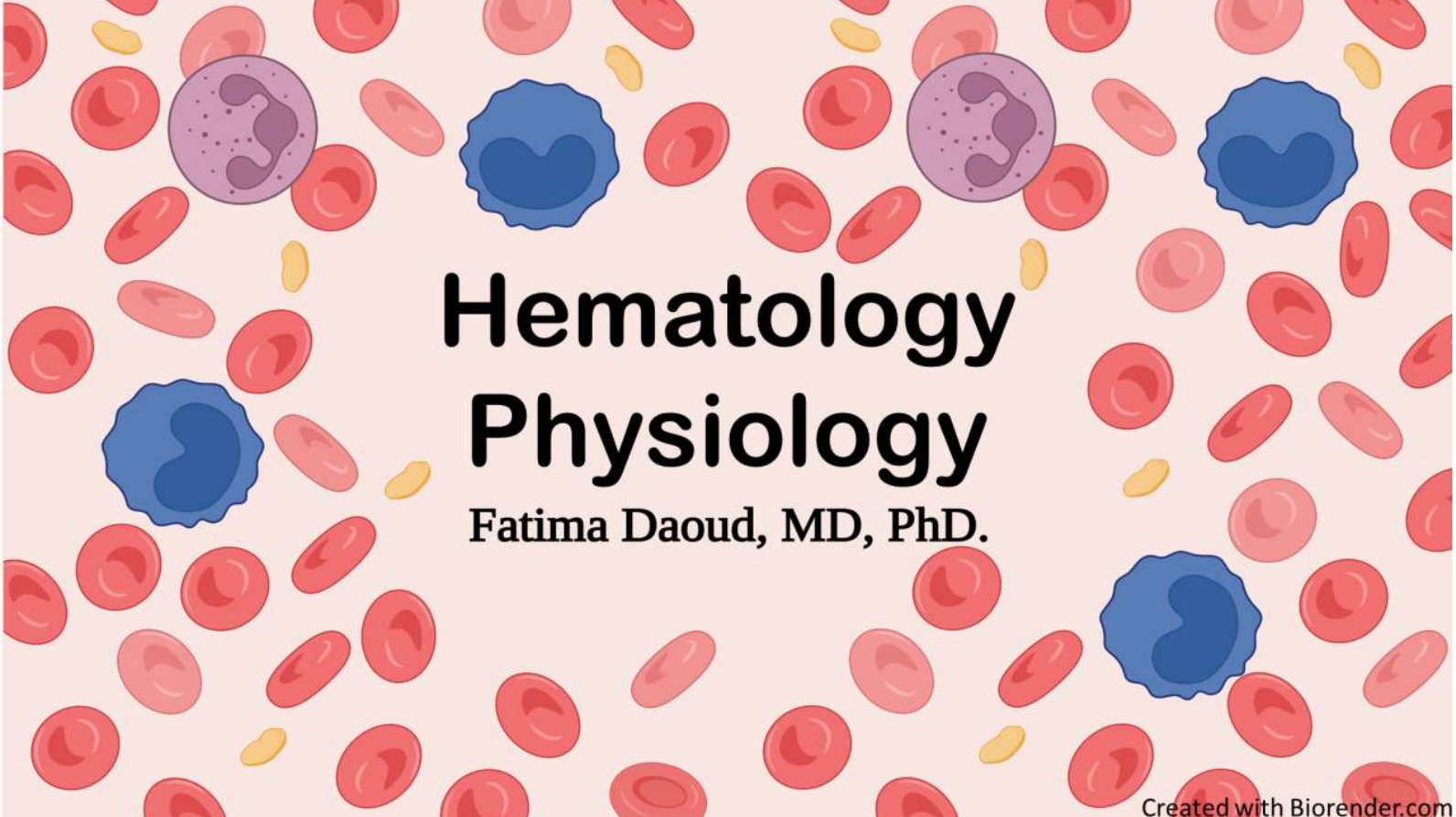
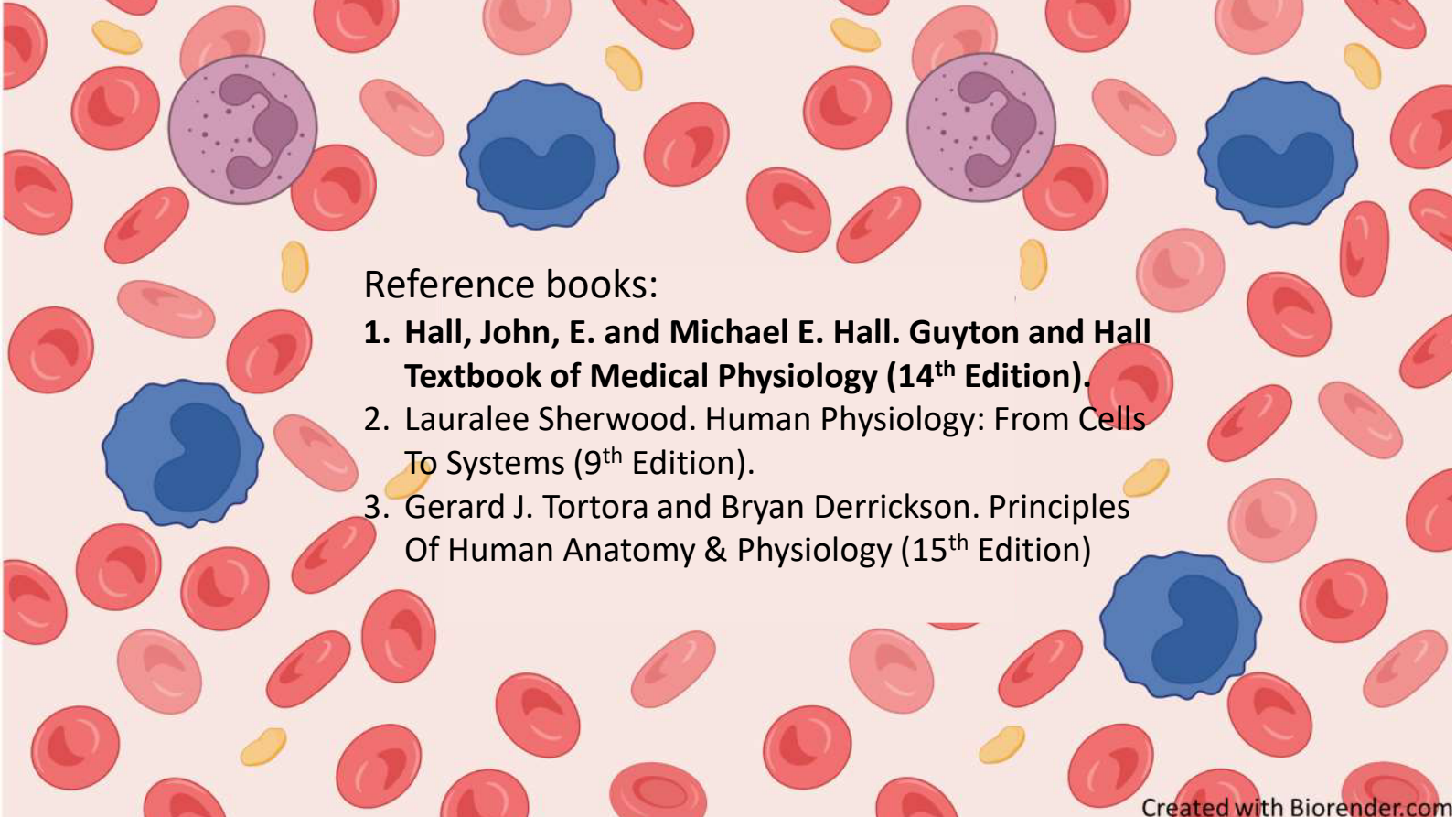

Hematology
Physiology
Fatima Daoud, MD, PhD.
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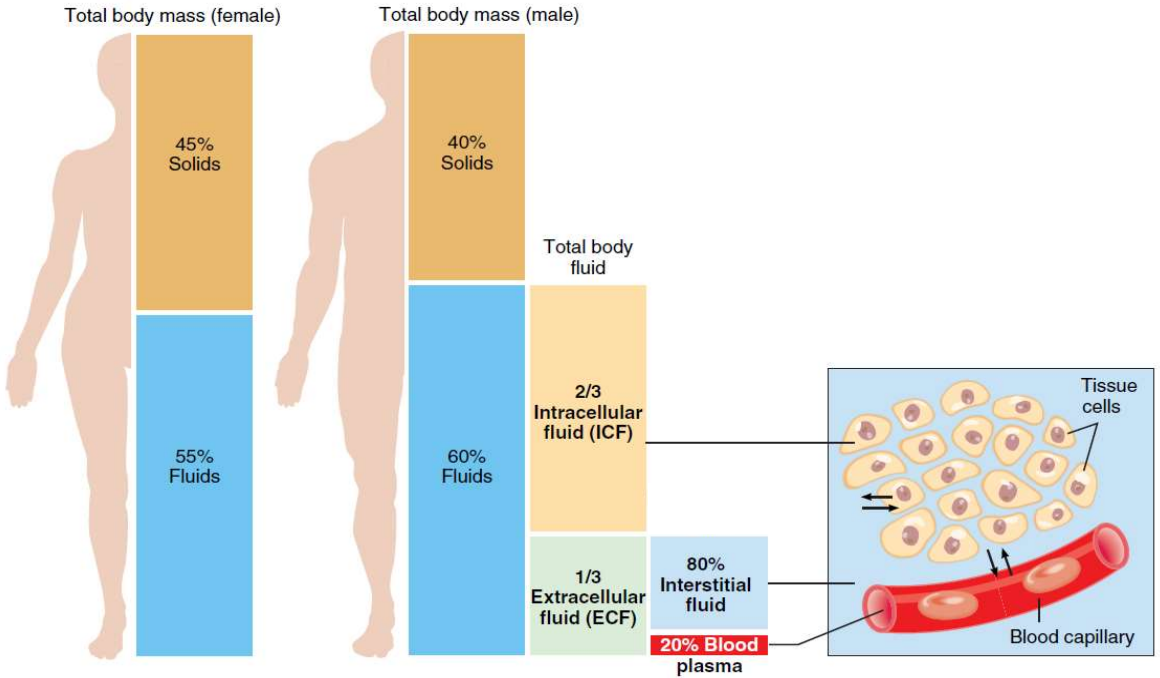


Reference books:

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)

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Hematology Body Fluids



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

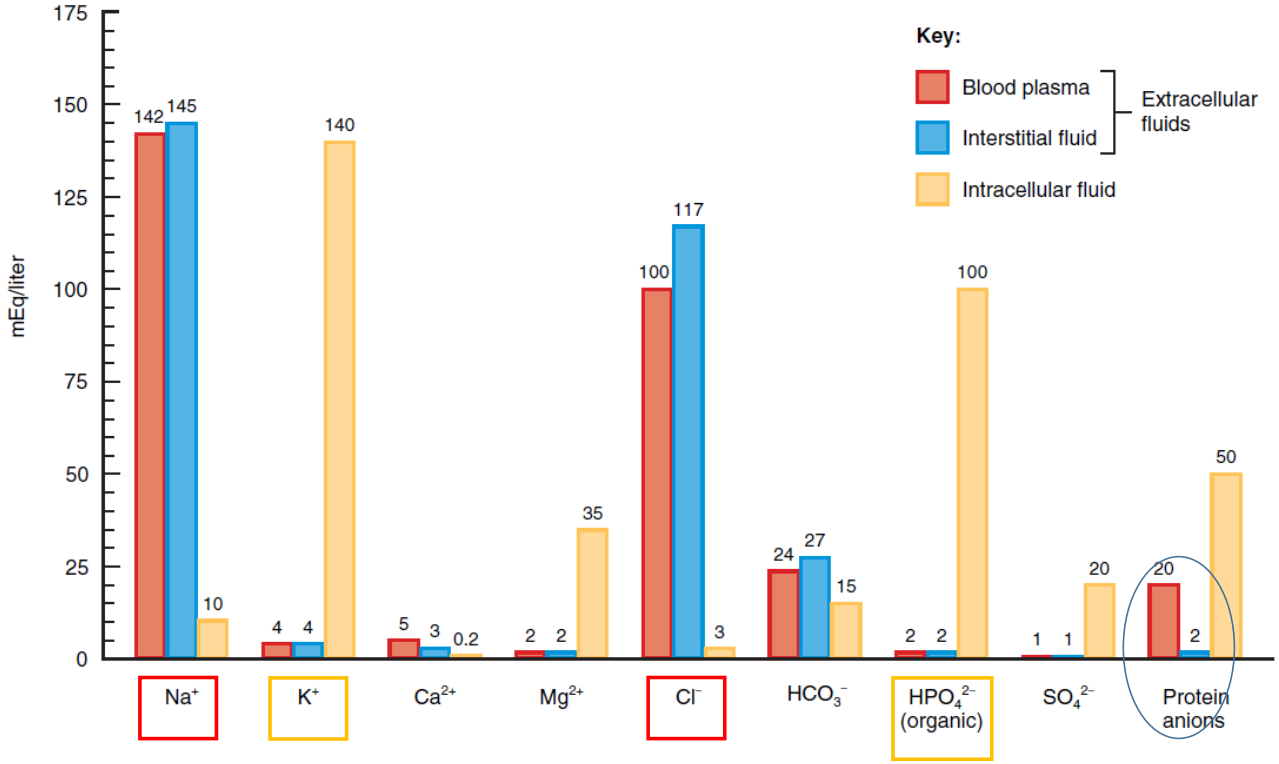
** About two-thirds of body fluid is **intracellular fluid (ICF).** The other third, called **extracellular fluid (ECF)** is outside cells.

** About 80% of the ECF is **interstitial fluid** and 20% of the ECF is **blood plasma**.

** Water content depends on age, gender, and the amount of adipose tissue present in the body.

** In the average 70-kg adult man, the total body water is about 60% of the body weight (42 L).

Hematology Body Fluids



**In extracellular fluid, the most abundant cation is Na^+, and the most abundant anion is Cl^-.
**In intracellular fluid, the most abundant cation is K^+, and the most abundant anions are proteins and phosphates.
** By actively transporting Na^+ out of cells and K^+ into cells, sodium–potassium pumps (Na^+–K^+ ATPases) play a major role in maintaining the high intracellular concentration of K^+ and high extracellular concentration of Na^+.
** The chief difference between the two extracellular fluids—blood plasma and interstitial fluid—is that blood plasma contains
many protein anions, in contrast to interstitial fluid, which has very few. Because normal capillary membranes are virtually impermeable to proteins, only a few plasma proteins leak out of blood vessels into the interstitial fluid.
This difference in protein concentration is largely responsible for the blood colloid osmotic pressure exerted by blood plasma.

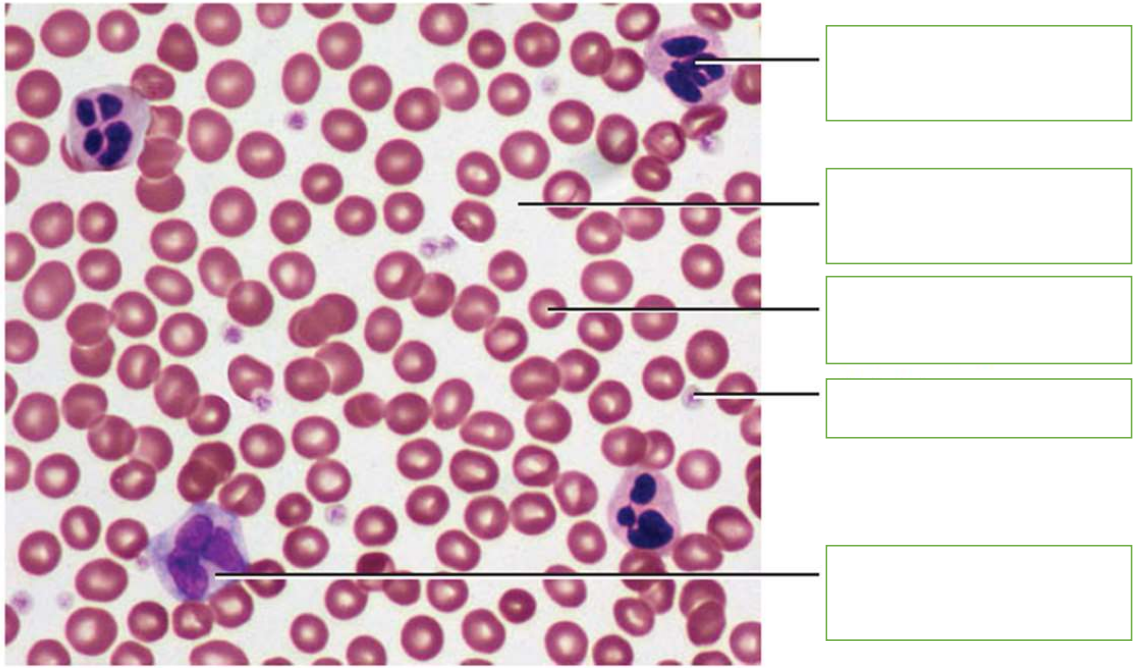
Hematology

Blood: general characteristics

- 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

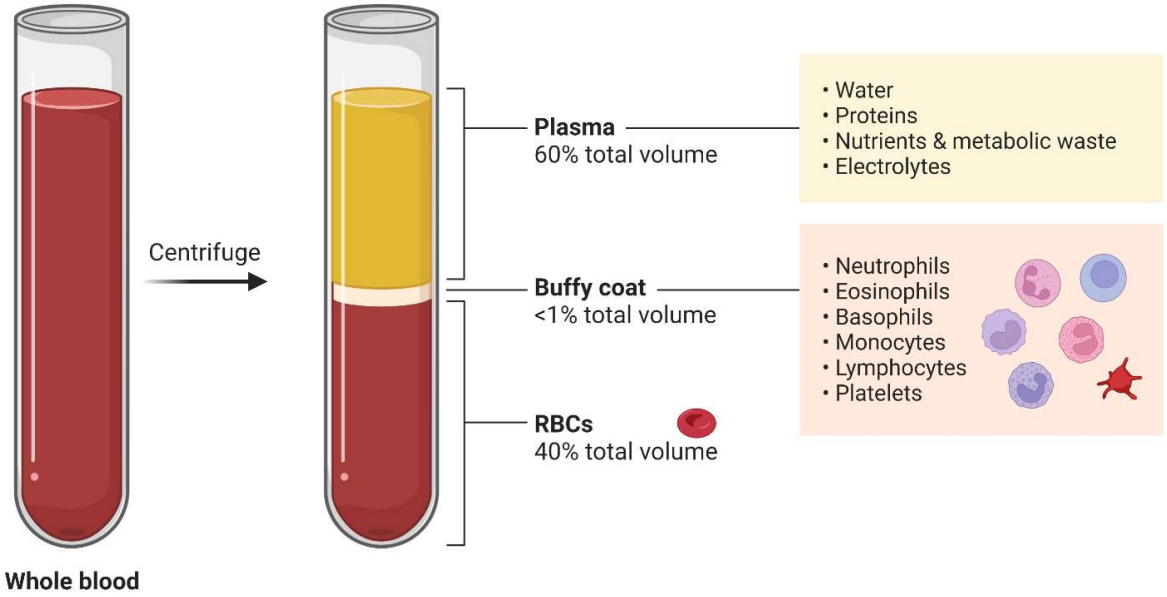
  unsaturated (O_2) → dark red

Blood volume varies with body size and physiological state. The approximate 5-L value is an orientation, not a universal normal value.



Hematology

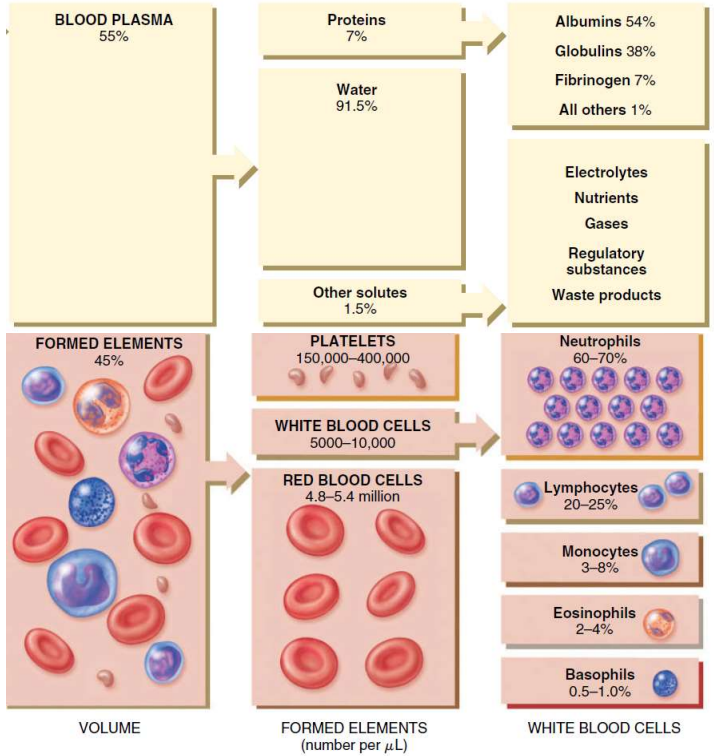
Blood and its components



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•The sample must contain an anticoagulant. Otherwise, clot formation changes what separates from the sample.

Blood and its components



•Whole blood = plasma + formed elements platelets are fragments derived from megakaryocytes, rather than complete nucleated cells.

Hematology | Plasma Protein

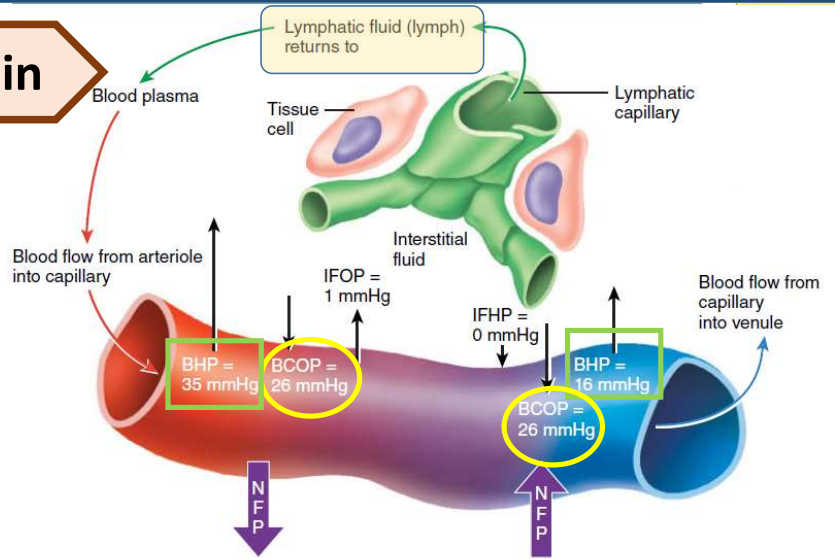
1. Establishment of colloid osmotic pressure.

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)



Albumin is the most abundant plasma protein.
Its osmotic effect helps retain water within the circulation.
Reduced plasma albumin lowers plasma oncotic pressure.
This can favor fluid accumulation in the interstitial space.

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.

Plasma proteins are synthesized by the liver, with the exception of antibodies, which are plasma cells derived from B lymphocytes

Principle roles of the blood

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

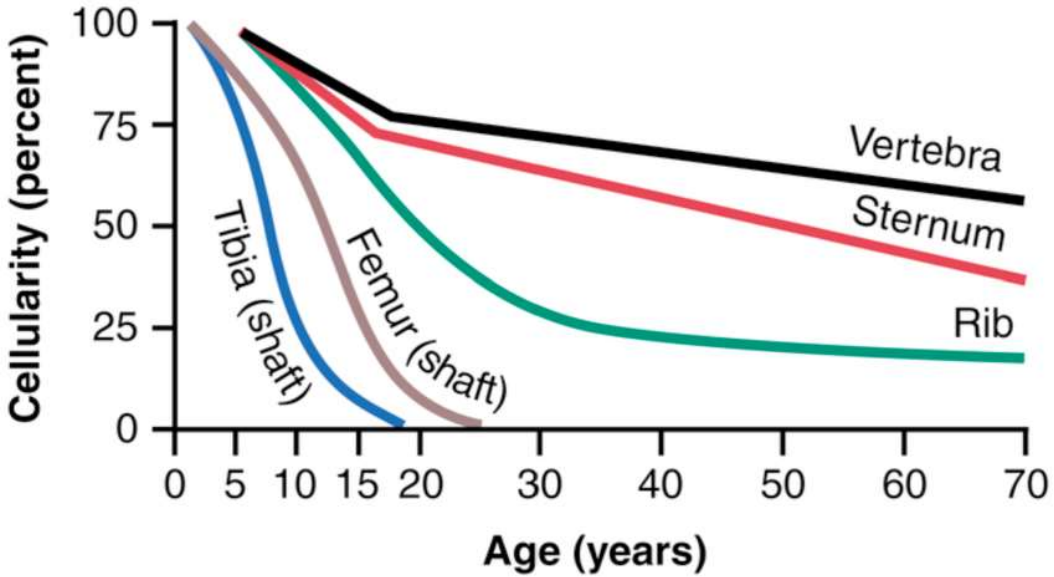
Hemopoiesis (formation of blood cells)

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.

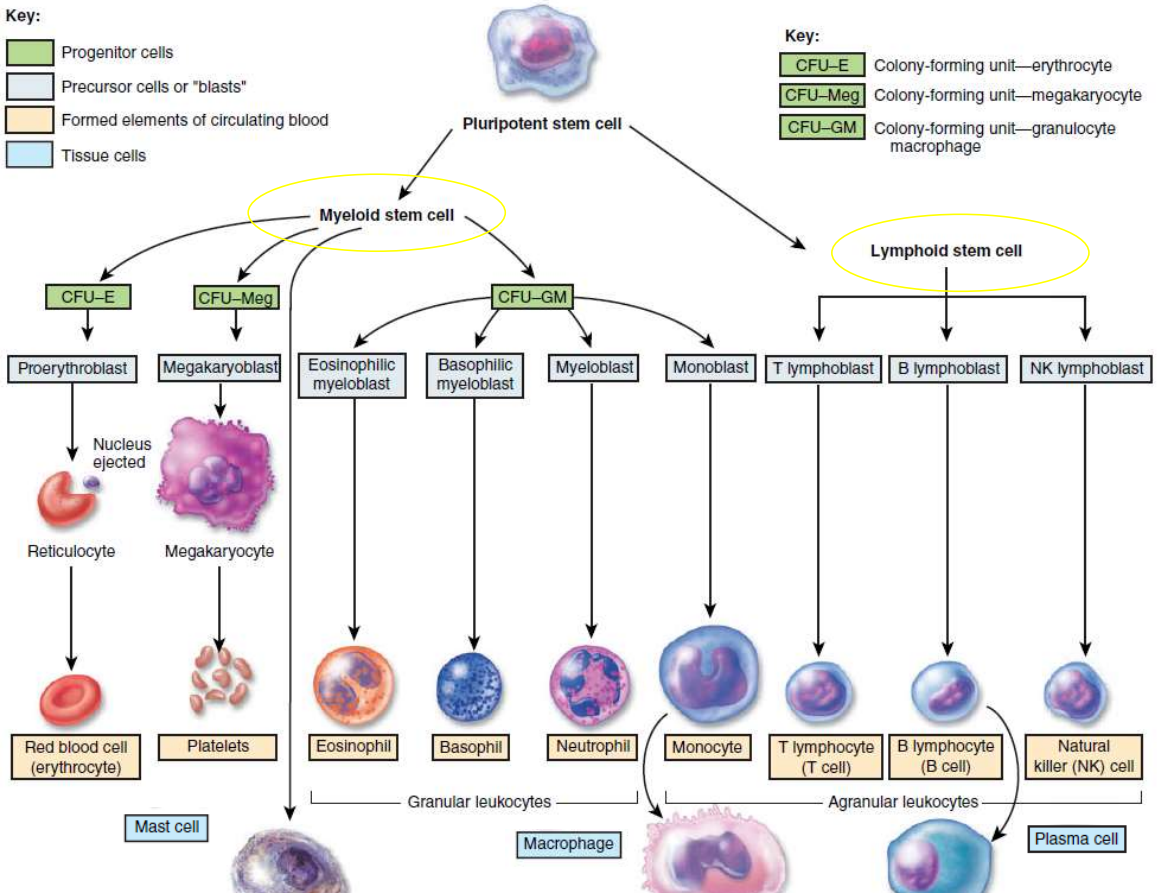
**In the early weeks of embryonic life, primitive nucleated RBCs are produced in the *yolk sac*.
**During the middle trimester of gestation, the *liver* is the main organ for RBC production but reasonable numbers are also produced in the *spleen* and *lymph nodes*.
** last month or so of gestation and after birth, RBCs are produced exclusively in the *bone marrow*.

Hematology

Hemopoiesis (formation of blood cells)



** the marrow of essentially all bones produces RBCs until a person is about 5 years old. The marrow of the long bones, except for the proximal portions of the humeri and tibiae, becomes fatty and produces no more RBCs after about the age of 20 years.
**Beyond 20, most RBCs continue to be produced in the marrow of the membranous bones, such as the vertebrae, sternum, ribs, and ilia.
**Bone marrow becomes less productive as age increases.



**pluripotent hematopoietic stem cells: constitute a population of adult stem cells found in bone marrow that are able to self-renew (their numbers diminish with age)
**The intermediate-stage cells are very much like the pluripotential stem cells, even though they have already become committed to a particular line of cells and are called committed progenitor cells *(CFU)*. The different committed progenitor cells, when grown in culture, will produce colonies of specific types of blood cells.

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

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

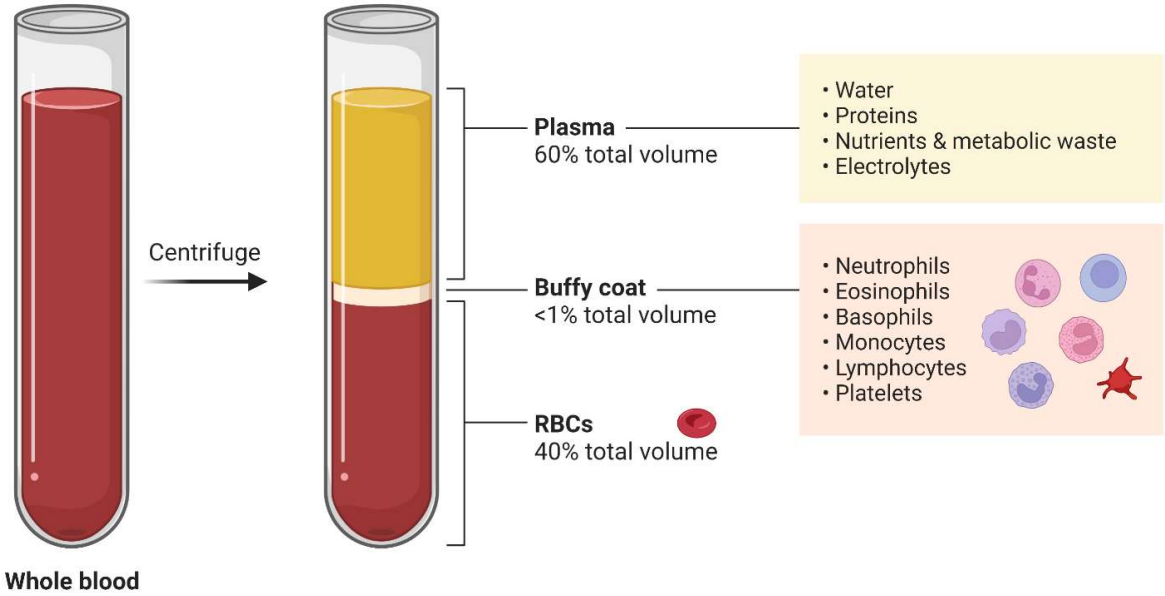
Hemopoiesis (Regulation)

- **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**

Body's need: Reduced oxygen availability in tissues, Infection

Hematology

Packed Red Cell Volume



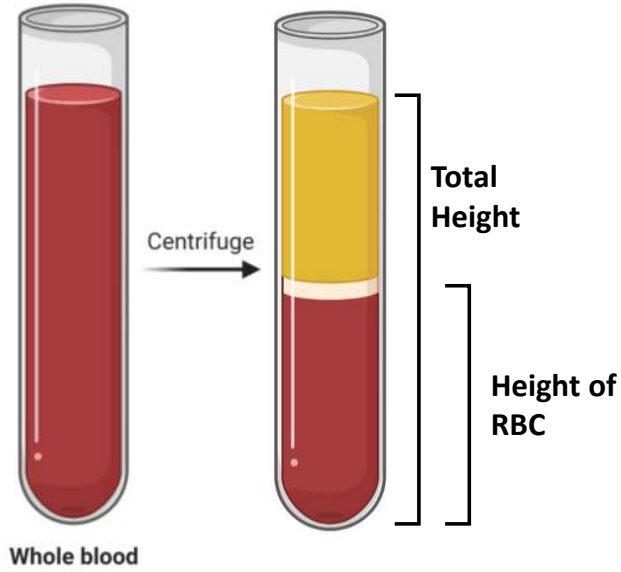
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Hematology > Hematocrit

- **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!!



Chapter 18, Boron Medical Physiology (3rd Edition)

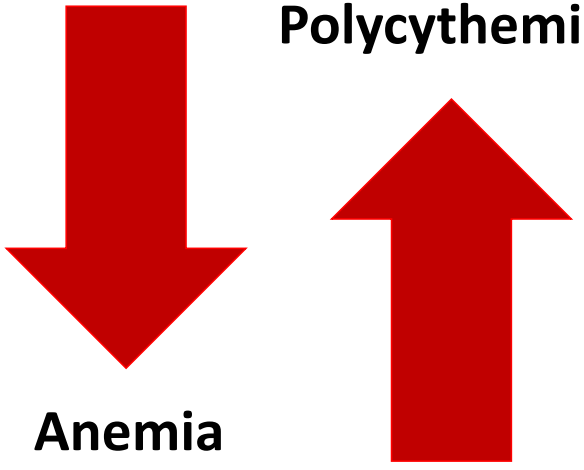
**The hematocrit is the fraction of the blood composed of red blood cells, as determined by centrifuging blood in a "hematocrit tube" until the cells become tightly packed in the bottom of the tube.

**Hematocrit measures a volume fraction. It does not directly measure the total number of RBCs in the body.

** **Hematocrit depends on both RBC volume and plasma volume.**

** HCT values are slightly less than PCV because there is no trapped plasma in an automated hematocrit calculation, as can occur with spun, packed cell values.

Hematology > Hematocrit

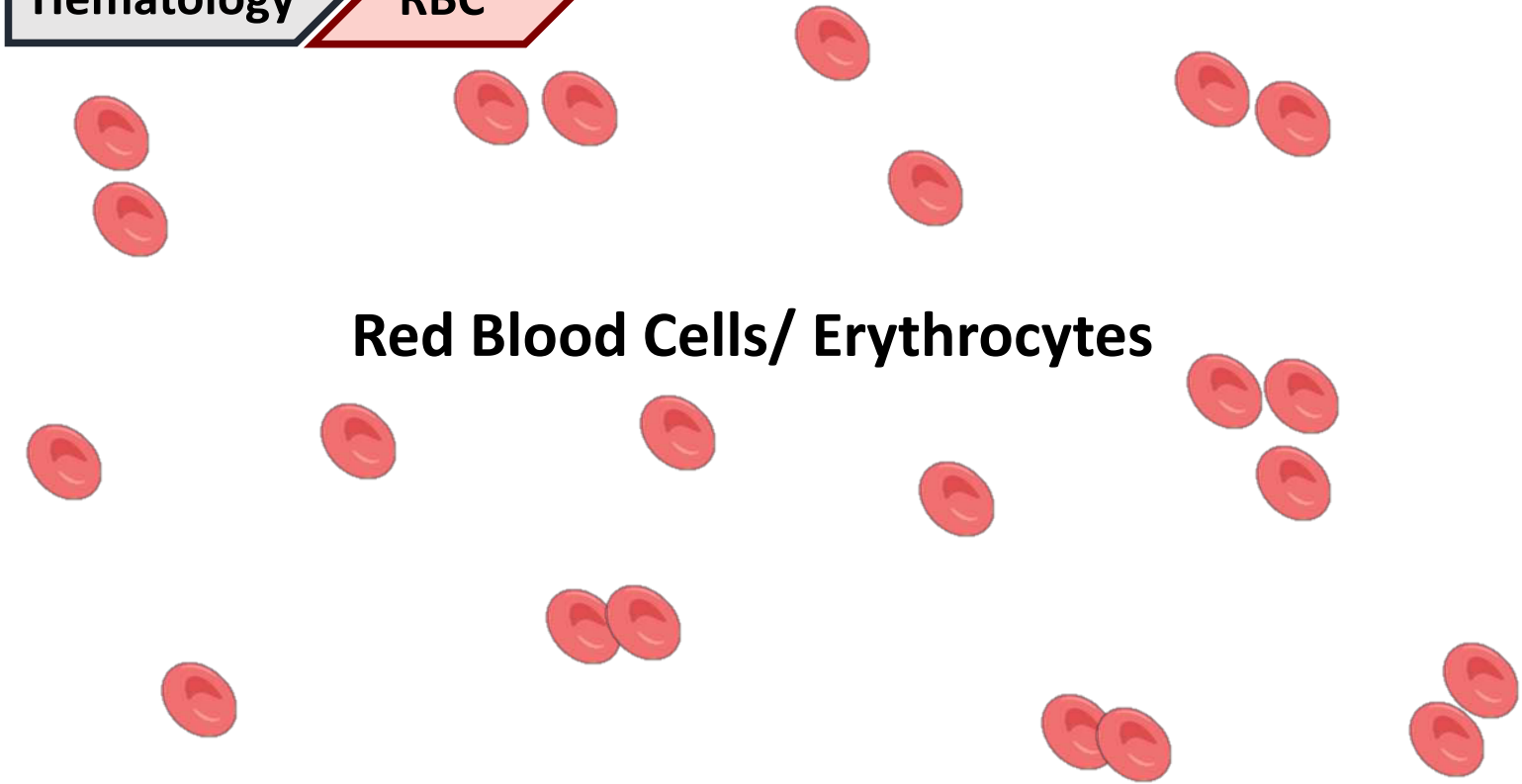


* An increased hematocrit can reflect more RBCs.
* It can also reflect less plasma.
* Clinical interpretation must distinguish the two.

****The hormone testosterone stimulates synthesis of erythropoietin that in turn stimulates production of RBCs.
** Lower values in women during their reproductive years also may be due to excessive loss of blood during menstruation
**Expansion of plasma volume in a pregnant woman reduces the hematocrit, whereas her total red cell volume also increases but less than plasma volume.
** Higher in dehydration.

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.

** The biconcave shape provides a larger surface area for diffusion of O2 from the plasma across the membrane into the erythrocyte than a spherical cell of the same volume would. Also, the thinness of the cell enables O2 to diffuse rapidly between the exterior and innermost regions of the cell.

**A second structural feature that facilitates RBCs' transport function is their flexible membrane (in great excess). Red blood cells, whose diameter is normally 8 um, can deform amazingly as they squeeze through capillaries. Because they are extremely pliant, RBCs can travel through the narrow, tortuous capillaries to deliver their O2 cargo at the tissue level without rupturing in the process.

The third and most important anatomic feature that enables RBCs to transport O2 is the hemoglobin they contain.

Cannot synthesize new components – no nucleus

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 count: cells per unit volume of blood.

Hematocrit: fraction of blood volume occupied by RBCs.

RBC Function

RBCs contribute to:

- **Oxygen transport** through hemoglobin.
- **Carbon dioxide transport**, including conversion of CO_2 to bicarbonate.
- **Acid–base buffering**, particularly through hemoglobin.

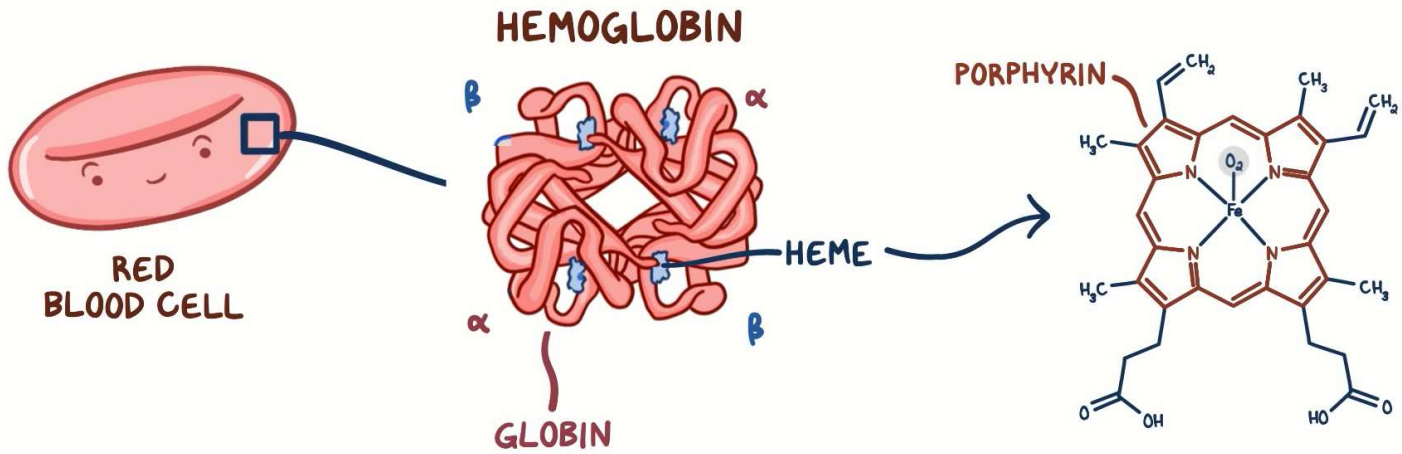
$$CO_2 + H_2O \leftrightarrow \underset{\text{carbonic acid}}{H_2CO_3} \leftrightarrow \underset{\text{bicarbonate}}{HCO_3^- + H^+}$$

** Erythrocytes contribute to CO2 transport in two ways—by means of its carriage on hemoglobin and its carbonic anhydrase–induced conversion to HCO3-.

**The red blood cells contain a large quantity of carbonic anhydrase, an enzyme that catalyzes the reversible reaction between carbon dioxide (CO2) and water to form carbonic acid (H2CO3), increasing the rate of this reaction several thousandfold. The rapidity of this reaction makes it possible for the water of the blood to transport enormous quantities of CO2 in the form of bicarbonate ion (HCO3−) from the tissues to the lungs, where it is reconverted to CO2 and expelled into the atmosphere as a body waste product.

**The hemoglobin in the cells is an excellent acid-base buffer (as is true of most proteins), so the red blood cells are responsible for most of the acid-base buffering power of whole blood.

RBC Hemoglobin



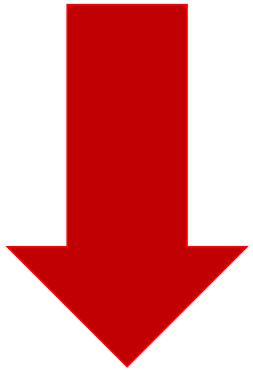
** Hemoglobin is a pigment (that is, it is naturally colored).
** Because of its iron content, it appears reddish when combined with O2 and bluish when deoxygenated.
** Therefore, when reticulocytes leave the bone marrow and pass into the blood stream, they continue to form minute quantities of hemoglobin for another day or so until they become mature erythrocytes.
** The most important feature of the hemoglobin molecule is its ability to combine loosely and reversibly with oxygen.

RBC Hemoglobin

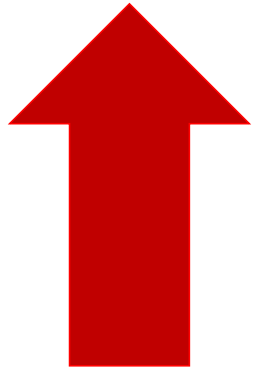
- The different types of chains are designated alpha chains, beta chains, gamma chains, and delta chains.
- The most common form of hemoglobin in the ADULT HUMAN, hemoglobin A, is a combination of two alpha chains and two beta chains.
- Iron ion can combine reversibly with one oxygen molecule
- Also 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

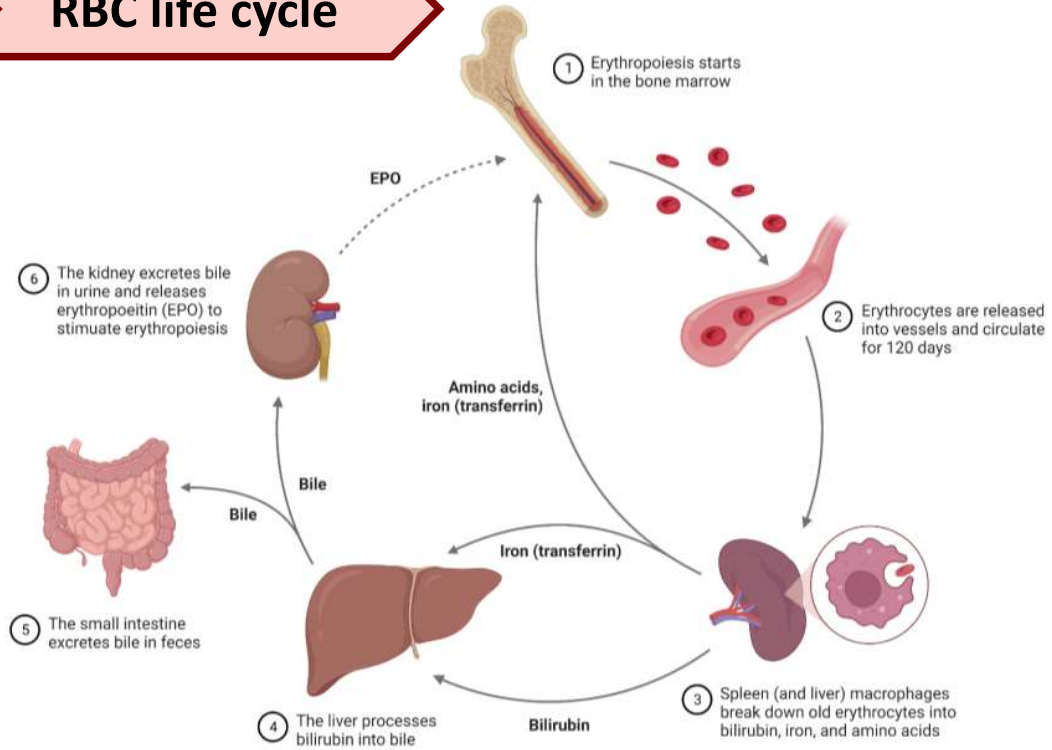
**the amount of Hb in whole blood

An Hb concentration of **15 g/dL means **15 grams of hemoglobin in 100 mL of whole blood**.

**Anemia means deficiency of hemoglobin in the blood, which can be caused by too few RBCs or too little hemoglobin in the cells.

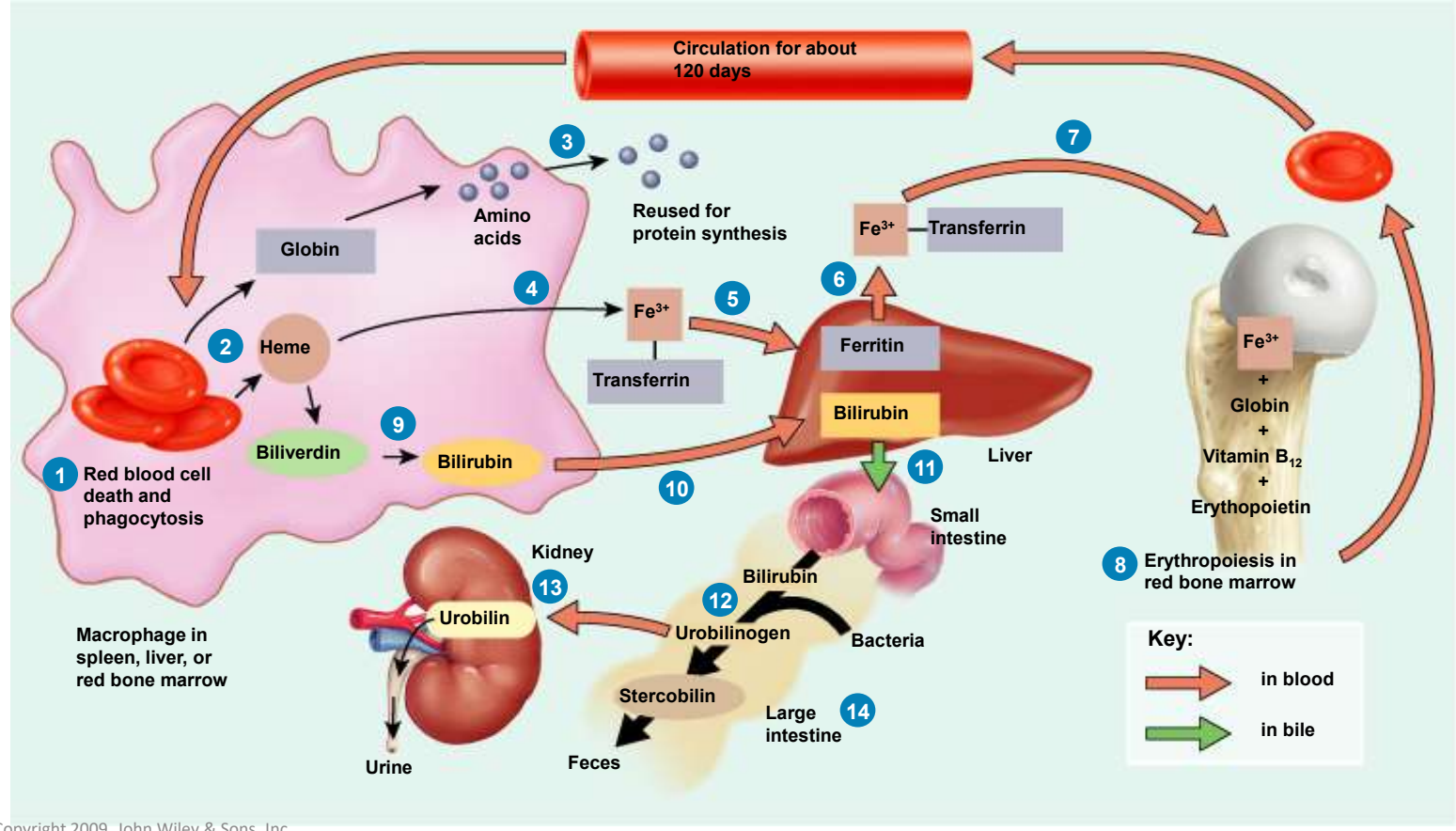
RBC

RBC life cycle



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**Live only about 120 days
**Cannot synthesize new components – no nucleus
**Ruptured red blood cells removed from circulation and destroyed by fixed phagocytic macrophages in spleen and liver
** Bone marrow replaces approximately 1% of the adult RBC every day.
** RBCs do have cytoplasmic enzymes that are capable of metabolizing glucose and forming small amounts of adenosine triphosphate. These enzymes also do the following: (1) maintain pliability of the cell membrane; (2) maintain membrane transport of ions; (3) keep the iron of the cells' hemoglobin in the ferrous form rather than the ferric form; and (4) prevent oxidation of the proteins in the RBCs. Even so, the metabolic systems of old RBCs become progressively less active, and the cells become more and more fragile, presumably because their life processes wear out.



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•Once the red cell membrane becomes fragile, the cell ruptures during passage through some tight spot of the circulation.
•Many of the red cells self-destruct in the spleen, where they squeeze through the red pulp of the spleen.
•Once the RBC membrane becomes fragile, the cell ruptures during passage through some tight spot of the circulation. Many of the RBCs self-destruct in the spleen, where they squeeze through the red pulp of the spleen. There, the spaces between the structural trabeculae of the red pulp, through which most of the cells must pass, are only 3 micrometers wide, in comparison with the 8-micrometer diameter of the RBC.
•Red blood cells burst and release their hemoglobin.
•The macrophages release iron from the hemoglobin and pass it back into the blood, to be carried by transferrin.
•Porphyrin is converted into the bile pigment *bilirubin.* Which is later removed from the body by secretion through the liver into the bile.

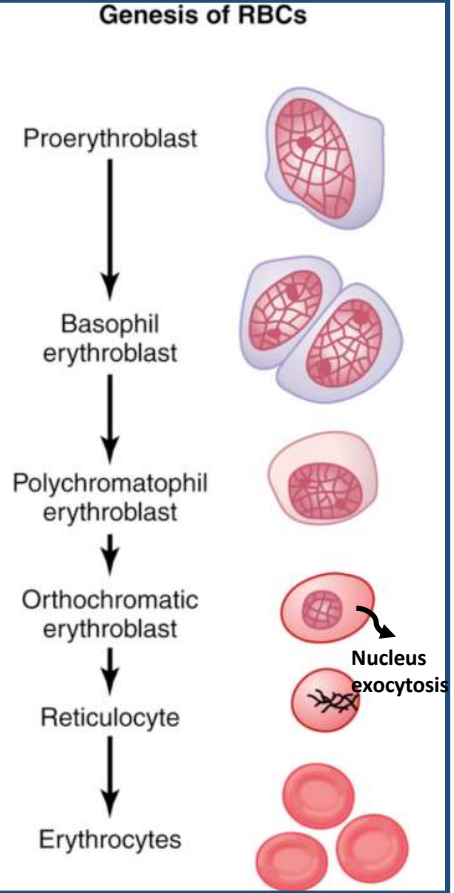
What happens to RBC components?

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.

**Under appropriate stimulation, large numbers of proerythroblast cells are formed from the CFU-E.



**Hemoglobin first appears in polychromatophil erythroblasts. In the succeeding generations, the cells become filled with hemoglobin to a concentration of about 34%, the nucleus condenses to a small size, and its final remnant is absorbed or extruded from the cell. At the same time, the endoplasmic reticulum is also reabsorbed.
**Reticulocyte: contains a small amount of basophilic material (ribosomal RNA), consisting of remnants of the Golgi apparatus, mitochondria, and a few other cytoplasmic organelles. During this reticulocyte stage, the cells pass from the bone marrow into the blood capillaries by diapedesis (squeezing through the pores of the capillary membrane).
**The remaining basophilic material in the reticulocyte normally disappears within 1 to 2 days, and the cell is then a mature erythrocyte. Because of this, their concentration among all the RBCs is normally slightly less than 1%.

**Changes: Hemoglobin accumulation, nuclear condensation, reabsorption of the endoplasmic reticulum.
** When reticulocytes leave the bone marrow and pass into the blood stream, they continue to form minute quantities of hemoglobin for another day or so until they become mature erythrocytes.

How much production maintains the pool?

5×10^6 RBCs/µL × 5×10^6 µL blood

≈ 25×10^{12} circulating RBCs

25×10^{12} ÷ 120 days ÷ 86,400 seconds/day

≈ 2.4 million RBCs replaced each second
≈208 billion RBCs/day"

A large circulating population requires continuous renewal.

** The total mass of RBCs in the circulatory system is regulated within narrow limits, and thus (1) an adequate number of RBCs are always available to provide sufficient transport of oxygen from the lungs to the tissues, yet (2) the cells do not become so numerous that they impede blood flow

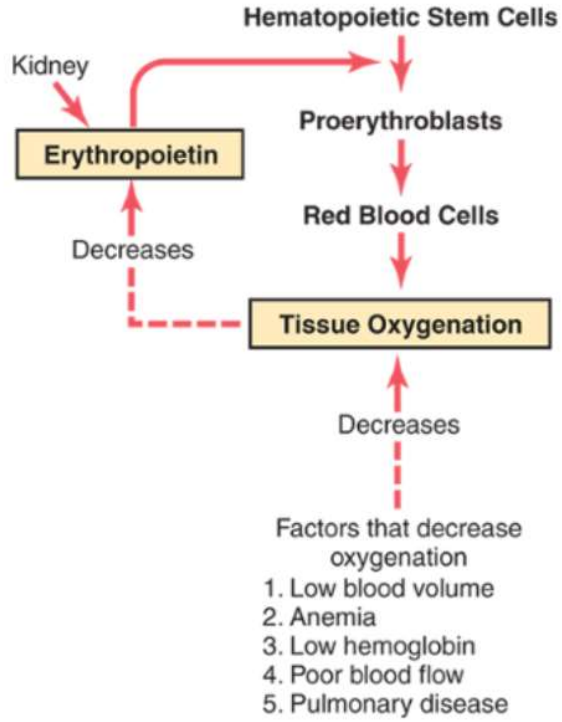
** Assumptions: 5 L blood, 5 million RBCs per microliter, 120-day mean lifespan and steady state. This explains the familiar approximation of 2–3 million cells per second. Production equals removal only when the pool is stable.

RBC Regulation of Erythropoiesis_ Erythropoietin (EPO)

- 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.

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

**** Renal tissue hypoxia leads to increased tissue levels of hypoxia-inducible factor-1 (HIF-1), which serves as a transcription factor for a large number of hypoxia-inducible genes, including the erythropoietin gene. HIF-1 binds to a hypoxia response element in the erythropoietin gene, inducing transcription of messenger RNA and, ultimately, increased erythropoietin synthesis.
**At times, hypoxia in other parts of the body, but not in the kidneys, stimulates kidney erythropoietin secretion, which suggests that there might be some nonrenal sensor that sends an additional signal to the kidneys to produce this hormone. In particular, norepinephrine and epinephrine and several of the prostaglandins stimulate erythropoietin production.

*At very **high altitudes**, where the quantity of oxygen in the air is greatly decreased, insufficient oxygen is transported to the tissues, and RBC production is greatly increased. In this case, it is not the concentration of RBCs in the blood that controls RBC production but the amount of oxygen transported to the tissues in relation to tissue demand for oxygen.

**In low oxygen atmosphere, erythropoietin begins to be formed within minutes to hours, and it reaches maximum production within 24 hours. Yet, almost no new RBCs appear in the circulating blood until about 5 days later

*Various diseases of the circulation **that decrease tissue blood flow**, particularly those that cause **failure of oxygen absorption** by the blood as it passes through the lungs, can also increase the rate of RBC production. This result is especially apparent in **prolonged cardiac failure and in many lung diseases**.

**When both kidneys are removed from a person, or when the kidneys are destroyed by renal disease, the person invariably becomes very anemic. This is because the 10% of the normal erythropoietin formed in other tissues (mainly in the liver) is sufficient to cause only one third to half the RBC formation needed by the body.

What stimulates the EPO response?

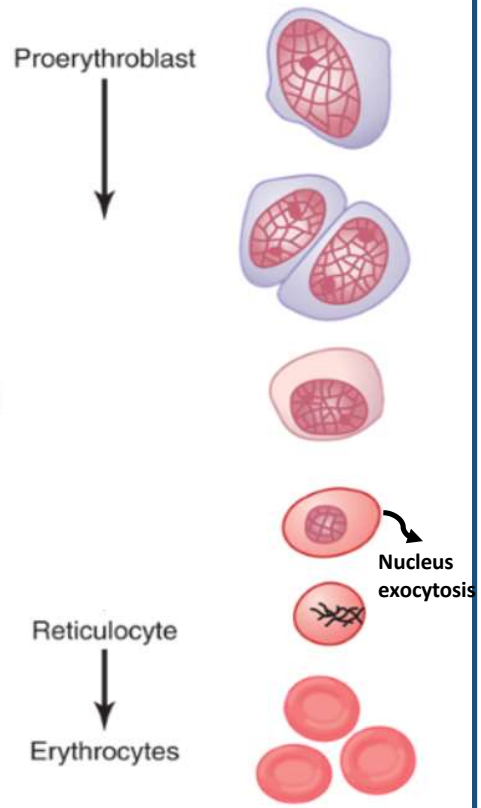
- **Anemia or blood loss:** less hemoglobin available to carry oxygen.
- **Low blood oxygen:** for example, at high altitude or with lung disease.
- **Reduced kidney blood flow:** less oxygen delivered to kidney tissue.

The shared signal is inadequate oxygen availability to renal tissue.

RBC Vitamins requirement

- Maturation of red blood cells requires vitamin 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 → 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



** The bone marrow are among the most rapidly growing and reproducing cells in the entire body.
**B12 or folate deficiency → impaired DNA synthesis → defective division and maturation → fewer, larger RBCs → megaloblastic anemia.
** Deficiency of vitamin B12 or folic acid causes maturation failure in the process of erythropoiesis à cells are capable of carrying oxygen normally, but their fragility causes them to have a short life.

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

Answer B. The key distinction is inadequate effective output. A confuses marrow activity with successful production. C produces hemoconcentration. D ignores the time required for cell maturation.

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

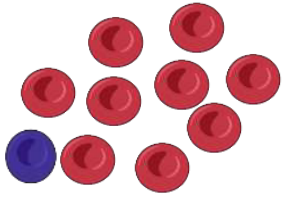
Aplastic anemia

Increased

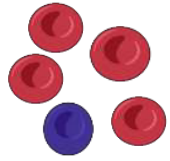
Hemolytic anemia
Post hemorrhage

** In the state of anemia, reticulocyte % is not a true reflection of reticulocyte production.
** A correction factor must be applied to not overestimate marrow production because each reticulocyte is released into whole blood containing few RBCs, which means low Hct, thus increasing the percentage.

RBC > Corrected Reticulocyte count



Retic = 1%
Hct = 45



Retic = 2%
Hct = 22.5

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

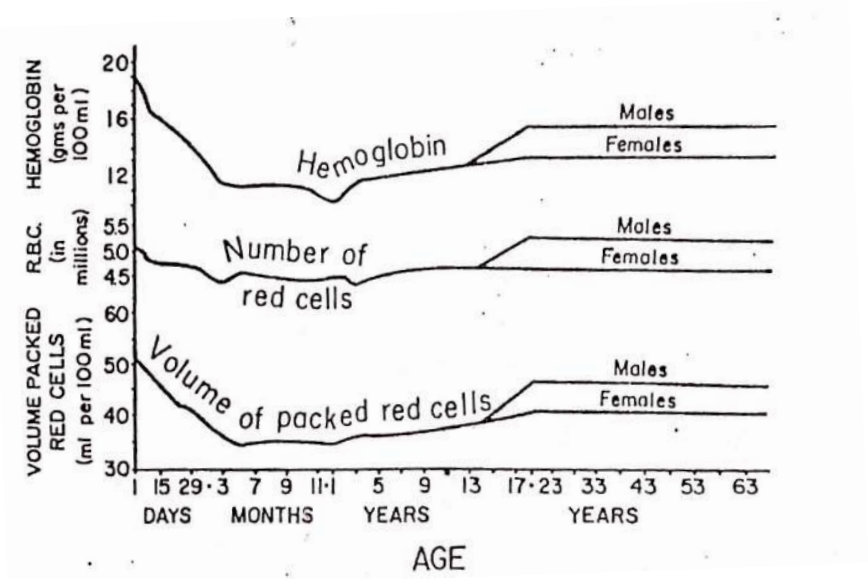
$$= 1\% \times \frac{45}{45}$$

= 1%

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

= 1%

** In the state of anemia, reticulocyte % is not a true reflection of reticulocyte production.
** A correction factor must not be applied to overestimate marrow production because each reticulocyte is released into whole blood containing few RBCs, which means low Hct, thus increasing the percentage.



Decline after birth
After birth, improved oxygenation suppresses EPO and reduces RBC production. Neonatal RBCs also have a shorter lifespan, and rapid growth expands blood volume. Together, these lower hemoglobin, producing the physiological nadir at about **2–3 months in term infants**.

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 (%)

- **RBC count: the number of cells**
- This is the number of RBCs in **one microliter of whole blood**.
- For example, **5 × 10^6/µL** 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:

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



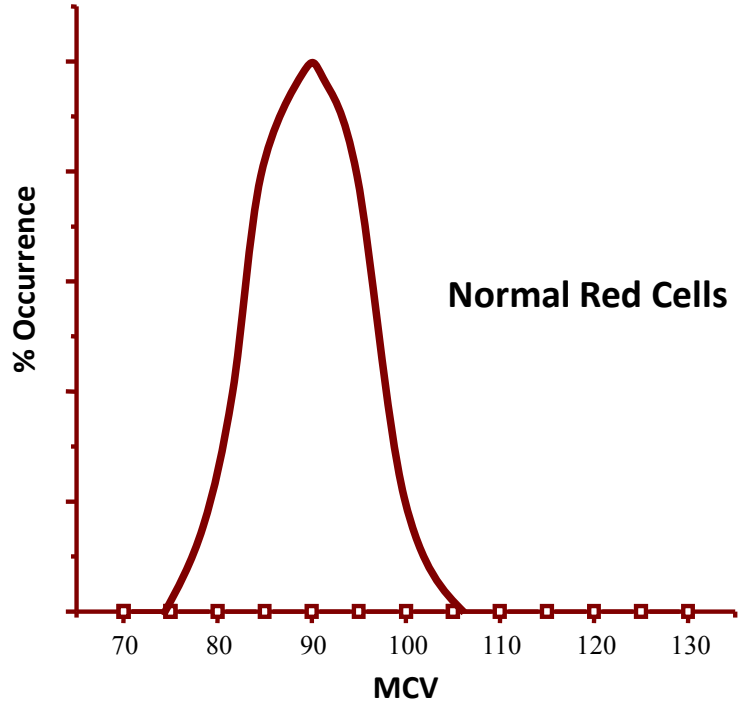
Macrocytic (>100)



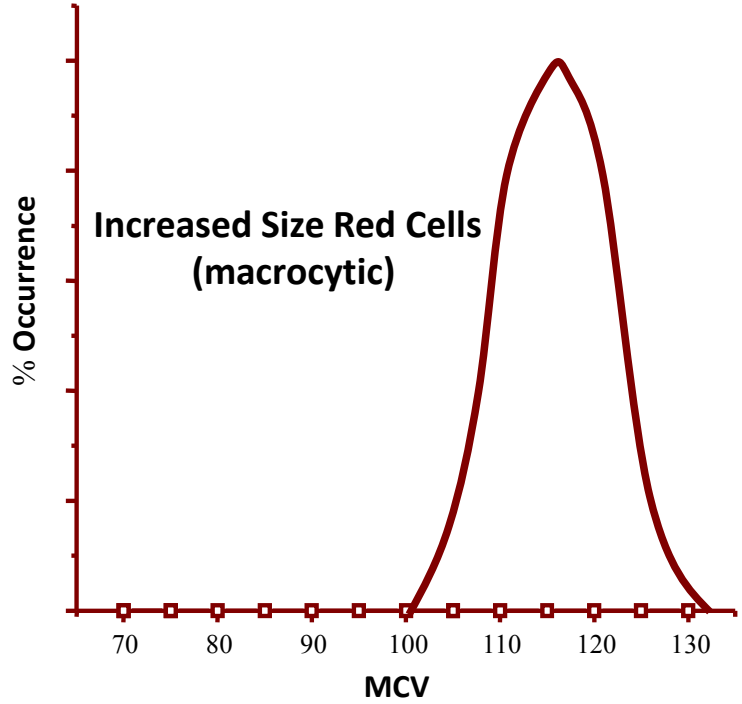
Normocytic (80-100)



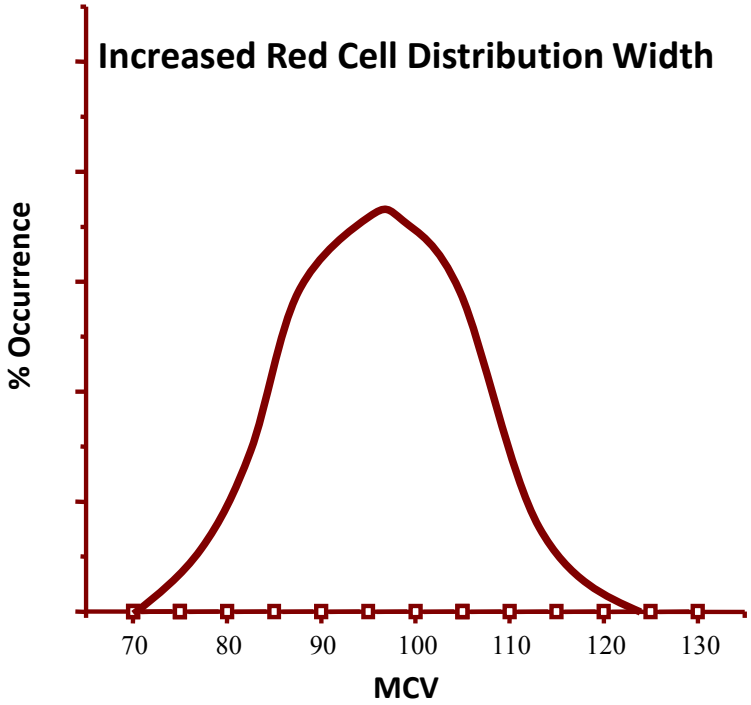
Microcytic (<80)


% Occurrence
Normal Red Cells
70
80
90
100
110
120
130
MCV

RBC > RBCs parameters > Distribution of RBCs sizes



- Measurement of RBC size variation (anisocytosis).
- RDW = [standard deviation/MCV] x 100.
- High RDW → large variation in RBC sizes
- Normal 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)

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**

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



Normochromic (30-36)



Hypochromic (<30)

MCHC=MCH/MCV

Mean corpuscular hemoglobin concentration expresses the amount of hemoglobin **relative to the volume of RBCs

For example, if a cell becomes larger and its hemoglobin amount increases proportionally, **MCH rises but MCHC stays the same.

RBC **RBCs parameters**

Hb = 8 g/dL
Hct = 28%
RBC count = 4 million/µL

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

Small RBCs — microcytic

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

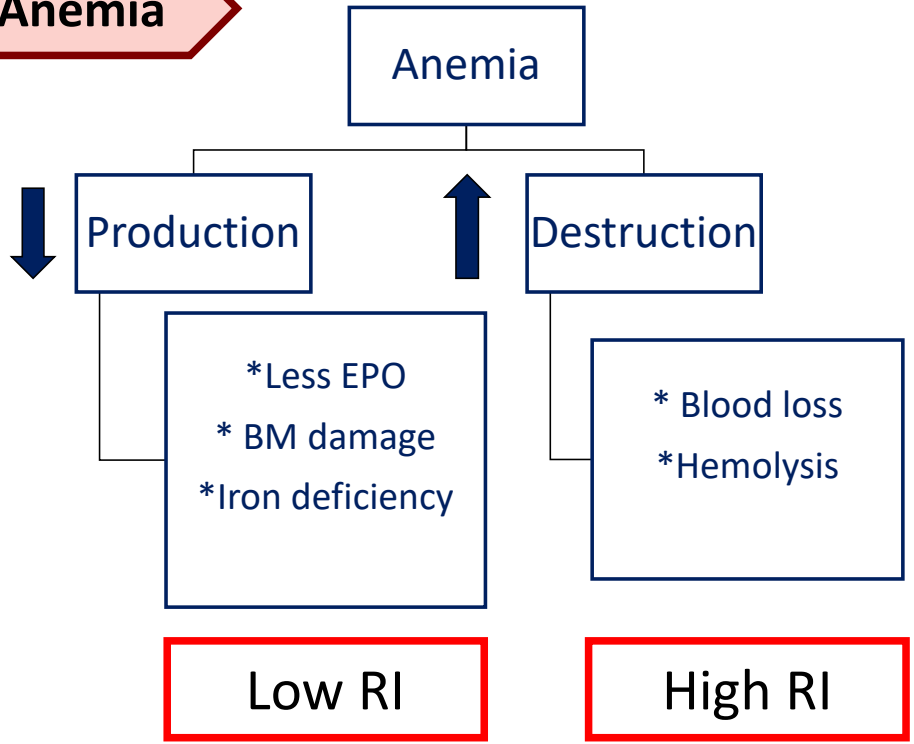
Reduced hemoglobin amount per RBC

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

Reduced hemoglobin concentration — hypochromic

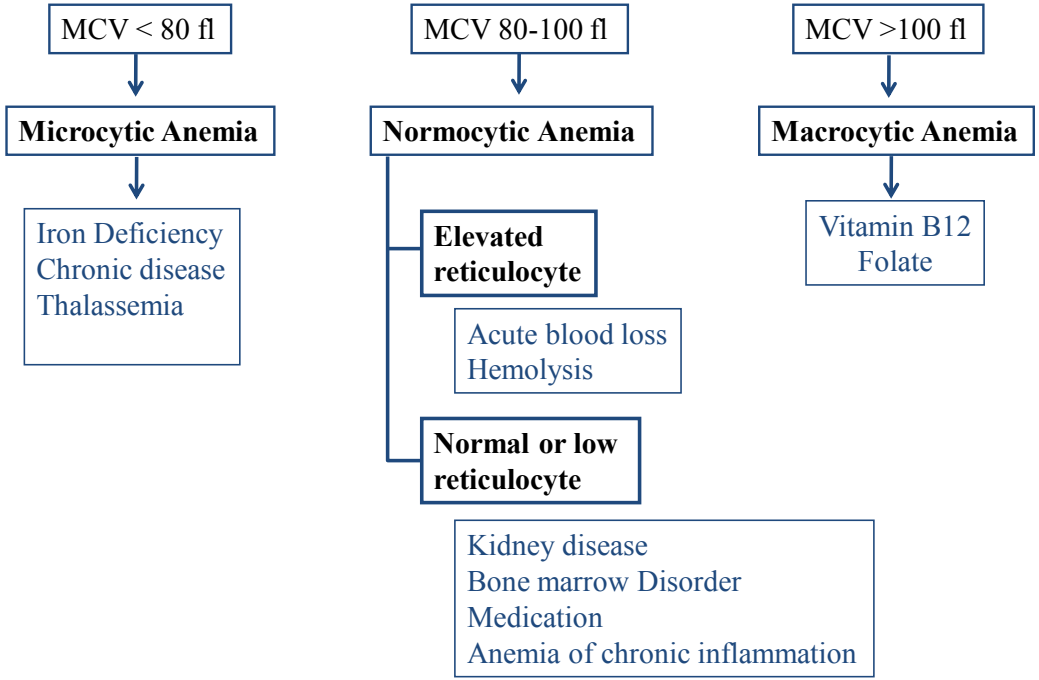
$$MCHC = \frac{MCH}{MCV} \times 100$$

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



****chronic inflammation is usually normocytic**, but can become microcytic—include it in both categories.

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?

RBC Effects of Anemia on Function of the Circulatory System

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?

Exercise increases the muscles' oxygen requirements. Normally, the heart responds by increasing cardiac output. In severe anemia, however, cardiac output is **already elevated at rest, leaving less capacity to increase it further—called **reduced cardiac reserve**. Consequently, oxygen delivery may fail to meet demand, causing **fatigue, breathlessness, and palpitations**.

RBC Effects of Polycythemia on Function of the Circulatory System

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

Effects of Polycythemia on Function of the Circulatory System

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

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

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.**

Effects of Polycythemia on Function of the Circulatory System

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**.