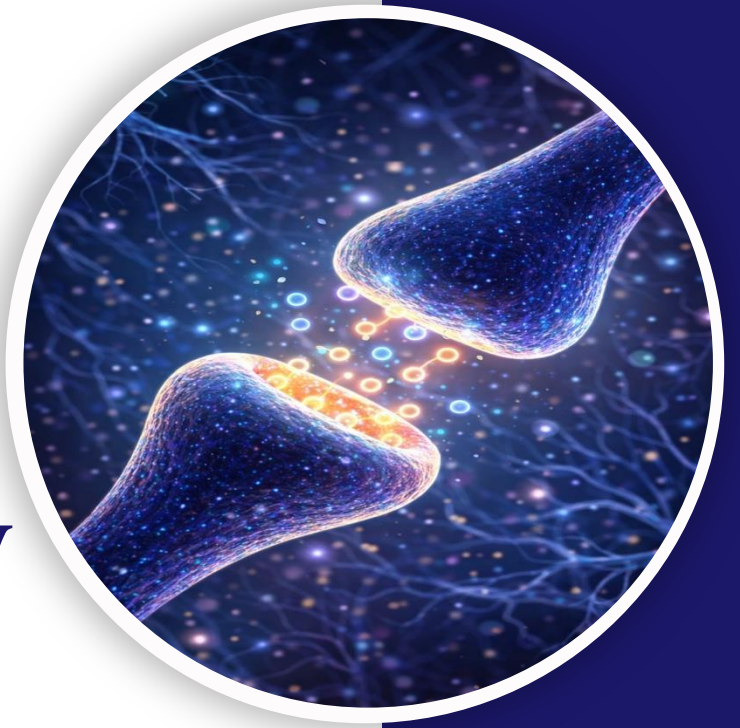
بسم الله الرحمٰن الرحيم

(وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ)

HLS Physiology | MID 1

Introduction to Hematology Physiology



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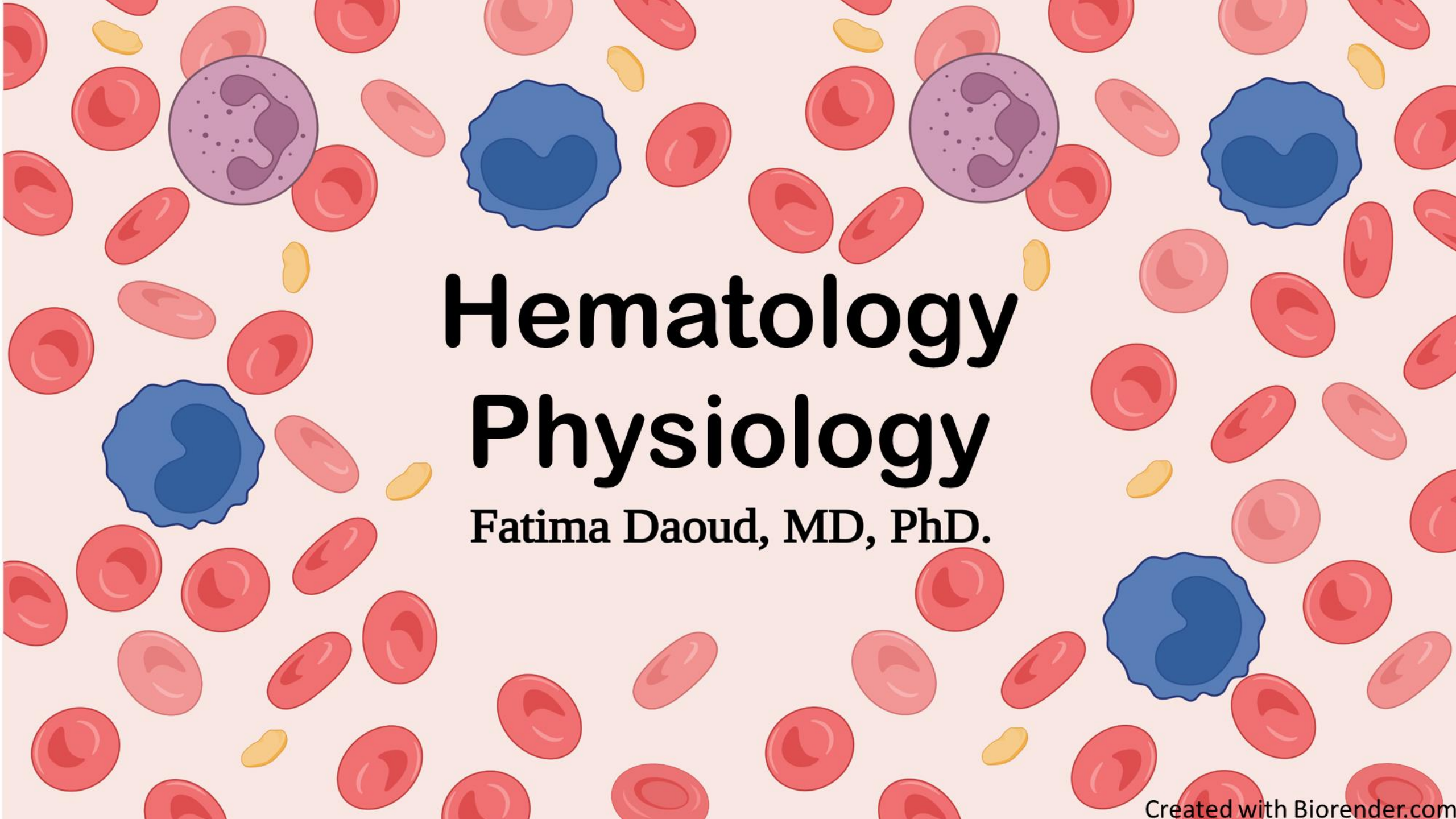

Hematology Physiology

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

Body Fluid Distribution

- Total Body Water (TBW) accounts for approximately 55%-60% of body weight.
- This percentage varies according to age ,sex and adipose tissue present in the body.

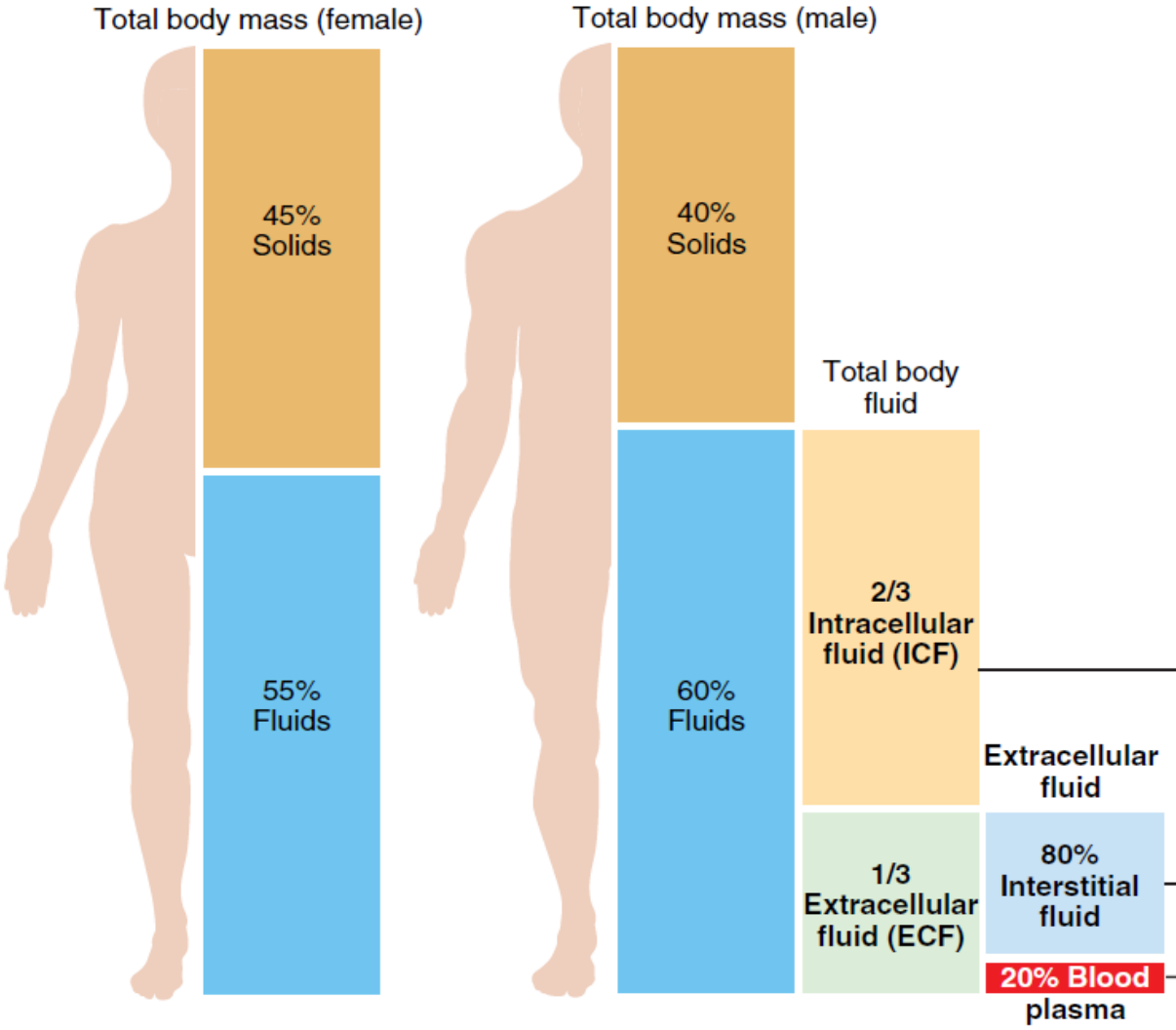
Body fluids are distributed into two main compartments:

1. Intracellular Fluid (ICF)
   - Represents approximately 2/3 of total body water.
   - It is the fluid found inside the cells.
2. Extracellular Fluid (ECF)
   - Represents approximately 1/3 of total body water.
   - It is the fluid found outside the cells.

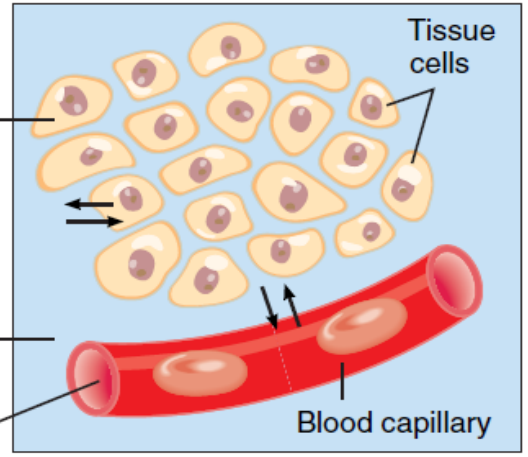
The extracellular fluid is further divided into:

- Intravascular fluid (20%): Fluid found inside blood vessels (plasma).
- Fluid found in the spaces between cells.

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

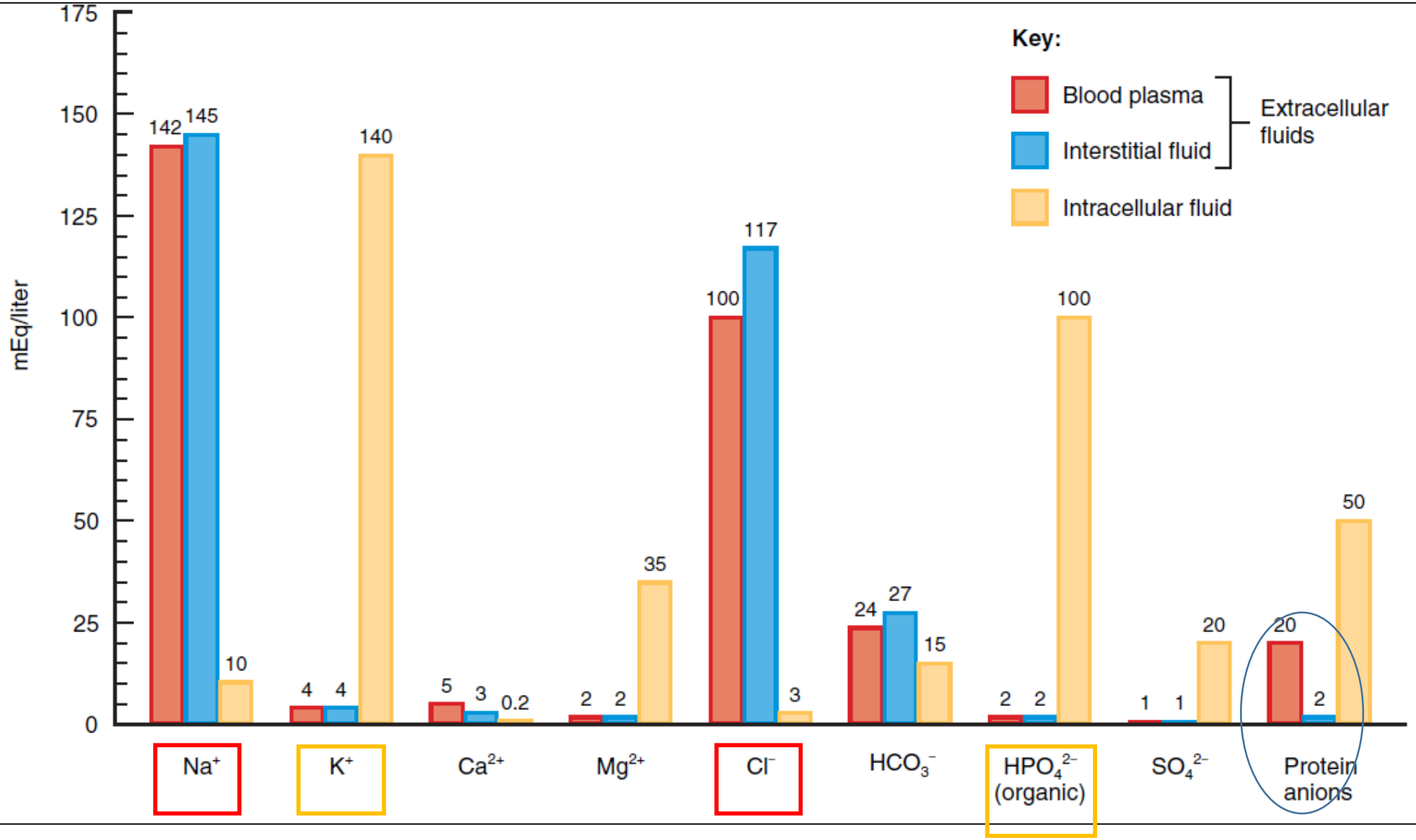


(a) Distribution of body solids and fluids in average lean adult female and male



(b) Exchange of water ar
body fluid compartme

Hematology Body Fluids



Differences Between Intracellular and Extracellular Fluid

The main difference between the intracellular (ICF) and extracellular (ECF) compartments lies in their electrolyte and protein composition.

The major electrolytes include:

- Sodium (Na^+) //Potassium (K^+) // Chloride (Cl^-) //Magnesium (Mg^{2+}) //Phosphate (HPO_4^{2-}) // Sulfate (SO_4^{2-})

Electrolyte distribution:

- Extracellular Fluid (ECF): Mainly rich in Na^+(most abundant cation) and Cl^-(most abundant anion).
- Intracellular Fluid (ICF): Mainly rich in K^+(most abundant cation in ICF), Mg^{2+}, phosphates, and proteins(the major source of negative charge).

Role of the Sodium-Potassium Pump (Na^+/K^+ ATPase)

The Na^+/K^+ ATPase pump plays a major role in maintaining the differences in electrolyte concentrations between intracellular and extracellular fluids. Actively transports Na^+ out of the cells and K^+ into the cells.

Maintains a high intracellular K^+ concentration and a high extracellular Na^+ concentration.

Uses ATP to transport 3 Na^+ out and 2 K^+ in.

Differences Between Plasma and Interstitial Fluid

Plasma and interstitial fluid have almost the same electrolyte composition, particularly in terms of Na^+, K^+, and Cl^- concentrations.

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**

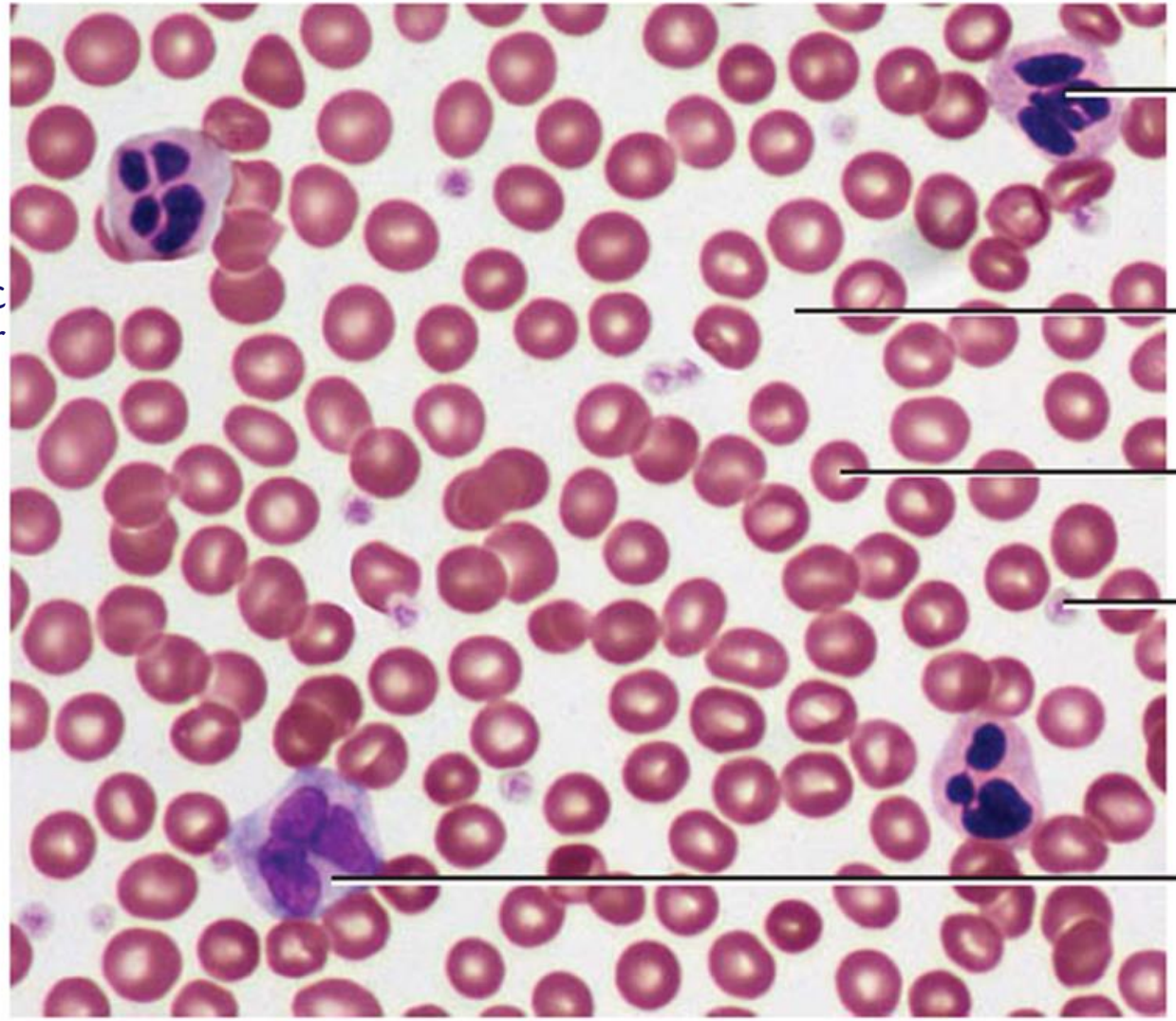
  unsaturated (O_2) → **dark red**

📌**NOTE**

Blood volume varies with body size and physiological state.

The approximate 5-L value is an orientation, not a universal normal value.

The shape of RBC pale in the center



White blood cell (leukocyte: neutrophil)

Blood plasma

Red blood cell (erythrocyte)

Most abundant component
Erythro=red // Cyte= cell

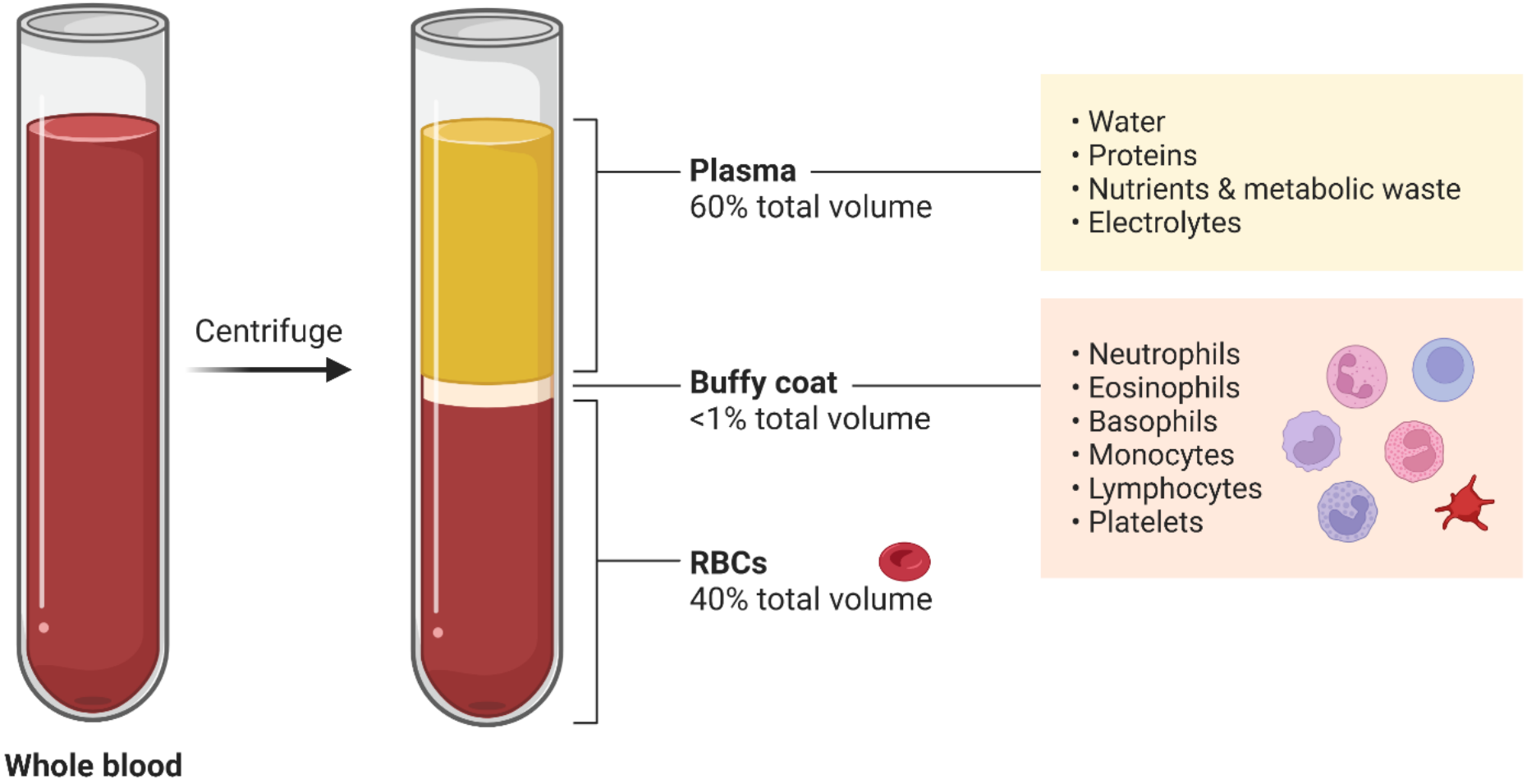
Platelet

Another name
Thrombocytes

White blood cell (leukocyte: monocyte)

Hematology

Blood and its components

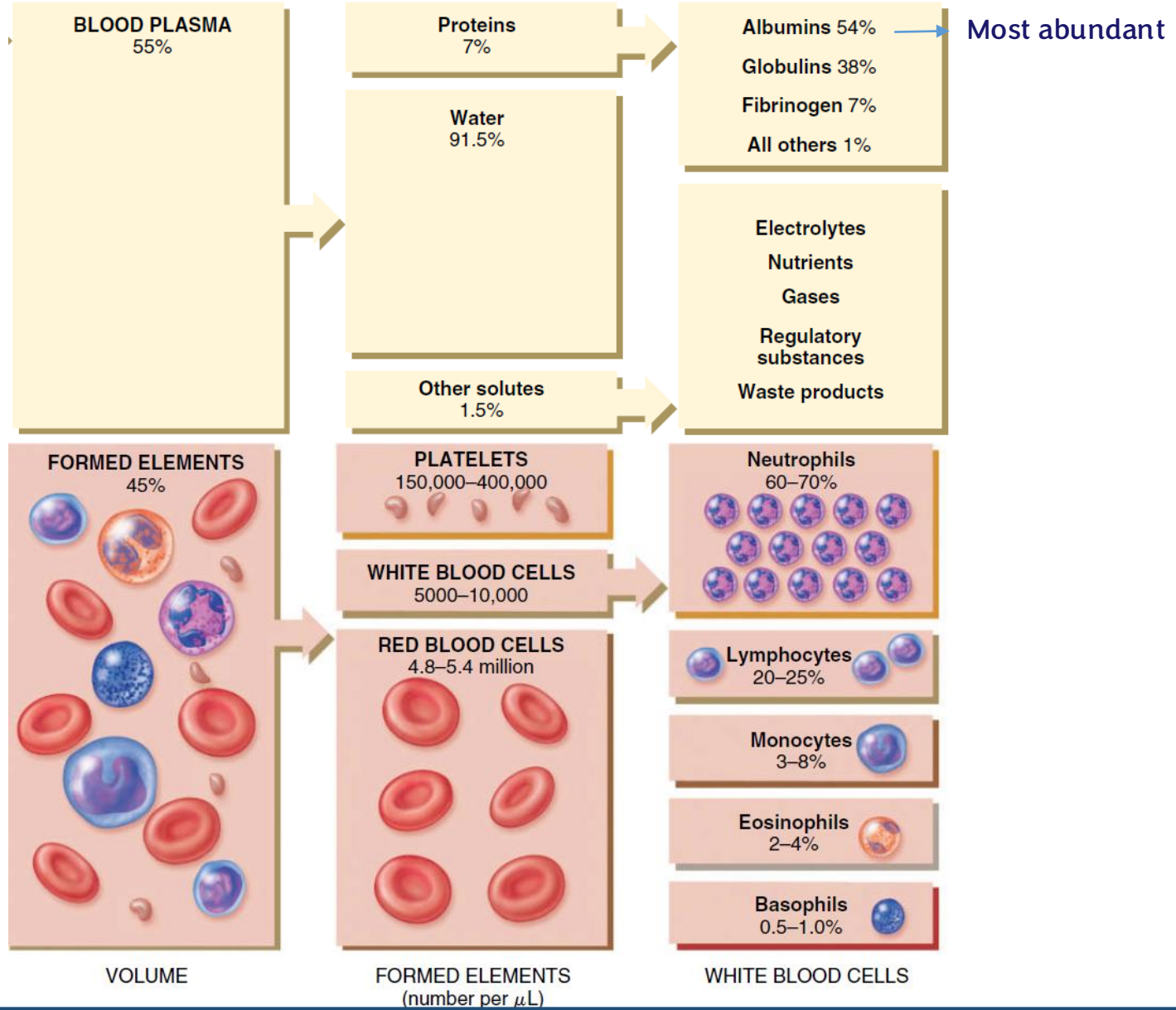


- The sample must contain an anticoagulant. Otherwise, clot formation changes what separates from the sample.

Hematology

Blood and its components

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



Very well explained through the lecture

Hematology | Plasma Protein

1. Establishment of colloid osmotic pressure.

Key:

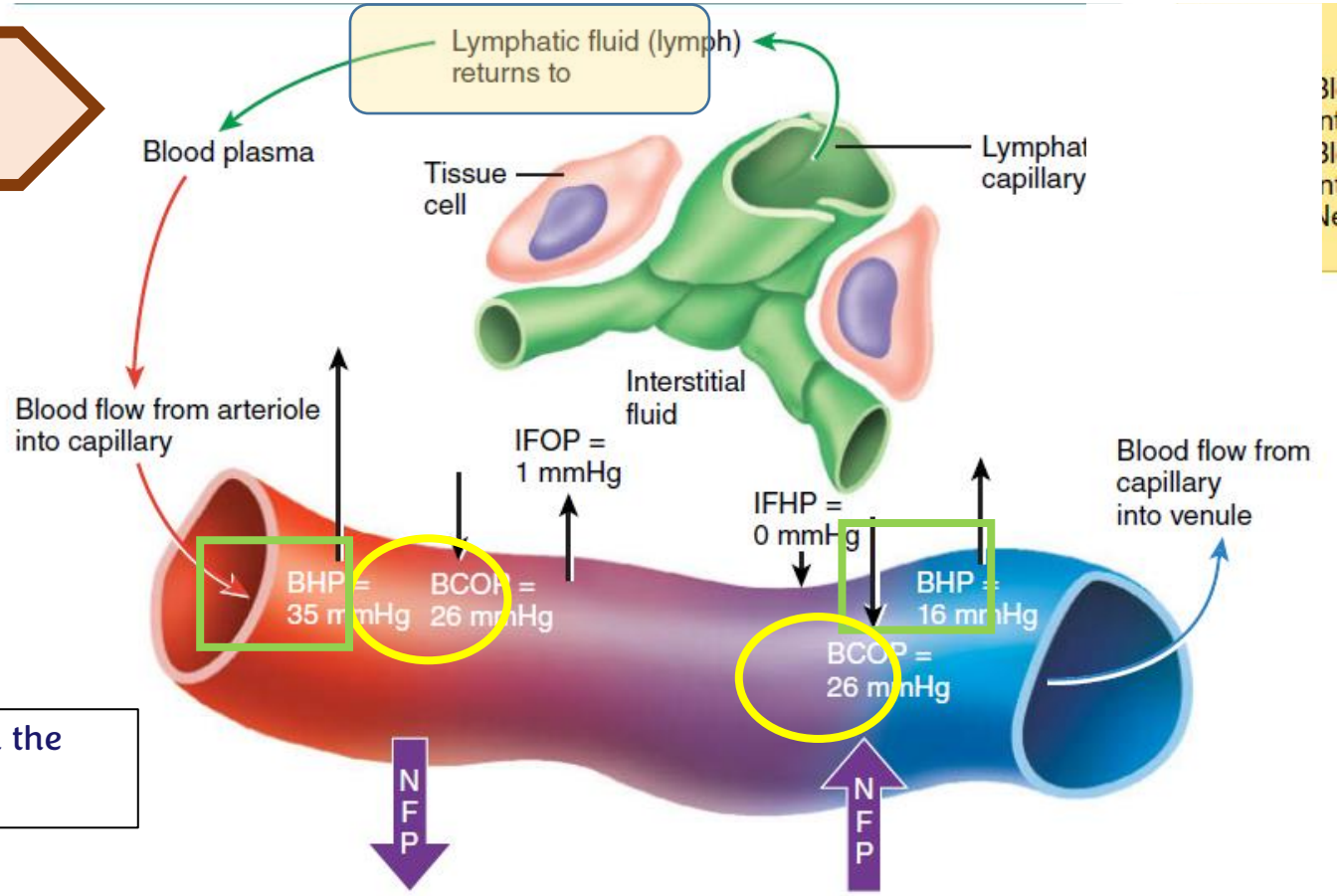
BHP = Blood hydrostatic pressure
IFHP = Interstitial fluid hydrostatic pressure
BCOP = Blood colloid osmotic pressure
IFOP = Interstitial fluid osmotic pressure
NFP = Net filtration pressure

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

Explanation in the next slide



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 — Plasma Protein

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

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: Functions

Plasma contains several proteins, with albumin being the most abundant plasma protein.

1. Transport of Substances (Carrier Function)

Plasma proteins act as carriers, transporting various substances through the bloodstream, particularly hydrophobic (water-insoluble) substances.
The main carrier proteins include:
-Albumin -α-globulins. -β-globulins.

2. Maintenance of Oncotic Pressure (Colloid Osmotic Pressure)

All plasma proteins contribute to maintaining oncotic pressure, but albumin is the major contributor.
There is a difference in protein concentration between plasma and interstitial fluid.—>Plasma contains a higher concentration of proteins than interstitial fluid.
This difference generates an osmotic pressure, which draws water toward the compartment with the higher protein concentration.
Fluid movement across capillaries is regulated by two opposing forces:
A. Filtration. Mainly driven by capillary hydrostatic pressure.
Pushes water out of blood vessels into the interstitial space.

B. Reabsorption. Favored by plasma oncotic pressure, primarily generated by albumin.
Draws water from the interstitial space toward the blood vessels.

c. Lymphatic Drainage. The balance between filtration and reabsorption determines the net movement of fluid across capillary walls.
When filtration exceeds reabsorption, fluid accumulates in the interstitial space.
Excess interstitial fluid is collected and drained by the lymphatic system.
The lymphatic system eventually returns this fluid to the bloodstream.

4. Immunity

- Gamma globulins (immunoglobulins) act as antibodies that recognize and neutralize foreign antigens.
- They play an important role in humoral immune defense.

5.Regulate the Temperature balance and fluid balance

6. Blood Clotting

Fibrinogen is an essential plasma protein involved in blood coagulation.
During clot formation, fibrinogen is converted into fibrin, which forms a meshwork that stabilizes the blood clot.

7. Acid-Base Balance

Plasma proteins act as buffers by accepting or releasing hydrogen ions (H^+).
This helps maintain a stable blood pH and prevents major changes in acidity.

8. Blood Pressure Homeostasis

Angiotensinogen, a plasma protein produced by the liver, contributes to blood pressure regulation.
It is converted into Angiotensin II, which causes vasoconstriction → ↑ Blood Pressure.

Clinical Significance: Edema Formation

Edema is the abnormal accumulation of excess fluid in the interstitial space.
The main causes include:
1. Decreased Protein Synthesis (Liver Diseases)
2. Increased Protein Loss (Kidney Diseases)
3. Impaired Lymphatic Drainage (Lymphatic Obstruction)

The concentration of proteins in blood ↓→ ↓ Plasma oncotic pressure → ↑ Net fluid filtration → Edema.

📌 Important Note: Unlike liver and kidney diseases, lymphatic obstruction does not necessarily decrease plasma protein concentration. Instead, it causes the accumulation of proteins and fluid within the interstitial space, resulting in edema.

Hematology

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 immunoglobulin and WBCs and prevention of blood loss fibrinogen and clotting factors in the plasma as well as platlet

Hematology

Hemopoiesis (formation of blood cells)

Hematopoiesis, also called hemopoiesis, is the process of blood cell formation .

.

The suffix ”siseiop-“means production or formation.

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.

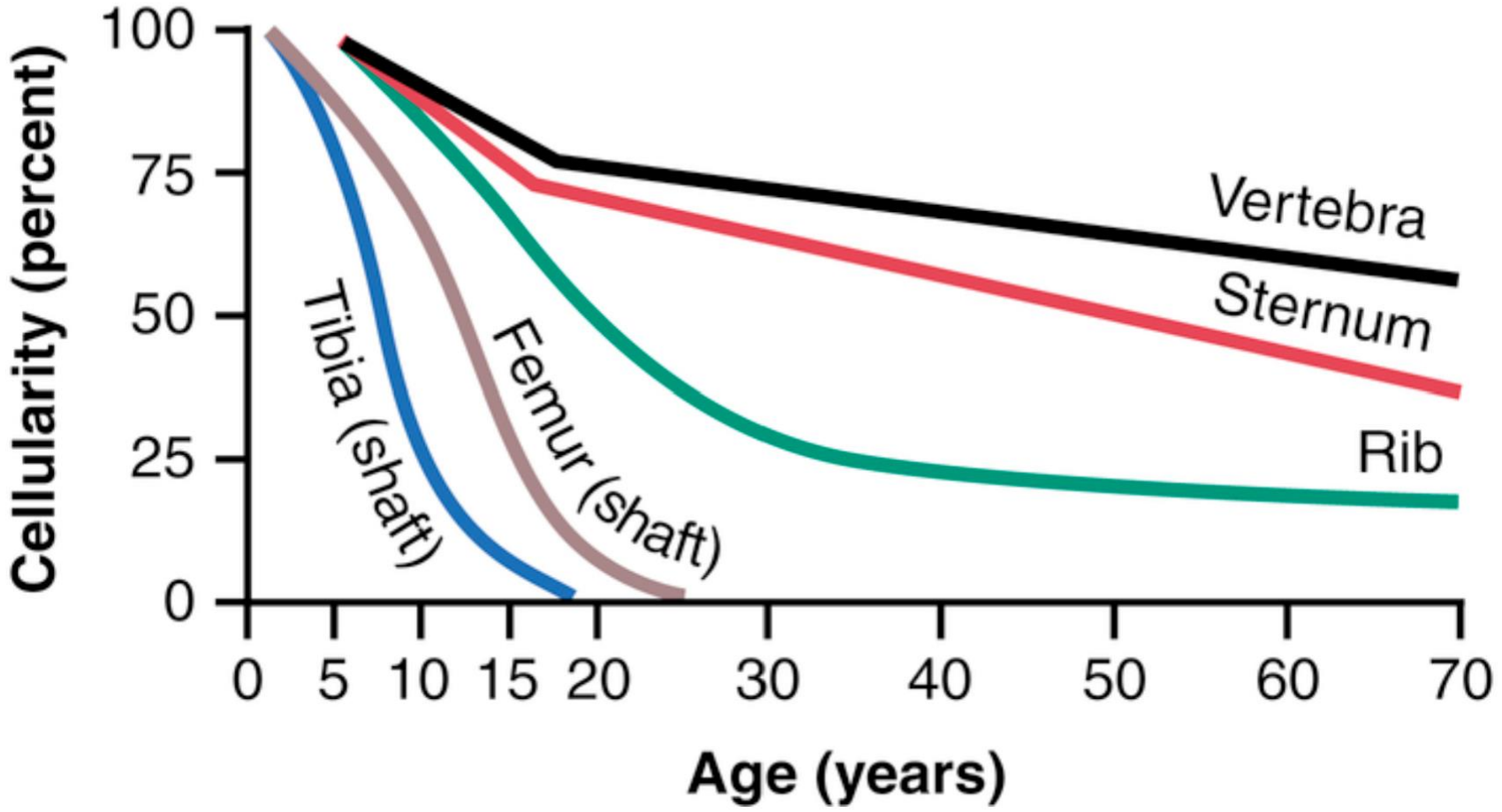
Hematology

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 sCBR tsom ,20 ni decudorp eb ot eunitnoc eht fo worram eht sa hcus ,senob suonarbmem ,sbir ,munrets ,earbetrev eht .aili dna

**Bone marrow becomes less productive as age increases.



Sites of Hematopoiesis During Fetal Life

.1Early Fetal Life: Yolk Sac

During early fetal life, blood cell formation begins in the yolk sac, where the first red blood cells (RBCs) are produced.

.2Middle Trimester of Pregnancy: Liver and Other Organs

As the fetus develops, the liver becomes the major site of blood cell formation. Other organs, such as the spleen, thymus, and lymph nodes contribute to this process.

.3Toward the End of Pregnancy and After Birth: Red Bone Marrow

As pregnancy progresses, the red bone marrow becomes increasingly important in blood cell formation. After birth, it becomes the main site of hematopoiesis and continues to produce blood cells throughout life.

Sites of Red Bone Marrow According to Age

What are the sites of red bone marrow?

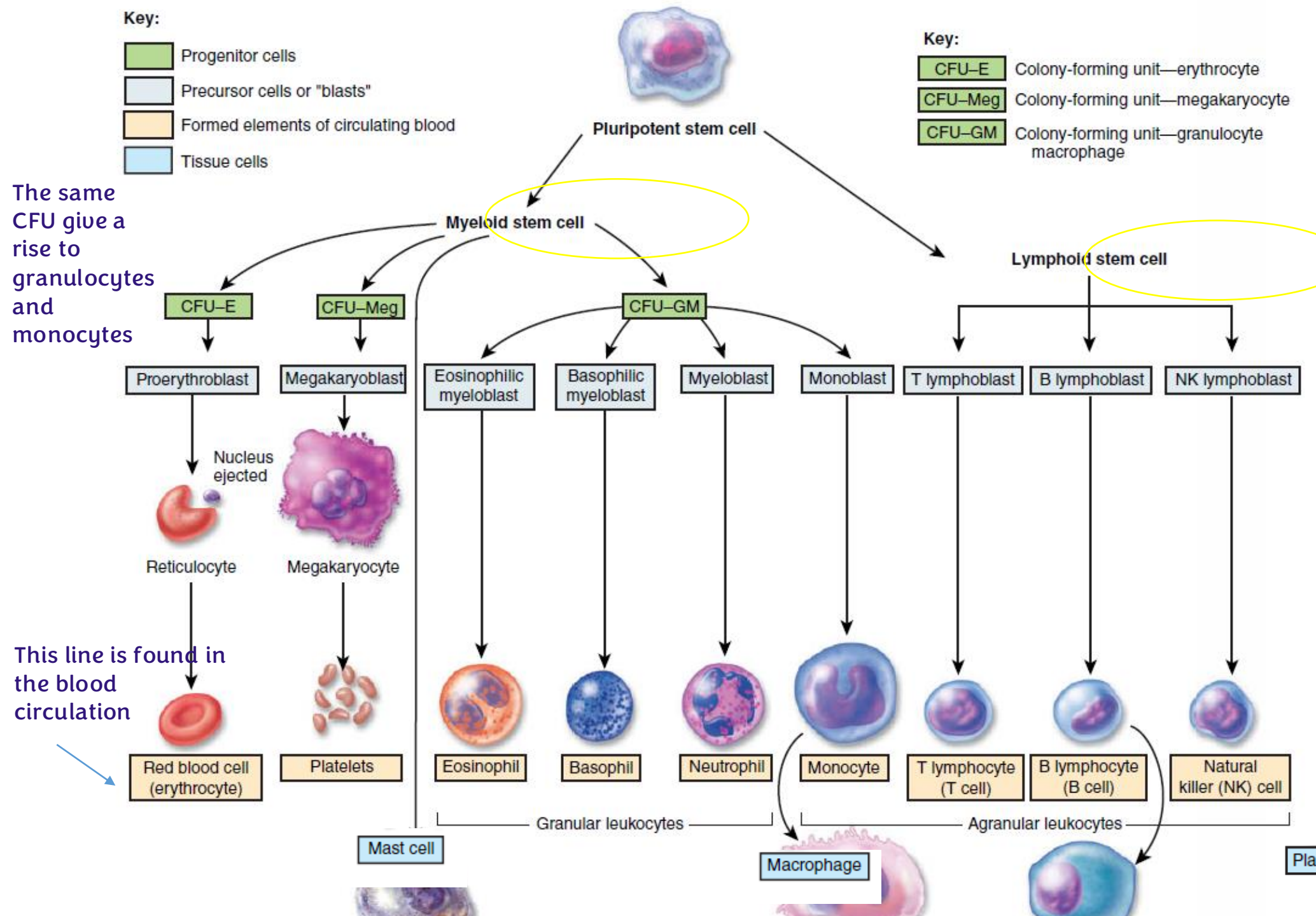
The distribution of red bone marrow changes as a person grows. At birth, red bone marrow is present in almost all bones. However, from around five years of age, red bone marrow gradually decreases in the shafts of long bones and becomes more restricted to other areas, especially the epiphyses and the axial skeleton.

As a person gets older, red bone marrow in the shafts of long bones is gradually replaced by yellow bone marrow, which contains more fat. By around the age of si tnemecalper siht ,20 eht ni dnuof ylniam si worram enob der ,stluda nI .senob gnol fo stfahs eht ni etelpmoc ylegral 30 fo sega eht neewteB .senob rehto niatrec dna noteleks laixaand niam eht era senob talf ,40 .worram enob der fo setis

With age, hematopoietic activity gradually decreases

Bone Marrow Biopsy and Aspiration

When a bone marrow sample is needed for examination, a bone marrow biopsy or aspiration can be performed. The posterior iliac crest is a common site for both procedures.



The same CFU give a rise to granulocytes and monocytes

This line is found in the blood circulation

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 ce

- ***Pluripotent Stem Cell (PHSC)***
- *Pluripotent: means* the ability of a cell to differentiate into different kinds of cells
- *stem cells:* are undifferentiated and immature cells. They have a high ability to Proliferate , as well as a very high ability to self-renewl

What do we mean by self-renewal?
Self-renewal means that stem cells can divide and produce new stem cells. This ability helps maintain the stem cell pool over time.

However, as shown in the previous chart, the ability of stem cells to self-renew decreases with time. This is related to a decrease in the stem cell pool, which means that the total number of stem cells becomes lower.

PHSC Differentiation

PHSC can differentiate into two main types of stem cells: myeloid stem cells and lymphoid stem cells.
Lymphoid stem cells give rise to all types of lymphocytes, including B cells, T cells, and NK cells (Natural Killer cells
Myeloid stem cells give rise to most blood cells, except lymphocytes and NK cells, which develop from lymphoid stem cells.
Moving to the myeloid stem cells, the next step is the formation of *colony-forming units (CFUs*.(

Colony-Forming Units
Colony-forming units are committed progenitor cells. This means that they are already committed to producing specific types of cells,

Why are they called colony-forming units?
Because when we take these cells and place them in a cell culture with specific substances and under specific conditions, they can grow and form colonies .

Each CFU is committed to producing a specific type of cells. For example, a CFU that produces red blood cells (RBCs) is called CFU-E (Colony-Forming Unit-Erythroid).
CFU-E gives rise to red blood cells.

If we take a myeloid stem cell and place it under specific conditions, we can influence its differentiation.
This means that the signals and conditions around the cell can affect which type of cell it will develop into.

The myeloid lineage gives rise to several types of blood cells, including:
-Red blood cells (RBCs).
-Platelets.
-Eosinophils.
-Basophils.
-Neutrophils.
-Monocytes.
The lymphoid lineage gives rise to:
-T lymphocytes.
-B lymphocytes.
-NK cells (Natural Killer cells).

All these cells eventually enter the circulation, meaning that they can be found in the bloodstream.

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)

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

- **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**

Growth inducer are signals that stimulate cell growth and division. They increase the number of cells by stimulating cell proliferation.

The most common growth inducer is interleukin- htworg rieht gnitalumits , CSHP no stca hcihw ,(3-LI)3 noitarefilorp dna

The release of IL-3 and other regulatory signals may depend on the body's needs. When the body needs more blood cells, these signals can stimulate the bone marrow to increase blood cell production. IL-3 supports this process by promoting the growth and proliferation of progenitor cells and helping them progress through differentiation toward mature blood cells,

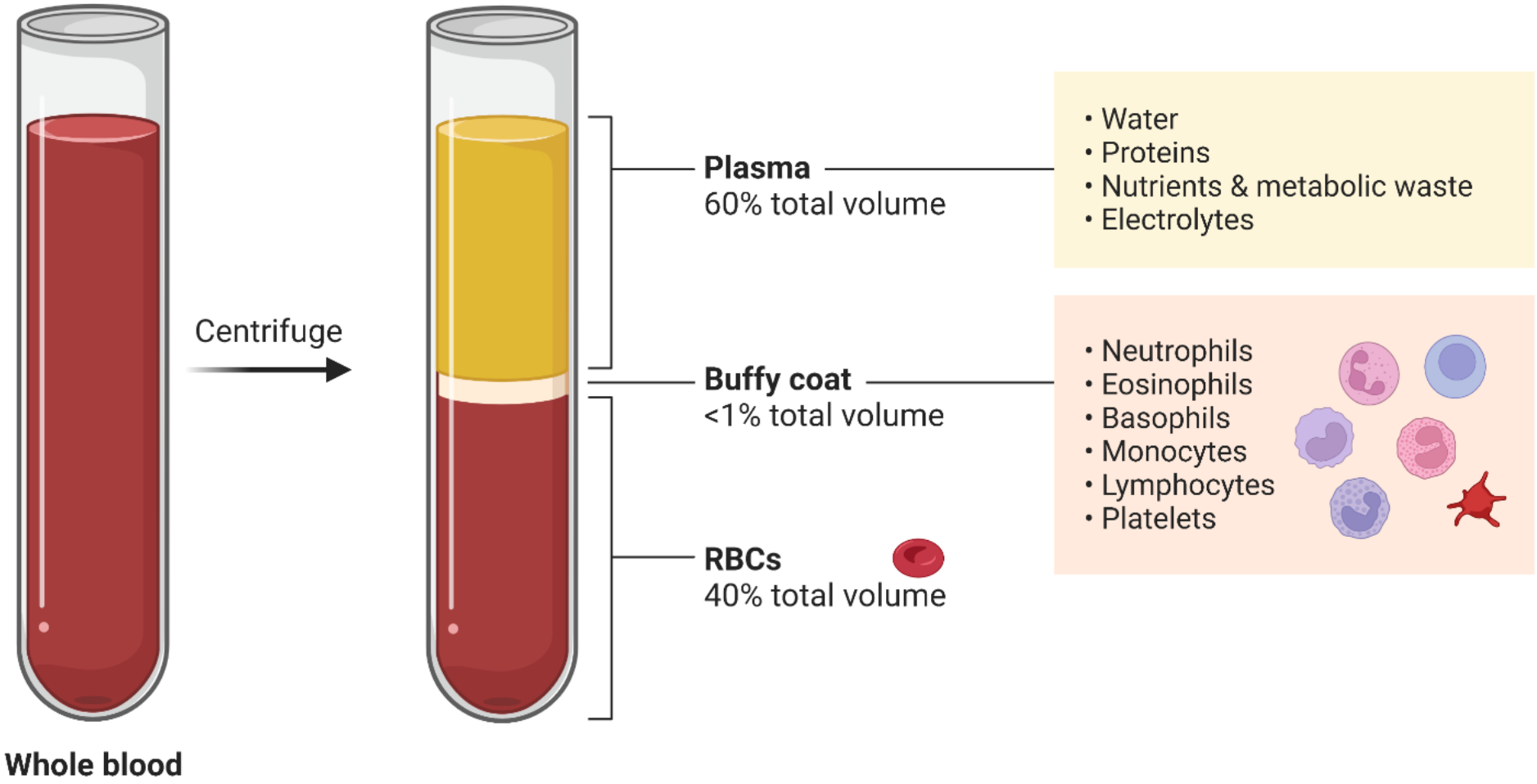
Bone Marrow and Cell Differentiation

The bone marrow provides signals that influence the differentiation of hematopoietic stem cells and progenitor cells. These signals guide the cells through the differentiation process and help determine which blood cell lineage they will develop into.

Depending on the signals they receive, the cells can follow different developmental pathways and become committed to specific blood cell lineages. IL-3 supports this process by stimulating the growth and proliferation of certain hematopoietic progenitor cells.

Hematology

Packed Red Cell Volume



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Hematology Hematocrit

**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.

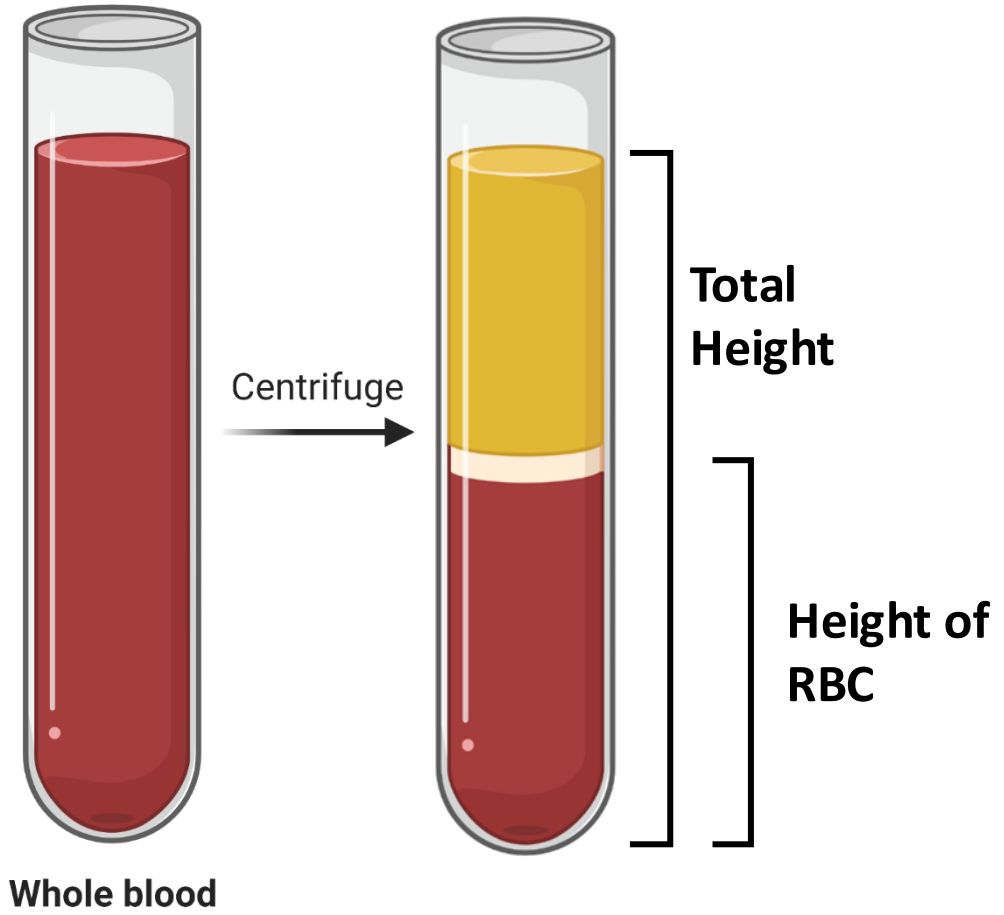
**Hematocrit measures a volume fraction. It does not directly measure the total number of RBCs in the body.

**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.

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

Ratio!!



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

Chapter 18, Boron Medical Physiology (3rd Edition)

Packed Cell Volume and Hematocrit

A blood sample is collected in a tube containing an anticoagulant to prevent clotting. The tube is then centrifuged to separate the blood components. After centrifugation, red blood cells (RBCs) settle at the bottom, while plasma remains at the top.

PCV and hematocrit represent the proportion of the total blood volume occupied by red blood cells. They can be determined using different methods:

-PCV: Traditionally measured manually by centrifuging the blood sample and measuring the packed red blood cell layer.
-Hematocrit : Commonly measured or calculated automatically by laboratory analyzers.

Measurement of PCV

PCV is calculated by comparing the height of the packed red blood cells with the total height of the blood sample.

PCV) = (Height of packed RBCs / Total height of blood) *

Therefore, PCV is expressed as a percentage of the total blood volume occupied by red blood cells.

PCV is generally higher in males than in females. It may be approximately 44% in males and is usually lower in females.

This difference is partly related to testosterone, which stimulates erythropoiesis (red blood cell production). Increased red blood cell production can increase PCV.
Females may also have a lower PCV partly because of menstrual blood loss.

Clinical Significance of PCV

PCV helps evaluate the proportion of red blood cells in the blood.

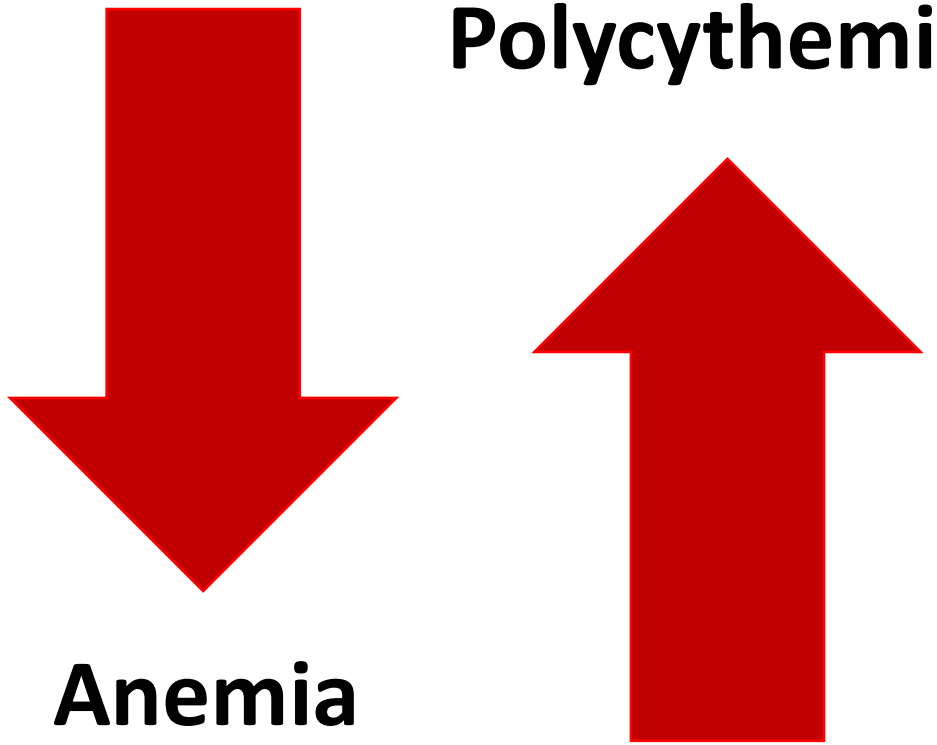
-Decreased PCV: May indicate anemia.
-Increased PCV: May indicate polycythemia, which is an increased proportion of red blood cells in the blood.

Increased PCV Due to Dehydration

An increased PCV does not always indicate polycythemia. It may also occur due to dehydration, which reduces the amount of plasma in the blood. As plasma volume decreases, the total blood volume decreases while the red blood cell volume remains relatively unchanged. Therefore, the proportion of red blood cells increases, resulting in a higher PCV.

This is called relative increase in PCV, because the percentage increases due to a decrease in plasma volume rather than an actual increase in red blood cell mass.

Hematology > Hematocrit



Polycythemia

Anemia

* 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 menstruatio.

**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.

رسالة من الفريق العلمي:

الزميل عون محمد العدوان تحت العناية المركزة أثر صعقة كهربائية، نتمنى من الجميع أن يتوجهوا إلى الله بالدعاء.

اللهم إنا نرفع إليك أكف الضراعة وقلوبنا معلقة برحمتك، لا نملك له من الأمر شيئًا، وأنت القادر على كل شيء، اللهم إن عجز الطب عن شيء، فأنت رب الطب لك ورب الدواء عن شيء، فأنت رب الطب ورب الدواء وإن ضعفت حيلتنا، فرحمتك أوسع من كل ضعف، وقدرتك أعظم من كل ألم.

اللهم أعد عون العدوان إلى أهله سالمًا معافى، وأقر أعين أحبته بشفائه، وأبدل خوفهم طمأنينة، ودموعهم فرحًا، ودعاءهم بشارة تُسَرّ قلوبهم.

اللهم لا تحرم أهله فرحة شفائه، ولا تكسر لهم قلبًا، ولا ترد لهم دعاء، واجعل له من كل ضيق فرجًا، ومن كل بلاء عافية، ومن كل ألم شفاء.

يا رب، إنا نرجوك رجاء لا يخيب، وندعوك دعاء المضطر الذي لا ملجأ له إلا أنت، فاشفه يا الله، واشرح صدره، ورد إليه عافيته ردًا جميلًا، واجعل القادم من أيامه أجمل مما مضى.

اللهم آمين، آمين، آمين يا رب العالمين...

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Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			