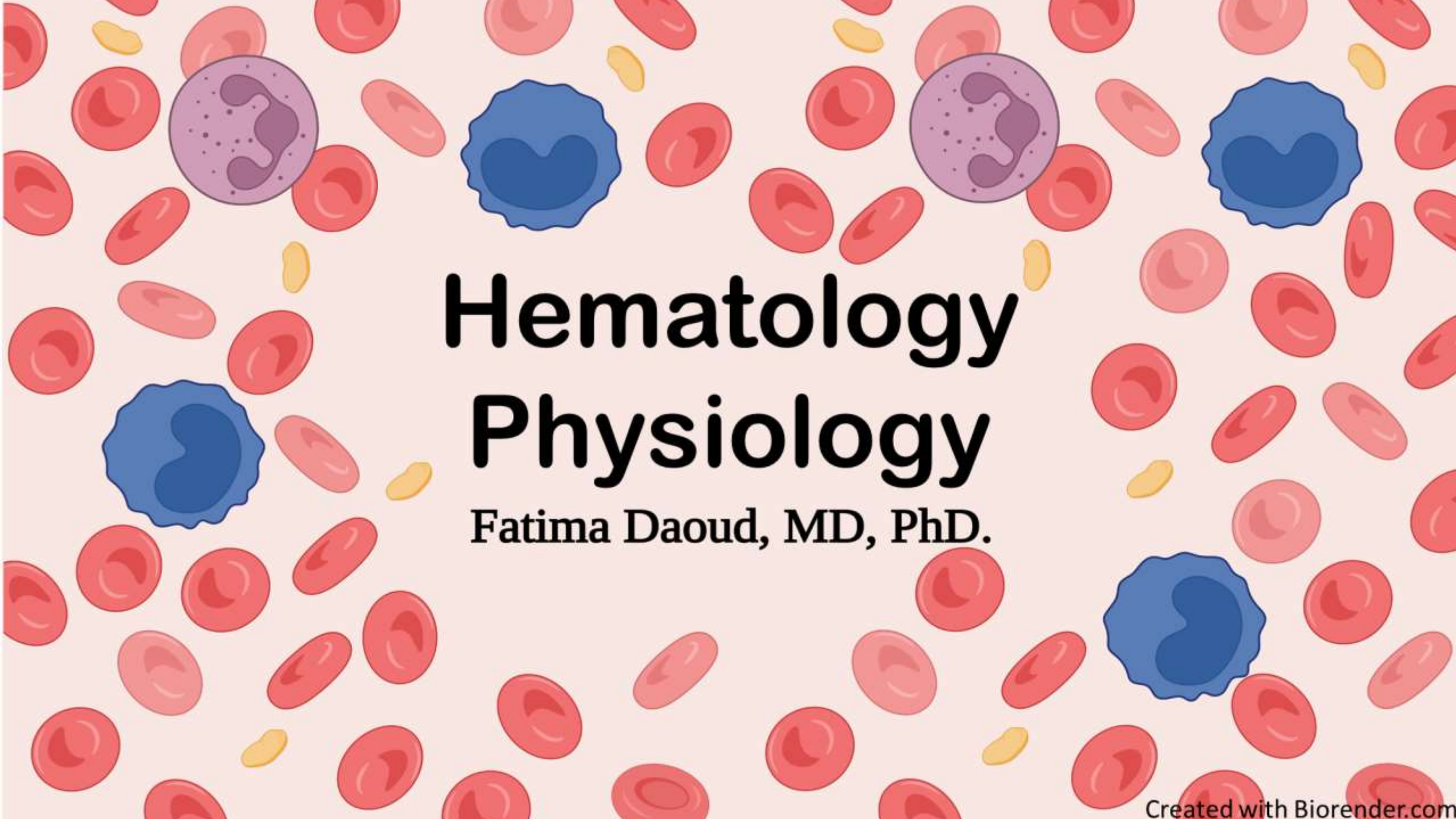
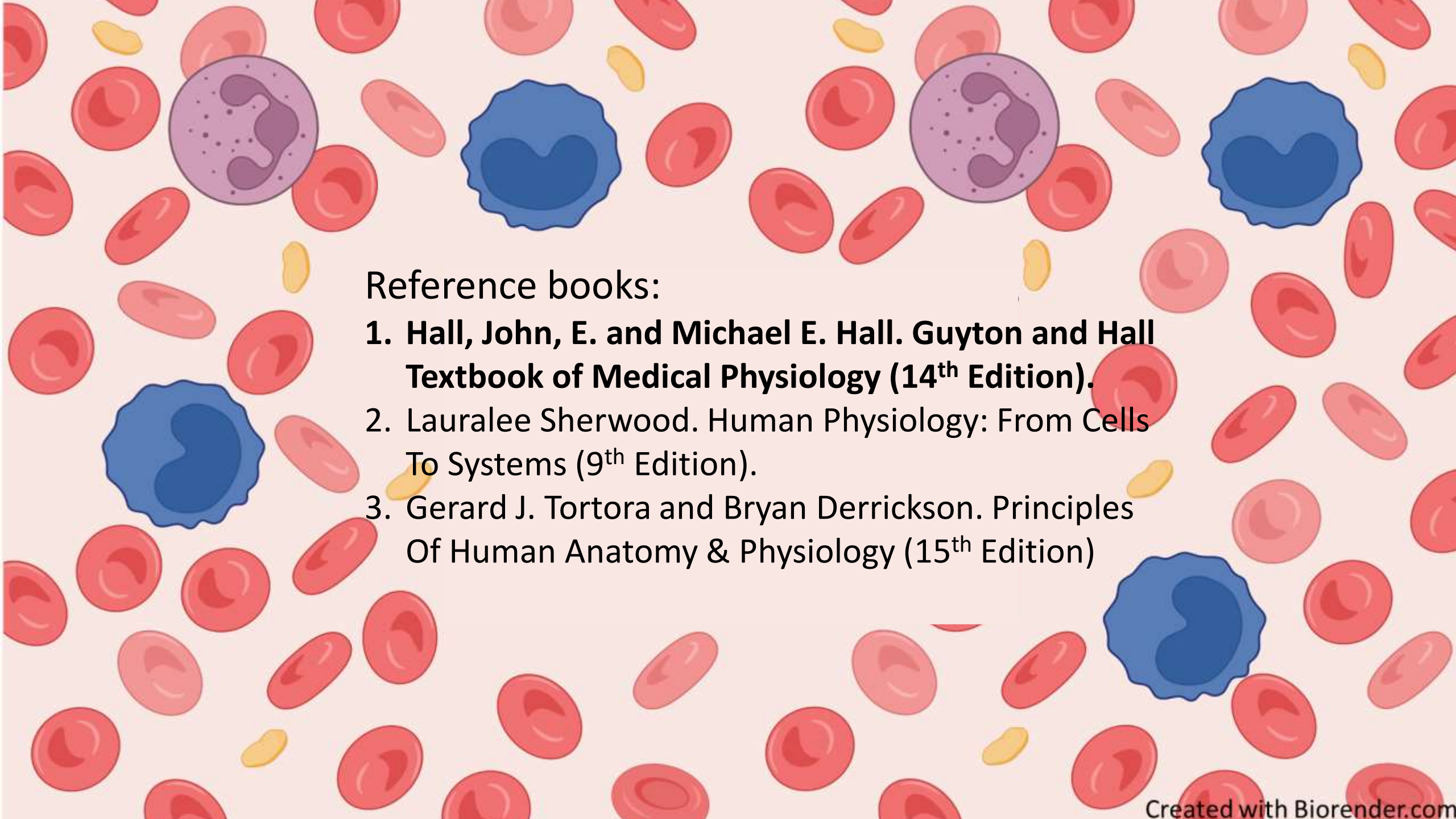


The background of the slide is a light pink color, populated with numerous stylized illustrations of blood cells. Red blood cells are depicted as red, biconcave discs. White blood cells are shown in two types: some with a multi-lobed purple nucleus and others with a large, dark blue, kidney-shaped nucleus. Small, yellow, bean-shaped cells are also scattered throughout. The text is centered in the middle of the slide.

Hematology Physiology

Fatima Daoud, MD, PhD.

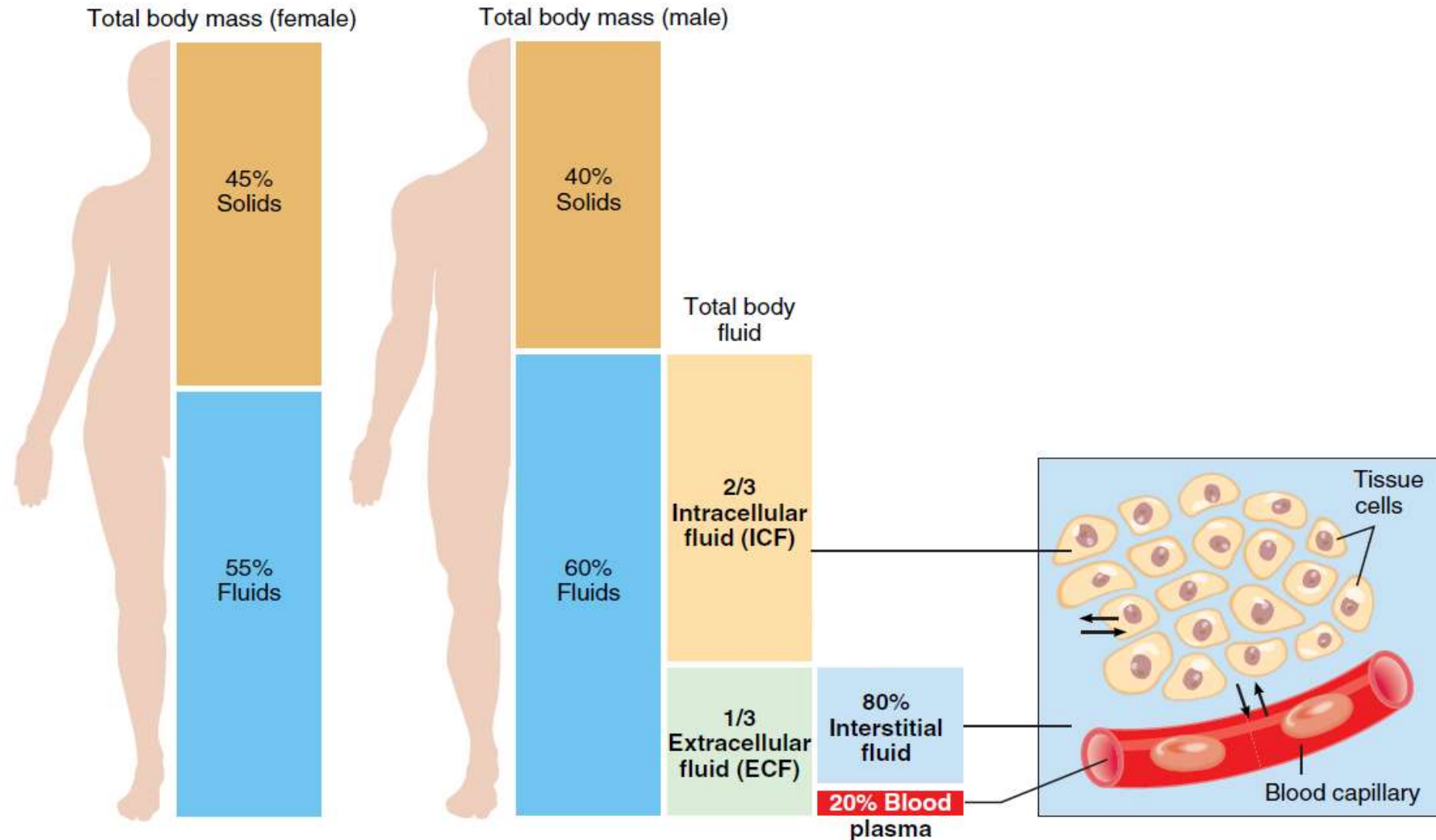
The background of the slide is a light pink color, populated with numerous stylized illustrations of blood cells. Red blood cells are depicted as red, biconcave discs of varying sizes. White blood cells are shown as larger, spherical cells with purple or blue nuclei and granular cytoplasm. Platelets are represented as small, yellow, oval-shaped cells. The cells are scattered across the entire background, creating a dense, microscopic appearance.

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

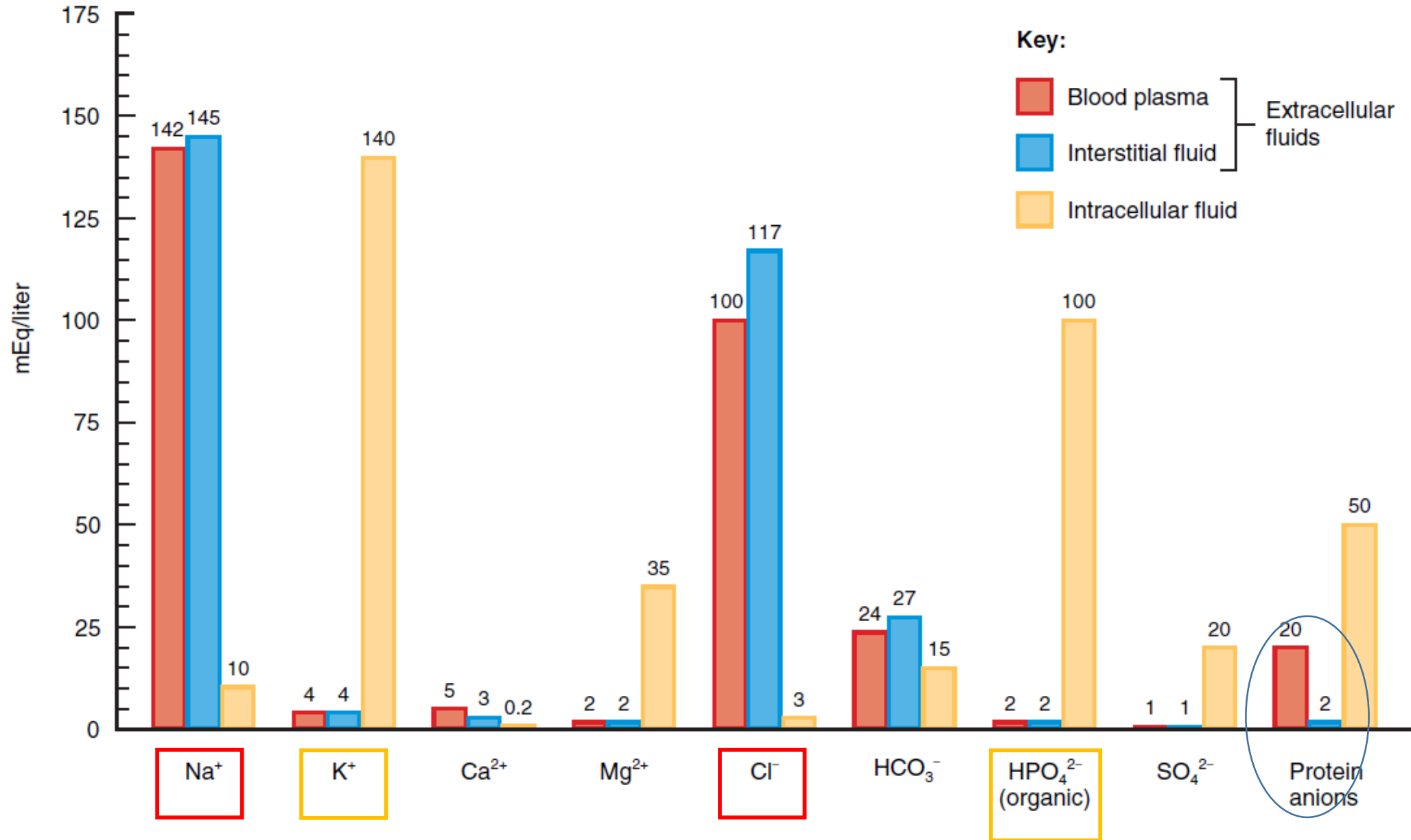
Body Fluids



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

Hematology

Body Fluids

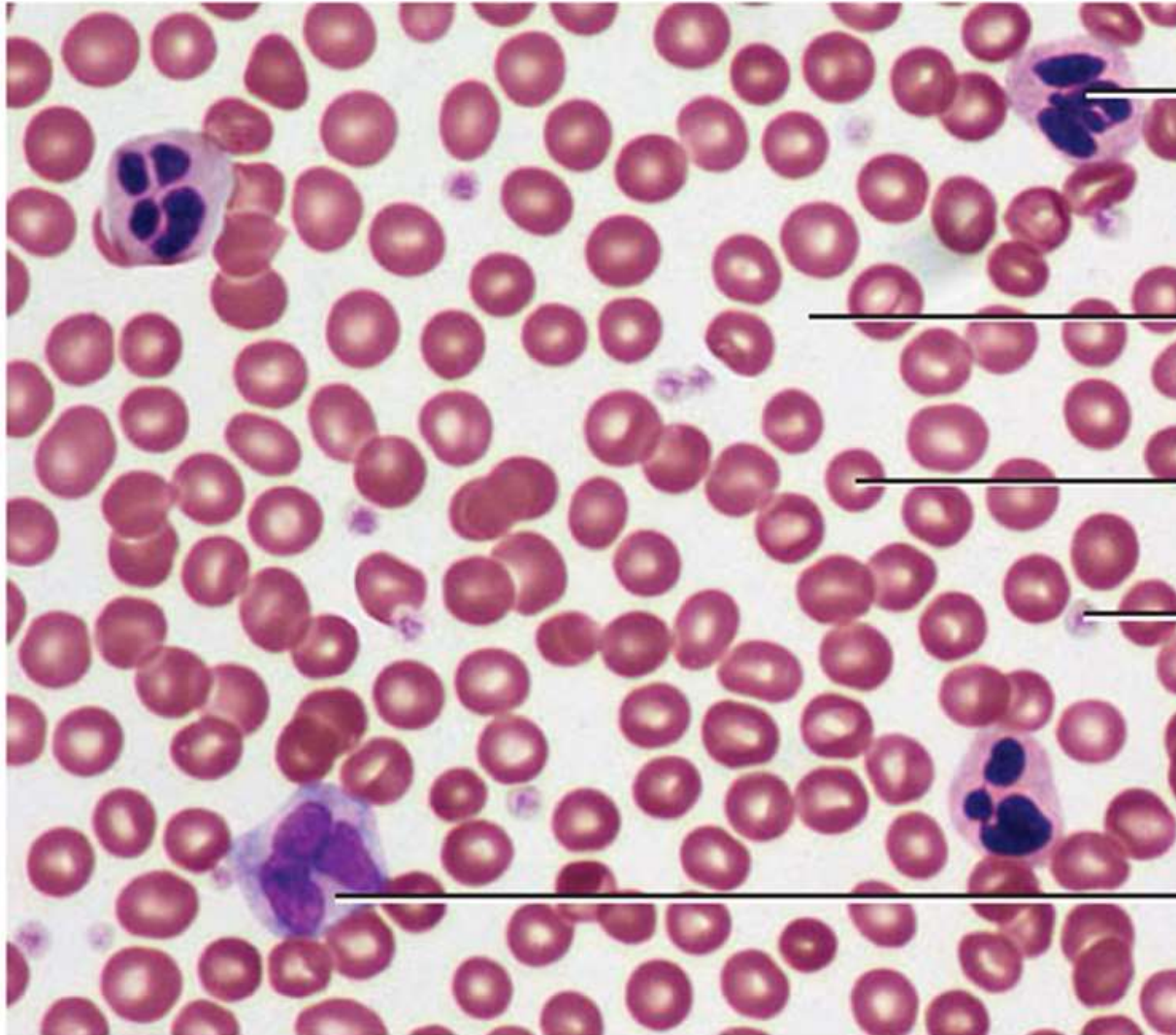


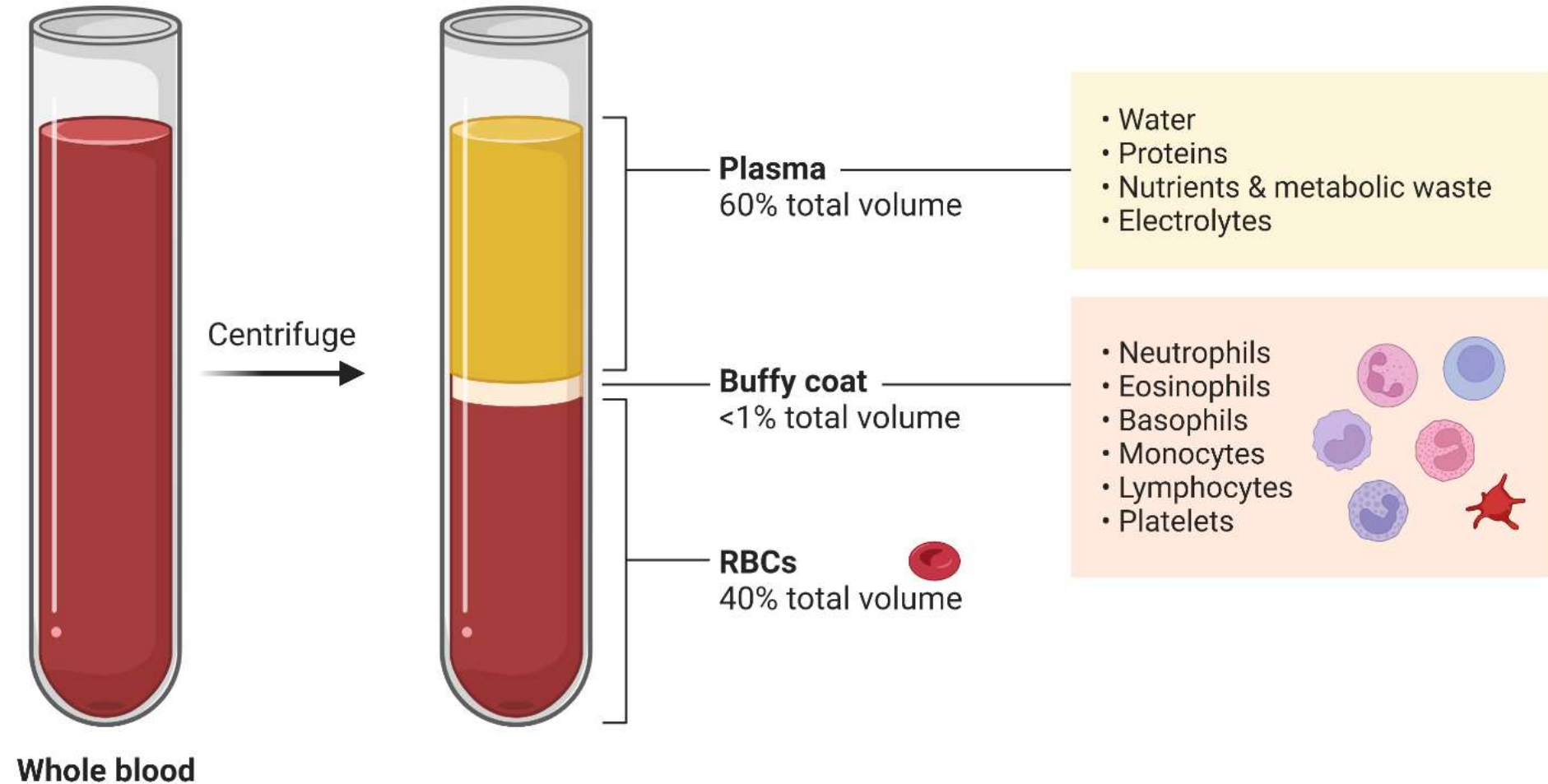
- The average blood volume of adults is about **7–8%** of body weight, or about 5 liters.
- Blood is connective tissue.
- Blood is denser and more viscous (thicker) than water.
- The temperature of blood is 38°C.
- Slightly alkaline pH ranging from 7.35 to 7.45 (average = 7.4).
- The color saturated (O_2) → bright red
unsaturated (O_2) → dark red

Hematology

Blood and its components

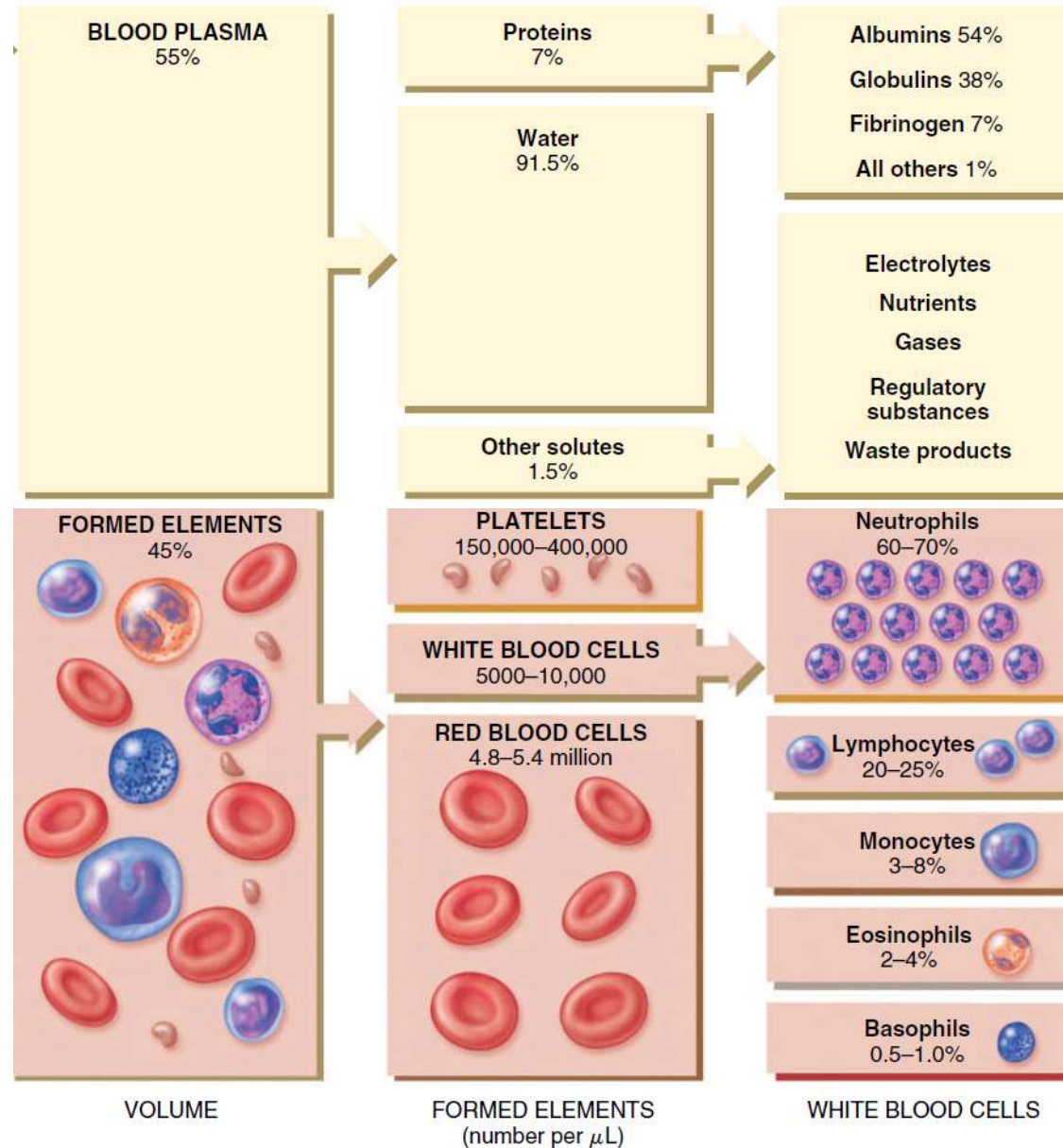
Blood smear





Hematology

Blood and its components



Hematology

Plasma Protein

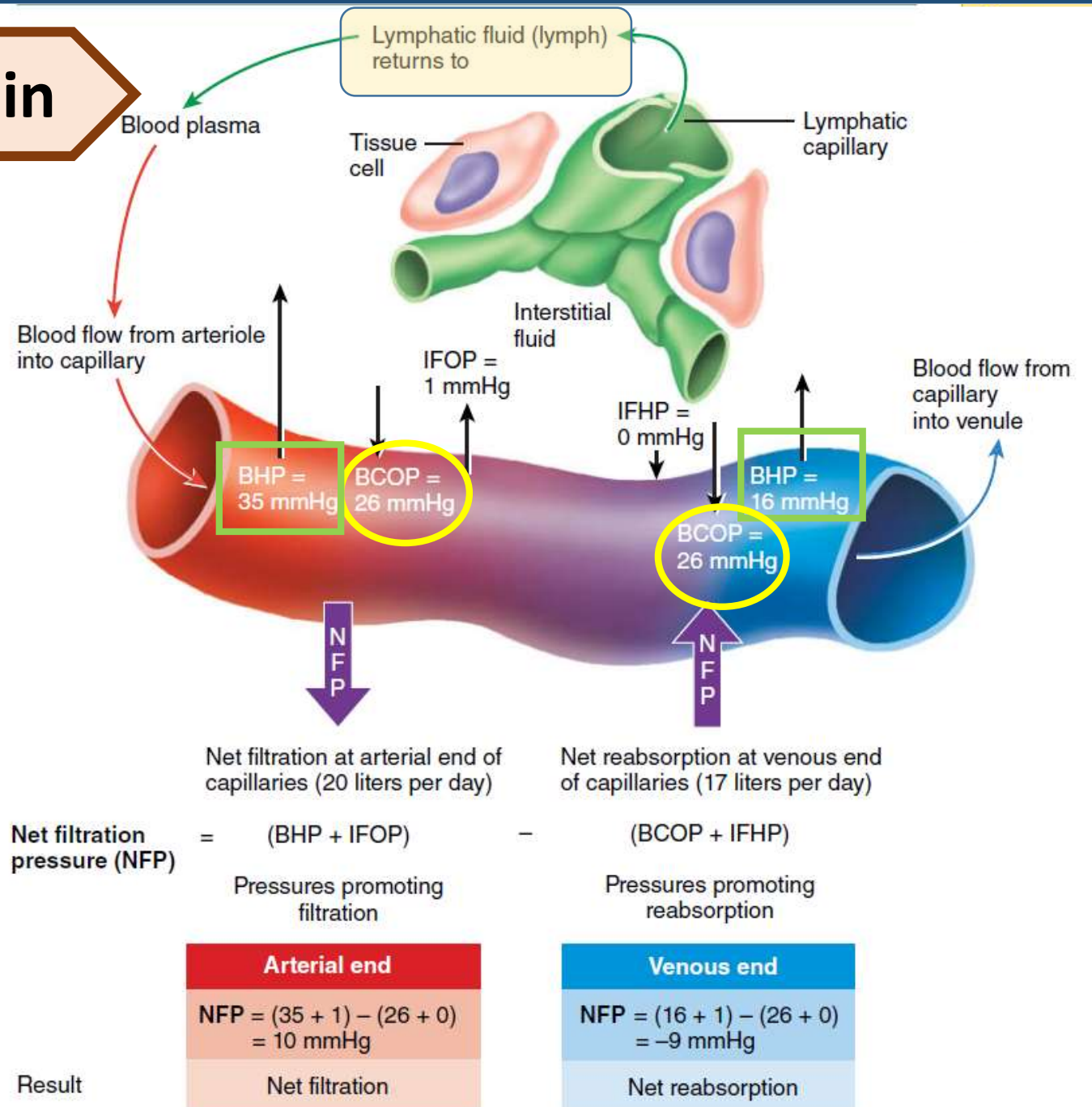
1. Establishment of colloid osmotic pressure.

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)



Hematology

Plasma Protein

2. Responsible for plasma's capacity buffer changes in pH.

Albumin

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

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.

Transportation

- Respiratory gases, nutrients, hormones, and metabolic wastes

Regulation

- Acid–base balance, heat distribution, and fluid balance

Protection

- Immune defense and prevention of blood loss

Hematology

Hemopoiesis (formation of blood cells)

Early fetal life

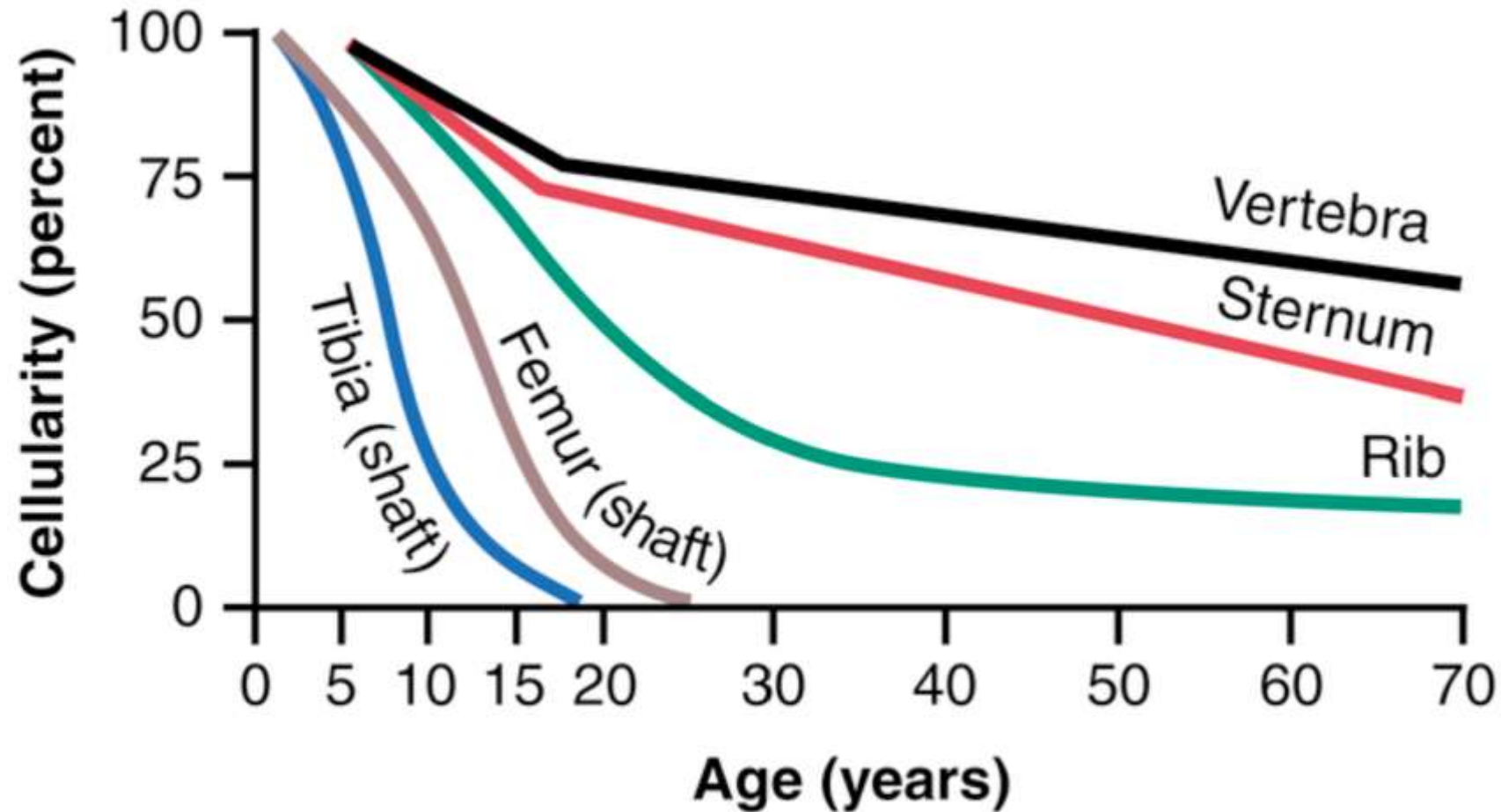
Occurs in the yolk sac of an embryo and later in the liver, spleen, thymus, and lymph nodes of a fetus.

last 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.

Hematology

Hemopoiesis (formation of blood cells)

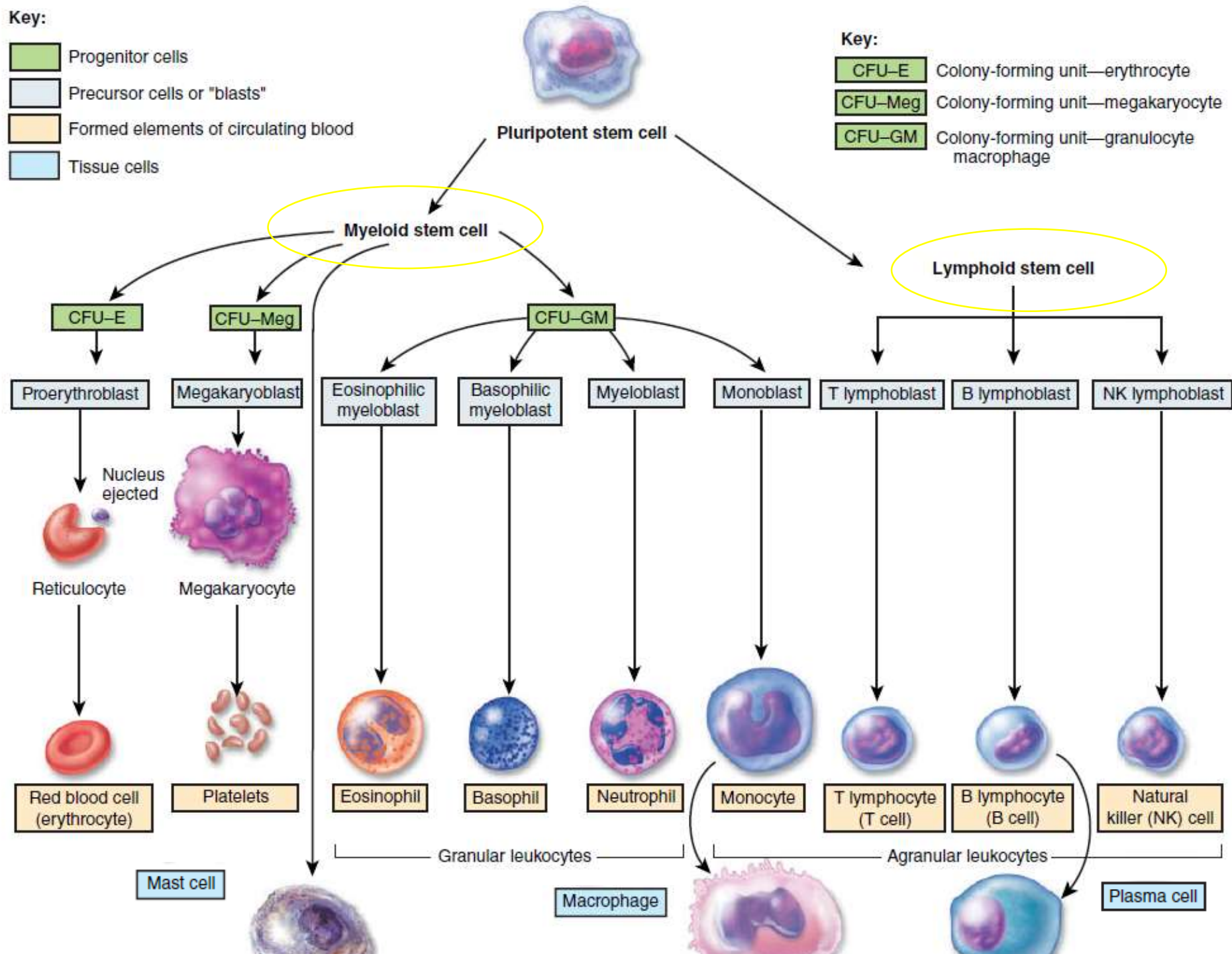


Key:

- Progenitor cells
- Precursor cells or "blasts"
- Formed elements of circulating blood
- Tissue cells

Key:

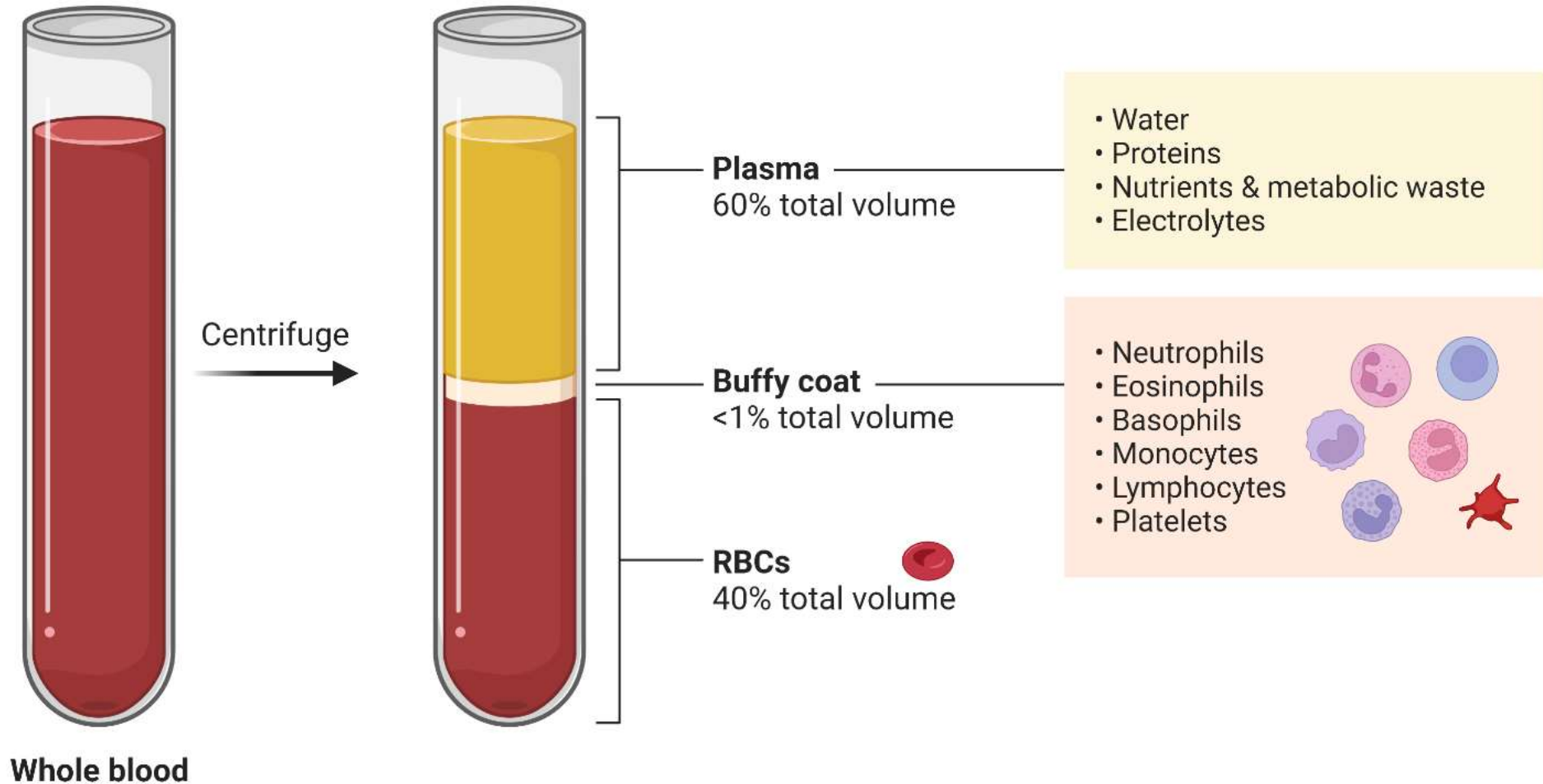
- CFU-E Colony-forming unit—erythrocyte
- CFU-Meg Colony-forming unit—megakaryocyte
- CFU-GM Colony-forming unit—granulocyte macrophage



- ✓ **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

- **Stem cells in bone marrow**
 - Reproduce themselves
 - Proliferate and differentiate
- **Formed elements do not divide once they leave red bone marrow**
 - Exception is lymphocytes

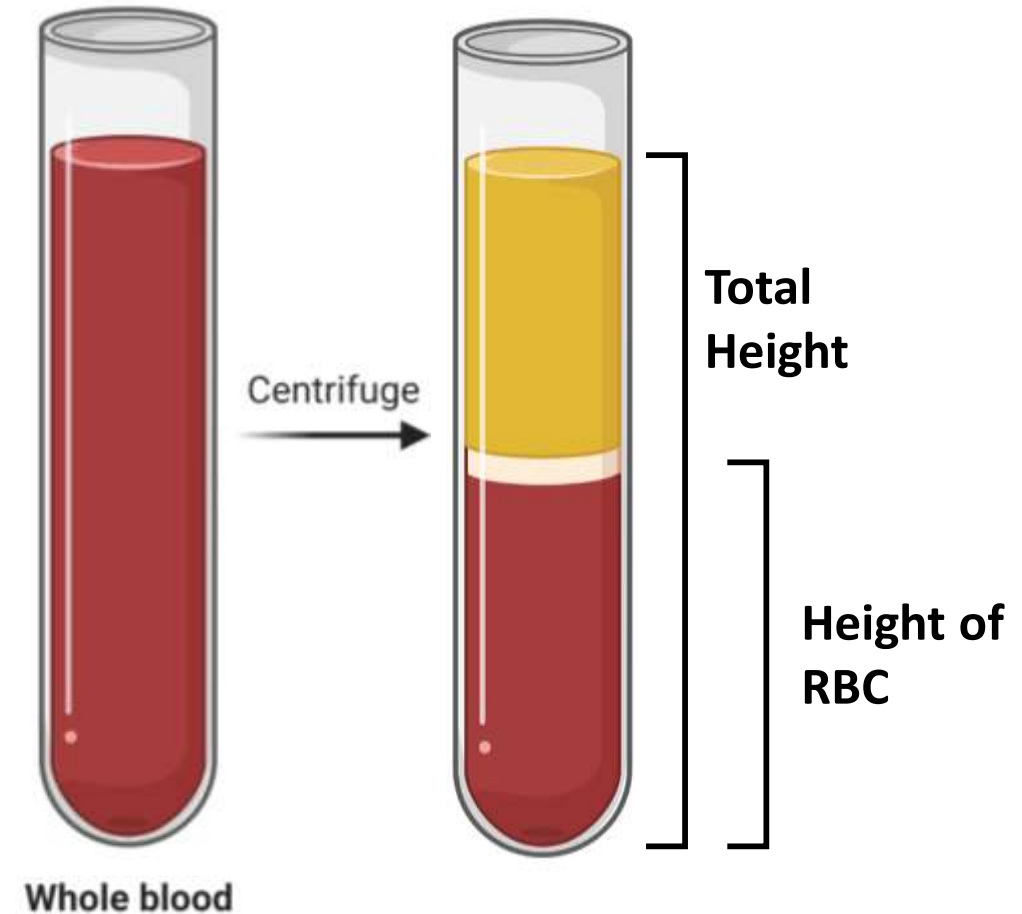
- **Growth inducers:** regulate growth and reproduction of the different stem. One of the growth inducers is **interleukin-3**, promotes growth and reproduction of virtually all the different types of committed progenitor cells. (**GM-CSF**, **G-CSF**, and **M-CSF**)
- **Differentiation inducers:** Each of these differentiation inducers causes one type of committed stem cell to differentiate one or more steps toward a final adult blood cell.
- Others: **Erythropoietin** – RBCs, **Thrombopoietin** – platelets
- **Signals from outside the marrow match production to the body's needs**



- **Hematocrit/ Packed Red Cell Volume**
- Adult males: 40–54% (avg = 45%).
- Adult females: 38–46% (avg = 42%)

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

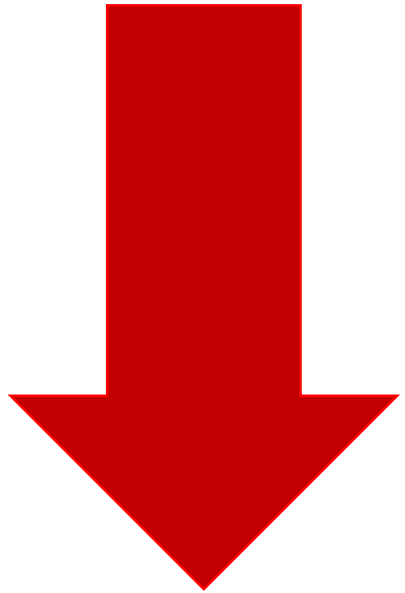
Ratio!!



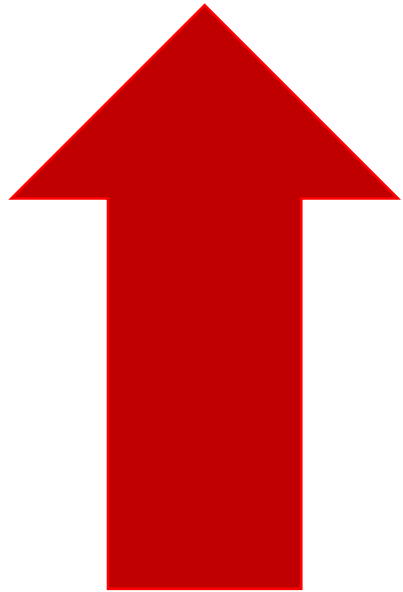
Hematology

Hematocrit

Polycythemia



Anemia

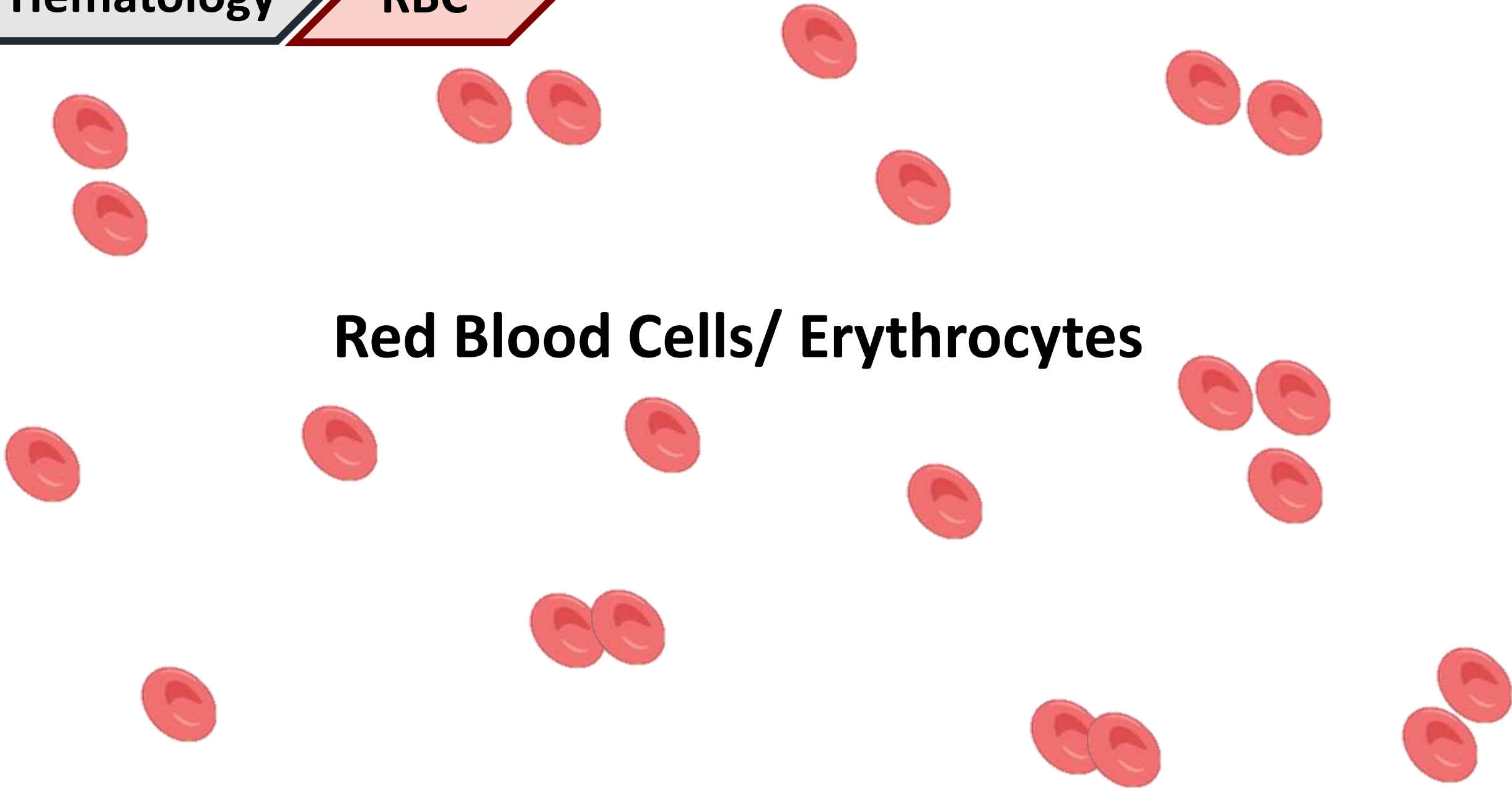


- * An increased hematocrit can reflect more RBCs.
- * It can also reflect less plasma.
- * Clinical interpretation must distinguish the two.

Hematology

RBC

Red Blood Cells/ Erythrocytes



RBC

RBC structure supports function

- Biconcave disc. (thickness of 2.5 μm at the thickest point and 1 μm or less in the center)
- Diameter is normally 7-8 μm .
- Strong, flexible plasma membrane.
- Lack nucleus and mitochondria.
- Contain oxygen-carrying protein (hemoglobin).
- Key erythrocyte enzymes: glycolytic enzymes and carbonic anhydrase.

RBC

General characteristics

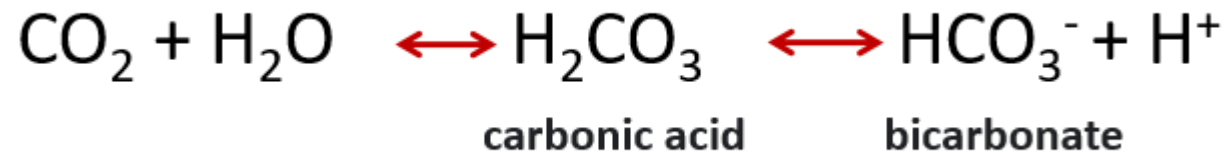
- Oligosaccharides in plasma membrane are responsible for ABO and Rh blood groups.
- 5,200,000/ μL in men; and 4,700,000/ μL in women.
- Production = destruction (2 million/ sec).

RBC

Function

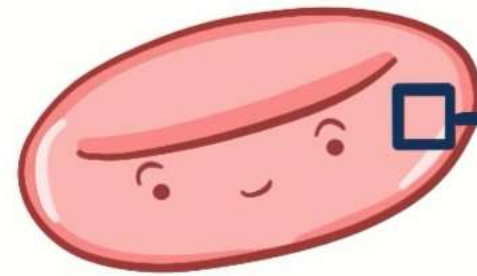
RBCs contribute to:

- **Oxygen transport** through hemoglobin.
- **Carbon dioxide transport**, including conversion of CO₂ to bicarbonate.
- **Acid–base buffering**, particularly through hemoglobin.



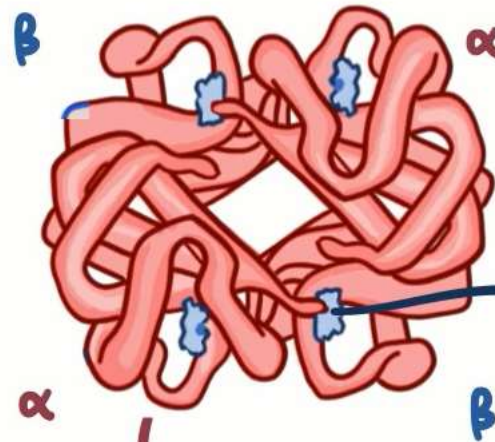
RBC

Hemoglobin



RED
BLOOD CELL

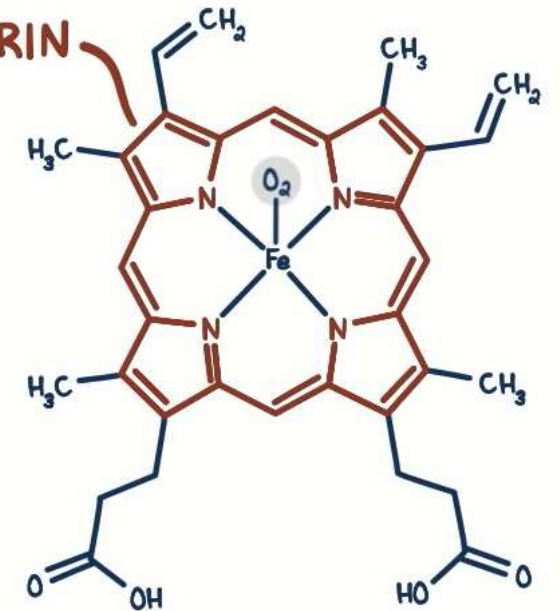
HEMOGLOBIN



GLOBIN

HEME

PORPHYRIN



RBC

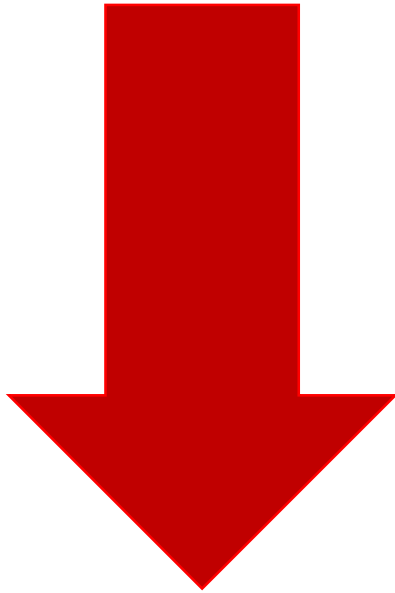
Hemoglobin

- 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).

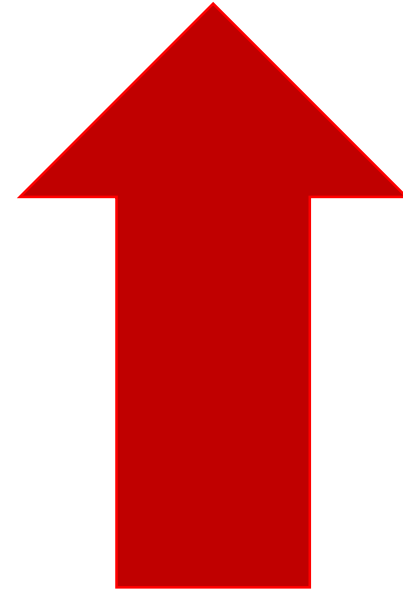
RBC

Hemoglobin

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



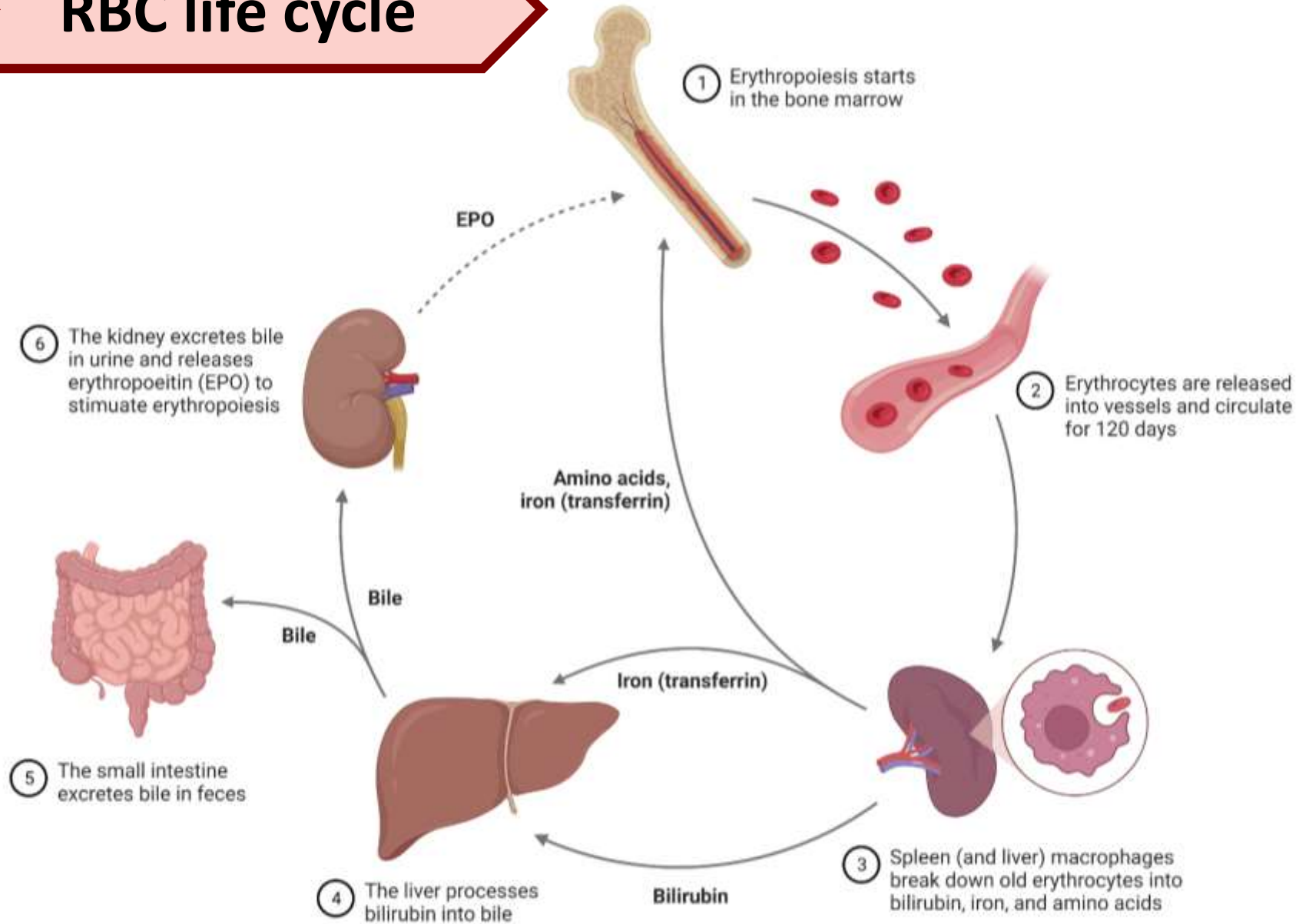
Anemia

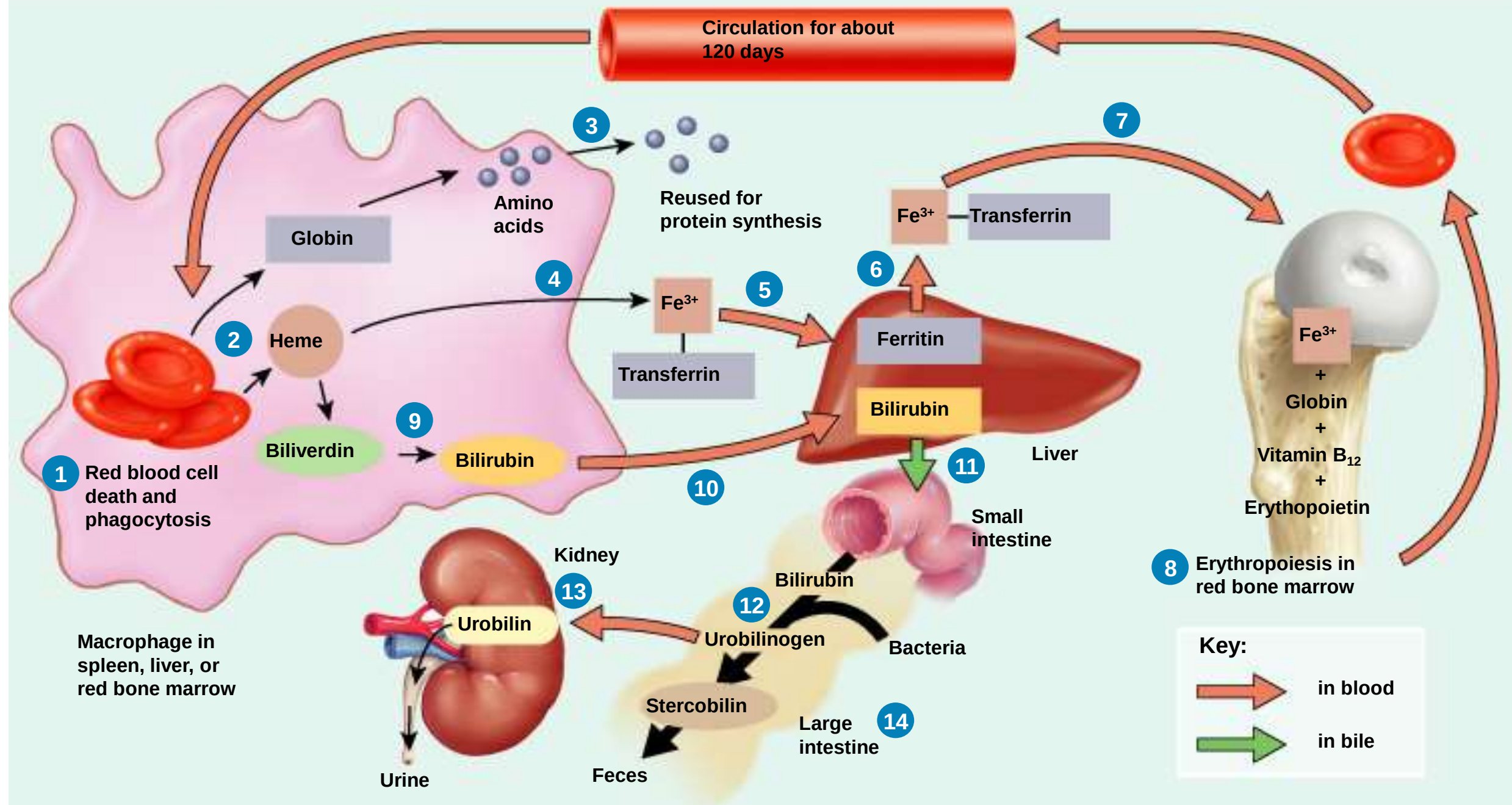


polycythemia

RBC

RBC life cycle





RBC

RBC life cycle

What happens to RBC components?

Component	Main fate
Globin	Breakdown to amino acids for reuse
Iron	Recovery and reuse in erythropoiesis or storage
Heme pigment remainder	Conversion to bilirubin and hepatic processing
Cell membrane	Macrophage degradation and recycling

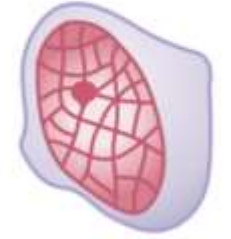
RBC

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.

Genesis of RBCs

Proerythroblast



Basophil erythroblast



Polychromatophil erythroblast



Orthochromatic erythroblast



Nucleus exocytosis

Reticulocyte



Erythrocytes



How much production maintains the pool?

$$5 \times 10^6 \text{ RBCs}/\mu\text{L} \times 5 \times 10^6 \mu\text{L blood}$$

$$\approx 25 \times 10^{12} \text{ circulating RBCs}$$

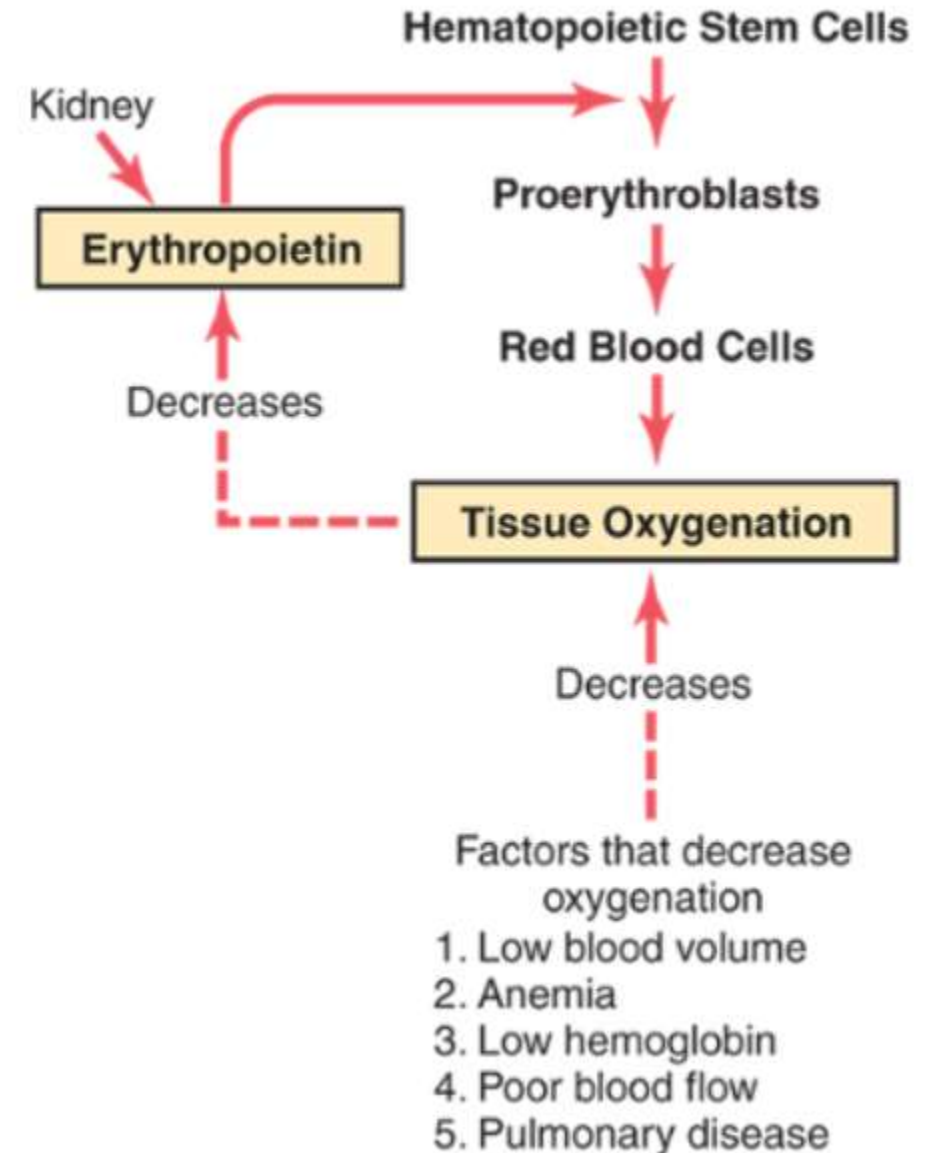
$$25 \times 10^{12} \div 120 \text{ days} \div 86,400 \text{ seconds/day}$$

$$\approx 2.4 \text{ million RBCs replaced each second}$$
$$\approx 208 \text{ billion RBCs/day}$$

A large circulating population requires continuous renewal.

- EPO 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.
- Negative feedback balances production with destruction.

- 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



What stimulates the EPO response?

- **Anemia or blood loss:** less hemoglobin available to carry oxygen.
- **Low blood oxygen:** for example, at high altitude or with lung disease.
- **Reduced kidney blood flow:** less oxygen delivered to kidney tissue.

The shared signal is inadequate oxygen availability to renal tissue.

RBC

Vitamins requirement

- Maturation of red blood cells requires vitamin B₁₂ (Cyanocobalamin) and folic acid.
- Both of these are essential for the synthesis of DNA (formation of thymidine triphosphate).
- lack of either vitamin B₁₂ or folic acid causes: abnormal and diminished DNA → failure of nuclear maturation and cell division → production of larger red cells called **macrocytes**, the cell itself has a flimsy irregular membrane → short life span

Proerythroblast



Nucleus
exocytosis



Reticulocyte



Erythrocytes



Check your understanding

Which finding best fits untreated B12-related maturation failure?

- A. High effective RBC output despite anemia
- B. Inadequate reticulocyte response with abnormal large RBCs
- C. Isolated loss of plasma volume
- D. Immediate normalization of RBC mass after EPO rises

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

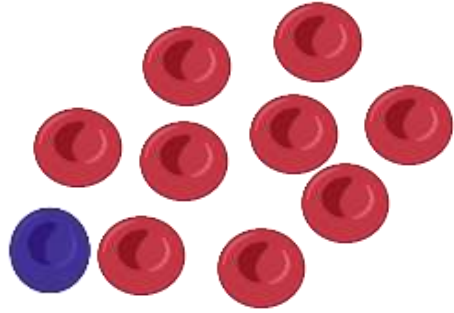
Aplastic anemia

Increased

Hemolytic anemia
Post hemorrhage

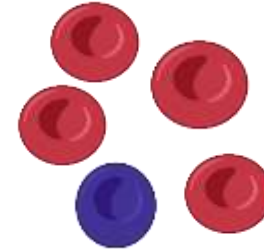
RBC

Corrected Reticulocyte count



Retic = 1%

Hct = 45



Retic = 2%

Hct = 22.5

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

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

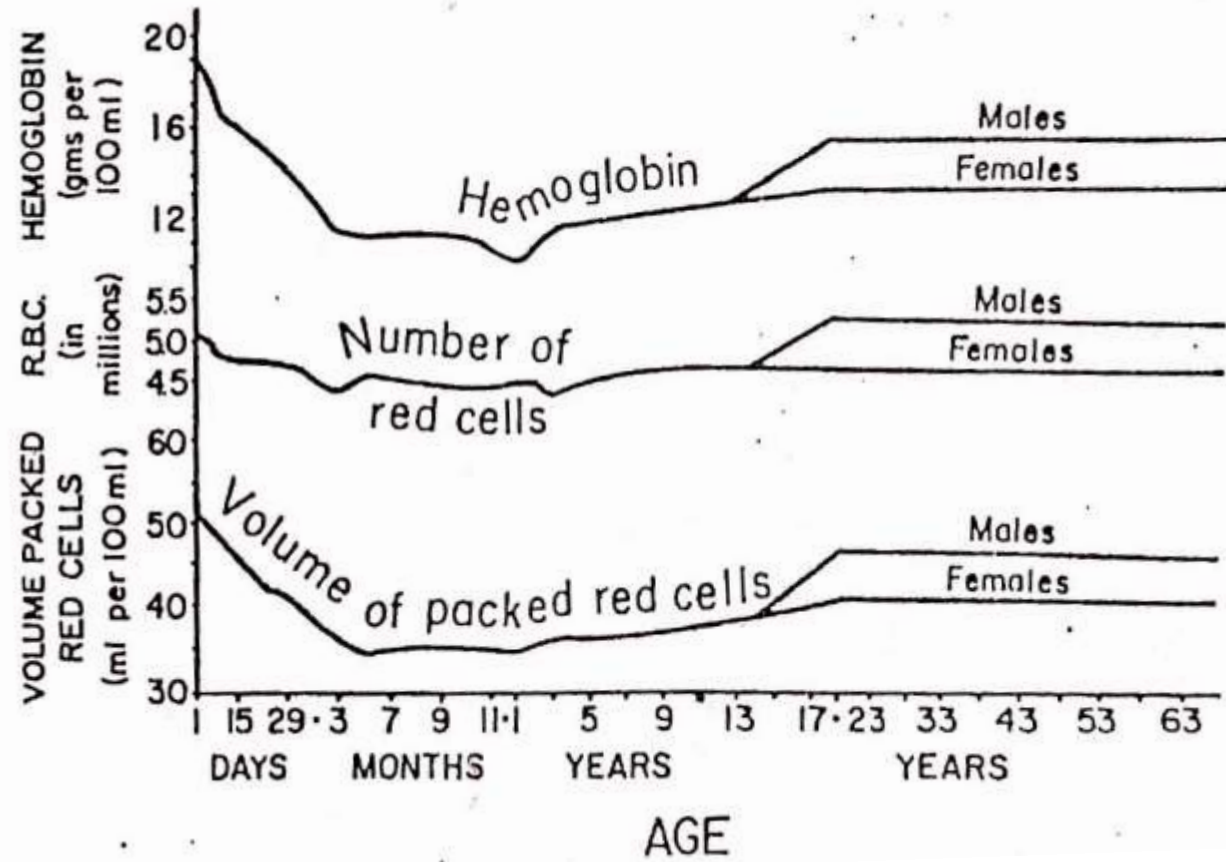
= 1%

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

= 1%

RBC

RBCs parameters



RBC

RBCs parameters

RBC count ($10^6/\mu\text{L}$ 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 (%)

RBC

RBCs parameters

RBC count

- **RBC count: the number of cells**
- This is the number of RBCs in **one microliter of whole blood**.
- For example, **$5 \times 10^6/\mu\text{L}$** means **5 million RBCs per microliter**.

RBC

RBCs parameters

MCV

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:

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



**Macrocytic
(>100)**



**Normocytic
(80-100)**

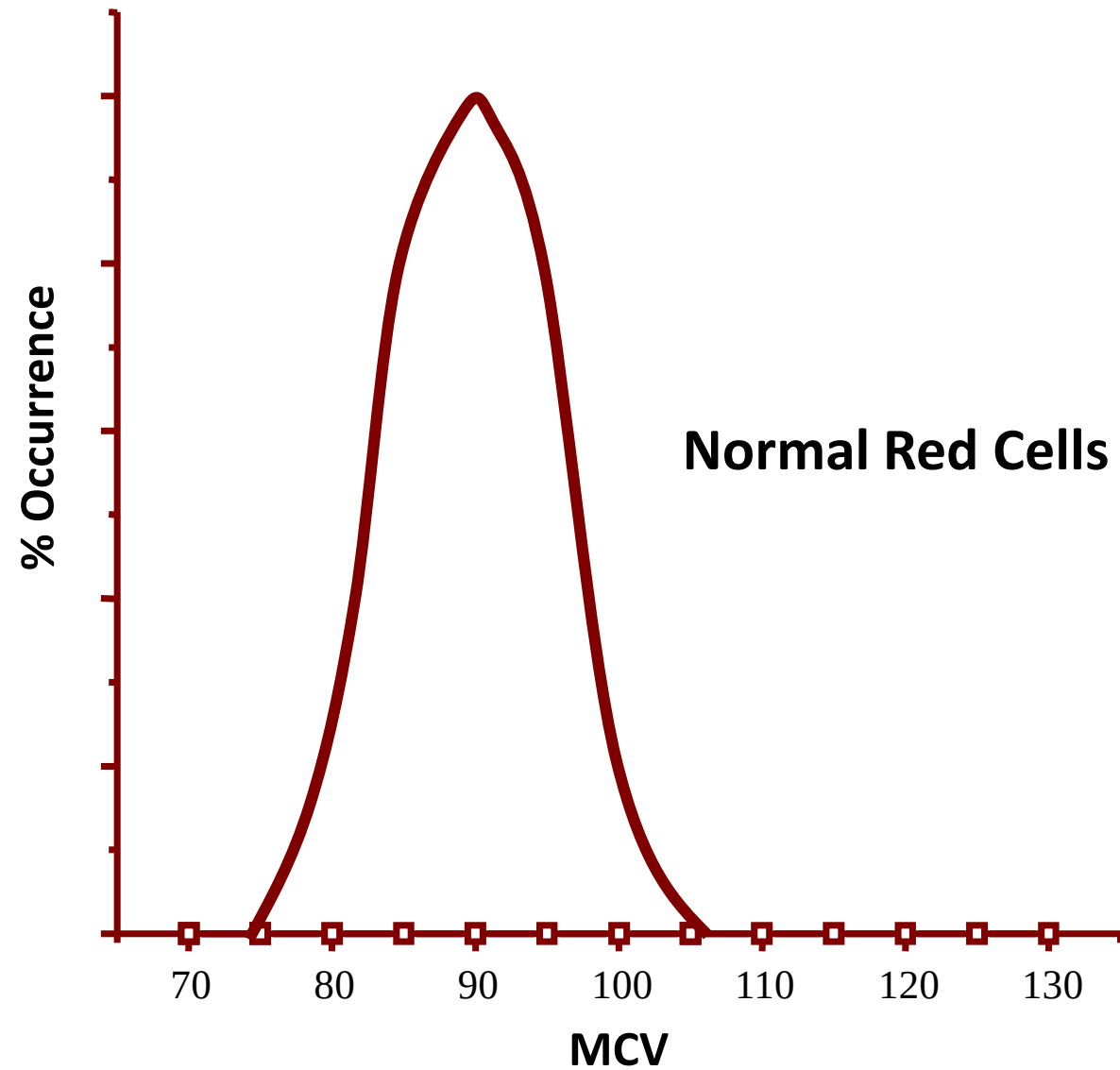


**Microcytic
(<80)**

RBC

RBCs parameters

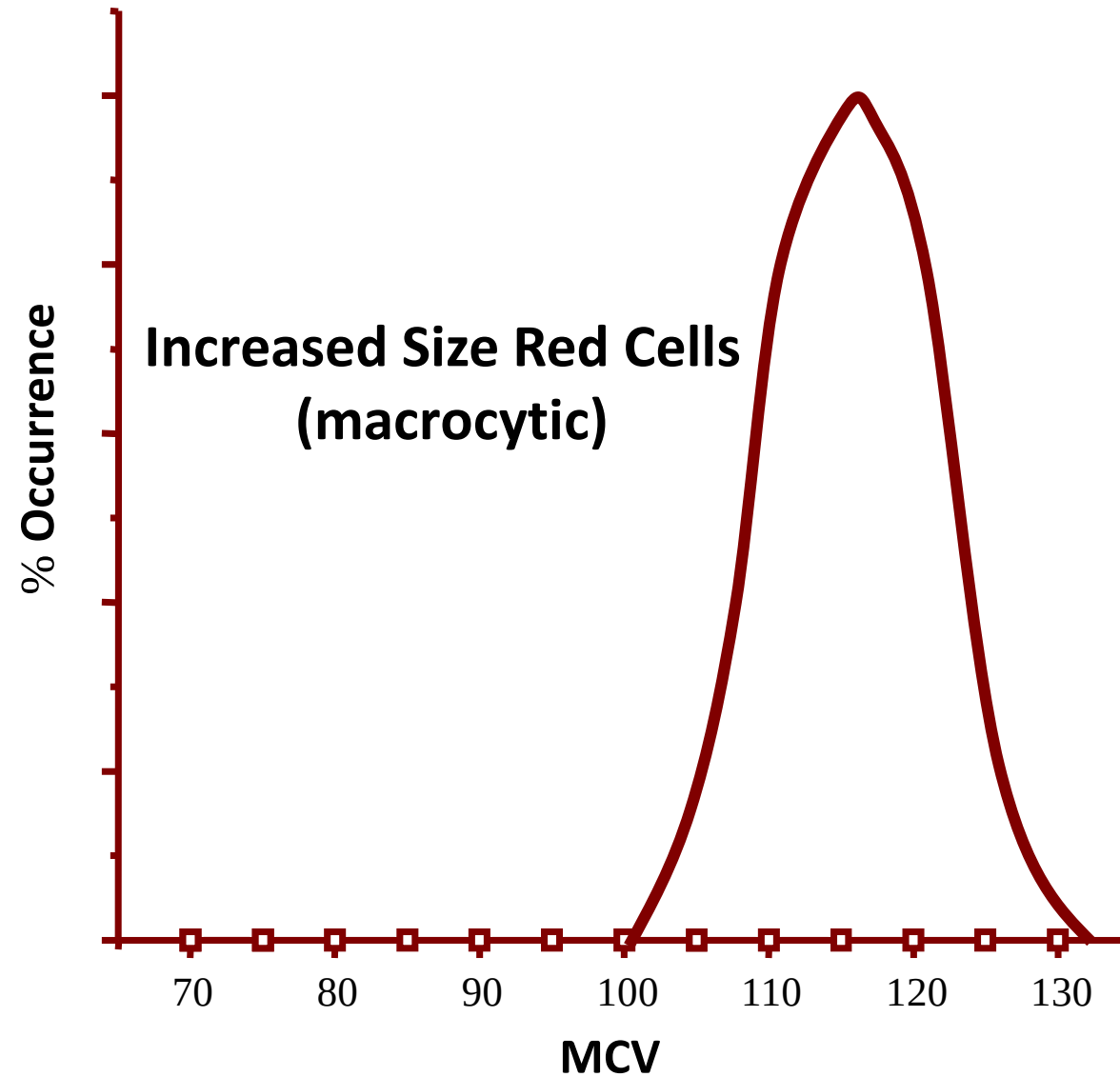
Distribution of RBCs sizes



RBC

RBCs parameters

Distribution of RBCs sizes

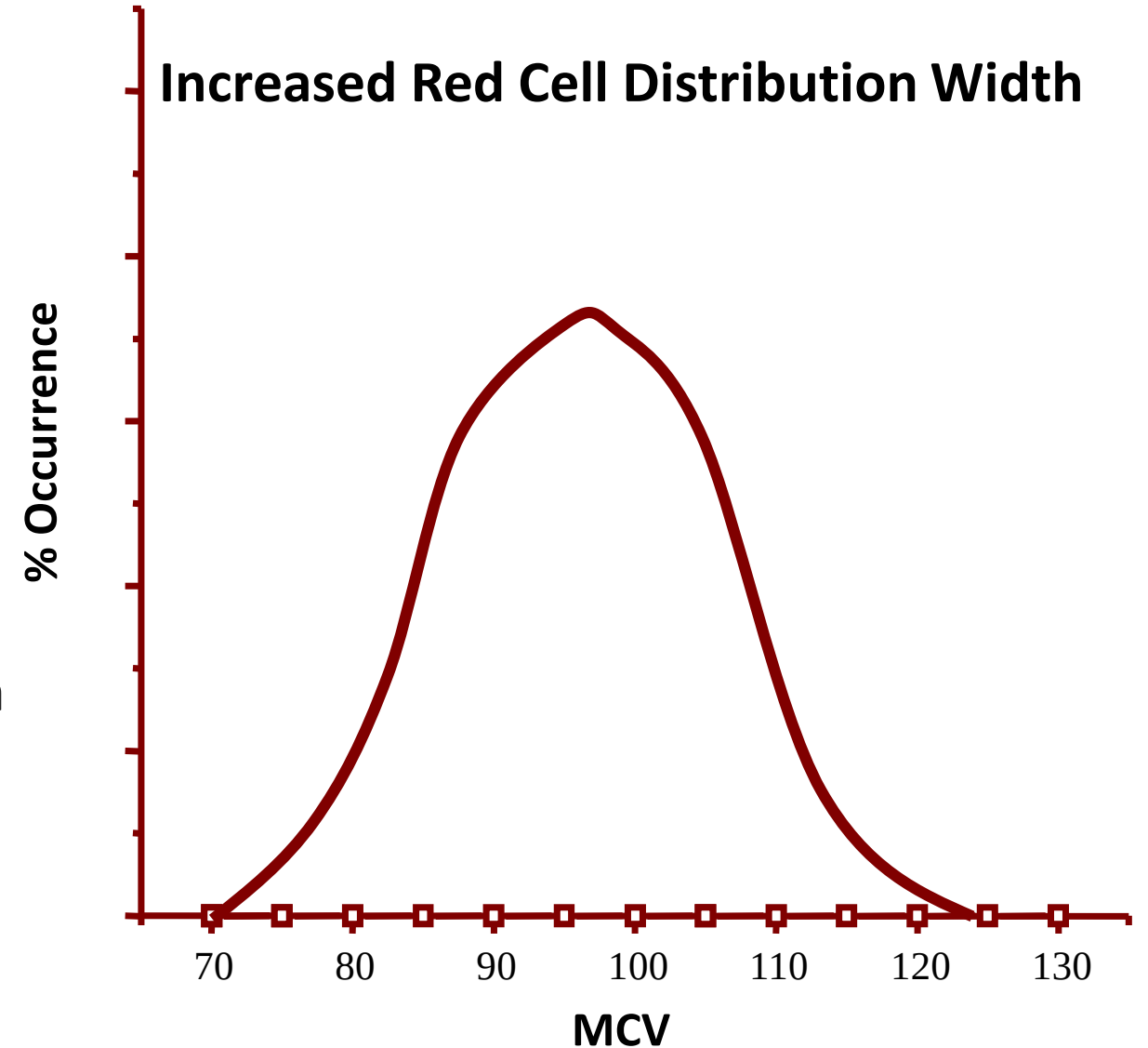


RBC

RBCs parameters

Red cell Distribution Width (RDW)

- Measurement of RBC size variation (anisocytosis).
- $RDW = [\text{standard deviation}/MCV] \times 100$.
- High RDW $\rightarrow$ large variation in RBC sizes
- Normal RDW $\rightarrow$ more homogeneous population of RBCs.
- A high RDW can be seen in a number of anemias, including iron deficiency, vitamin B12 or folate deficiency.



RBC

RBCs parameters

MCH

Mean cell hemoglobin concentration (pg/ cell)

- Is the average hemoglobin content in a RBC.

$$= \frac{\text{Hemoglobin [g/dL]} \times 10}{\text{RBC count [in millions}/\mu\text{L}]}$$

- 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)**

RBC

RBCs parameters

MCHC

Mean cell hemoglobin concentration (g/dL RBC)

- Is the average hemoglobin concentration per RBC.
- expresses the amount of hemoglobin **relative to the volume of RBCs**

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



**Normochromic
(30-36)**



**Hypochromic
(<30)**

RBC

RBCs parameters

Hb = 8 g/dL

Hct = 28%

RBC count = 4 million/ μ L

$$\text{MCV} = \frac{\text{Hct} \times 10}{\text{RBC count}} = \frac{28 \times 10}{4} = 70 \text{ fL}$$

Small RBCs — microcytic

$$\text{MCH} = \frac{\text{Hb} \times 10}{\text{RBC count}} = \frac{8 \times 10}{4} = 20 \text{ pg}$$

Reduced hemoglobin amount per RBC

$$\text{MCHC} = \frac{\text{Hb} \times 100}{\text{Hct}} = \frac{8 \times 100}{28} = 28.6 \text{ g/dL}$$

Reduced hemoglobin concentration — hypochromic

RBC

Anemia

Anemia

Production

Destruction

- *Less EPO
- * BM damage
- *Iron deficiency

- * Blood loss
- *Hemolysis

Low RI

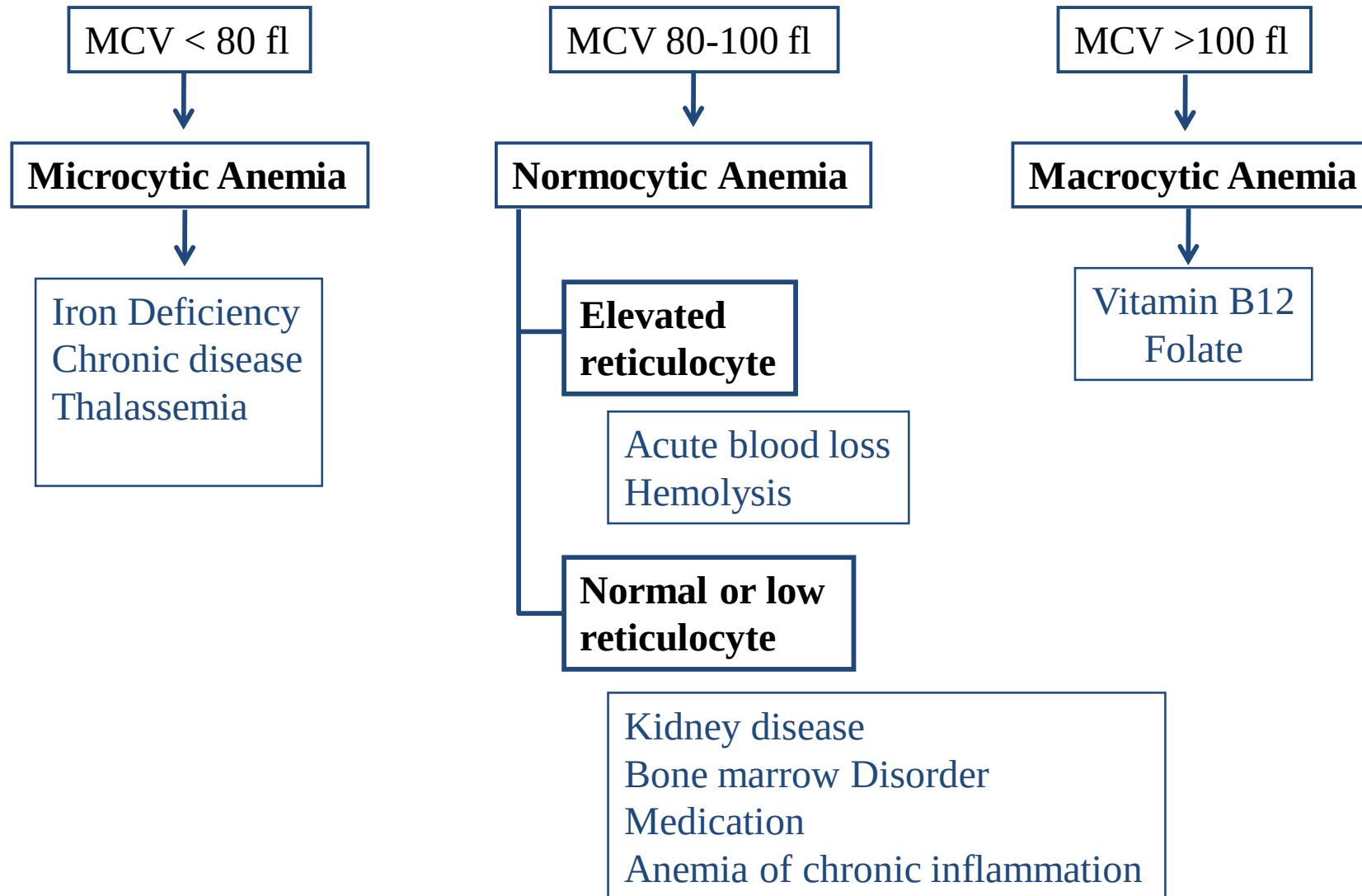
High RI



RBC

Anemia classification

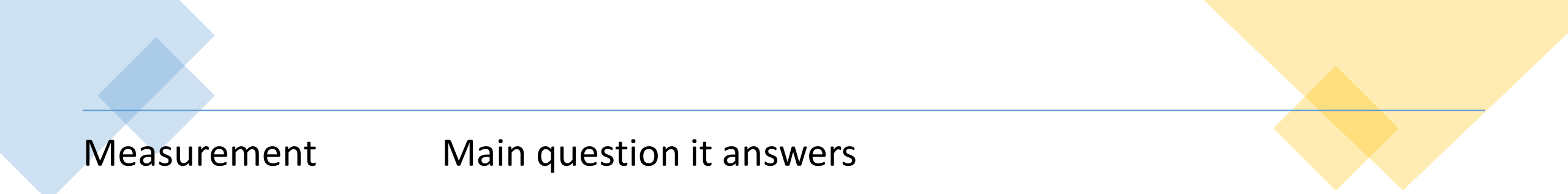
Anemia confirmed by low hemoglobin → classify by MCV



RBC

Anemia classification

(MCV)	(MCHC)	Typical causes
Normocytic	Usually normochromic	Chronic kidney disease, anemia of chronic inflammation, acute blood loss, many hemolytic anemias, marrow failure
Macrocytic	Usually normochromic	Vitamin B12 or folate deficiency; also liver disease, alcohol use, certain medications
Microcytic	Often hypochromic	Iron deficiency, thalassemia, sometimes anemia of chronic inflammation



Measurement

Main question it answers

RBC count

How many red cells are present?

Hematocrit (Hct)

How much of the blood's volume is occupied by RBCs?

Hemoglobin (Hb)

How much hemoglobin is present in whole blood?

MCV

How large is the average RBC?

MCH

How much hemoglobin is in the average RBC?

MCHC

How concentrated is hemoglobin inside the RBCs?

RDW

How much do RBC sizes differ from one another?



In anemia, each milliliter of blood carries less oxygen, so the body compensates by circulating more blood per minute. This increases the heart's workload

$$\text{Oxygen delivery} = \text{Cardiac output} \times \text{Blood oxygen content}$$

Change in anemia	Effect on circulation
Lower hematocrit → lower blood viscosity	Blood flows more easily, reducing resistance in the circulation.
Reduced oxygen delivery → tissue arterioles dilate	Wider vessels further reduce resistance and allow more blood through the tissues.

This compensation can maintain adequate oxygen delivery **at rest**, despite the anemia.

Why does exercise become difficult?

Polycythemia means an increased concentration of RBCs in the blood. The higher hematocrit makes blood more viscous “thicker” and harder to move through blood vessels.

1. Cardiac output: two opposing effects

Change	Effect on blood returning to the heart
Increased viscosity	Increases resistance to flow → tends to decrease venous return
Increased blood volume, as can occur in polycythemia vera	Increases the pressure driving blood back to the heart → tends to increase venous return

2. Blood pressure: thicker blood does not automatically mean hypertension

Mean arterial pressure $\approx$ Cardiac output $\times$ Systemic vascular resistance

Higher viscosity tends to increase vascular resistance and therefore blood pressure. However, adjustments in vessel diameter, cardiac output, and fluid balance can compensate. **Hypertension develops when compensation is insufficient.**

Skin color: why it may look reddish or dusky

The **subpapillary venous plexus** is a network of small veins just beneath the skin's surface.

In polycythemia vera:

- More blood and hemoglobin in these vessels give the skin a **ruddy or reddish appearance**.
- Sluggish flow allows tissues to extract more oxygen from passing blood.
- The increased amount of **deoxygenated hemoglobin** can add a **dusky or bluish tinge**.