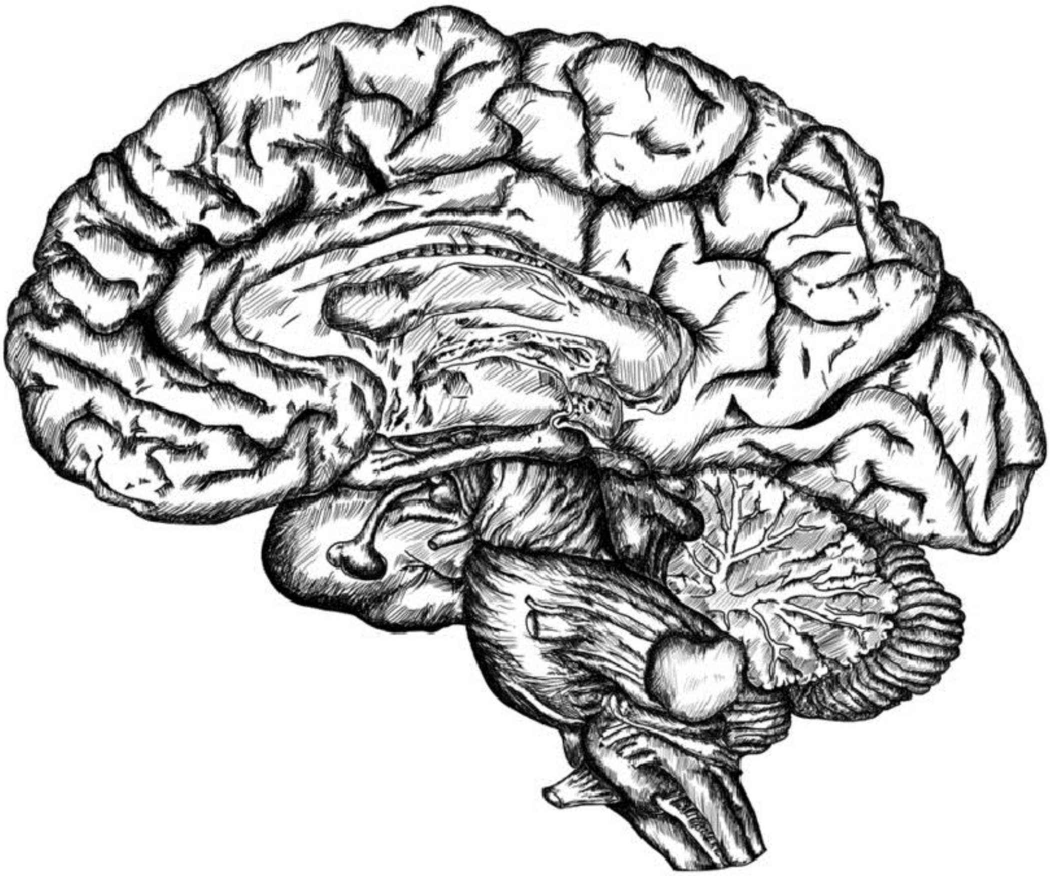
PHYSIOLOGY



☑ Sheet ☐ Slides ☐ Handout

Lecture No.: 21

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Review:

In the previous lecture, we have seen how to measure total body fluids volume by using tritiated water (water that has hydrogen atoms with one proton and two neutrons) or by using Antipyrine.

Also, we saw how we measure extra-cellular fluids (ECF) by using radioactive Na (in this case we measure Na space and from this we can measure the ECF), also, we can use radioactive Iodine Thalamate (^{125}I-iothalamate) or by using Thiosulfate or by using Inulin (in this case we measure Inulin space).

We said that **we can't measure intra-cellular fluid** (ICF) because we have substances that can only be distributed inside cells. But we can calculate ICF (ICF = Total - ECF).

Review is over.

Measuring intra-vascular fluid:

We may measure **plasma volume** only or **total blood volume**.

If we centrifuged a blood sample, blood cells will be deposited down, and what remains up is the **plasma** (**Figure 1**).

So, Plasma = Blood – Cells

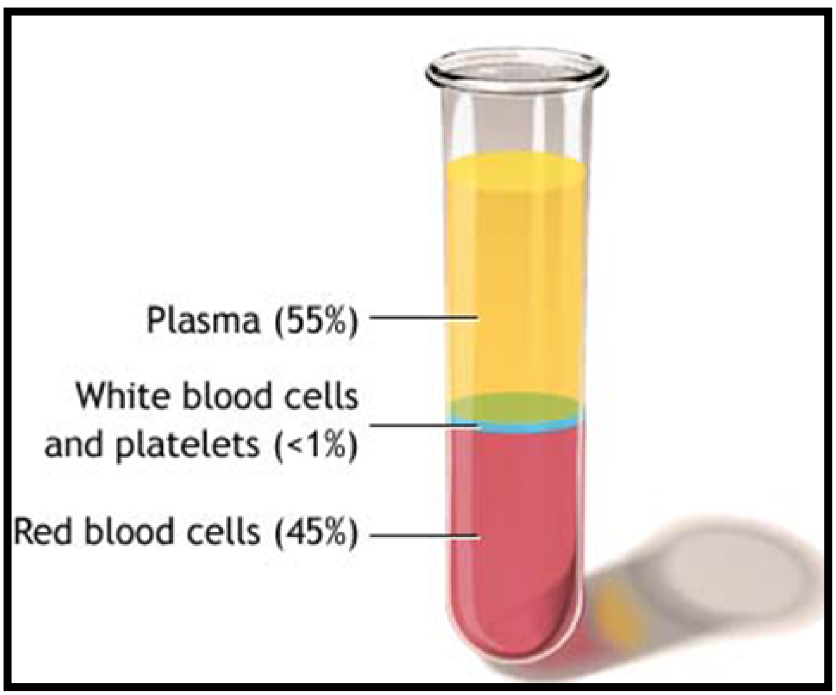


Figure 1: Centrifuged blood.

Note: If you coagulate all the blood sample at first (this will consume all the coagulation proteins -including fibrinogen- on the blood), and then centrifuged the sample, we will get cells and **serum** instead of plasma.

The volume percentage (%) occupied by blood cells is called the **Hematocrit** (also known as packed cell volume -PCV-), we get this percentage by calculating $\frac{\text{Blood cells volume}}{\text{Total blood volume}} \times 100\%$

(This is calculated using a sample –not whole body blood volume)

or by calculating $\frac{\text{Blood cells height}}{\text{Total blood height}} \times 100\%$

(Normally, the Hematocrit is around 43-45%).

Note: Anemia test and some other test are done by measuring the Hematocrit.

Plasma is composed of: - Water (>90%) - Small molecules (2%)
- Proteins: 60-80 gram of proteins per 1 liter of plasma, most of these proteins is albumin (40-50 g/L = 54%), also there is globulin (α_1, α_2, β, γ) (20-30 g/L = 38%), and fibrinogen which is involved in coagulation process (7%).

Note: γ globulins are the anti bodies.

Note: We will not be asked on all these details, we shall know them just in brief.

Now, the thing that is important to us is methods used to measure the plasma volume.

There is two methods:

1- ^{125}I-Albumin: Most of the proteins are found in plasma (mostly albumin), and very low amount is found in the interstitial fluid, so we can use **radio iodine serum albumin** (radioactive I-albumin) to measure the plasma volume.
2- **Evans Blue**: We can use substances that bind to proteins, once these substances bind we can assay them and measure plasma volume.

To measure total blood volume, we have two methods:

1- We can use **red blood cells labeled by radioactive chromium** (^{51}Cr). By introducing these labeled cells we can measure total blood volume using the **indicator-dilution principle**.
2- We can **calculate** total blood volume, but firstly we must know plasma volume and the Hematocrit then we can use this equation to calculate the total blood volume.

$$\text{Total blood volume} = \frac{\text{Plasma volume}}{1 - \text{Hematocrit}}$$

Exercise: If the hematocrit is 0.40 (40%) and total blood volume is 5 liters, calculate:

a- Plasma volume.   b- Blood cells volume.

Solution:

a- $\text{Total blood volume} = \frac{\text{Plasma volume}}{1 - \text{Hematocrit}}$

   5 = Plasma volume / 1 - 0.40 → Plasma volume = 3 liters.

b- We can calculate it in two ways:
   - Hematocrit = Cells volume / Total volume.
   - Total volume = Plasma volume + Cells volume.

By using the first method: Cells volume = Total volume × Hematocrit = 5 × 0.40 = 2 liters.

Regulation of fluids volume:

The amount of fluid in our bodies is very well regulated, this regulation involves **regulation of osmolality** and **regulation of volume of ECF**.

Note: There are many mechanisms for these regulations and these mechanisms are overlapped and confusing. Actually, different body systems use these mechanisms.

1- Regulation of osmolality:

Osmolality depends mainly on Na^+ concentration in our bodies, so we need to regulate Na^+ concentration to regulate osmolality.

Ex: A- If there was an increment in Na^+ concentration in the body, the body fluids will become hypertonic. There are receptors in the body that sense these changes in fluids, if it sensed an increment, the **hypothalamus** will respond by making the body feel **thirsty**. By drinking water, the osmolality will decrease and return normal (**Regulation of intake**) (this is the simplest way).

B- Also increment in osmolality will stimulate **ADH** (Antidiuretic hormone), which in its role, will act over the kidney to get **more reabsorption of water** and as a result the osmolality will decrease (**Regulation of output**).

So, the purpose of these two mechanisms is decreasing of osmolality.

2- Regulation of ECF volume:

Ex: A- If there was a decrement in volume, this will result in decrement of blood flow toward kidneys, this will activate Juxtaglomerular cells, and this will result in releasing Renin.

Renin converts Angiotensinogen to Angiotensin I. Angiotensin I usually converted to Angiotensin II (the active form) by lung tissue. Then Angiotensin II will stimulate the release of **Aldosterone**. Aldosterone will result in an **increment of Na^+ reabsorption** which will increase osmolality, this increment in osmolality acts on the hypothalamus centers to increase ADH, as ADH increases the volume will increase as a result of water reabsorption (This method is called **renin-angiotensin mechanism**).

B- Also volume may be regulated by **ANP** which activates releasing of Aldosterone (it has many other effects).

Note: Don't pay much attention to method B, you just should know that the ECF volume can be regulated by ANP.

You must not know all the details, as a summary:

- Thirst and ADH are involved in regulating osmolality.
- Renin-angiotensin mechanism (which results in secretion of Aldosterone) is involved in regulating volume (Aldosterone increase Na^+ absorption which will finally result in an increment of water reabsorption).

Note: Aldosterone is secreted from **Suprarenal gland (Adrenal gland)**.

Note: Aldosterone is also called mineralocorticoid.

Disorders of Volumes:

Increment in volume is called **Hypervolemia**.

Decrement in volume is called **Hypovolemia**.

Hypovolemia results by high loss of water (by sweating, urination, vomiting, diarrhea…).

Medical applications:

- Osmotic diuresis (**ادرار البول التناضحي**): in this disease there are high glucose concentration in urine, this will cause more attraction of water, and as a result patient will have high urination → Hypovolemia.
- Diabetes insipidus (**مرض السكري الكاذب**): in this disease there will be a decrement in ADH, this will cause more loss of water → Hypovolemia.

Hypervolemia results by high intake of water, or by disturbances of the mechanisms examined earlier.

Ex: If there is high increment of ADH (abnormal case), this will result in more reabsorption of water which will cause hypervolemia.

Note: In hypovolemia the osmolality increases and in hypervolemia the osmolality decreases. So, we get a change in composition of fluids also (not only in volume).

Disorders of Osmolality:

Increment in osmolality is called **Hypernatremia**.

Decrement in osmolality is called **Hyponatremia**.

Hyponatremia results by:

- Excessive loss of Na^+.
- Administration of <u>hypotonic</u> fluids.
- Loss of <u>hypertonic</u> fluids.
- Increment in ADH (reabsorption of water).
- Decrement in Aldosterone.

Hypernatremia results by:

- Excessive intake of Na^+.
- Administration of <u>hypertonic</u> fluids.
- Loss of <u>hypotonic</u> fluids.
- Decrement in ADH (Loosing more water).
- Increment in Aldosterone.

So, these disorders may happen by disturbances of regulatory mechanisms not only by intake or loss of hypertonic fluids or hypotonic fluids or so on.

Note: Always there is a relation between volume and osmolality.

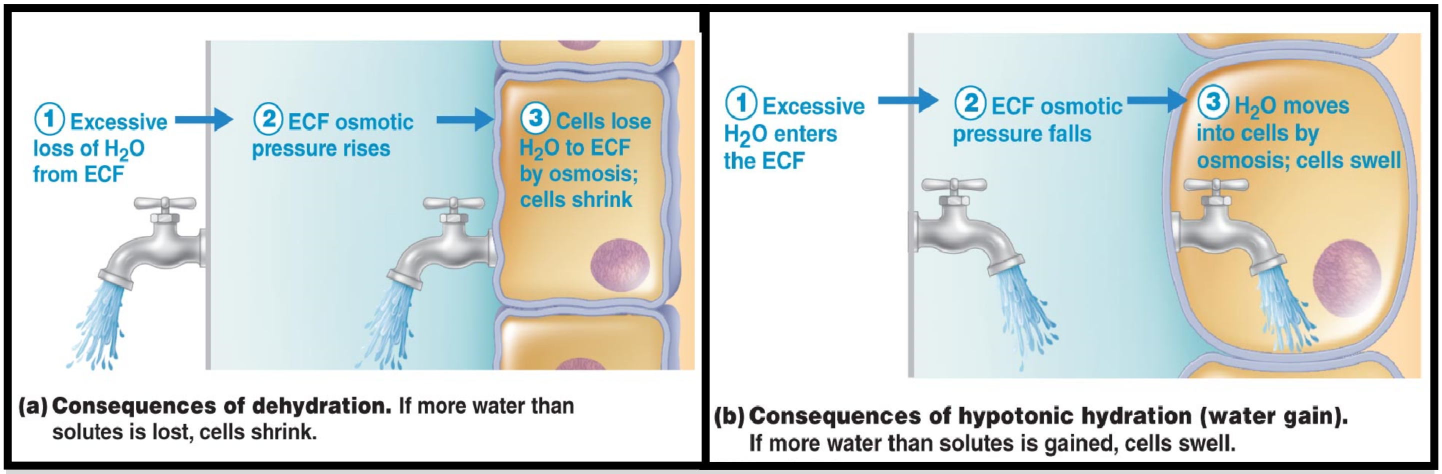
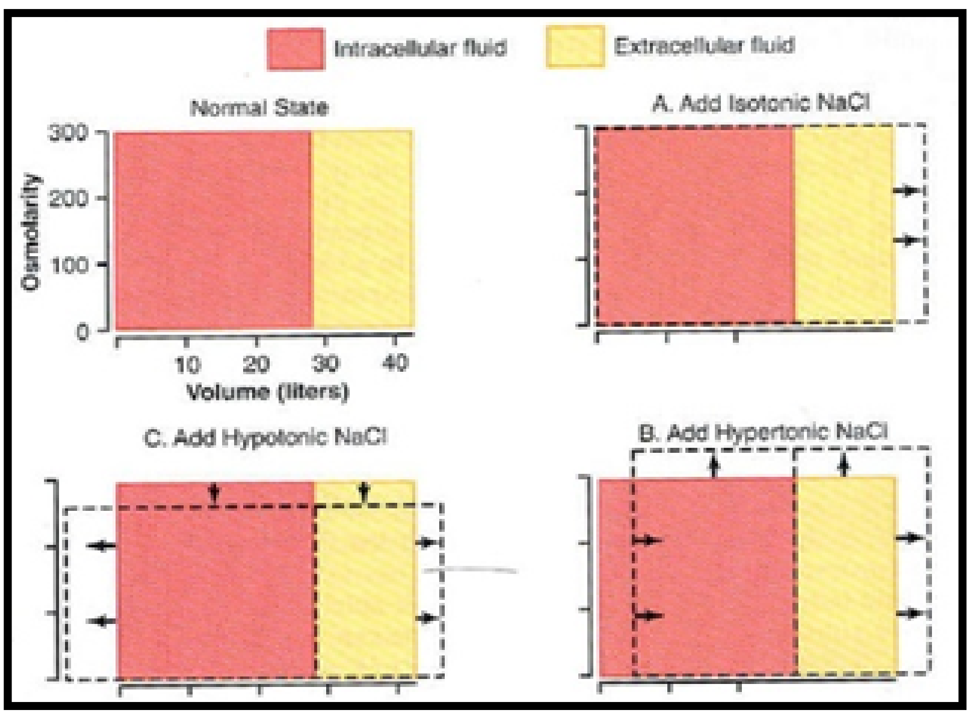


Figure 2: Dehydration and over hydration.

See **figure 2**, assuming that the water is hypotonic. If we have excessive loss of water like in (a), this will result in increasing of osmolality in ECF and water will move from inside cells toward ECF. As a result, cells will shrink (This is called **Dehydration**).

If we have excessive intake of water like in (b), this will result in decreasing of osmolality in ECF and water will move from ECF and enters cells. As a result, cells will swell (This is called **Overhydration**).

Figure 3: Effects of isotonic, hypertonic and hypotonic solutions.



See **figure 3**.

- If we give **normal saline** (isotonic solution) to a normal body as in (A), this will result in **increasing of ECF volume**, **without any change in ICF volume or osmolarities**.
- If we give **hypertonic** solution to a normal body as in (B), this will result in **increasing of ECF volume and osmolarity**, this will cause fluid to move from ICF to ECF, as a result, **ICF volume decreases and its osmolarity increases**.
- If we give **hypotonic** solution to a normal body as in (C), this will result in **increasing of ECF volume and decreasing of its osmolarity**, this will cause fluid to move from ECF to ICF, as a result, **ICF volume increases and its osmolarity decreases**.