when needed

No nucleus.

Last for 10 days.




Transmission Electron Micrograph (TEM) of platelets. Within a platelet plug the platelet "streams" its plasma membranes as pseudopods. These pseudopods reach out and "grab" fibrin strands then pull back. This "tightens" the platelet plug and helps to stop the bleeding. After this happens, in a superficial wound, you can see an almost clear fluid (serum) being forced out of the platelet plug.


Note: This is called the platelet plug

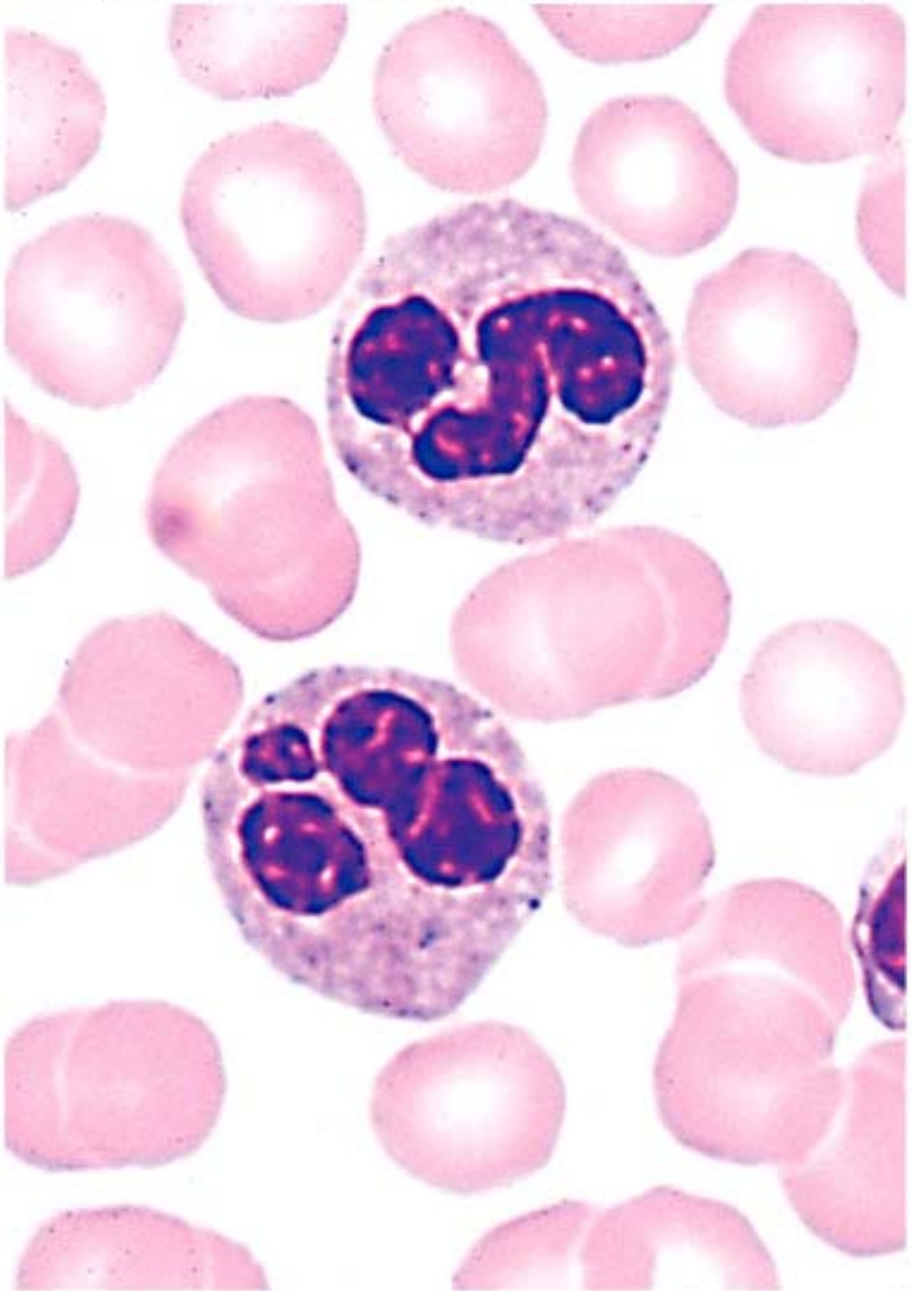
# Leukocytes (White Blood Cells / WBCs)

## Granulocytes

- Neutrophils
- Eosinophils
- Basophils

## Agranulocytes

- Lymphocytes
- Monocytes




**Neutrophils**

Percent of WBCs = 60-70%

Mean count = 4,150 cells / uL

Diameter = 9-12 um

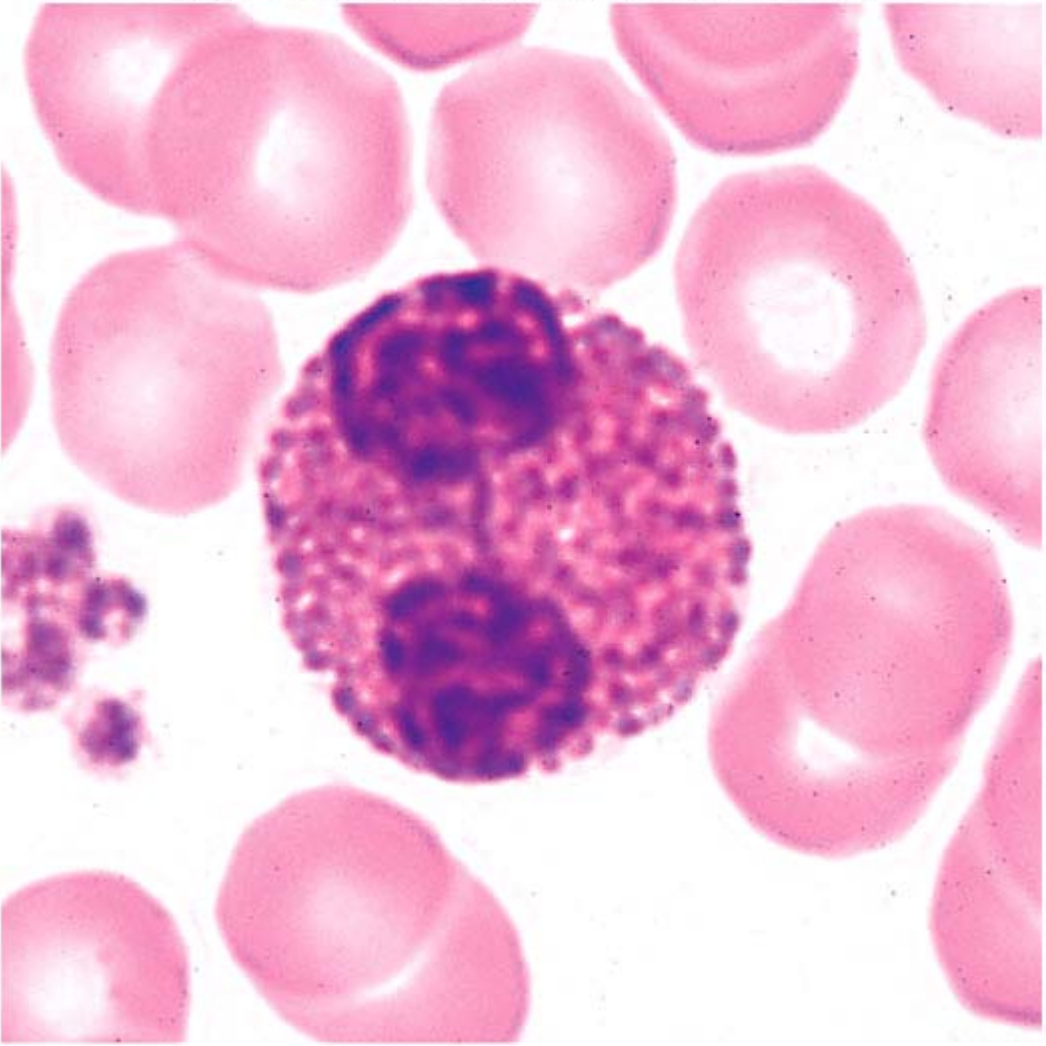
Nucleus usually with 3-5 lobes in S or C shape.

Fine reddish to violet granules in cytoplasm.

Increased numbers in bacterial infections

Phagocytize bacteria

Release antibicrobial chemicals.



Eosinophil

10 µm

Percent of WBCs = 2 - 4%

Mean count = 165 cells / uL

Diameter = 10 – 14 um

Nucleus usually has two large lobes connected by thin strand

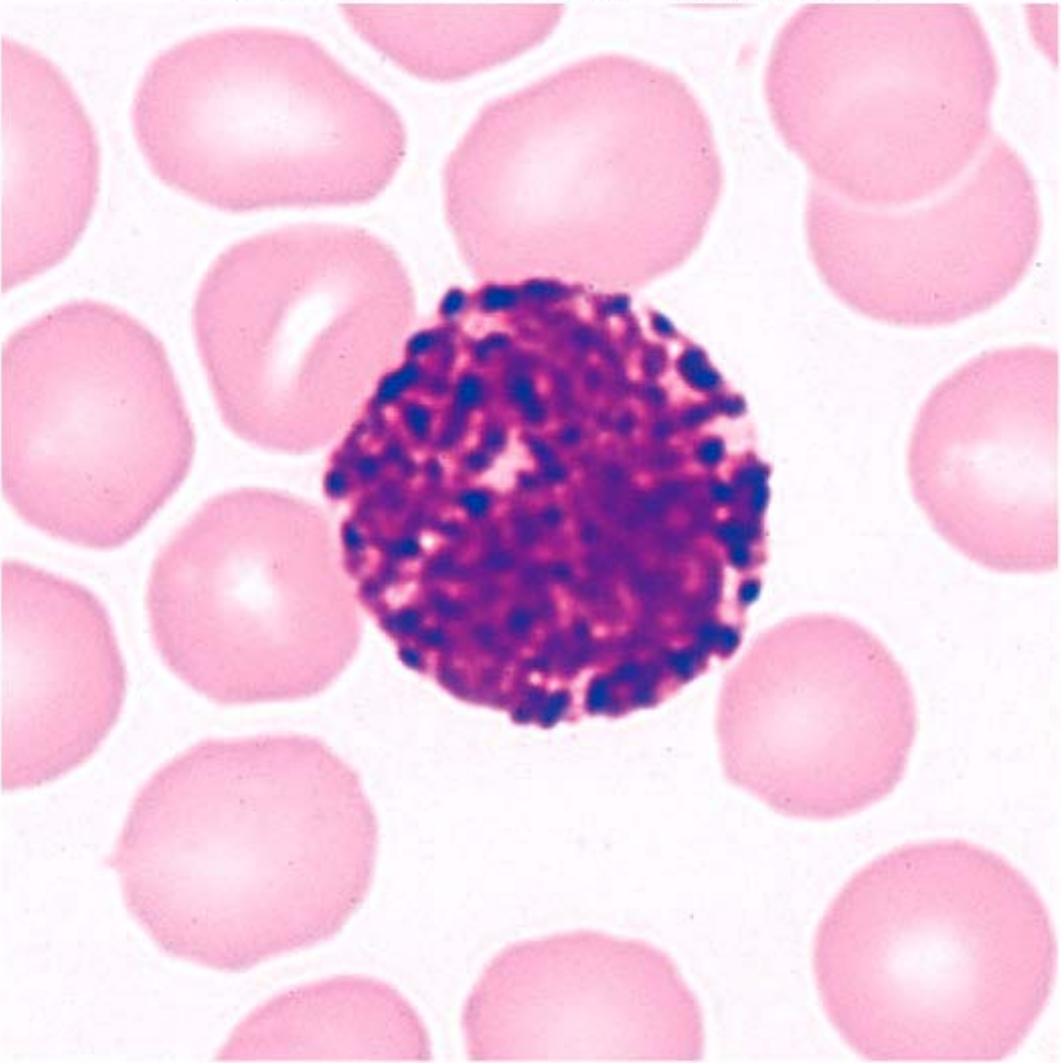
Large orange-pink granules in cytoplasm

Number fluctuates greatly from day to night, seasonally, and with phase of menstrual cycle.

Increases in parasitic infections, allergies, collagen diseases, and diseases of spleen and central nervous system.

Phagocytize antigen-antibody complexes, allergens, and inflammatory chemicals.

Release enzymes that weaken or destroy parasites such as worms.



Basophil

10 µm

Percent WBCs = less than 0.5 – 1%

Mean count 44 cells / uL

Nucleus large and u to s shaped, but typically pale and obscured from view

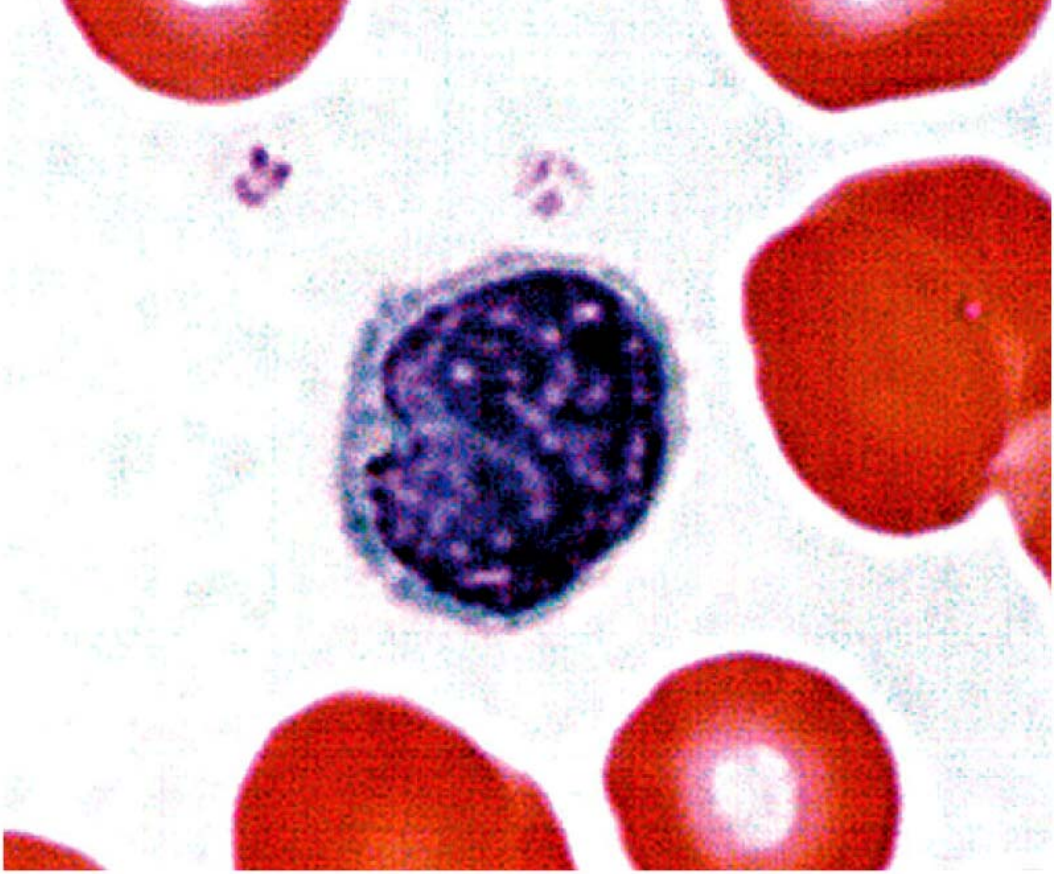
Coarse, abundant, dark violet granules in cytoplasm

Relatively stable

Increases in chicken pox, sinusitis, diabetes mellitus, myxedema, and ploycythemia

Secrete histamine which increases blood flow to a tissue

Secrete heparin, which promotes mobility of other WBCs by prventing clotting



**Lymphocyte**

10 μm

Percent of WBCs = 25 – 33%

Mean count = 2,185 / uL

Diameters (small class = 5 – 8 um / medium class = 10 – 12 um / large class = 14 – 17 um)

Nucleus round, ovoid, or slightly dimpled on one side, of uniform dark violet color

In small lymphocytes, nucleus fill nearly all of the cell and leaves only a scanty rim of clear, light blue cytoplasm

In larger lymphocytes, cytoplasm is more abundant; large lymphocytes may be hard to differentiate from monocytes

Increases in diverse infections and immune responses

Several functional classes usually indistinguishable by light microsocopy

Destroy cancer cells, cells infected with viruses, and foreign cells

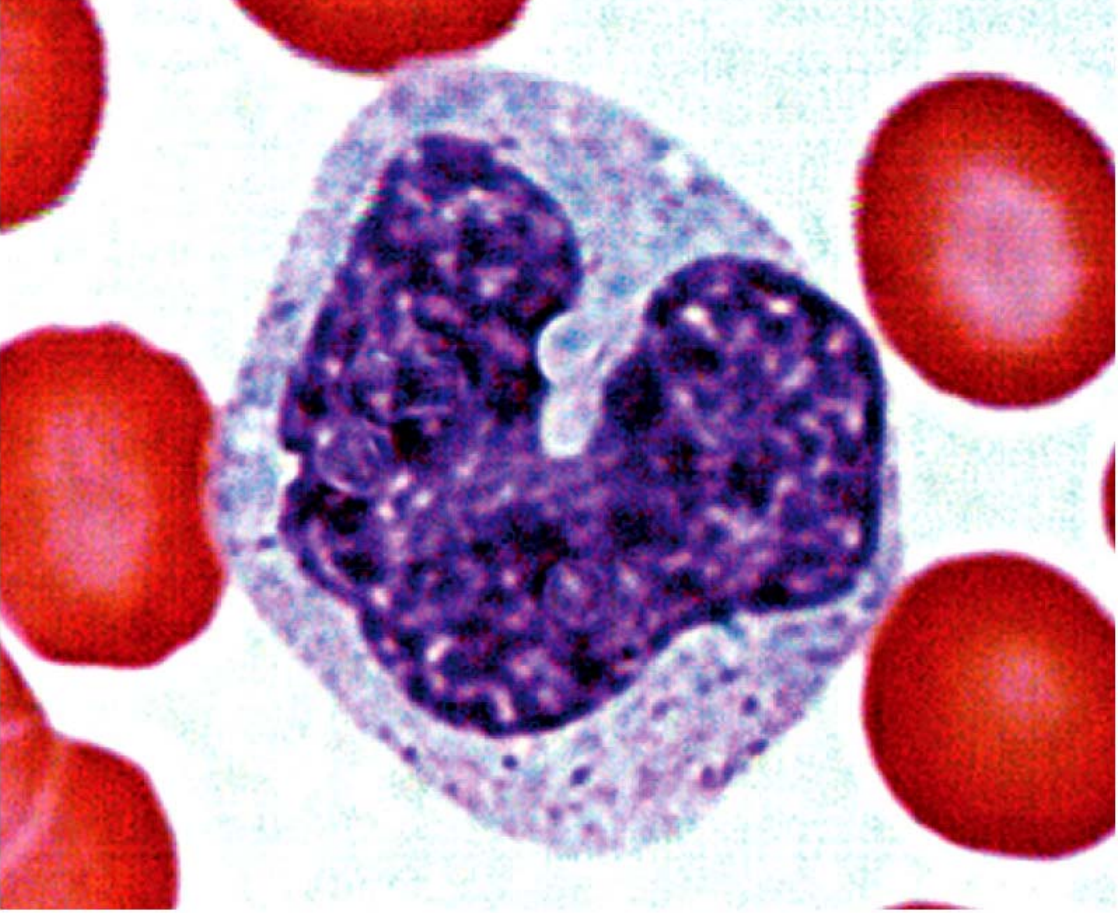
“Presents” antigens to activate other cells of immune system

Coordinate actions of other immune cells

Secrete antibodies

Serve in immune memory

Precursor for T and B cells



**Monoocyte**

10 μm

Percent WBCs = 3 – 8%

Mean count = 456 cells / uL

Diameter = 12 – 15 um

Nucleus ovoid kidney-shaped or horseshoe-shaped; light violet

Abundant cytoplasm with sparse, fine granules

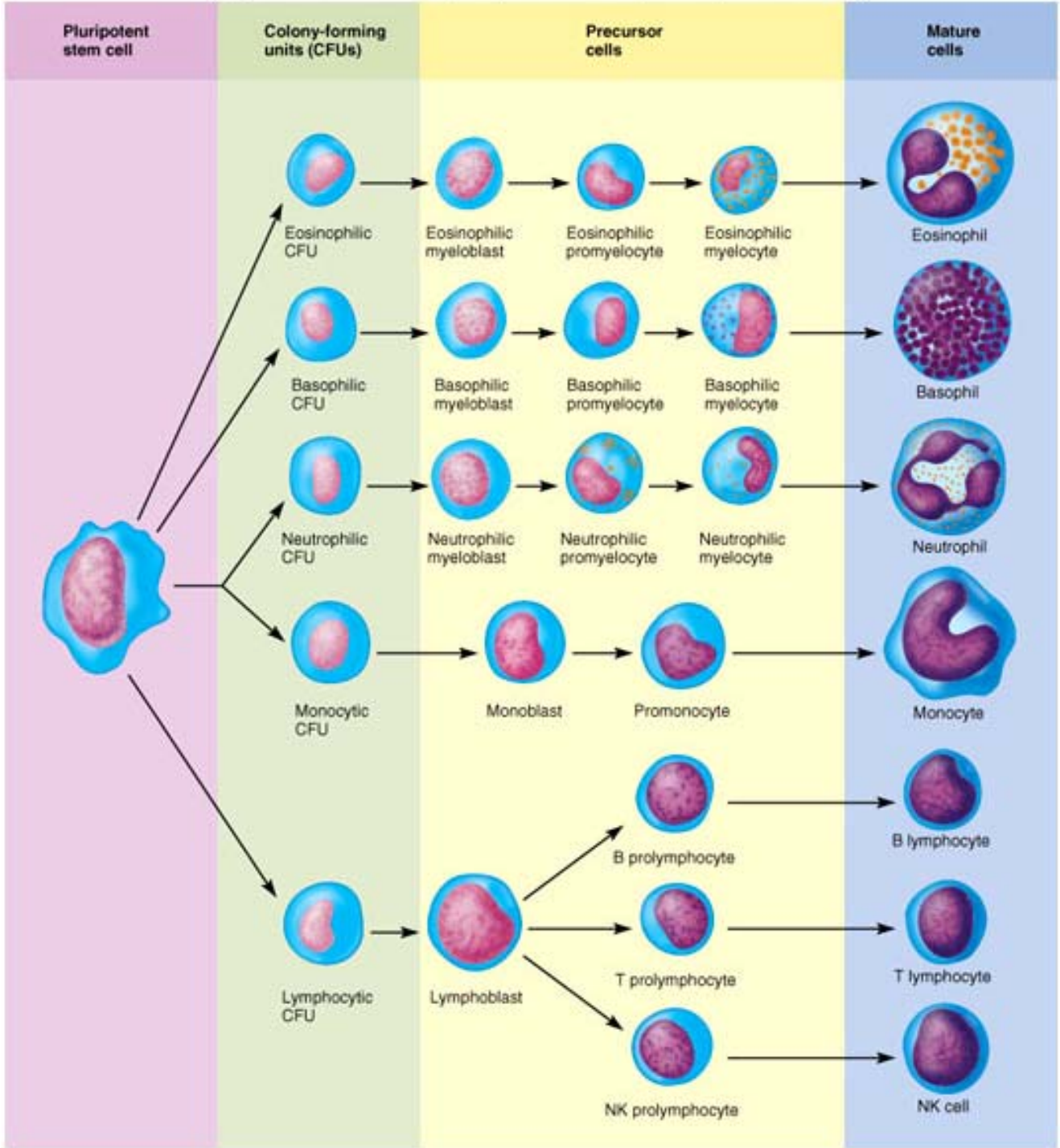
Sometimes very large with stellate or polygonal shapes

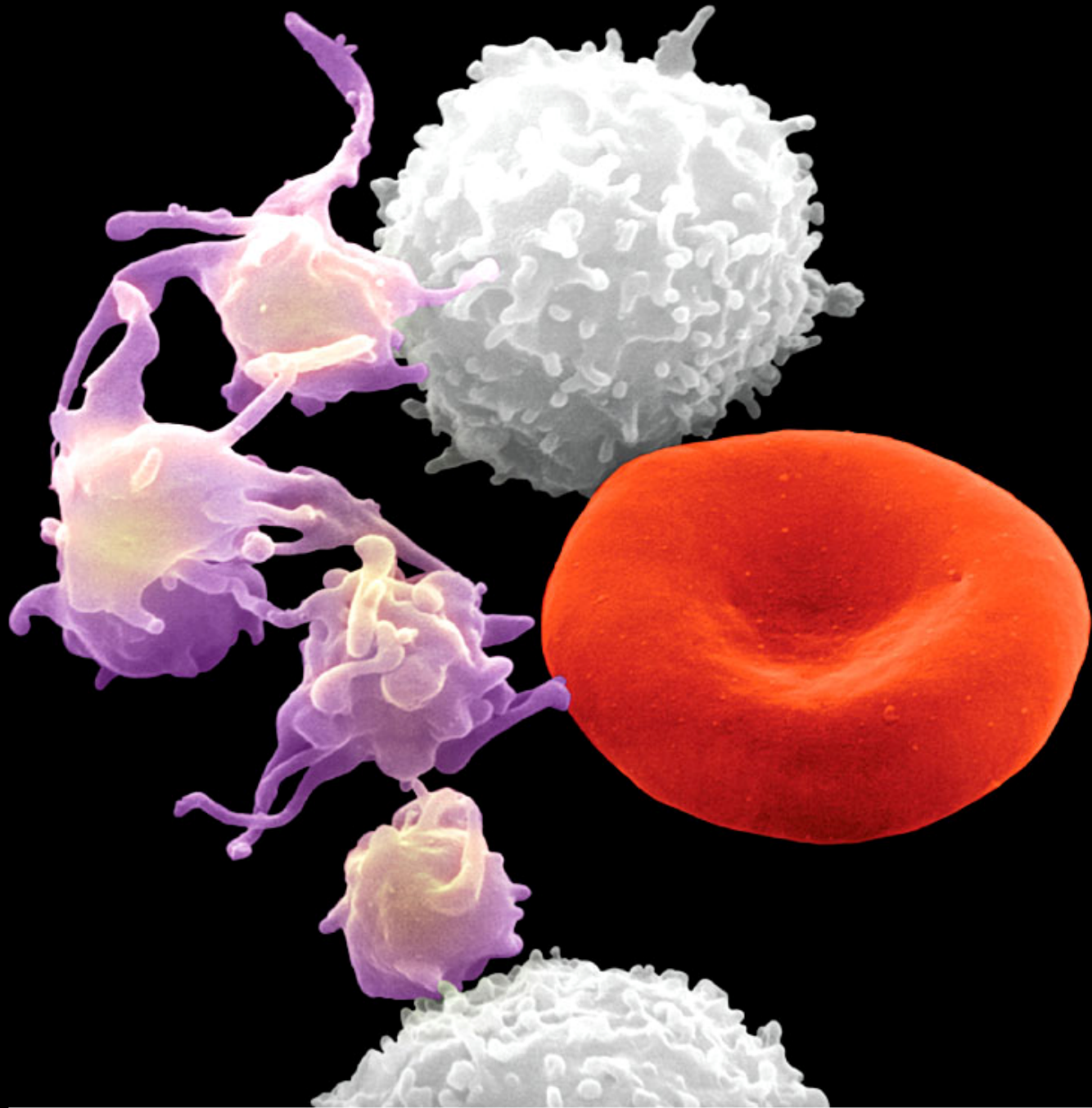
Increases in viral infections and inflammation

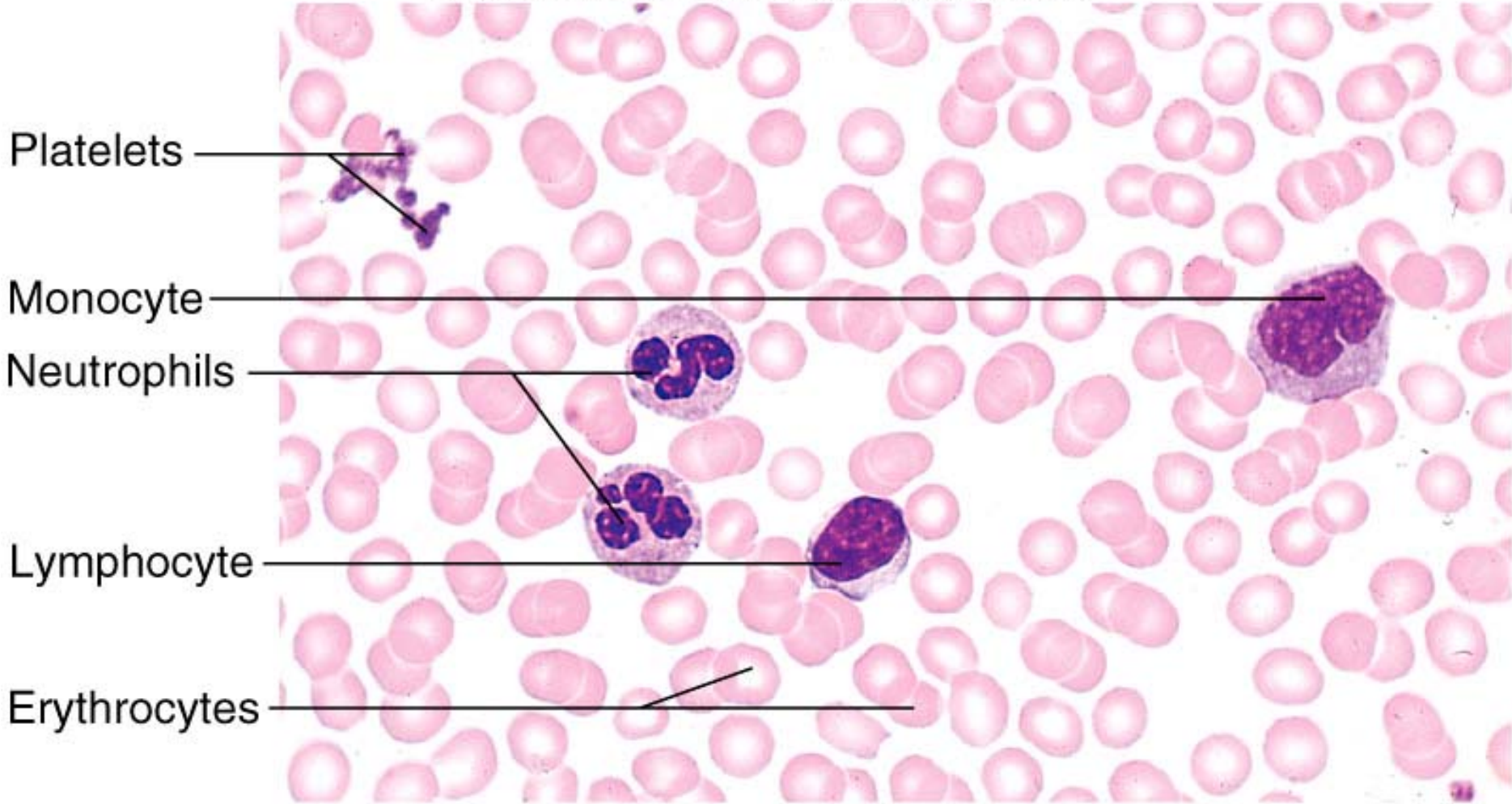
Differentiate into macrophages, large phagocytic cells of the tissue

Phagocytize phathogens, dead neutrophils, and debris of dead cells

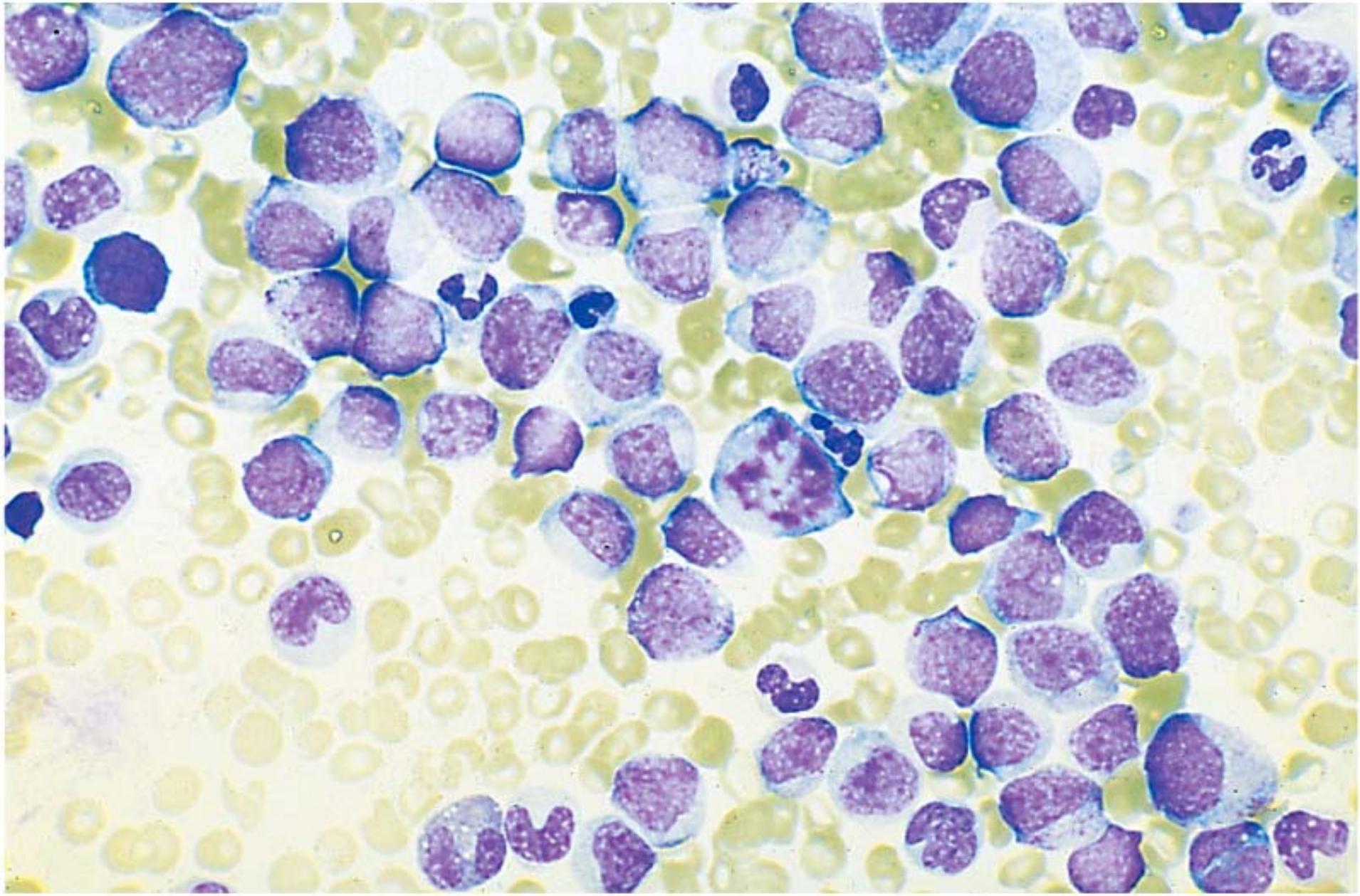
“Present” antigens to activate other cells of immune system


Pluripotent stem cell
Colony-forming units (CFUs)
Precursor cells
Mature cells
Eosinophilic CFU
Eosinophilic myeloblast
Eosinophilic promyelocyte
Eosinophilic myelocyte
Eosinophil
Basophilic CFU
Basophilic myeloblast
Basophilic promyelocyte
Basophilic myelocyte
Basophil
Neutrophilic CFU
Neutrophilic myeloblast
Neutrophilic promyelocyte
Neutrophilic myelocyte
Neutrophil
Monocytic CFU
Monoblast
Promonocyte
Monocyte
B prolymphocyte
B lymphocyte
T prolymphocyte
T lymphocyte
Lymphocytic CFU
Lymphoblast
NK prolymphocyte
NK cell






**(a)** Normal blood smear.




(b) Blood from a patient with acute monocytic leukemia. Note high number of WBCs, especially monocytes