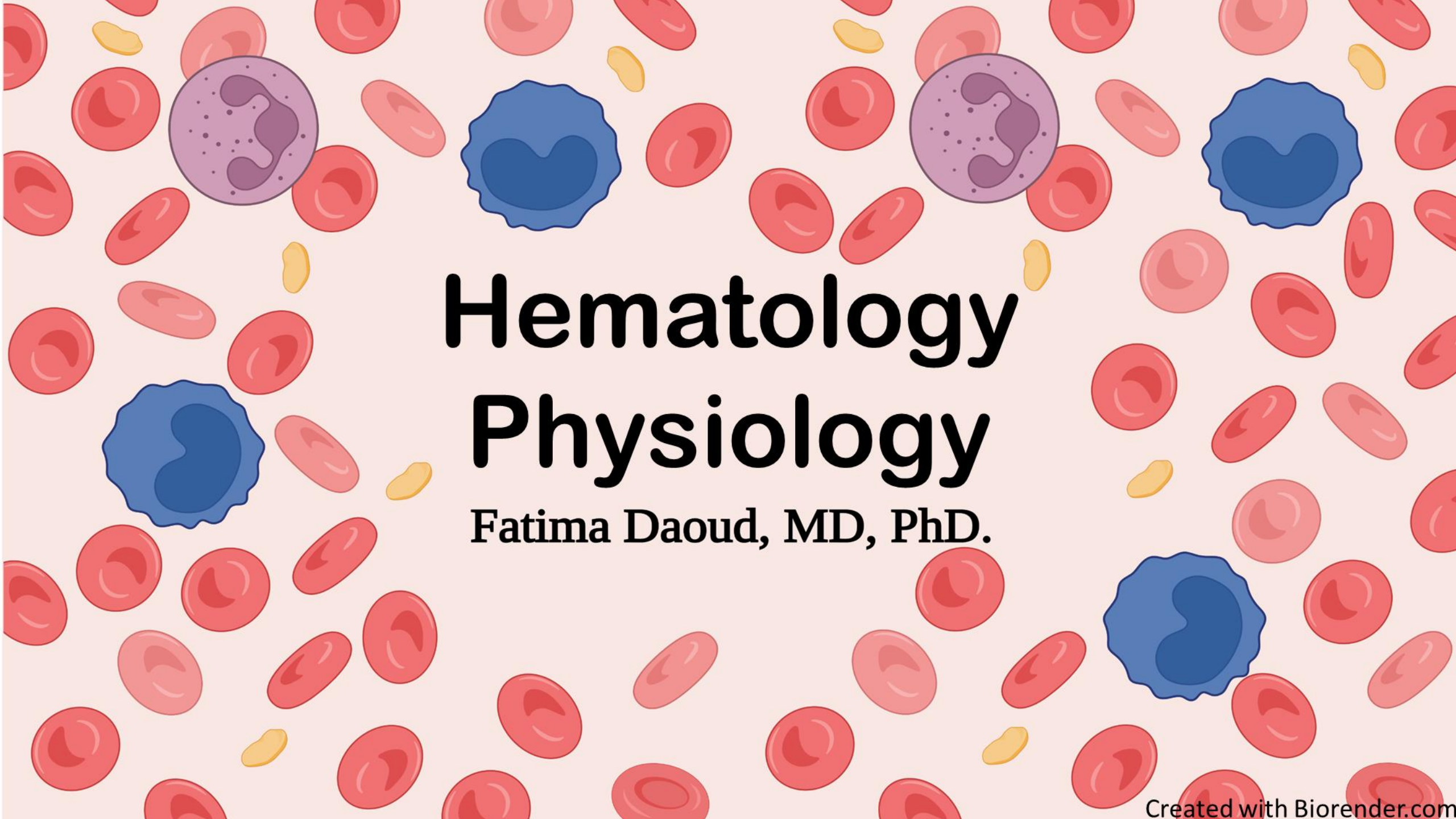


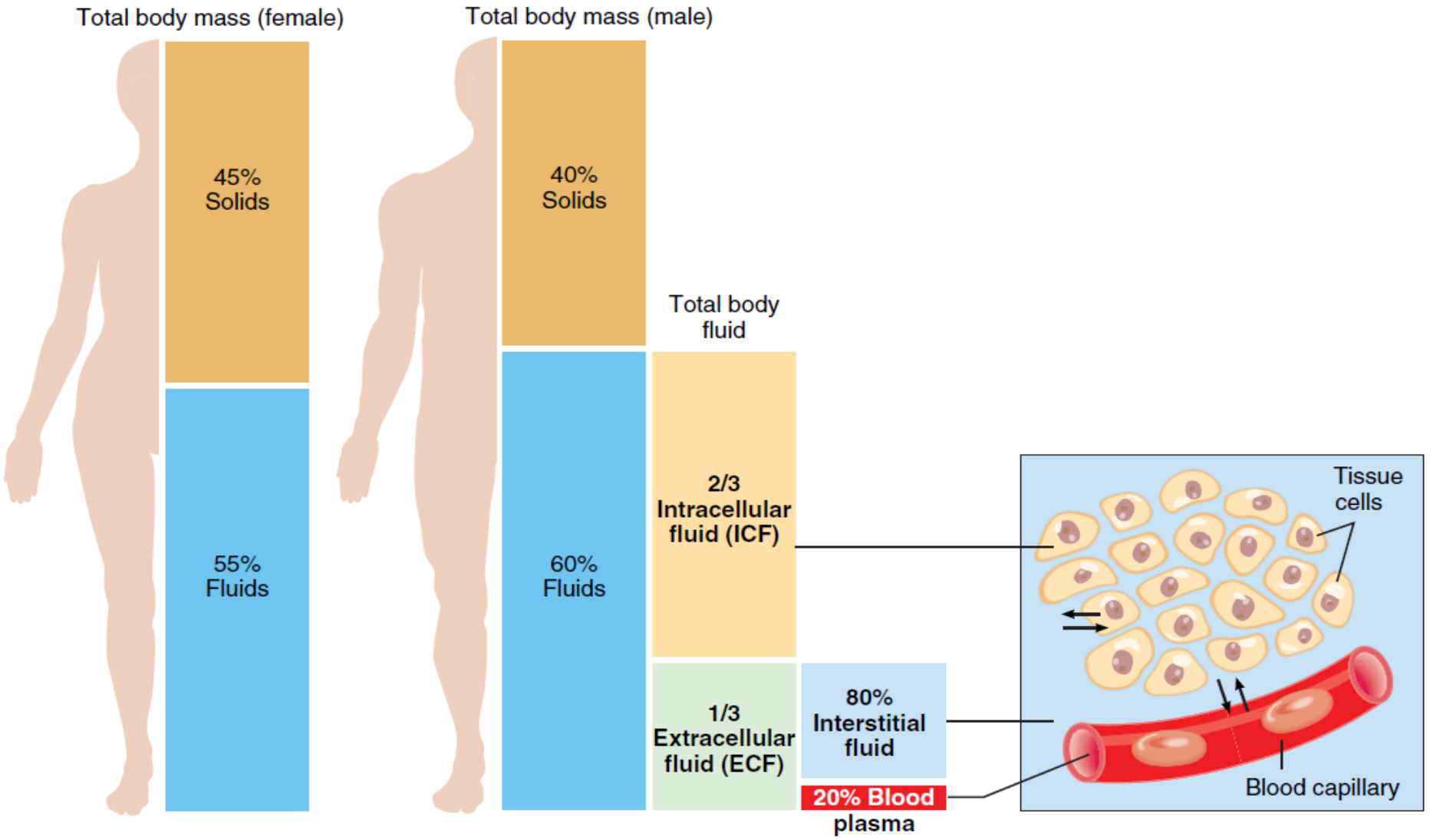
Hematology Physiology

Fatima Daoud, MD, PhD.

Reference books:

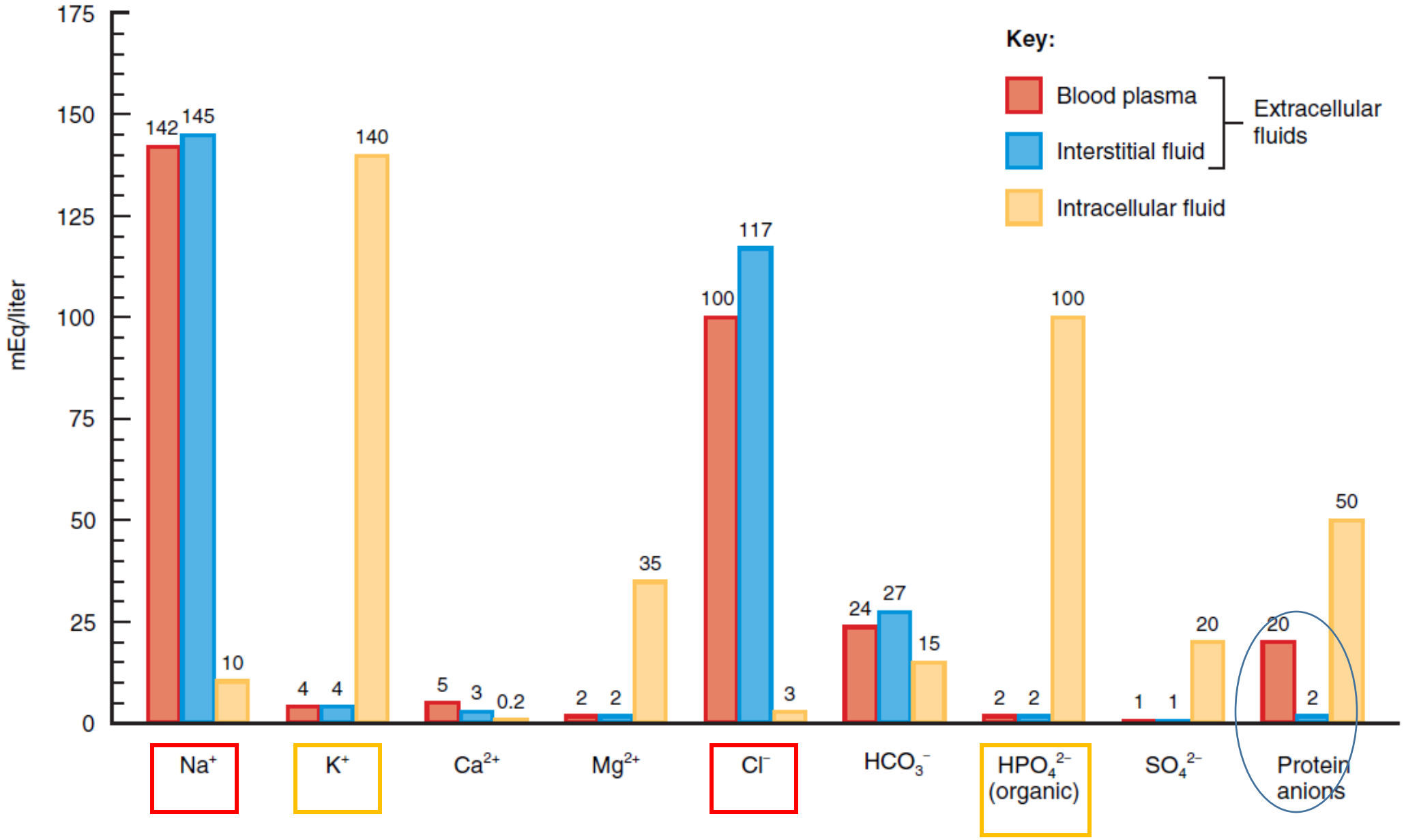
1. **Hall, John, E. and Michael E. Hall. Guyton and Hall Textbook of Medical Physiology (14th Edition).**
2. Lauralee Sherwood. Human Physiology: From Cells To Systems (9th Edition).
3. Gerard J. Tortora and Bryan Derrickson. Principles Of Human Anatomy & Physiology (15th Edition)

Hematology Body Fluids



(a) Distribution of body solids and fluids in average lean adult female and male

Hematology Body Fluids



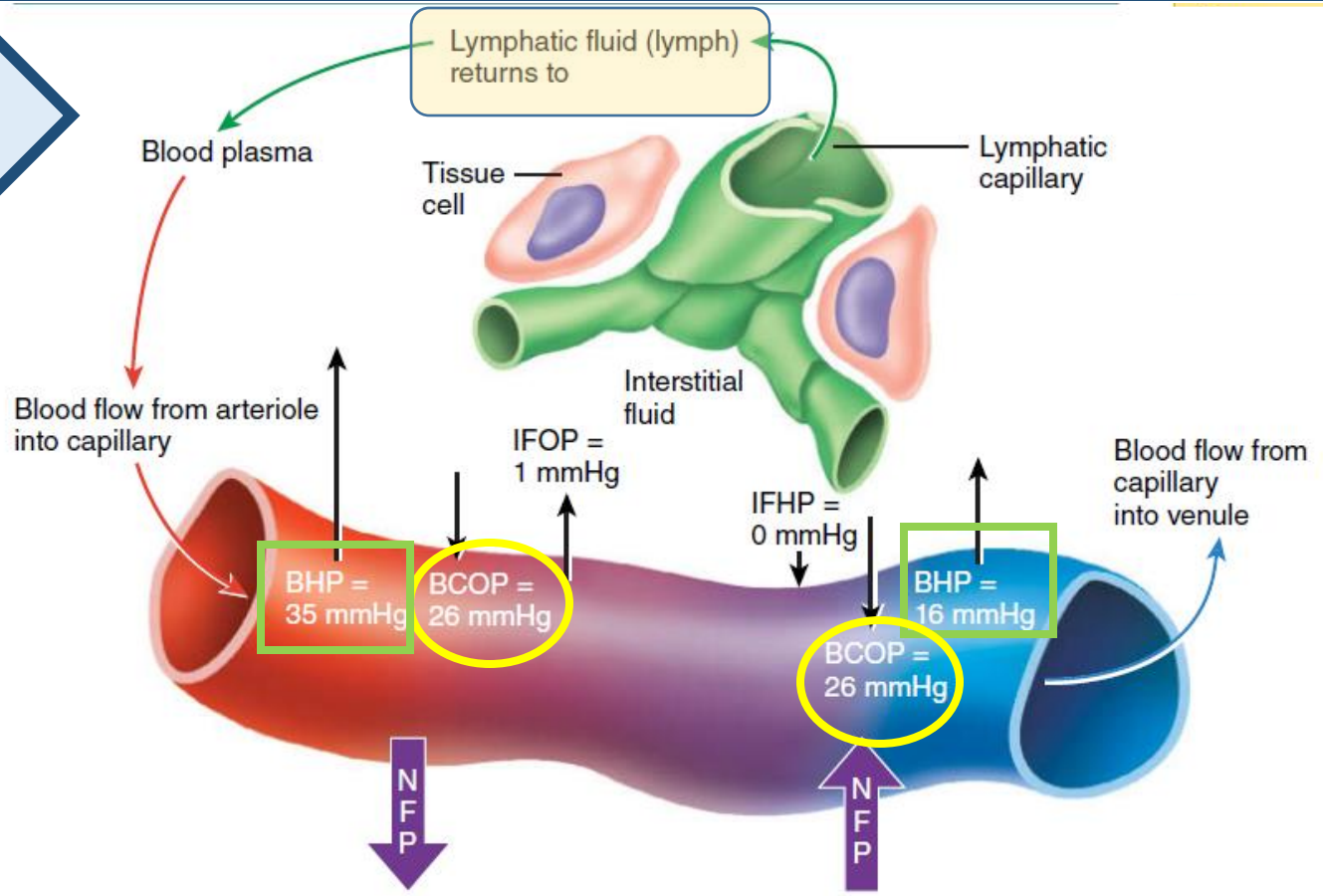
Hematology Body Fluids

Key:

BHP = Blood hydrostatic pressure
IFHP = Interstitial fluid hydrostatic pressure
BCOP = Blood colloid osmotic pressure
IFOP = Interstitial fluid osmotic pressure
NFP = Net filtration pressure

Blood hydrostatic pressure pushes fluid out of capillaries (filtration)

Blood colloid osmotic pressure pulls fluid into capillaries (reabsorption)



Net filtration at arterial end of capillaries (20 liters per day)

Net reabsorption at venous end of capillaries (17 liters per day)

Net filtration pressure (NFP) = (BHP + IFOP) − (BCOP + IFHP)

Pressures promoting filtration

Pressures promoting reabsorption

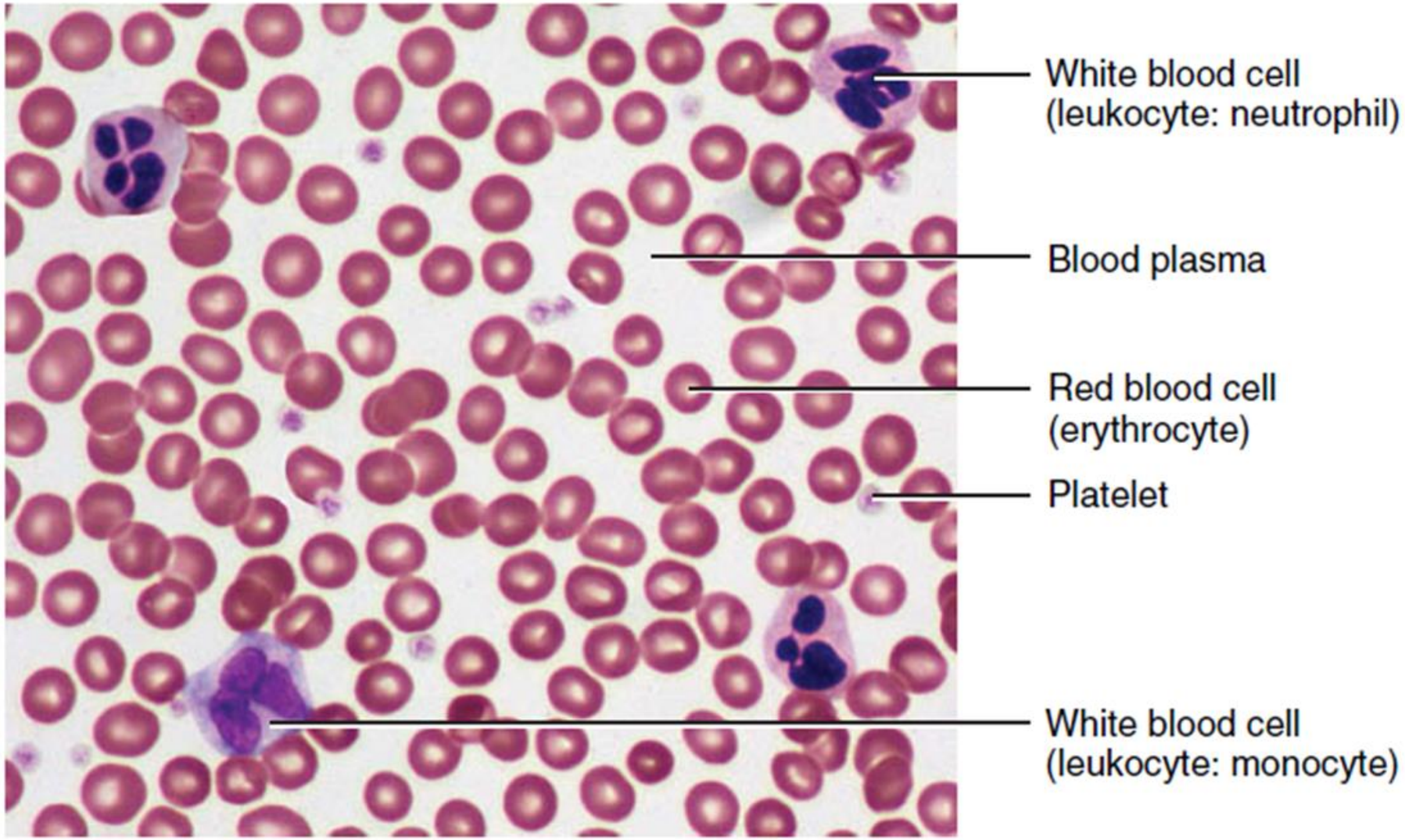
	Arterial end	Venous end
	NFP = (35 + 1) − (26 + 0) = 10 mmHg	NFP = (16 + 1) − (26 + 0) = −9 mmHg
Result	Net filtration	Net reabsorption

Hematology

Blood and its components

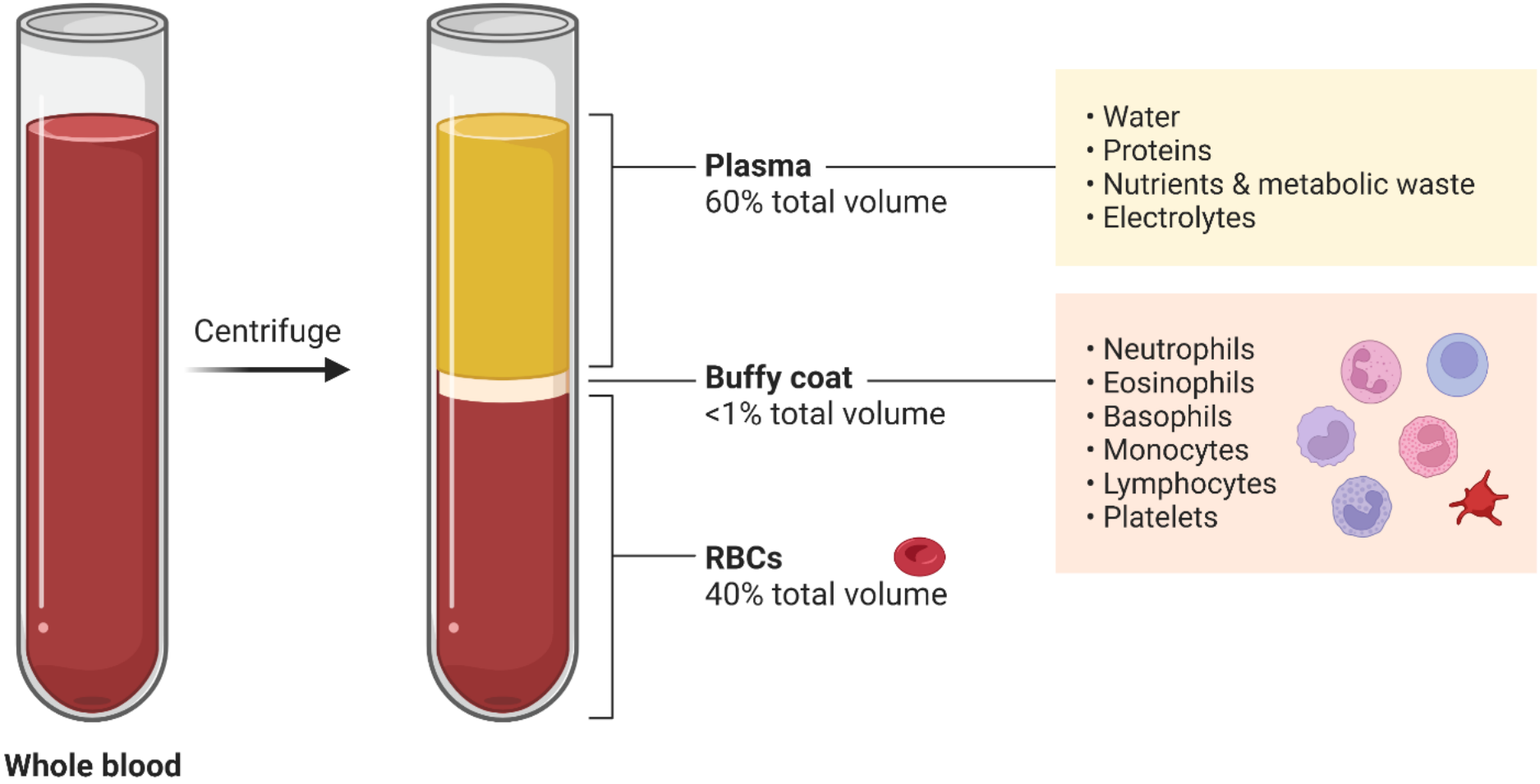
- The average blood volume of adults is about 7% of body weight, or about 5 liters.
- Blood is connective tissue.
- Blood is denser and more viscous (thicker) than water.
- The temperature of blood is 38°C.
- Slightly alkaline pH ranging from 7.35 to 7.45 (average = 7.4).
- The color saturated (O_2)→ bright red

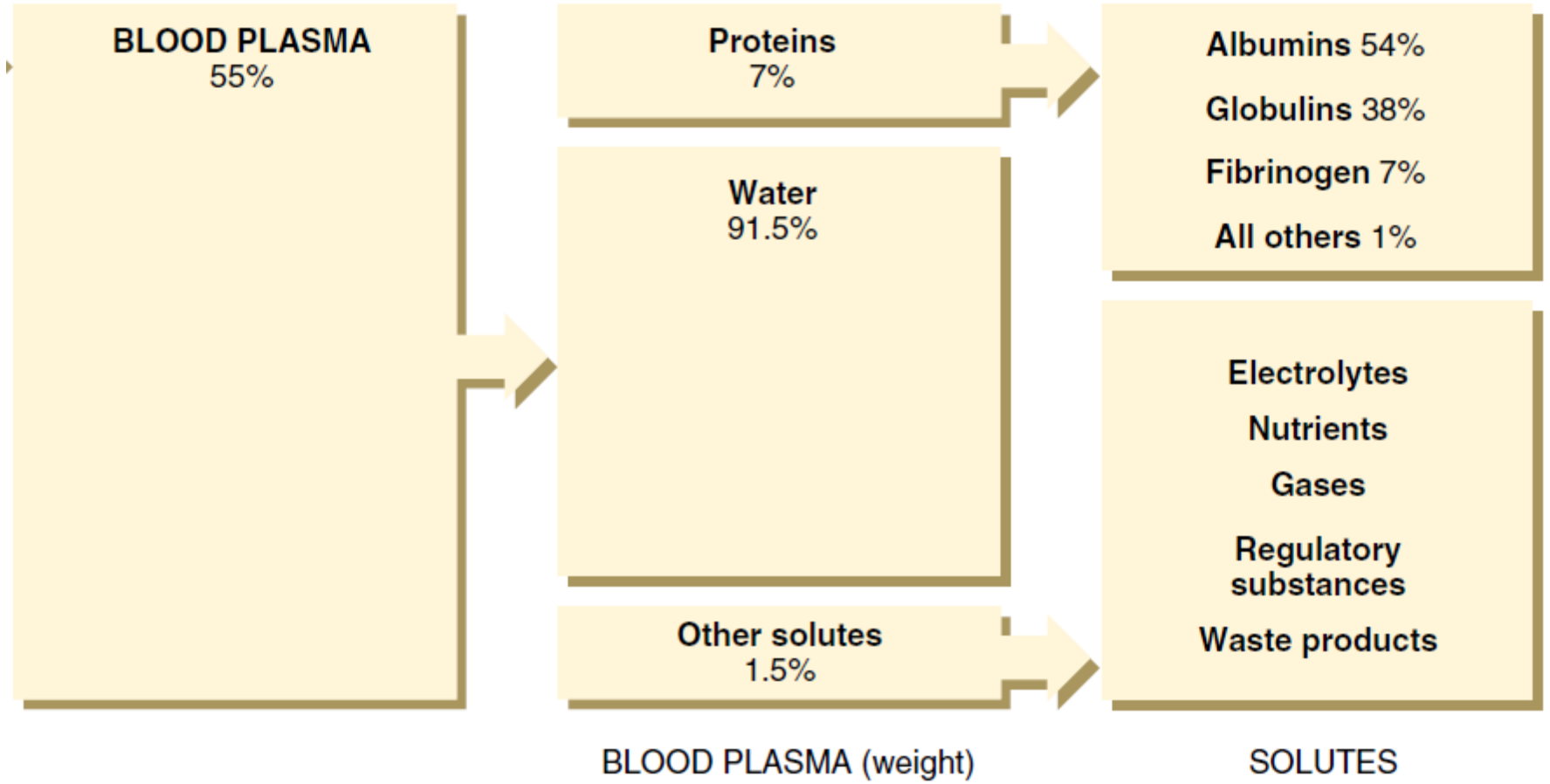
  unsaturated (O_2) → dark red


White blood cell
(leukocyte: neutrophil)
Blood plasma
Red blood cell
(erythrocyte)
Platelet
White blood cell
(leukocyte: monocyte)

Hematology

Blood and its components




BLOOD PLASMA
55%
Proteins
7%
Water
91.5%
Other solutes
1.5%
Albumins 54%
Globulins 38%
Fibrinogen 7%
All others 1%
Electrolytes
Nutrients
Gases
Regulatory substances
Waste products
BLOOD PLASMA (weight)
SOLUTES

1. Establishment of colloid osmotic pressure.
2. Responsible for plasma's capacity buffer changes in pH.

Albumin

Nonspecifically binds substances that are poorly soluble in plasma (bilirubin)

Fibrinogen

Is an inactive precursor for a clot's fibrin meshwork

Globulins

α & β

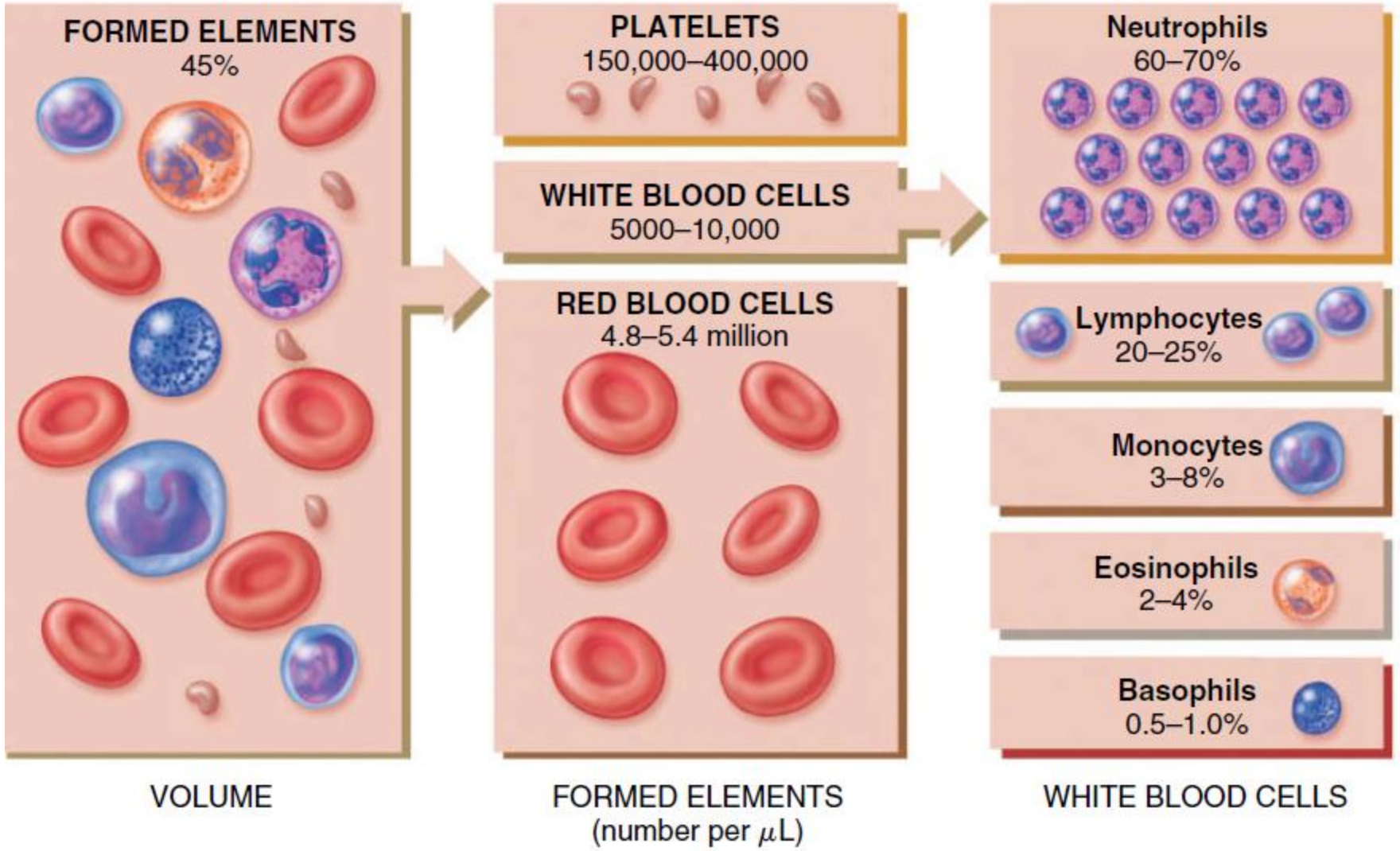
- Specifically bind poorly water-soluble substances (thyroid hormone, cholesterol, and iron).
- Involved in blood-clotting.
- Angiotensinogen.

γ

Antibodies/ immunoglobulins.
Body's defense mechanism.

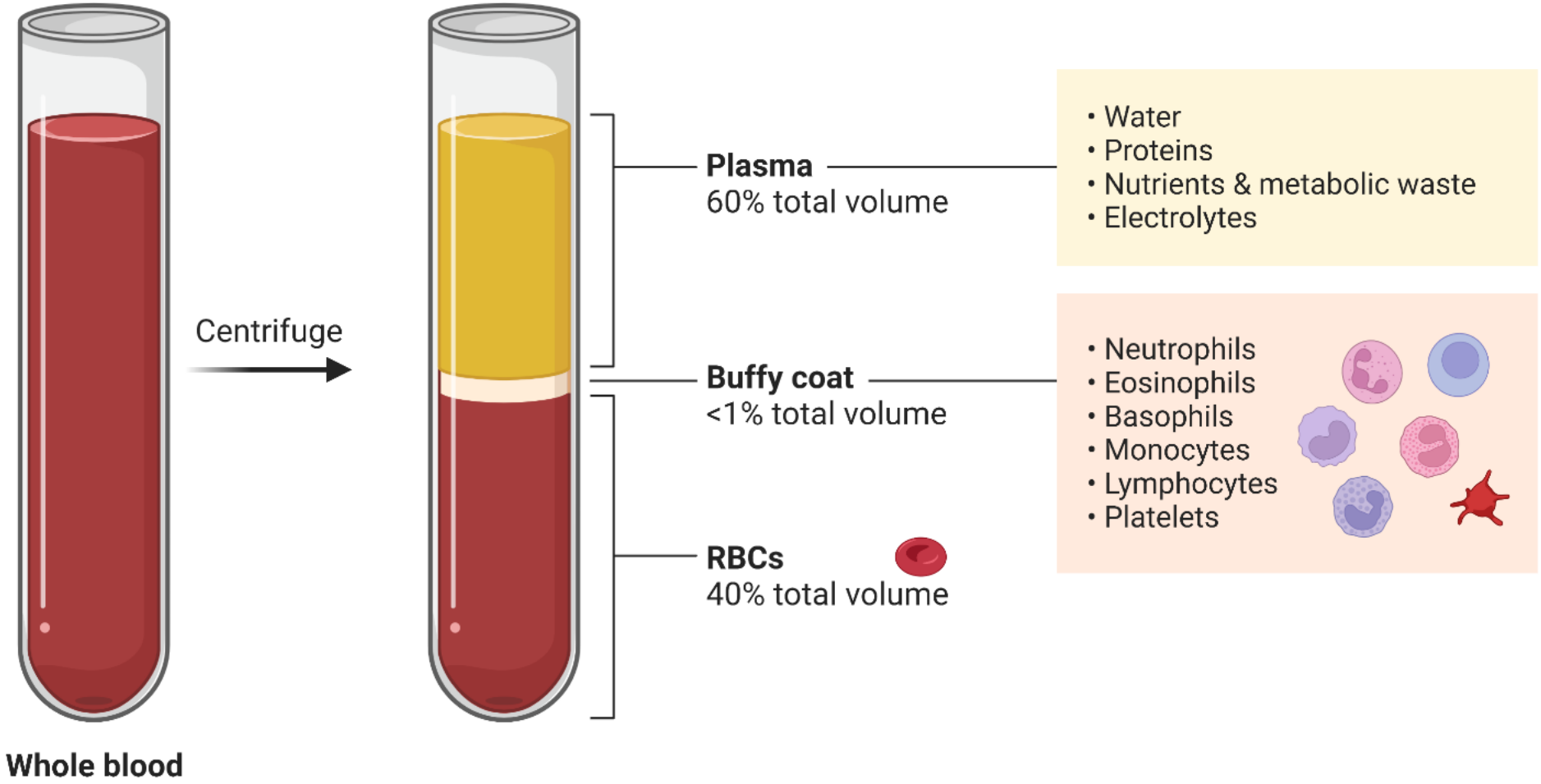
Hematology

Blood and its components



Hematology

Packed Red Cell Volume

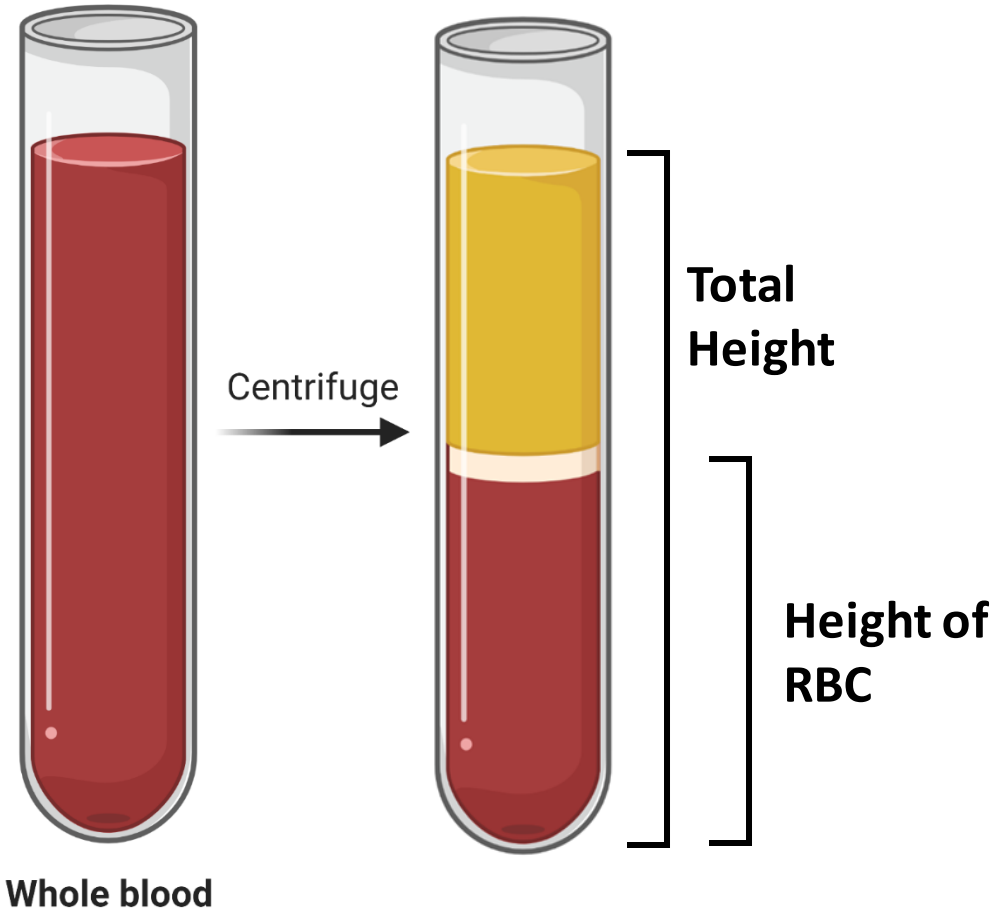


Hematology Hematocrit

- **Hematocrit/ Packed Red Cell Volume**
- Adult males: 40–54% (avg = 47%).
- Adult females: 38–46% (avg = 42%)

$$\text{Hematocrit} = \frac{\text{Height of RBCs}}{\text{Total height}} \times 100\%$$

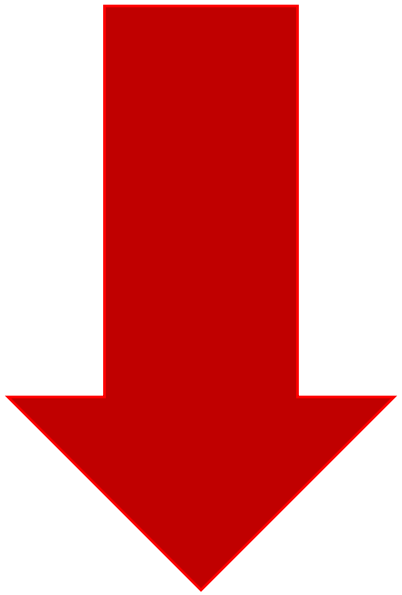
Concentration!!

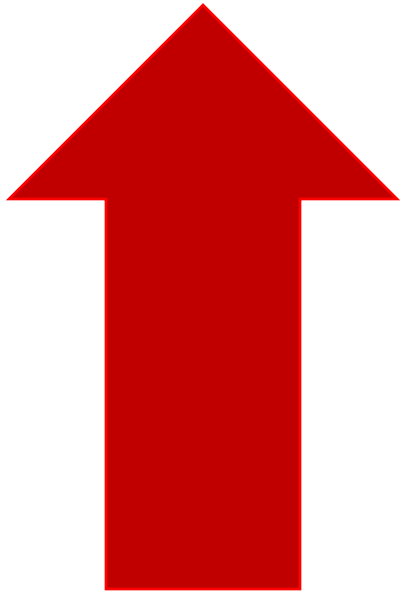


Chapter 18, Boron Medical Physiology (3rd Edition)

Hematology > Hematocrit

Polycythemia





Anemia

Hematology

Principle roles of the blood

Transportation	• Gases, nutrients, hormones, waste products.
Regulation	• pH, body temperature, water content (osmotic pressure)
Protection	• Clotting, white blood cells,antibodies

Hematology

Hemopoiesis (formation of blood cells)

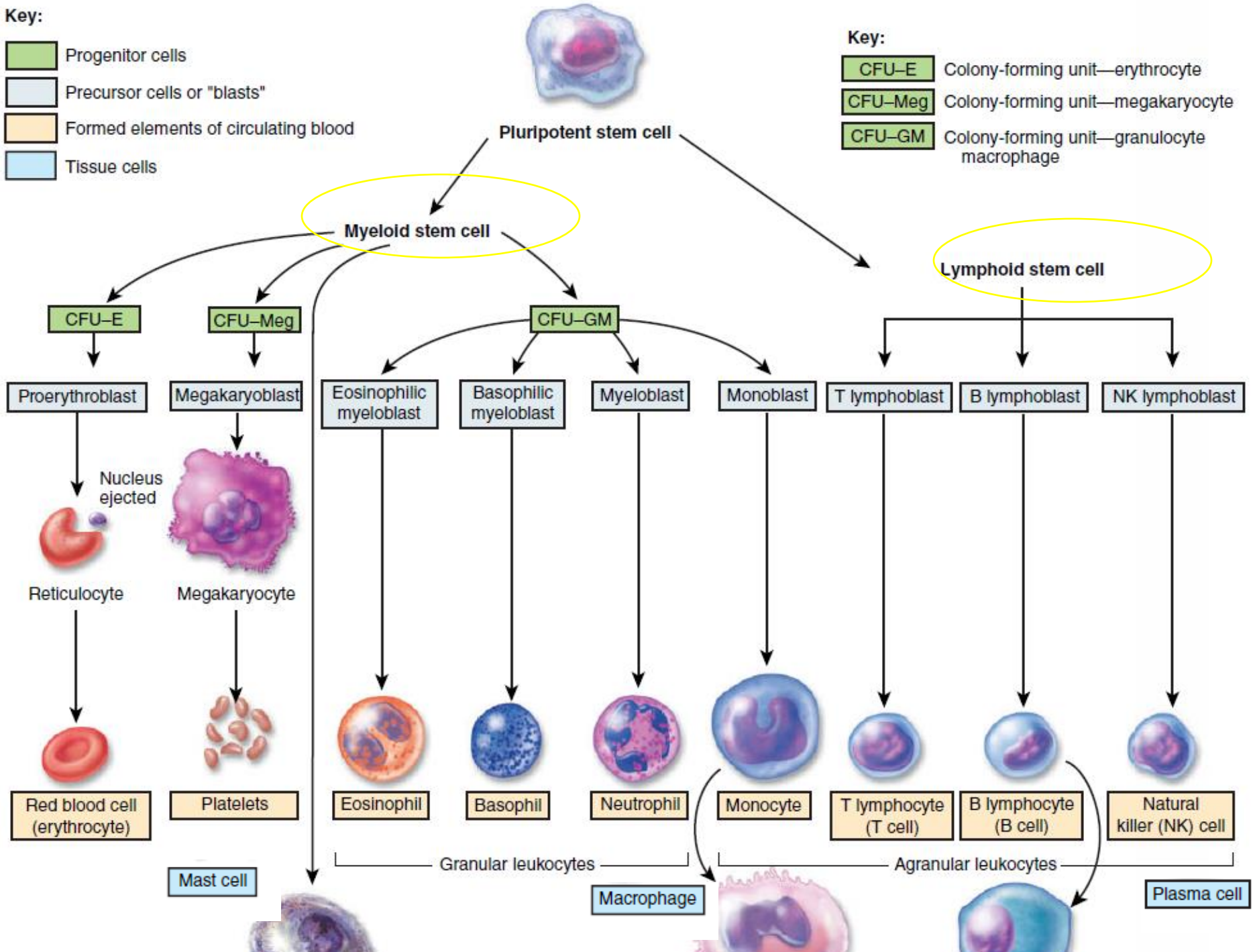
Early fetal life

Occurs in the yolk sac of an embryo and later in the liver, spleen, thymus, and lymph nodes of a fetus.

last 3 gestational months- death

*Red bone marrow becomes the primary site of hemopoiesis in the, and continues as the source of blood cells after birth and throughout life.

*axial skeleton, pectoral and pelvic girdles, and the proximal epiphyses of the humerus and femur.


Key:
Progenitor cells
Precursor cells or "blasts"
Formed elements of circulating blood
Tissue cells
Key:
CFU–E
Colony-forming unit—erythrocyte
CFU–Meg
Colony-forming unit—megakaryocyte
CFU–GM
Colony-forming unit—granulocyte macrophage
Pluripotent stem cell
Myeloid stem cell
Lymphoid stem cell
CFU–E
CFU–Meg
CFU–GM
Proerythroblast
Megakaryoblast
Eosinophilic myeloblast
Basophilic myeloblast
Myeloblast
Monoblast
T lymphoblast
B lymphoblast
NK lymphoblast
Nucleus ejected
Reticulocyte
Megakaryocyte
Red blood cell (erythrocyte)
Platelets
Eosinophil
Basophil
Neutrophil
Monocyte
T lymphocyte (T cell)
B lymphocyte (B cell)
Natural killer (NK) cell
Granular leukocytes
Agranular leukocytes
Mast cell
Macrophage
Plasma cell

Hemopoiesis (formation of blood cells)

- **Stem cells in bone marrow**
  - Reproduce themselves
  - Proliferate and differentiate

- **Formed elements do not divide once they leave red bone marrow**
  - Exception is lymphocytes

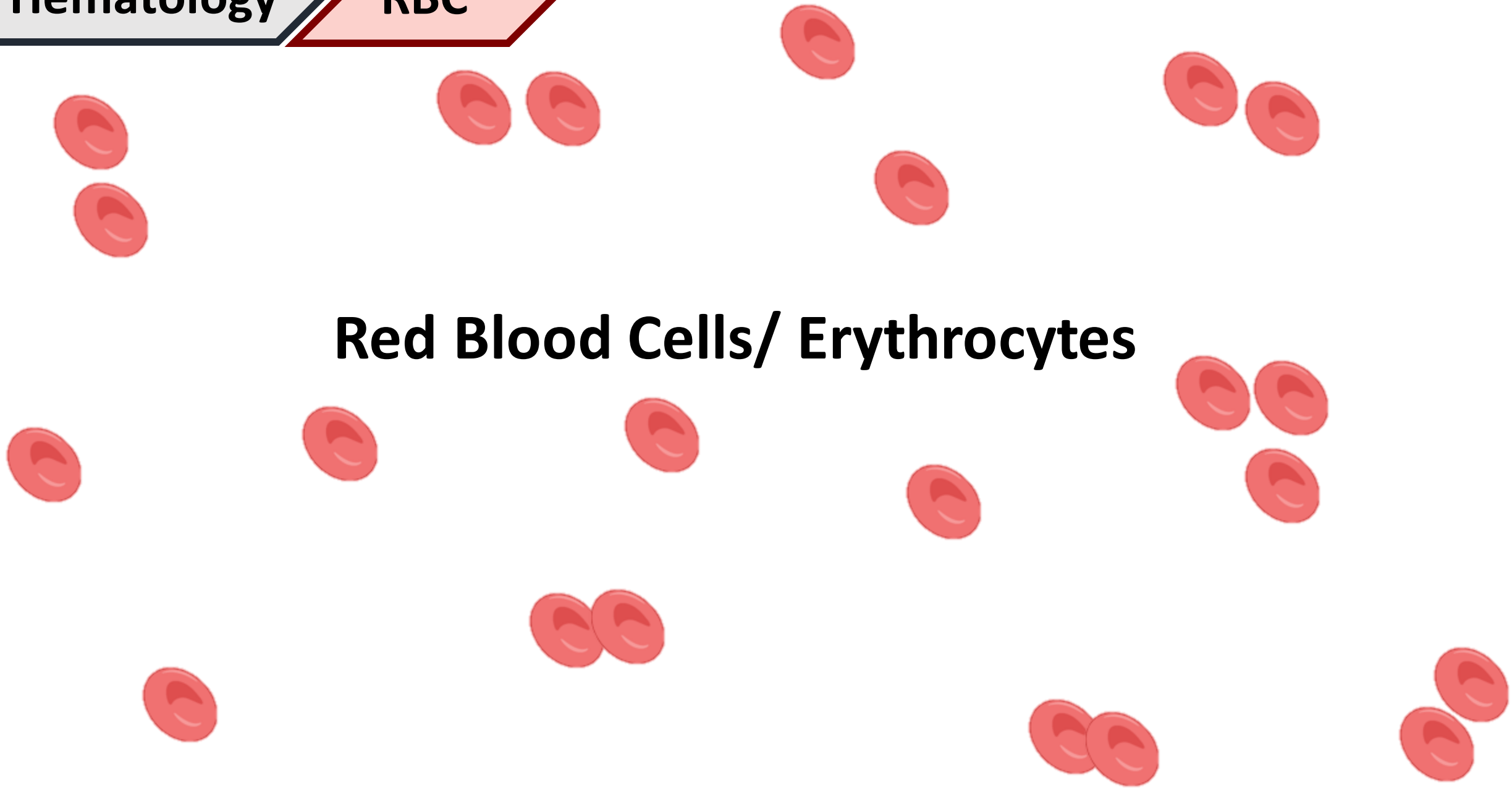
Hematology

Hemopoiesis (formation of blood cells)

- ✓ **Myeloid stem cells**
  - Give rise to red blood cells, platelets, monocytes, neutrophils, eosinophils and basophils
- ✓ **Lymphoid stem cells** give rise to
  - Lymphocytes and natural killer cells

- ✓ Hemopoietic growth factors regulate differentiation and proliferation
  - Erythropoietin – RBCs
  - Thrombopoietin – platelets
  - Colony-stimulating factors (CSFs) and interleukins – WBCs

Red Blood Cells/ Erythrocytes



RBC General characteristics

- Biconcave disc.
- Diameter is normally 8 μm.
- Strong, flexible plasma membrane.
- Lack nucleus and other organelles
- Lack mitochondria.
- Key erythrocyte enzymes: glycolytic enzymes and carbonic anhydrase.
- Contain oxygen-carrying protein (hemoglobin).

RBC General characteristics

- Oligosaccharides in plasma membrane are responsible for ABO and Rh blood groups.
- 5,200,000/ mm^3 in men; and 4,700,000/ mm^3 in women.
- Production = destruction (2 million/ sec).

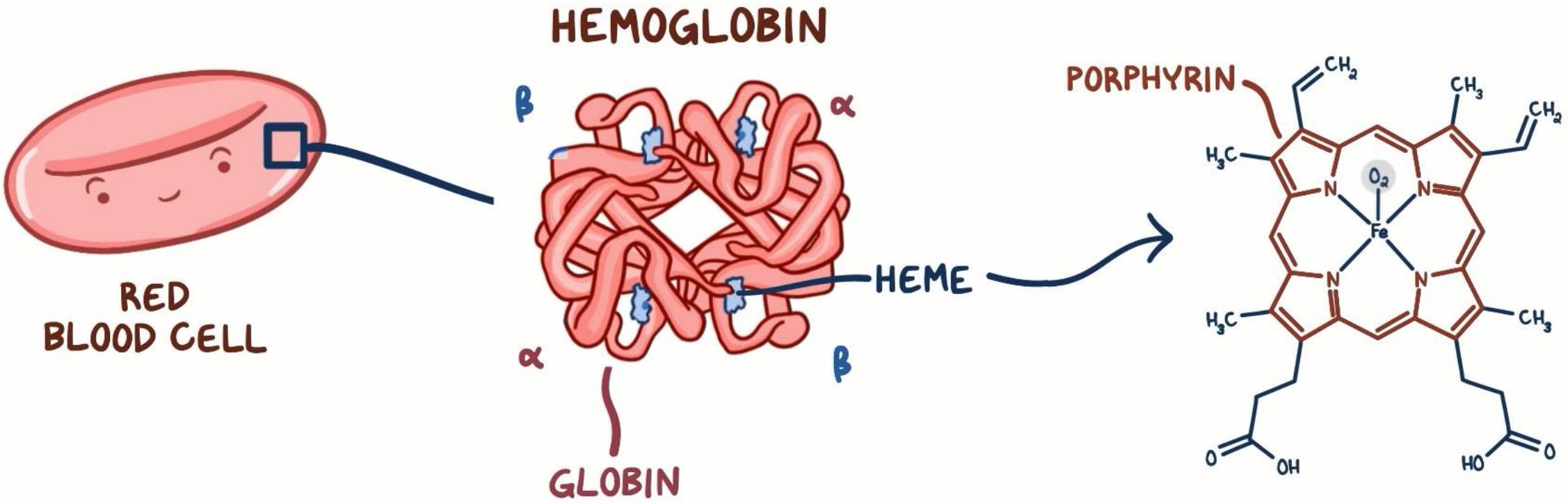
RBC Function

- Oxygen and CO_2 transport (hemoglobin).
- Contain a large quantity of carbonic anhydrase → increasing the rate of this reaction several thousand folds.
- Responsible for most of the acid-base buffering power of whole blood (hemoglobin).

$$CO_2 + H_2O \longleftrightarrow H_2CO_3 \longleftrightarrow HCO_3^- + H^+$$

carbonic acid bicarbonate

RBC Hemoglobin

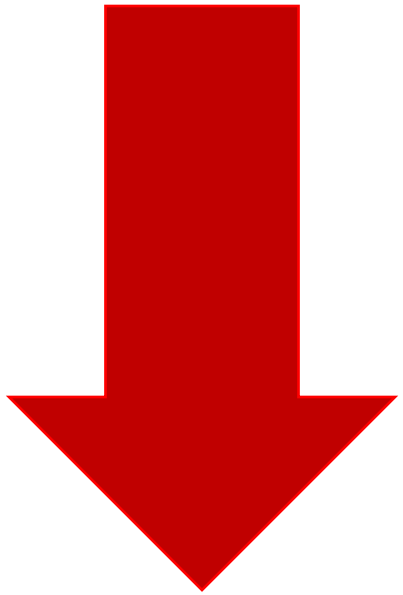


RBC Hemoglobin

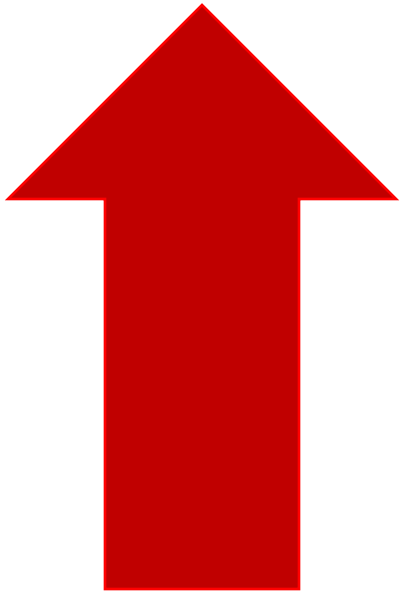
- The different types of chains are designated alpha chains, beta chains, gamma chains, and delta chains.
- The most common form of hemoglobin in the ADULT HUMAN, hemoglobin A, is a combination of two alpha chains and two beta chains.
- Iron ion can combine reversibly with one oxygen molecule
- Also transports 23% of total carbon dioxide (Combines with amino acids of globin).

RBC Hemoglobin

- Normal blood hemoglobin content is ~14.0 g/dL in the adult female and ~15.5 g/dL in the adult male.



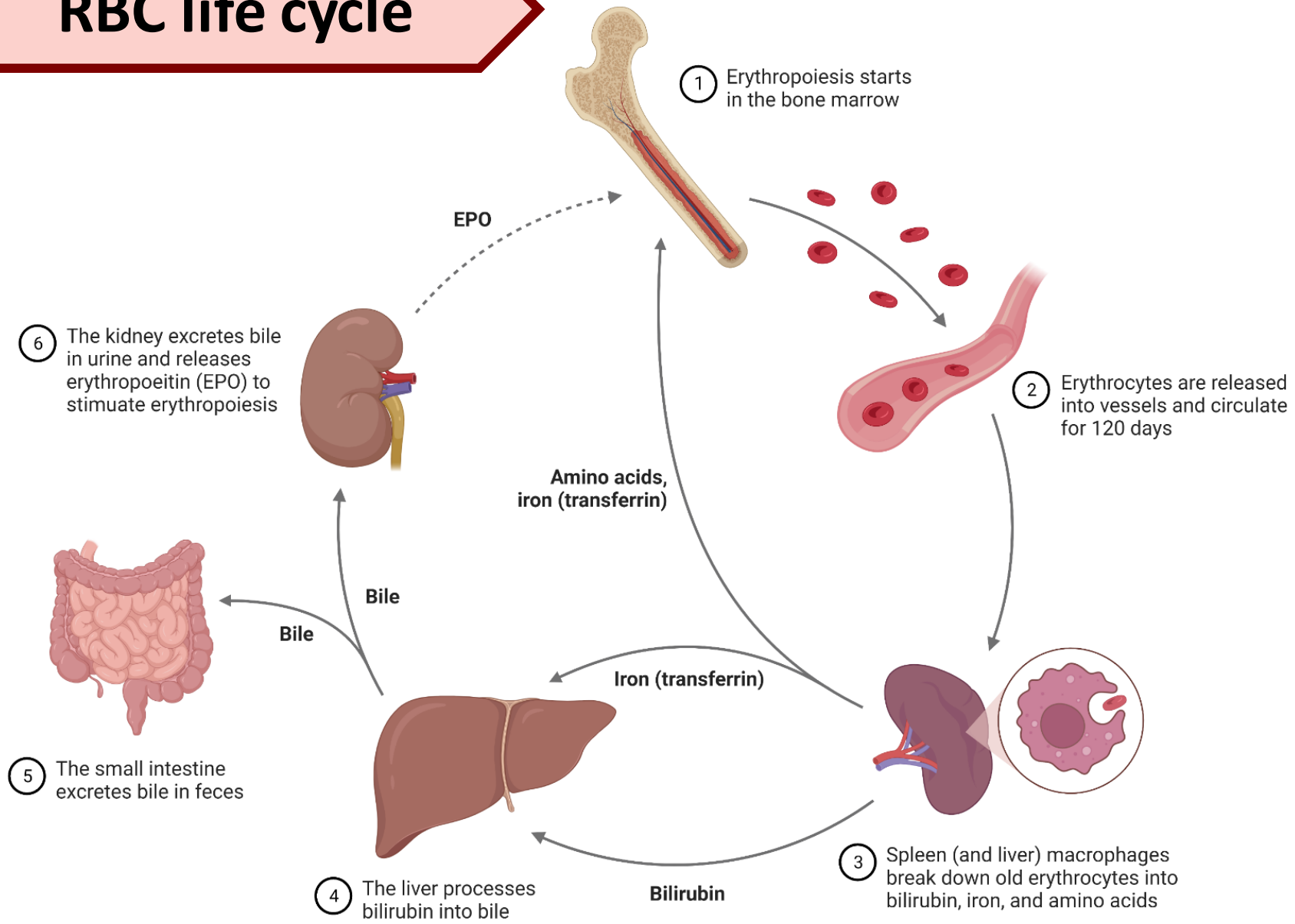
Anemia



polycythemia

RBC

RBC life cycle



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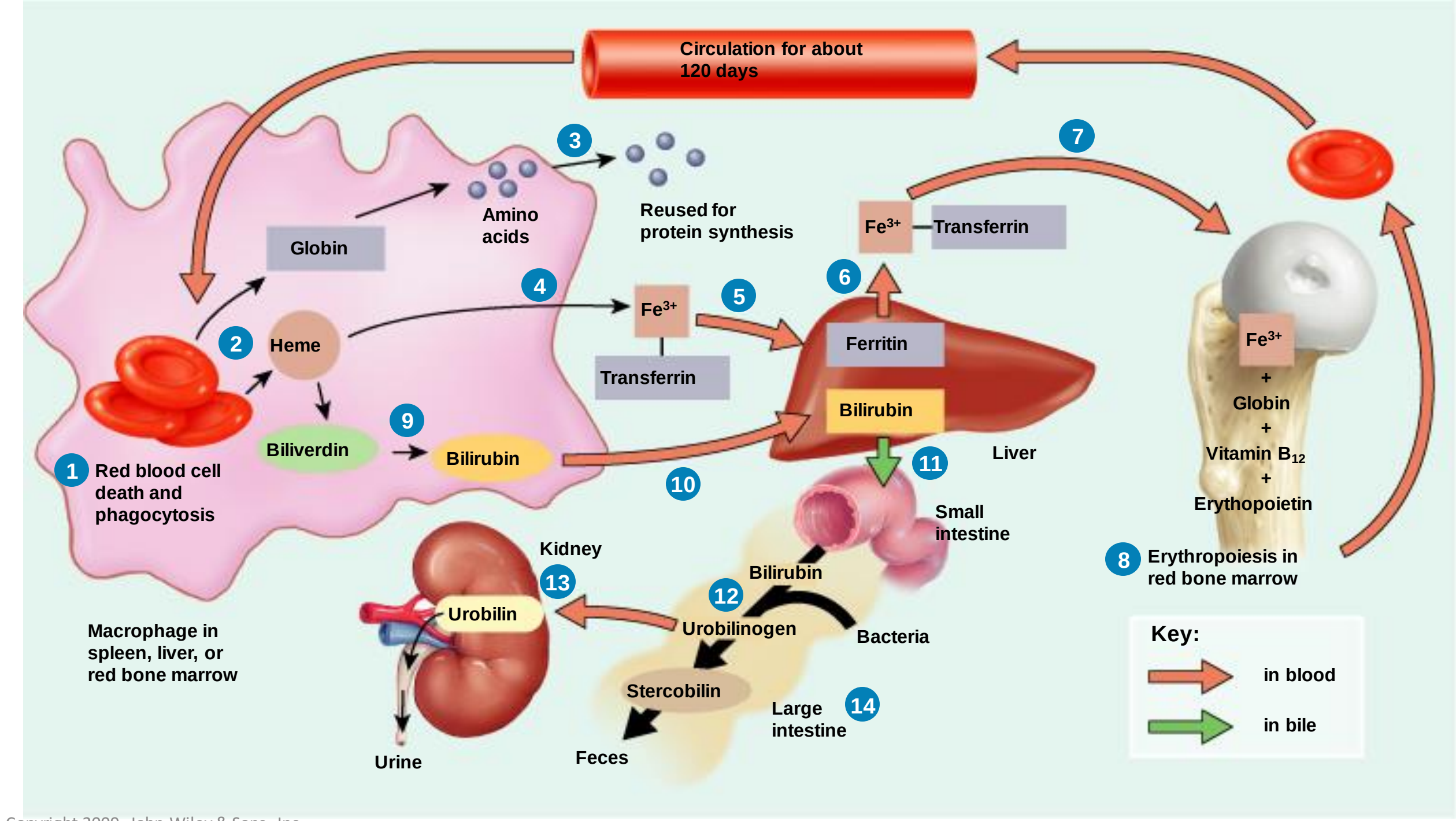


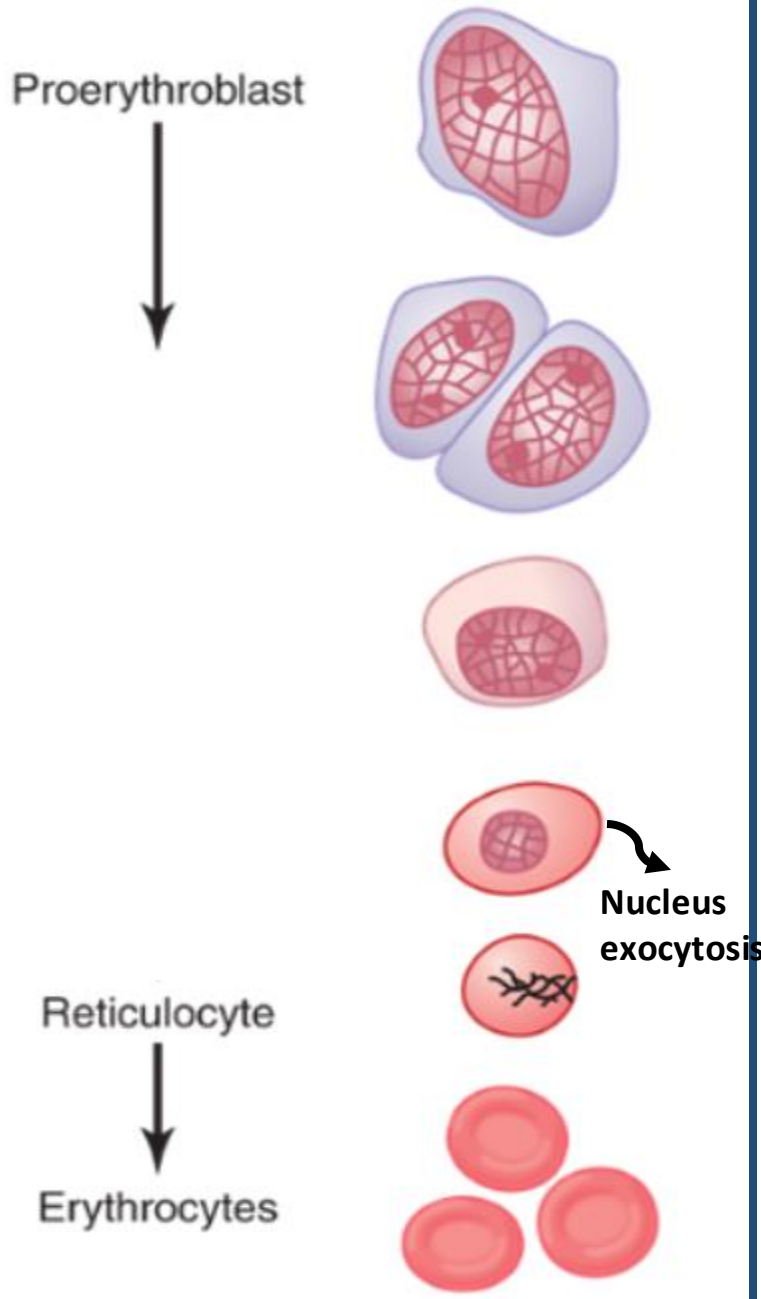
RBC life cycle

Breakdown products recycled

- Globin's amino acids reused
- Iron reused
- Non-iron heme ends as yellow pigment urobilin in urine or brown pigment stercobilin in feces

RBC Erythropoiesis

- Starts in red bone marrow with proerythroblast.
- Cell near the end of development ejects nucleus and becomes a reticulocyte which develop into mature RBC within 1-2 days.
- The remaining basophilic material in the reticulocyte normally disappears within 1 to 2 days, and the cell is then a mature erythrocyte.



RBC → **Reticulocyte count** <2% in normal adult

$$\text{Reticulocyte count} = \frac{\text{Number of reticulocyte}}{\text{Number of RBCs}} \times 100\%$$

Importance: Reticulocytes count help in diagnosis and typing of anemia

Decreased

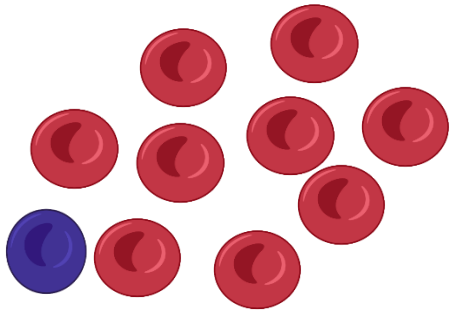
Aplastic anemia

Increased

Hemolytic anemia
Post hemorrhage

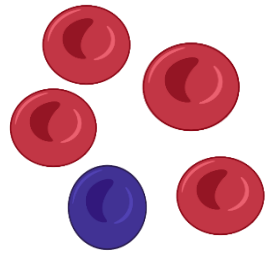
RBC

Corrected Reticulocyte count



Retic = 1%

Hct = 45



Retic = 2%

Hct = 22.5

$$\text{Corrected reticulocyte count} = \text{Reticulocyte count} \times \frac{\text{Actual Hct}}{\text{Normal Hct}}$$

$$= 1\% \times \frac{45}{45}$$

= 1%

$$= 2\% \times \frac{22.5}{45}$$

= 1%

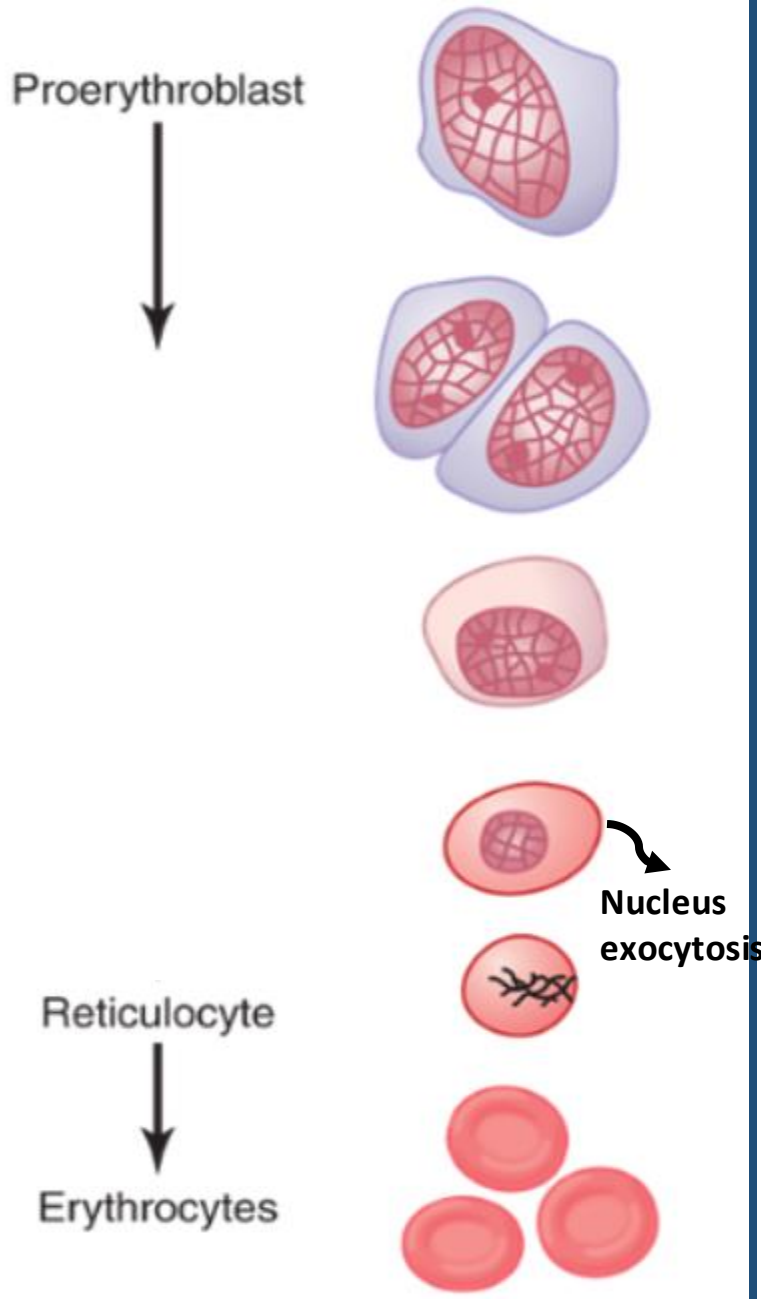
RBC Vitamins requirement

- Maturation of red blood cells requires vitamin B_{12} (Cyanocobalamin) and folic acid.
- Both of these are essential for the synthesis of DNA (formation of thymidine triphosphate).

- lack of either vitamin B_{12} or folic acid causes:

**abnormal and diminished DNA and, consequently, failure of nuclear maturation and cell division.

** production of larger red cells called **macrocytes** and the cell itself has a flimsy irregular membrane.

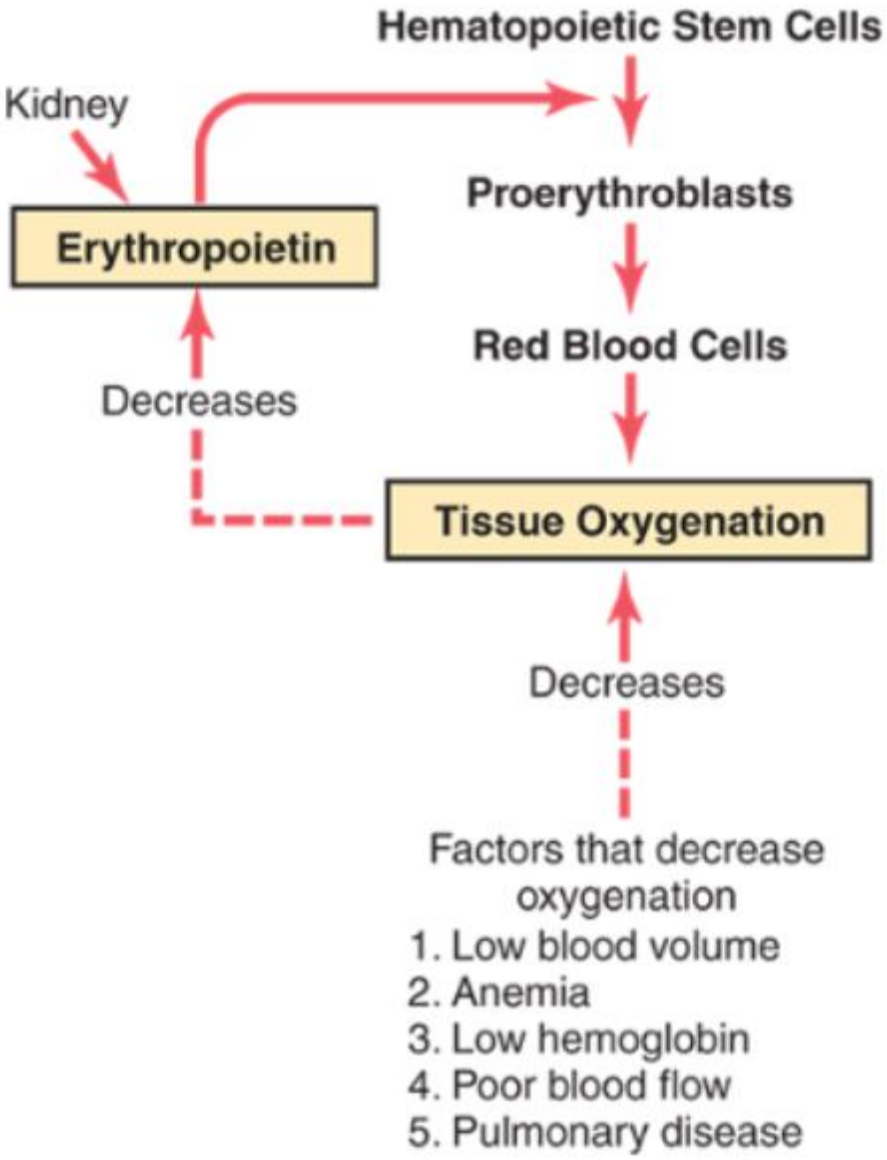


RBC Regulation of Erythropoiesis_ Erythropoietin (EPO)

- Negative feedback balances production with destruction.
- Is a glycoprotein that normally formed in the kidneys (90%); the remainder is formed mainly in the liver.
- It is essential to stimulate the production of proerythroblasts from hematopoietic stem cells in the bone marrow.
- EPO causes these cells to pass more rapidly through the different erythroblastic stages.

RBC Regulation of Erythropoiesis_ Erythropoietin (EPO)

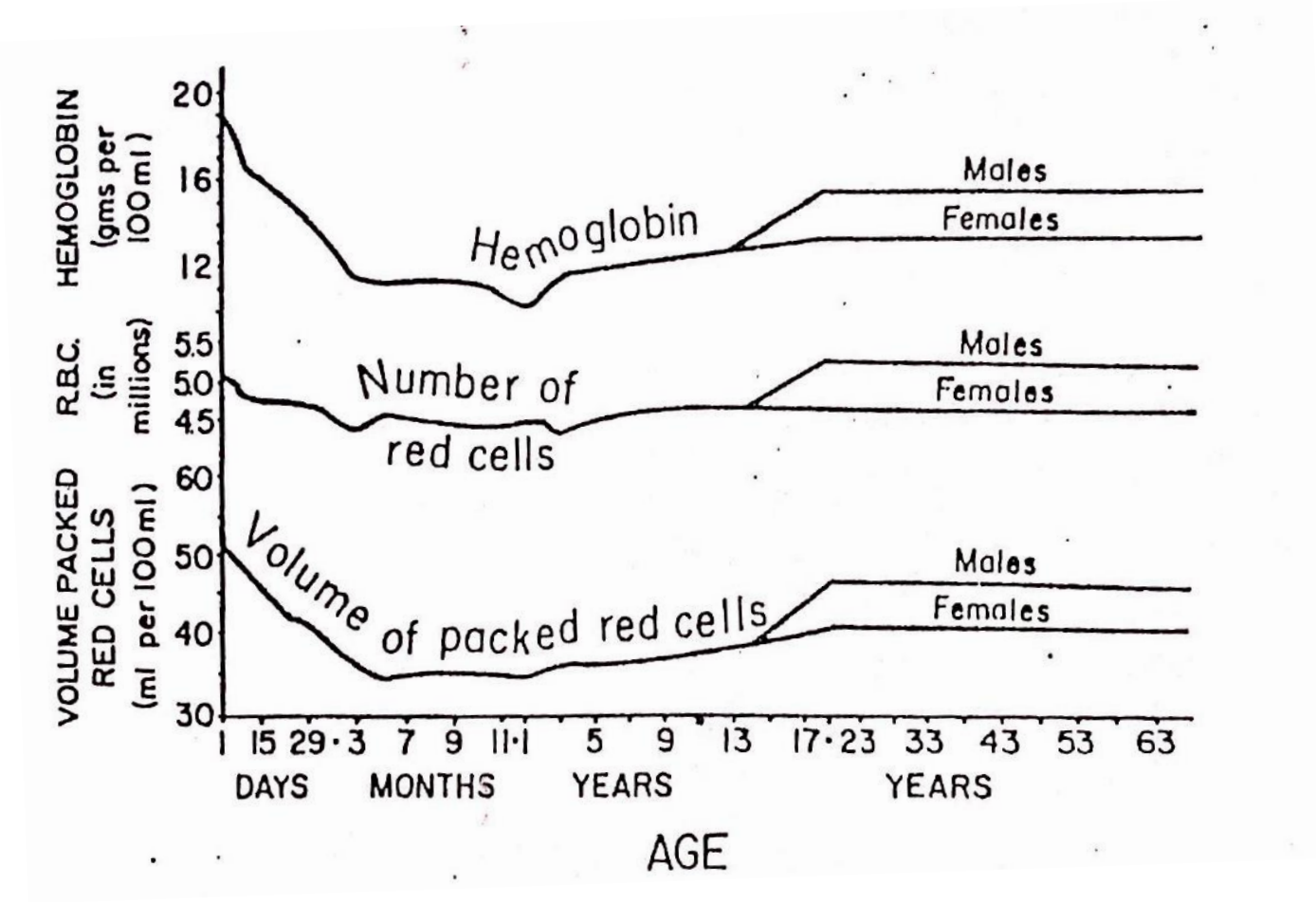
- Hypoxia causes a marked increase in erythropoietin production.
- With renal failure, EPO release slows and RBC production is inadequate. This leads to a decreased hematocrit.



- P.s. Hypoxia is insufficient O_2 at the cellular level

RBC

RBCs parameters



RBC

RBCs parameters

RBC count (10^6/μL blood)
Hematocrit (%)
Hemoglobin (g/dL blood)
Mean red cell volume, MCV (fL/cell)
Mean red cell hemoglobin, MCH (pg/cell)
Mean cell hemoglobin concentration, MCHC (g/dL RBCs)
Red cell distribution width, RDW (%)

Mean cell volume (fL/cell)

- Is the average volume (size) of the RBCs.
- It can be measured, as it is in automated cell counters, or calculated:

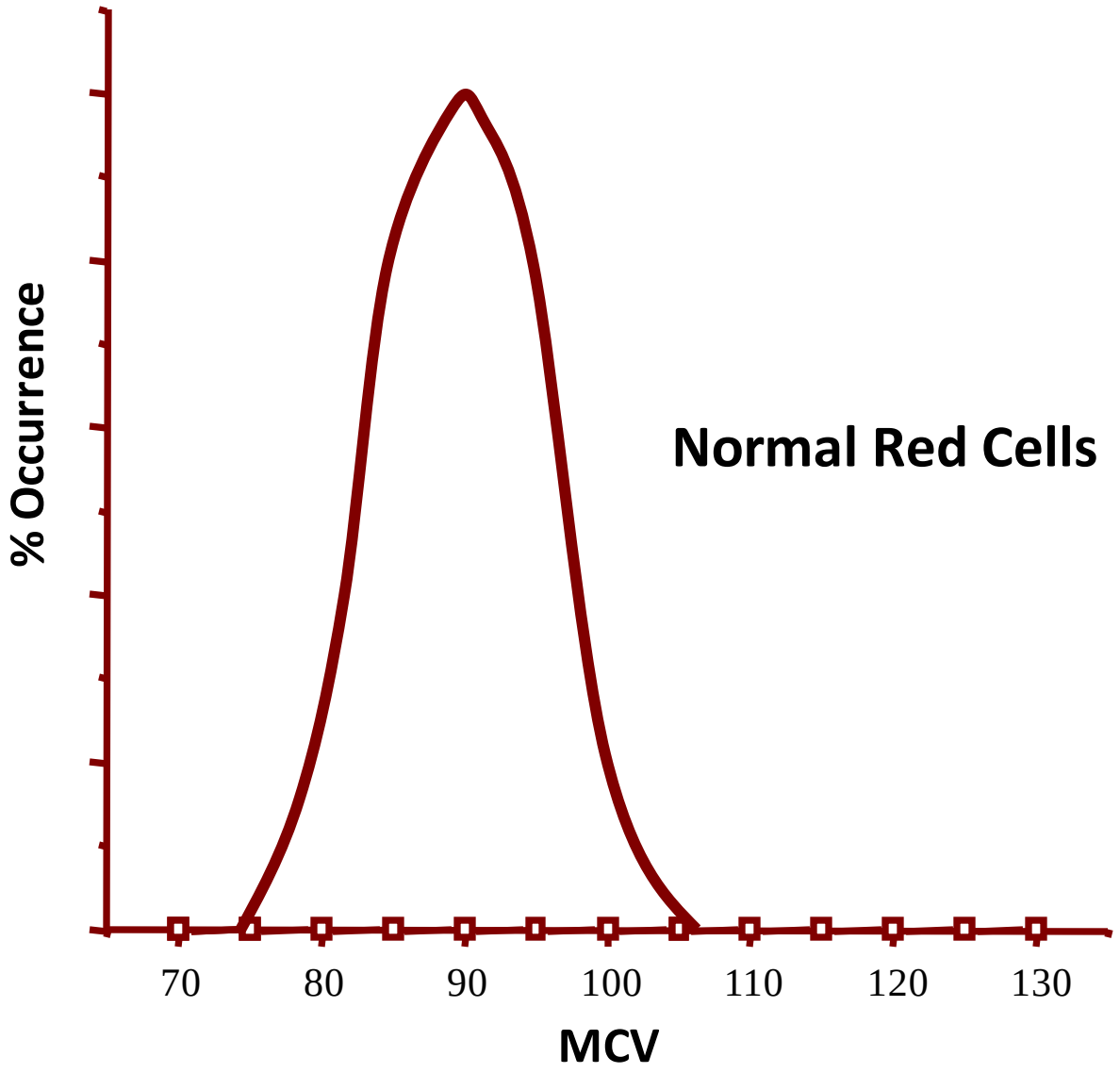
$$= \frac{\text{Hct [\%]} \times 10}{\text{RBC count [in millions/µL]}}$$

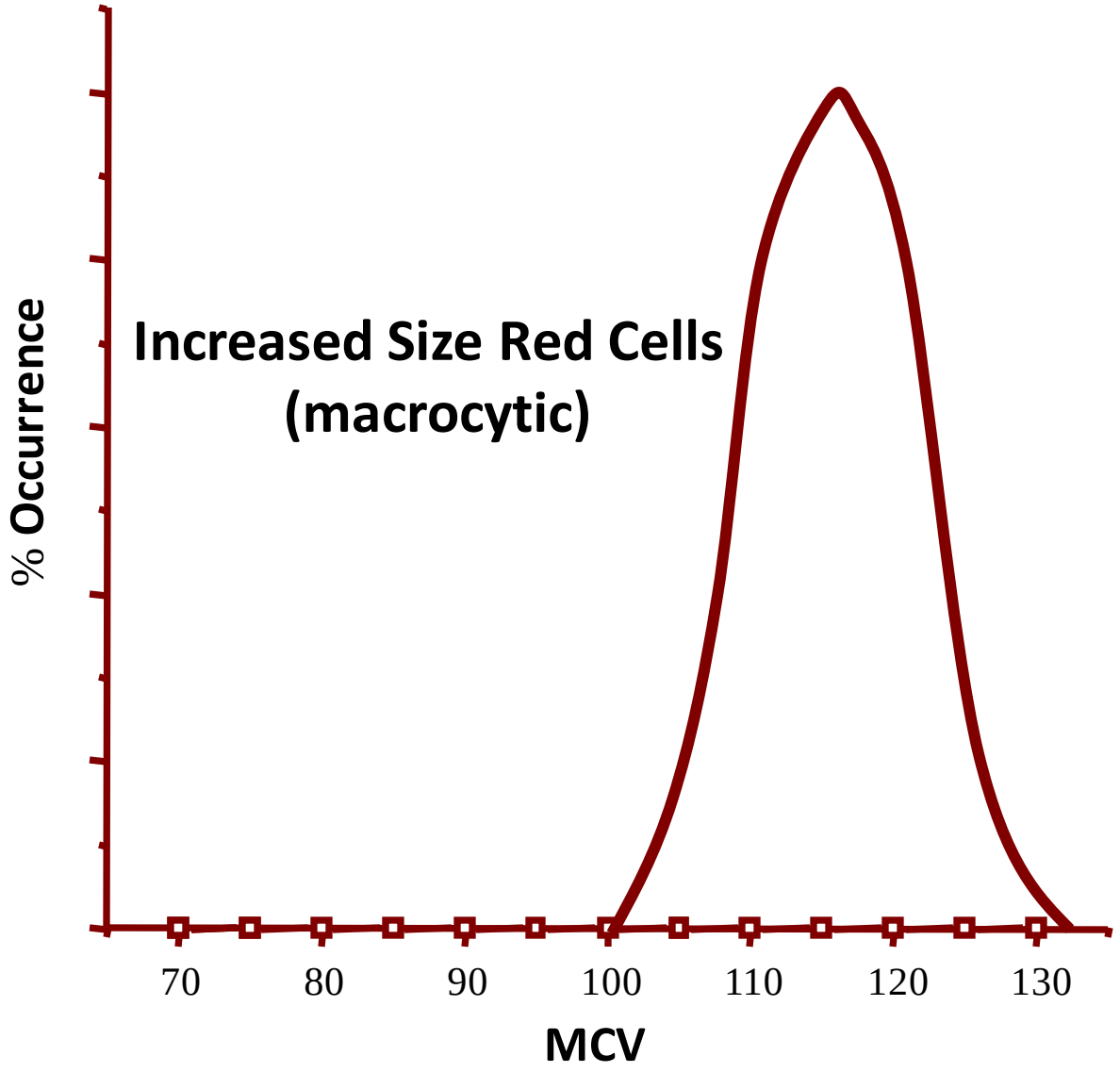
Macrocytic (>100)

Normocytic (80-100)

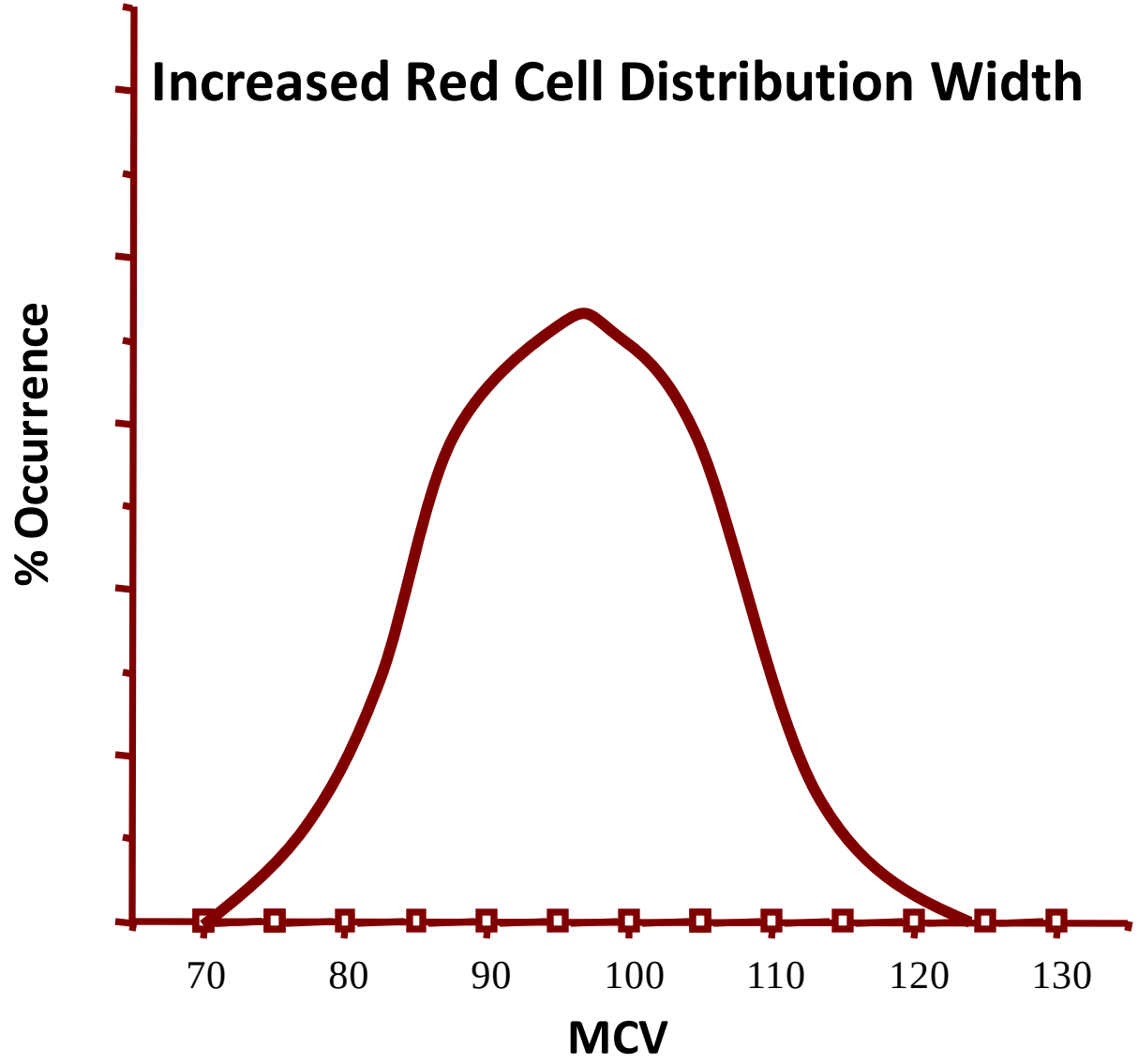
Microcytic (<80)

RBC > RBCs parameters > Distribution of RBCs sizes




% Occurrence
Increased Size Red Cells
(macrocytic)
70
80
90
100
110
120
130
MCV

- Measurement of RBC size variation (anisocytosis).
- RDW = [standard deviation/MCV] x 100.
- A high RDW → large variation in RBC sizes
- A low RDW → more homogeneous population of RBCs.
- A high RDW can be seen in a number of anemias, including iron deficiency, vitamin B12 or folate deficiency.



Mean cell hemoglobin concentration (pg/ cell)

- Is the average hemoglobin content in a RBC.

$$= \frac{\text{Hemoglobin [g/dL] x 10}}{\text{RBC count [in millions/µL]}}$$

- A low MCH is typically reflected in an enlarged area of central pallor in RBCs on the peripheral blood smear (greater than one-third of the RBC diameter)

Normochromic (30-34)

Hypochromic (<30)

Mean cell hemoglobin concentration (g/dL RBC)

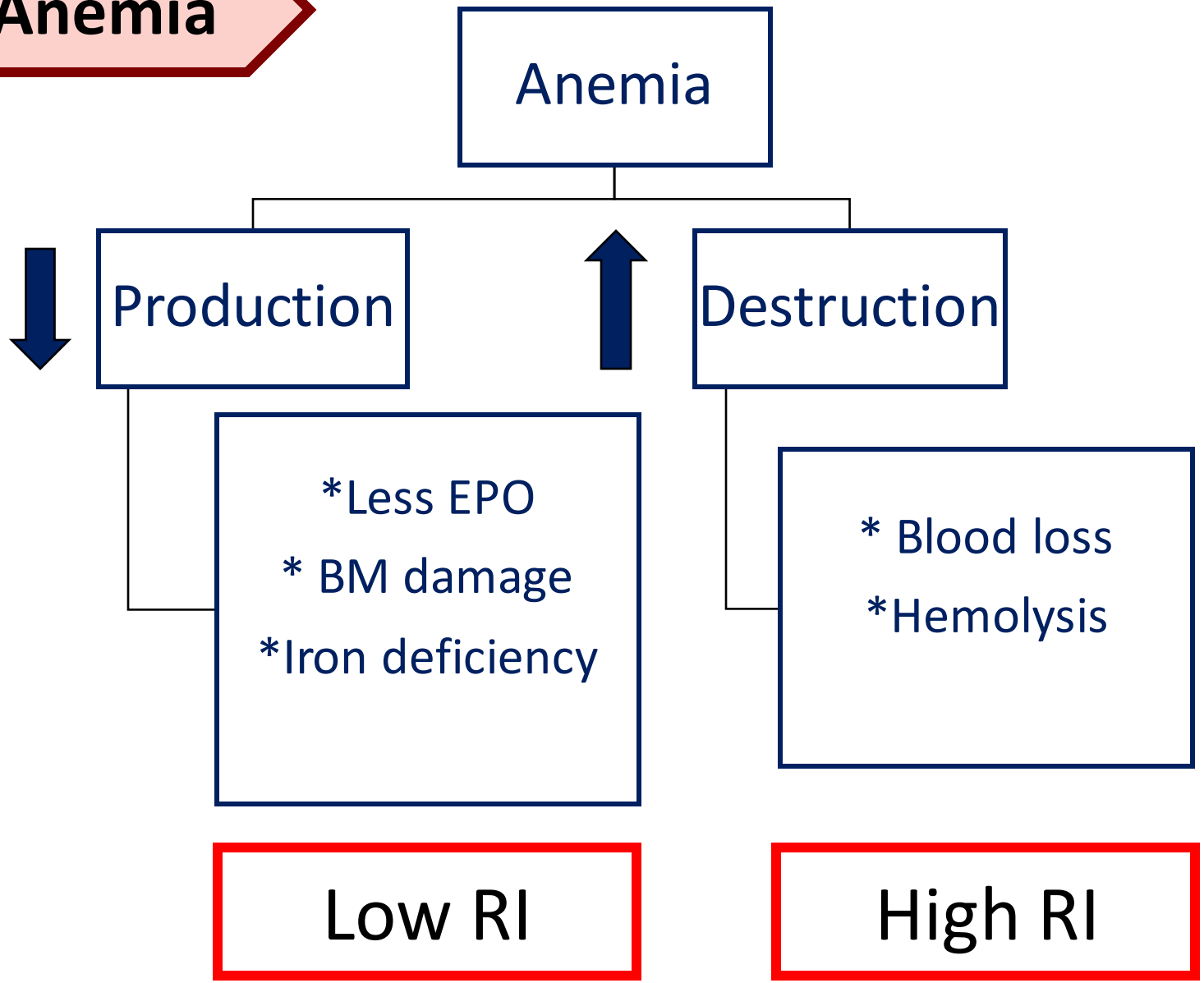
- Is the average hemoglobin concentration per RBC.

$$= \frac{\text{Hemoglobin [g/dL] x 100}}{\text{Hct [\%]}}$$

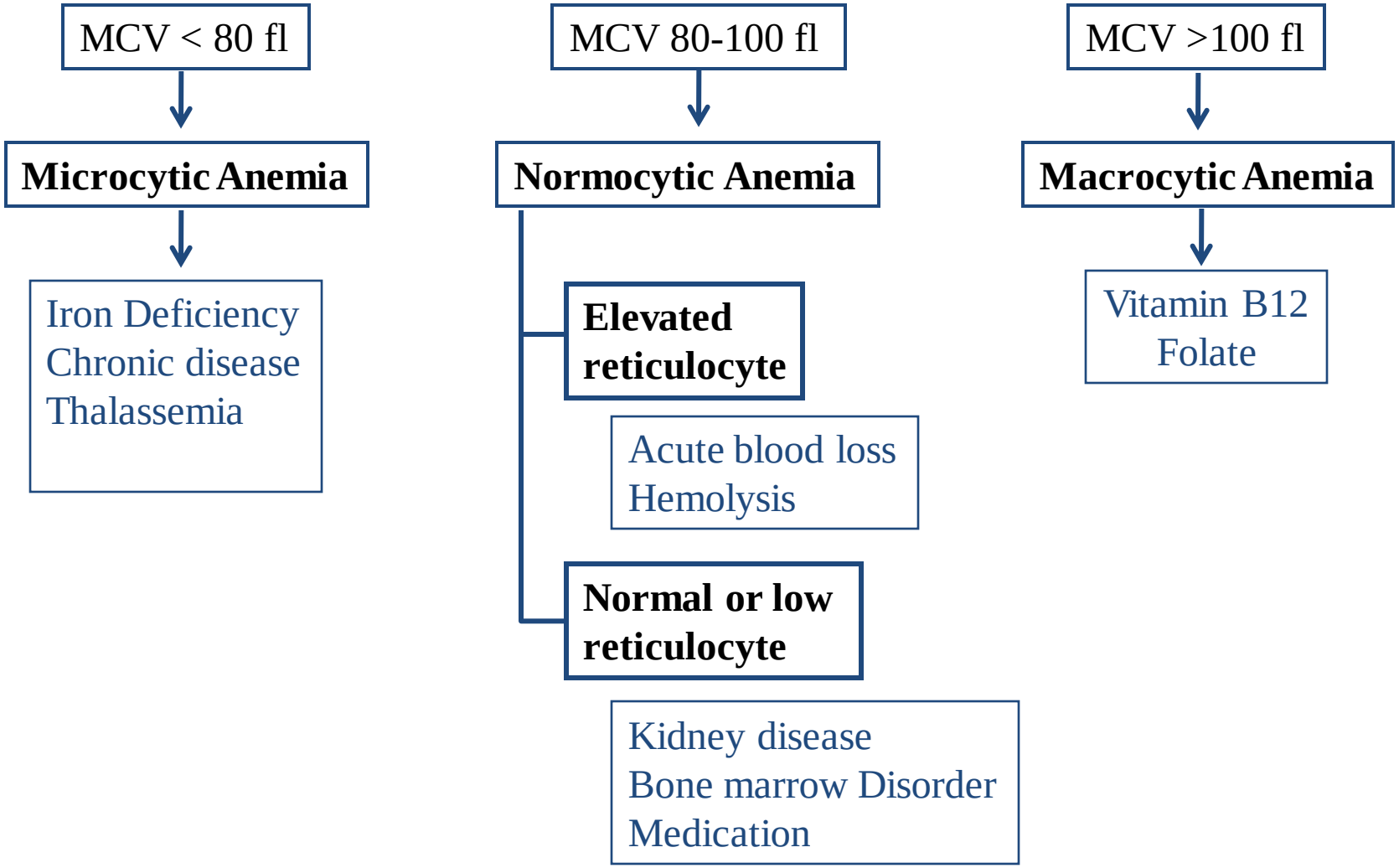
Normochromic (30-36)

Hypochromic (<30)

RBC Anemia


Anemia
Production
Destruction
*Less EPO
* BM damage
*Iron deficiency
* Blood loss
*Hemolysis
Low RI
High RI

RBC Anemia classification



RBC Anemia classification

MCV	Hb Content (MCH)	Causes
Normocytic	Normochromic	Bone marrow failure, renal disease, hemolytic anemia
Macrocytic	Normochromic	vitamin B_{12}, folic acid deficiency
Microcytic	Hypochromic	Iron deficiency, chronic diseases, Thalassemia

RBC Effects of Anemia on Function of the Circulatory System

- Blood viscosity is decreased.
- This decreases the resistance to blood flow in the peripheral blood vessels.
- Greater quantities of blood return to the heart.
- Increased cardiac output.

- ***Thus, one of the major effects of anemia is greatly increased cardiac output, as well as increased pumping workload on the heart***.