Physiology
Sheet No. 20

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Body fluids

Water is forming around 60% of the total body mass in males and around 55% of the total body mass in females (the difference in percentage is because females have more fats than males).

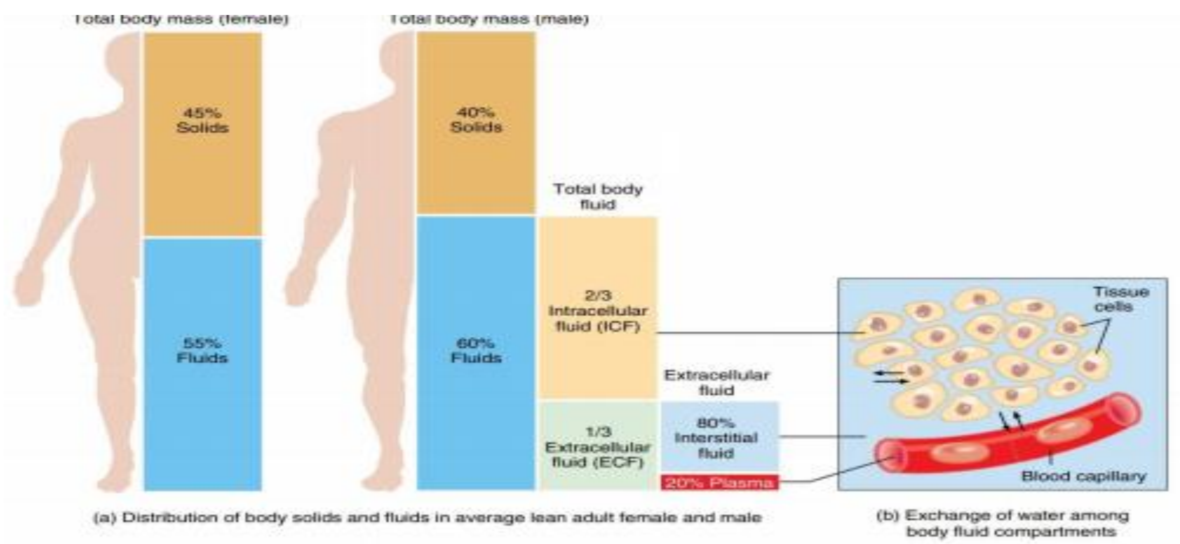
These fluids are distributed inside cells and outside cells forming 2 compartments:

1) 2/3 of these fluids are found inside cells forming intracellular fluid compartment.

2) 1/3 of these fluids are distributed outside cells forming extracellular fluid compartment (ECF):

   A- 80% of (ECF) are found between cells forming interstitial fluid.

   B- around 20% of (ECF) are found inside vessels forming plasma (which is around the red blood cells and the blood cells inside vessels).



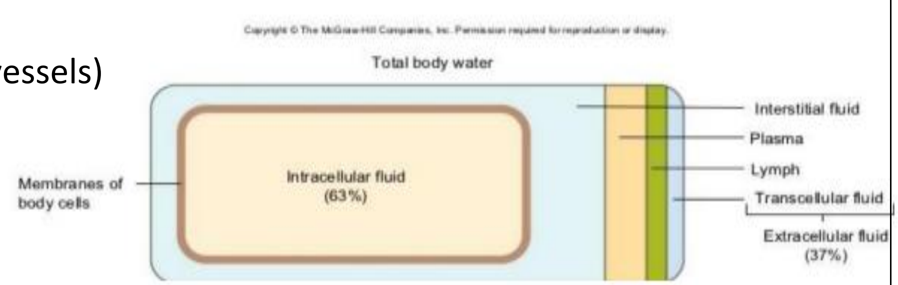
(a) Distribution of body solids and fluids in average lean adult female and male
(b) Exchange of water among body fluid compartments

Extracellular fluid can be:

A. plasma   B. lymph (in lymphatic vessels)

C. small amount transcellular fluid

(in certain cavities in our body).



❖ Transcellular fluid can be found in:

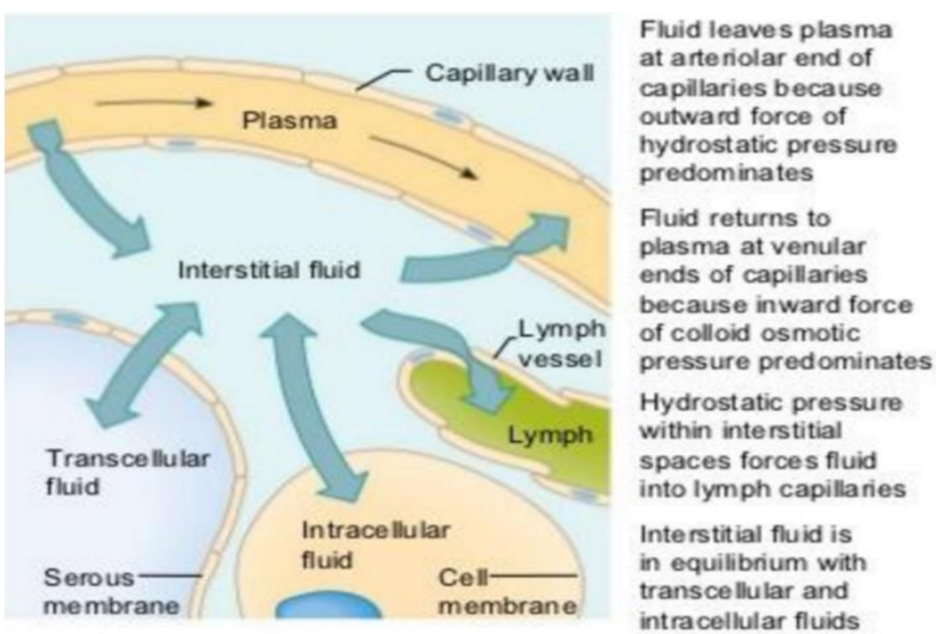
- Synovial fluid (Joints).
- Pericardial fluid (around the heart).
- Pleural fluid (around the lungs).
- Peritoneal fluid (gastrointestinal fluid).
- Ocular fluid (in the eye).
- Cerebrospinal fluid (around neural tissue in CNS).

❖ Movement of Fluids between compartments

These fluids that are found inside body are not static all the time we have exchange between different compartments (as arrows) the movement of fluid is regulated by certain factors as:

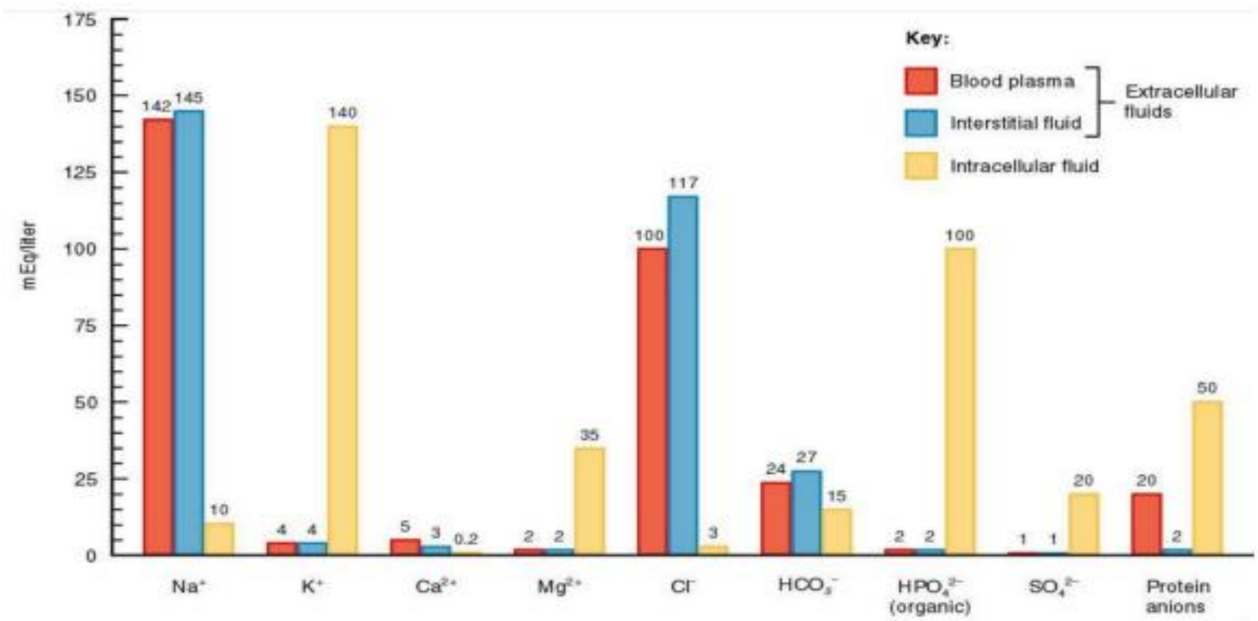
1- **osmotic pressure**

2- **hydrostatic pressure**



water moves between these compartments according to **the pressure** we are having in these compartments; the composition of these fluid may vary according to compartments (example: Na+ in extracellular compartment is high while K+ in intracellular fluid is high and we have low K+ in ECF)

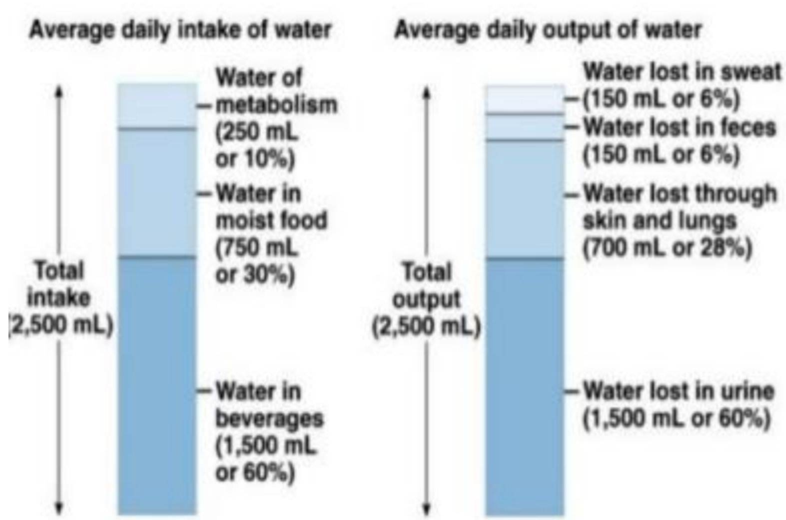
- There are also differences between sub compartments (example: higher amount of protein in plasma than in interstitial fluid both belong to ECF).



❖ Water Balance: Water input = Water output

In any body all the time water is in balance, at any time there is an increase in water output by more loss of water there is increase in water input (and any increase in water input there is increase in output to keep the balance).

1.Water input



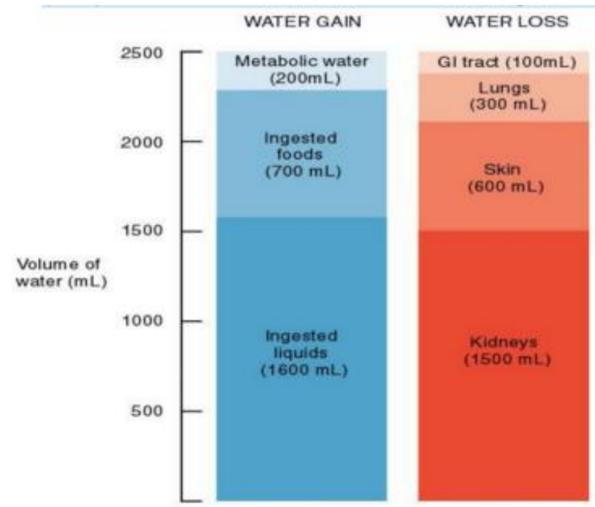
The volume of water gained daily varies among individuals, averaging about 2500 mL/day (2.5 liters/day).

a. 60% Drinking.

b. 30% moist food (ingested food).

c. 10% Metabolic processes in the body after oxidative phosphorylation (the final degradation of nutrients resulting of water and CO2).

2.Water output



Water normally enters the body only through the mouth, but it can be lost by a variety of routes, including:

a. Urine (60% loss). b. Feces (6% loss).

c. Sweat (sensible perspiration) (6% loss).

d. Evaporation from the skin (insensible perspiration).

e. The lungs during breathing. (also insensible perspiration)

(Evaporation from the skin and the lungs is a 28% loss that loss is called insensible loss)

- We talked about water intake and loss in our bodies, and we said that there is a balance between water intake and water loss. But the question is:

How can we keep the balance between water intake and loss, and keep the volume of water roughly fixed in our bodies??

By asking this question, we should conclude that water balance is highly regulated in our bodies. There are many systems that are involved in the regulation of water's amount in our bodies and **the regulation of fluids and electrolytes**, like:

- Urinary system
- Cardiovascular system
- Endocrine system, through (Pituitary, parathyroid and adrenal glands)
- Respiratory system (Lungs participate in this process of regulation)

- Fluids in our bodies are not static, rather they are **Dynamic**. That's why you always have movement of fluids between interstitial fluid and other fluids (intracellular fluid, transcellular fluid, plasma and lymph fluid) Check the picture in page 3
- The regulation of fluids and electrolytes in our bodies leads to **Homeostasis**

- Now, what are the factors that regulate this movement and exchange of water?
  1- Osmolarity or Osmolality (**Osmotic pressure**)

  2- **Volume of ECF** (related to hydrostatic pressure)

  Note: In this sheet you don't need to differentiate between osmolarity and osmolality (You can use any of them, it doesn't matter)

We will focus on the regulation of water and sodium, and before starting…. you should know that there is an overlapping in the mechanisms involved in the regulation of water and Na^+:

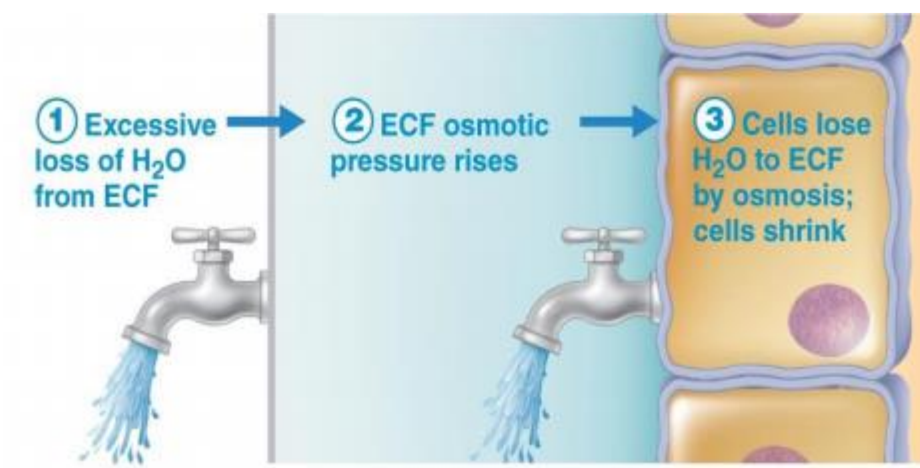
THE REGULATION OF WATER AND SODIUM Na^+

Let's start,

Firstly, **What is the importance of water and Na^+ regulation?**

To answer this question, imagine that we have excessive **loss of water** from the body (water without Na^+). In this case, **ECF volume will decrease**, so **the osmolarity of the ECF will increase** and this will cause **water to move from inside the cells towards ECF** and this will end with **shrinkage** of cells.

This process is called **Dehydration** of cells (we are decreasing the volume of water inside the cells).



(a) Consequences of dehydration. If more water than solutes is lost, cells shrink.

Now, let's think of it in the opposite way. What will happen if we have excessive **intake of water**? Surely, you will say that **ECF volume will increase** and the **osmolarity of ECF will decrease**. As a result, **water will move from ECF towards cells**. This will end with **swelling** of cells.

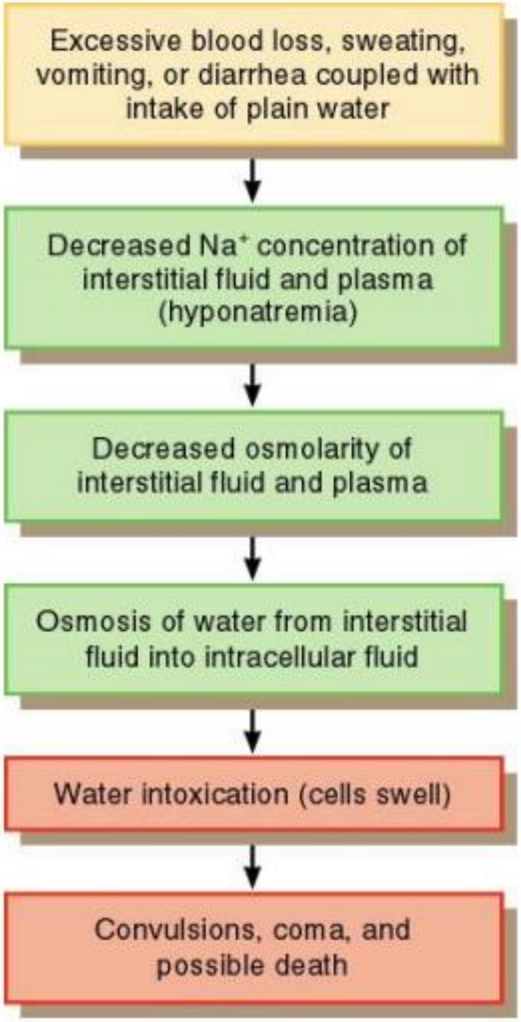
This is important for you as a doctor, because when this happens in some tissues and organs, it leads to **Oedema.**

(b) Consequences of hypotonic hydration (water gain).
If more water than solutes is gained, cells swell.

You should know that neither **dehydration** nor **swelling** is healthy.

EXAMPLE:

To deeply understand the following example, you have to know that in blood loss, sweating, vomiting or diarrhea, the body loses water and ions. While the intake of plain water replaces the water but not the ions. So, this changes the osmolarity of fluids inside your body.



>> Intake of plain water happens by drinking

>> Water moves from low osmolarity area into high osmolarity area.

>> The brain tissue is the most sensitive to water intoxication, so those people are subjected to convulsions ,(تشنجات) coma and possible death.

Don't forget that we were trying to understand the importance of regulation of water and sodium, and now I think that you are aware of it.

Measurements of body fluids

We will study the **dilutional method** to measure body fluids' volume in our bodies, and this method can be done in different ways. In order to understand these ways, we have to discuss **Dilution Principle**.

Don't worry you already know it ☺

Dilution Principle

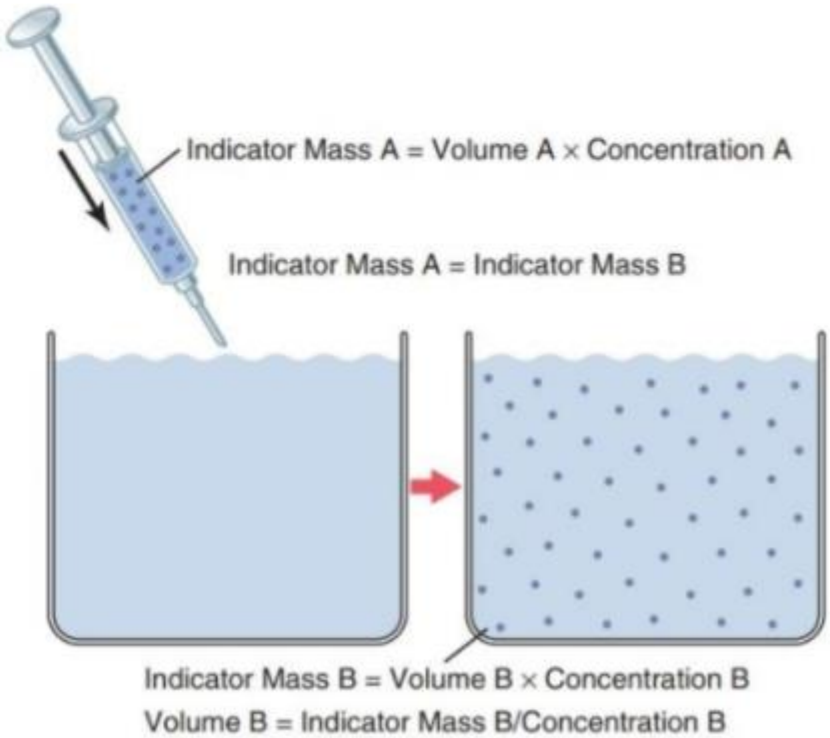


Figure 25-4. Indicator-dilution method for measuring fluid volumes.

In the picture above, we have injected 1mL of a 10mg/mL solution (let's say it's a dye) into a fluid compartment that we don't know its volume. **After injection**, the final concentration was 0.01mg/mL. Using these information, we can know the volume of the fluid compartment. We say that:

Volume B = (Volume A * Concentration A) / Concentration B

= (1mL * 10mg/mL) / 0.01mg/mL = 1000mL

Remember from chemistry 101

Vi*Mi=Vf*Mf

Not required, but to understand

no. of moles in the dye before injection = no. of moles after injection

$Concentration_{before} * Volume_{before} = Concentration_{after} * Volume_{after}$

$Volume_{after} = (Concentration_{before} * Volume_{before}) / Concentration_{after}$

Volume B = (Volume A * Concentration A) / Concentration B

Now we will talk about dilution method,

☒ What kind of dyes can we use?

We use the ideal dye (ideal tracer) that must:

• be **nontoxic**

• be **rapidly and evenly distribute** throughout the nominated compartment and does not enter any other compartment.

• **not be metabolized.**

• **not be excreted** (or excretion is able to be corrected for) during the equilibration period.

• be **easy to measure**

• **does not interfere with body fluid distribution**

- To get an overview about what we will be talking about:

We will measure the following body fluids' volume:

* **Total body water** ***ECF** ***ICF** ***Total blood** ***Plasma**

Total body water measurement

❖ We should use a substance that can be distributed in all compartments, because we want to measure **Total** body water volume.

We can use:

1. **Radioactive water (^3H_2O, T_2O, Tritium)** or **heavy water (^2H_2O, D_2O, Deuterium)**. This will mix with the total body water in just a few hours and the dilution method for calculation can be used.
   Notes:
   *Radioactive water and heavy water are radioactive, but they differ in radioactivity
   *we use these substances in tiny concentrations

Example:

You inject someone with 1mL of heavy water (with known radioactivity) and after a few hours it will mix with the total body water, then you take 1mL of blood and you will find that radioactivity is less than that you have injected and using calculations (dilution principle) you can measure water volume in the body. **(Radioactivity is related to concentration, so you can use dilution principle)**

2. **Antipyrine** (It isn't radioactive)

Extracellular fluid (ECF) measurement

To measure ECF volume, we can use:

1. **$^{22}Na^{+}$ (Sodium space)**. It is radioactive. We can use sodium to measure ECF volume because sodium is mainly found in ECF.
2. **^{125}I-iothalamate**. It is also radioactive.
3. **Thiosulfate.**
4. **Inulin (Inulin space).**

The measurement should be in (30-60) minutes, before the substance gets exchanged between ECF and ICF.

Intracellular fluid (ICF) measurement

To measure ICF volume, we can say:

ICF = Total body water – ECF

There is **no need** to use substances

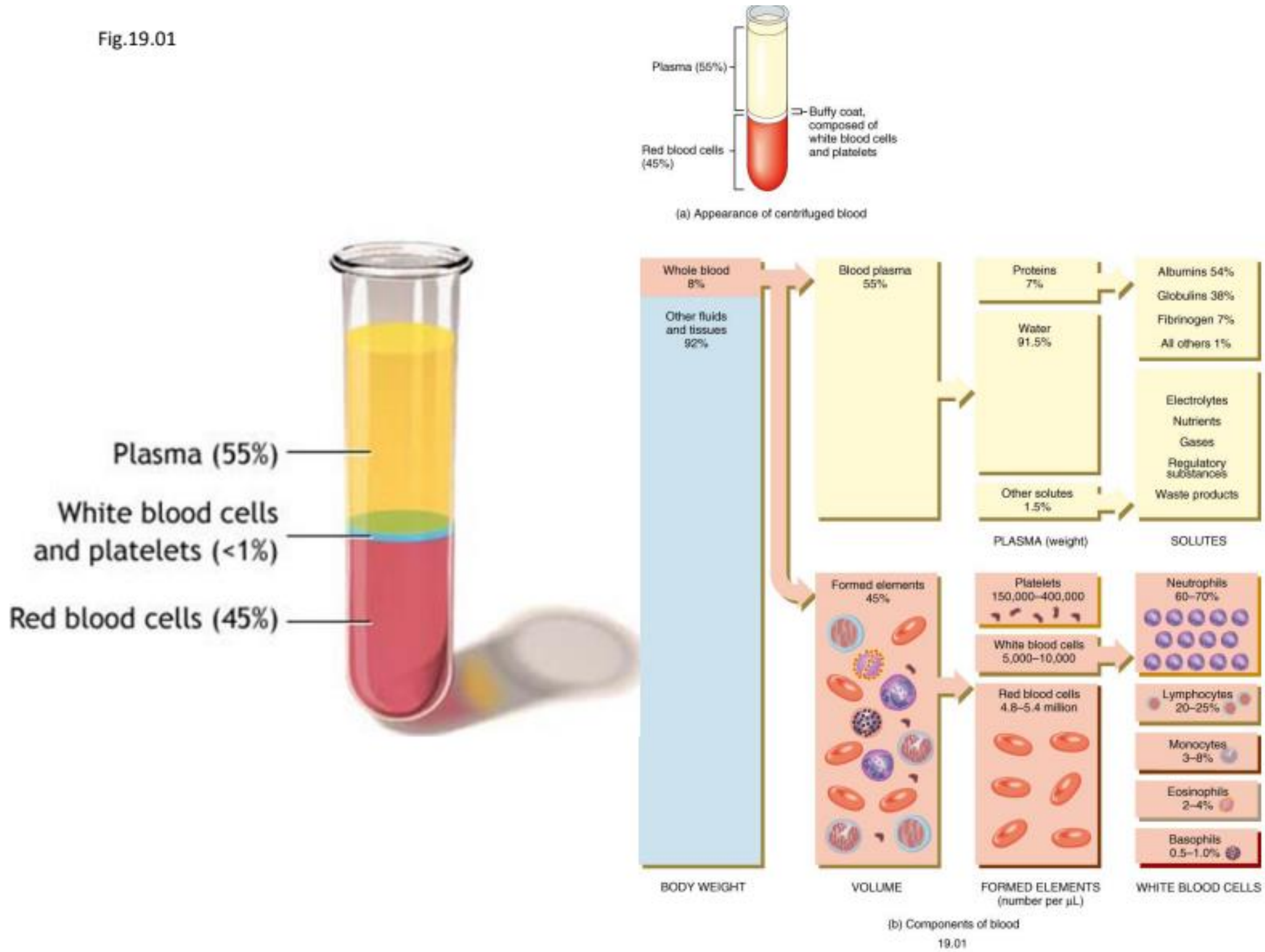
Measurement of intravascular fluids

*Total blood volume *Plasma

You may ask: **What's the difference between blood and plasma?**

If you have a blood sample and you centrifuge it (separate its components), you will find that plasma represents 55% of the blood. RBCs represent 45% of the blood, while white blood cells and platelets represent less than 1%. (If you ask about the proportions, how can they be more than 100%? I will tell you that these proportions are not exact, rather they are approximate proportions), Check the picture below!

Fig.19.01



Plasma composition

• Water: > 90%

• Small molecule: 2%, it is electrolytes, nutriment, metabolic products, hormones, enzymes, etc.

• Proteins : 60-80 g/L, plasma protein include **albumin** (40-50 g/L) (54%), **globulins** (20-30 g/L) (α1 -, α2 , β-, γ-) (38%) and **fibrinogen** (7%). Most of albumin and globulin made from liver

Notes :

1. We have high amount of proteins in plasma
2. γ- globulins are antibodies
3. Fibrinogen is important for the process of coagulation (تخثر الدم)

After discussing the difference between plasma and blood, and the components of each one, let's talk about the measurement of plasma volume and total blood volume

Measurement of plasma volume

We can use:

1. **^{125}I-Albumin (RISA)** (Radio iodide albumin)

It can't be distributed out of the vascular fluid
It is radioactive (you can know this from its name)
Of course, we use dilution principle

2. **Evans Blue (Dye (T1824))**

Measurement of total blood volume

*We can use **^{51}Cr- labeled red blood cells** (We label RBCs with iodide chromium (^{51}Cr), then we inject them in the blood. After that, we use dilution principle)

*We can use **Fluoroscent dyes** rather than radioactive dyes (if we use fluorescent dyes, we measure the fluorescence not the radioactivity), but you should know that radioactive products are more accurate

*We can calculate the total blood volume as the following:

Plasma volume / (1- Hematocrit)

> **Hematocrit** : The volume percentage of RBCs in blood

Or simply, think of it as the following:

If you know the volume of plasma, you can know the total volume of blood since plasma represents 55% of the blood and vice versa (if you know the volume of blood, you can know the volume of plasma)

Let's return to our basic concept, we said that we have different regulatory machanisms in our bodies to regulate Na^+ and water that are involved in the regulation of **osmolality** and **volume of ECF**

Remember: There is an overlapping in the regulatory mechanisms of water and Na^+

Osmoregulation

We have in our bodies receptors that are called **osmoreceptors** (they sense changes in osmolarity)

If there is an increase in body fluids' osmolarity, this means that we need water. And the body will try to collect water in different ways to decrease the osmolarity and bring it back to normal (Negative feedback system). These ways involve increasing water intake and reducing water loss

1. Increasing water intake (Regulation of intake)

Simply, if there is an increase in the osmolarity of your body fluids, you will have a lot of signals going towards thirst centers in the hypothalamus and you will feel thirsty, so you will drink water. And by this we have increased water intake. In order to do this, there are different ways and here are some of them:

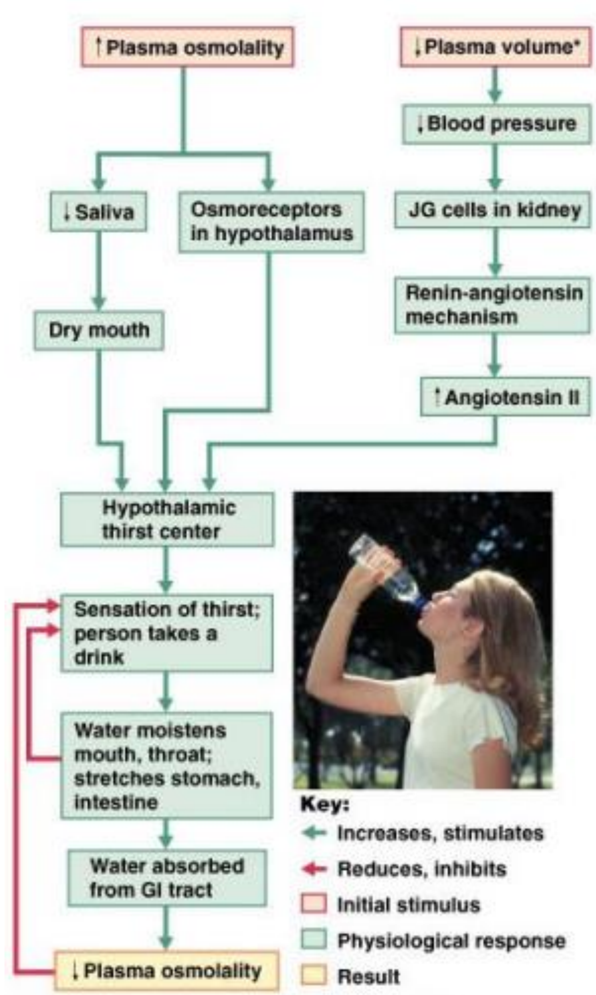
*You should know that hypothalamic thirst centers are activated by **dry mouth**. So the first way to increase water intake:

Increased osmolarity reduces salivation, so the mouth will be dry and this activates thirst centers

*The second way is through **osmoreceptors** in hypothalamus (They sense an increase in the osmolarity and send signals to thirst centers)

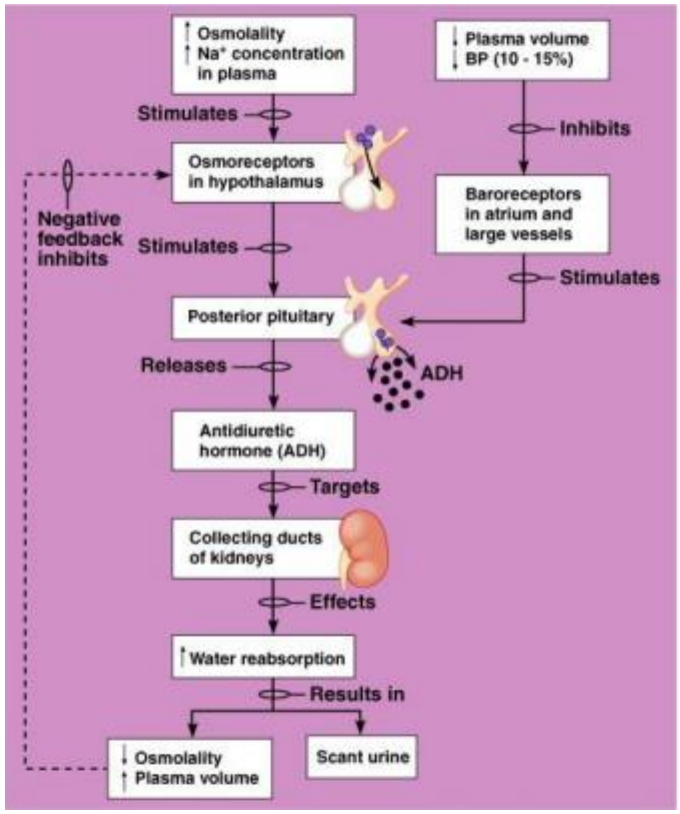
*The third way:

Decreased plasma volume means decreased BP (blood pressure) and this will activate JG (juxtaglomerular) cells in the kidney to activate a system known as "Renin-angiotensin-aldosterone" and this system activates thirst centers in hypothalamus through **angiotensin II** –we will study this system with more details-



2. Decreasing water output (Regulation of output)

Increased osmolarity stimulates the release of ADH (antidiuretic hormone) from posterior pituitary gland which acts on renal collecting ducts and increases water reabsorption. And this is how water output decreases



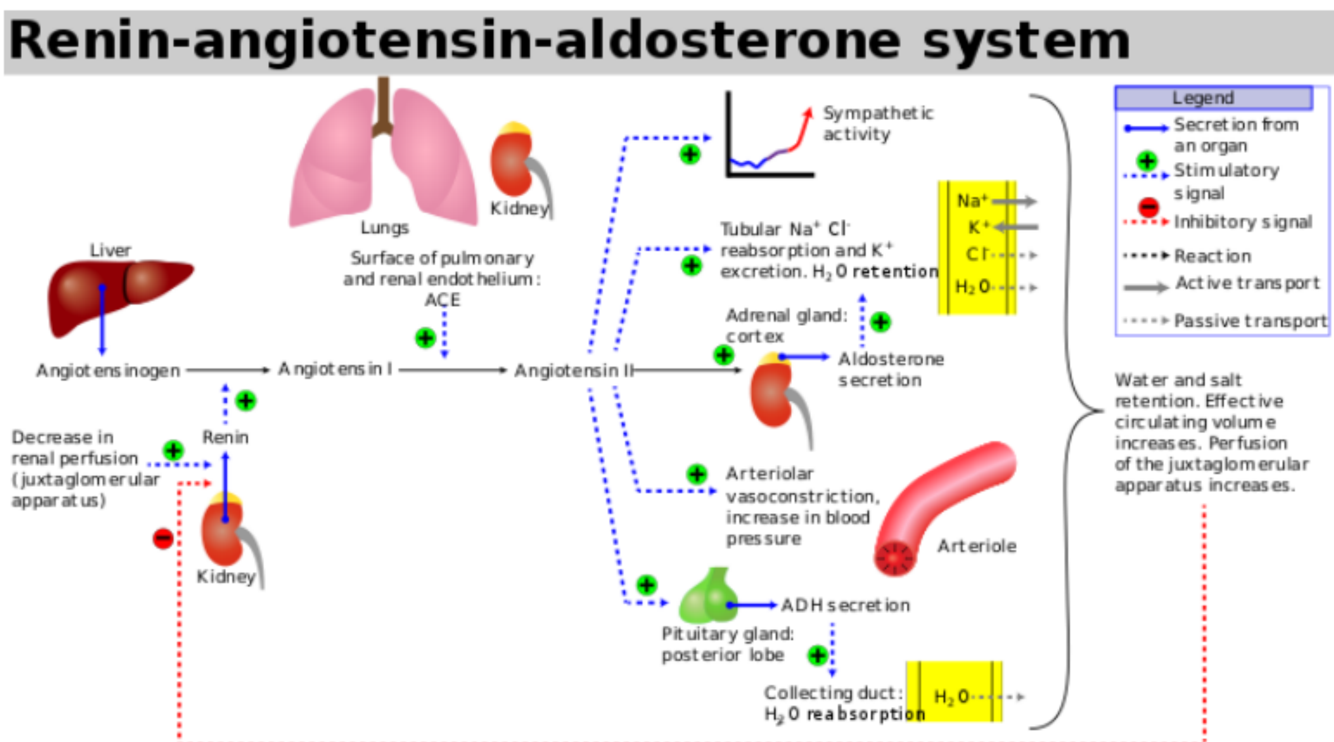
Regulation of ECF volume

The regulation of ECF volume depends on **Na^+ excretion in urine** and it is controlled by **Renin-Angiotensin-Aldosterone** system (yes I told you that there is overlapping in the regulatory mechanisms!!)

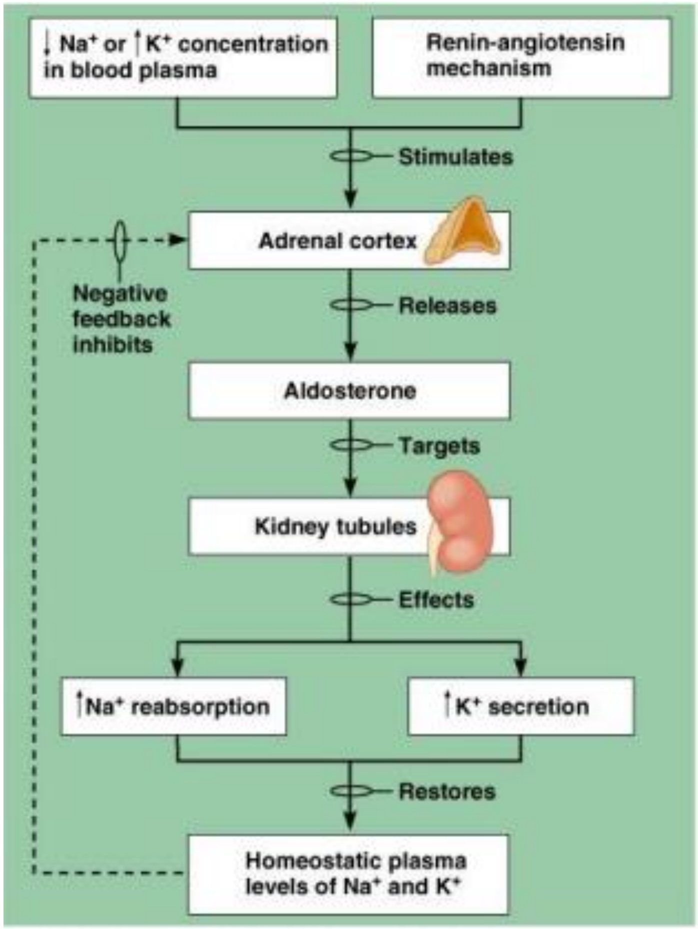
Let's start and activate this system,

Once there is a decrease in blood flow in our kidneys, that can happen when volume of ECF is reduced→ Juxtaglomerular Cells (in Kidney) release Renin → Angiotensinogen (from liver) (by renin enzyme) is converted into Angiotensin I → Angiotensin I (by Angiotensin converting enzymes (ACE) which is produced in lungs) is converted into Angiotensin II → Angiotensin II acts on adrenal (suprarenal) gland → to stimulate release Aldosterone from adrenal cortex → Aldosterone acts on the kidney and increases reabsorption of sodium and secretion of K^+ → increase osmolality → water retention → the volume of ECF will increase.

* To know: ACE enzyme is the target of covid virus



* Notice that this system is also involved in the homeostasis of Na^+ and K^+



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