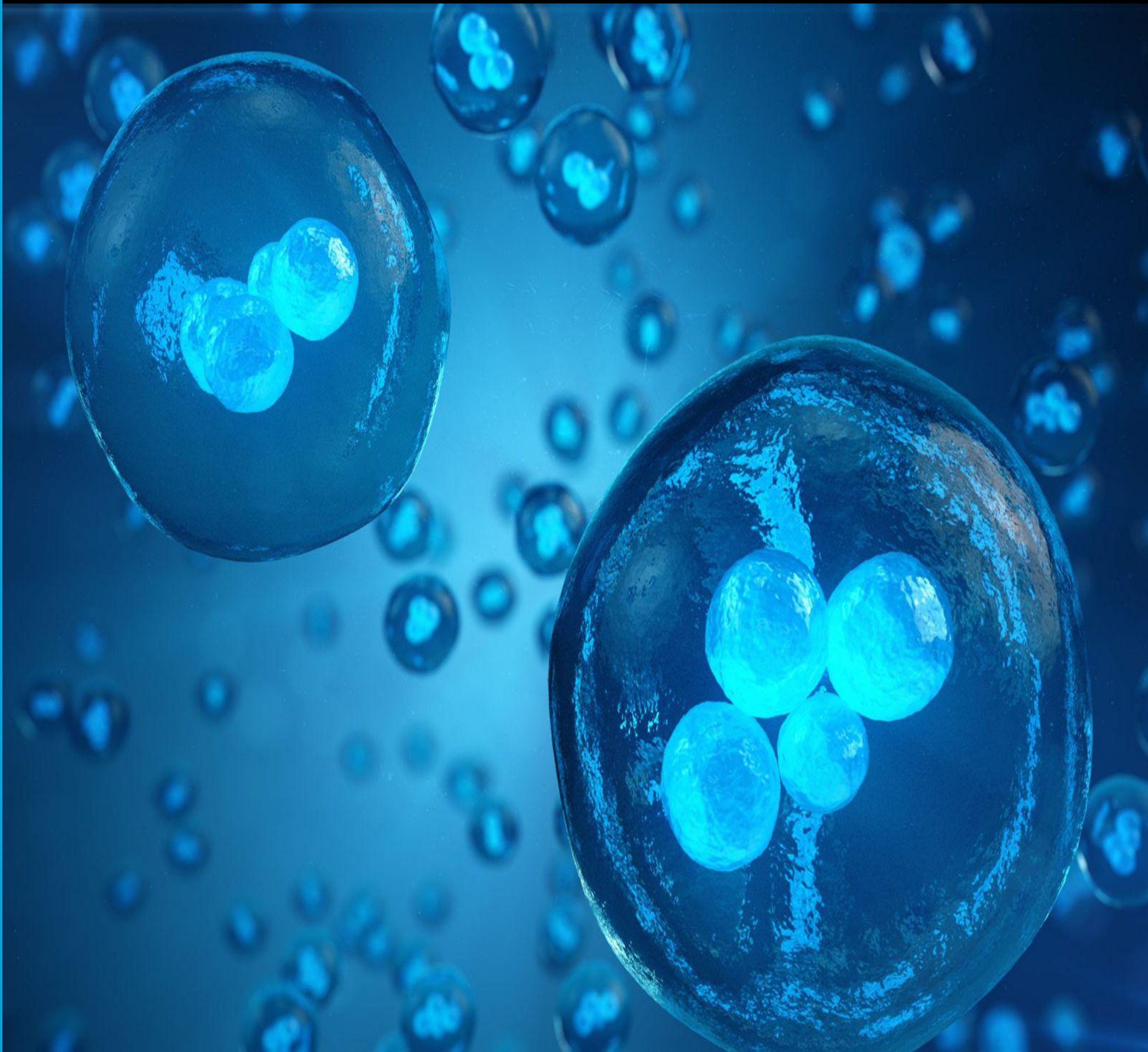
Body fluids



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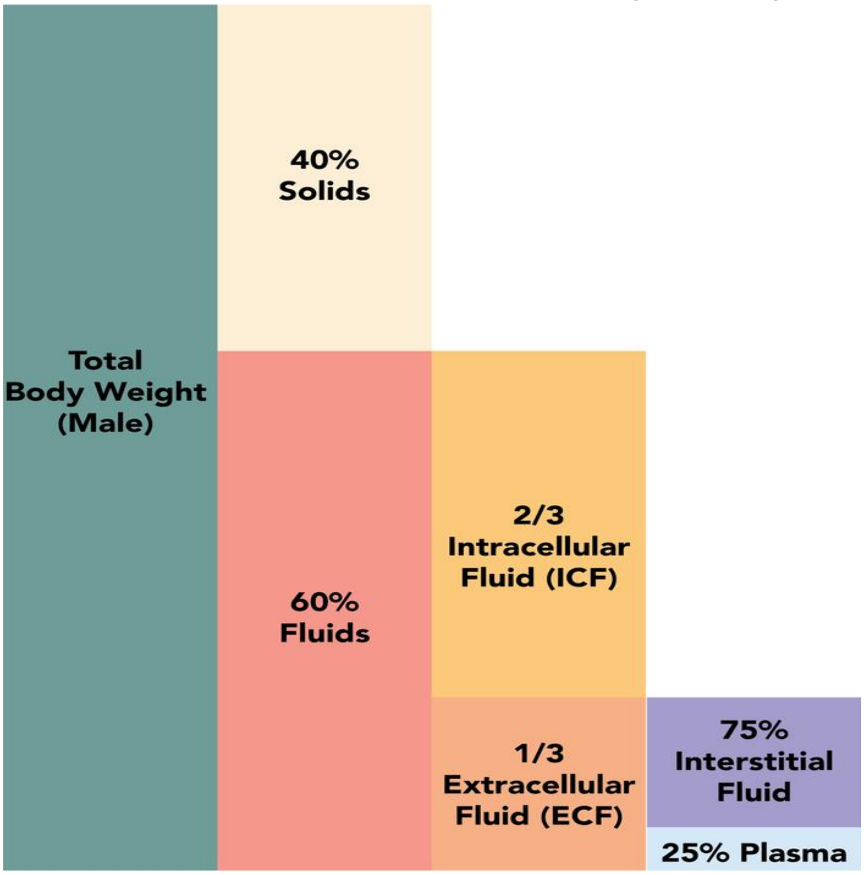
Introduction: -

-60% of our total body weight is formed by water (in males), and about 52% - 55%(in females), this difference is due to the higher amount of fat in females than in males, keep in mind that fat cells contain a very little amount of water inside it, now please ponder the plot below:



-quick reminder for this terminology: -

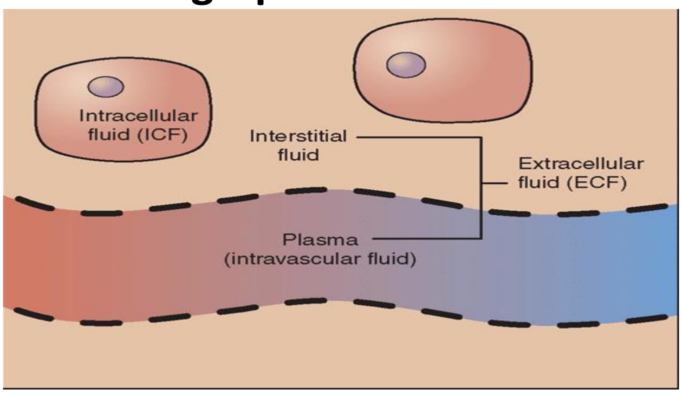
1-Intracellular fluid: the fluid contained within cells

2-Extracellular fluid: the fluid outside the cells

3-Interstitial fluid: body fluid between blood vessels and cells

4-Plasma: the clear, straw-colored liquid portion of blood that remains after red blood cells, white blood cells, platelets and other cellular components are removed.

Now this graph will make it easier for you to visualize:-



- Some boring notes here:
- 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).**

- another boring notes:
=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).
=WATER OUTPUT:
- Urine 60%
- Feces 6%
- Sweat (sensible perspiration) 6%
***sensible means that you can feel the loss of water and you can measure it.**
- Evaporation from skin and lungs (insensible perspiration) 28%
***Insensible means that you don't feel the loss of water and it's hard to be measured.**

= 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).

Movement of body fluids

- Interstitial fluid is very similar to plasma:
- Now imagine the plasma with all it's components, and you've filtered it from proteins and protein-bound substances, just like that, eventually you will have the interstitial fluid.

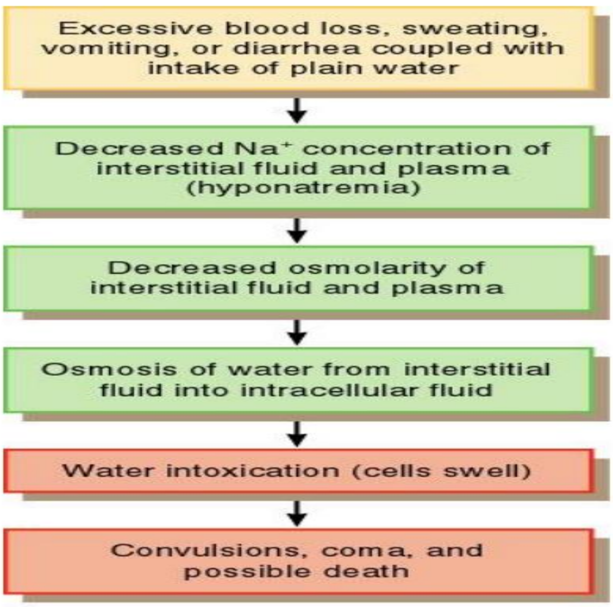
- if you take one liter of the extracellular fluid, then all cations and anions together will produce osmotic power to hold water , this equals about 290 osmole per that liter of water, and this is the normal osmolarity in the human body fluid, of course main contribution is done in the exotic by sodium and chloride.
And so if anyone asked you about the osmolarity of pure water, you better answer him immediately: zero, there is no osmotically active particles in pure water, the amount of water in any compartment is proportionate to the number of osmatically active particles, which are the solutes that can't pass a given semi-permeable membrane, in fact, fluids love to be with solutes, (you can revise osmosis from past lectures for further understanding).

- I think you already know that cells are bags of potassium ions, so the major component of the intracellular fluid is K+, and obviously Na+ is the major component of the extracellular fluid.

- keep in mind that the biological partition between plasma and the interstitial fluid is the capillary membrane, and capillary membrane is very permeable and so it doesn't offer any barrier to the movement of sodium and chloride, because capillary membrane is highly porous (has a lot of pores), that means: sodium and chloride concentration will be

always equal in plasma and in the interstitial fluid, the opposite case related to cell membrane which doesn't allow sodium chloride to move freely, now why is this so important? Go ahead and read the following:

- Now imagine that there is a high concentration of sodium chloride in an extracellular compartment, sodium will not be able to enter the cells, and it will concentrate outside, due to that, osmotically active particles will be more outside the cell (it's hyperosmolar outside) then in this case plasma of the blood will become more salty, and there is a high osmotic pressure in the extracellular fluid, so the solute in the extracellular will drag the water toward itself, remember: water move from hypotonic to hypertonic (from low effective osmotic pressure to high effective osmotic pressure).
- Now imagine that you have eaten a salty potato chips, in this case extracellular fluid will become more hypertonic than the intracellular fluid, and so cell will shrink due to the movement of water from inside the cell toward the extracellular compartments which will expand, (EXTRACELLULSR EDEMA), okay, imagine a giant salty potato chips instead.
- Now imagine the opposite case, that you have drunk 10 liter of pure water, then extracellular fluid will become more hypotonic than the intercellular, and so, cell will expand, and extracellular compartment will shrink, (INTRACELLULAR EDEMA).
**too many imagination, بهنّيك



- Note that whenever we make a description like: hypertonic, hypotonic, isotonic, hyperosmolar and hypoosmolar, we are referring exclusively to the extracellular fluid not the intracellular fluid, keep this in your mind.

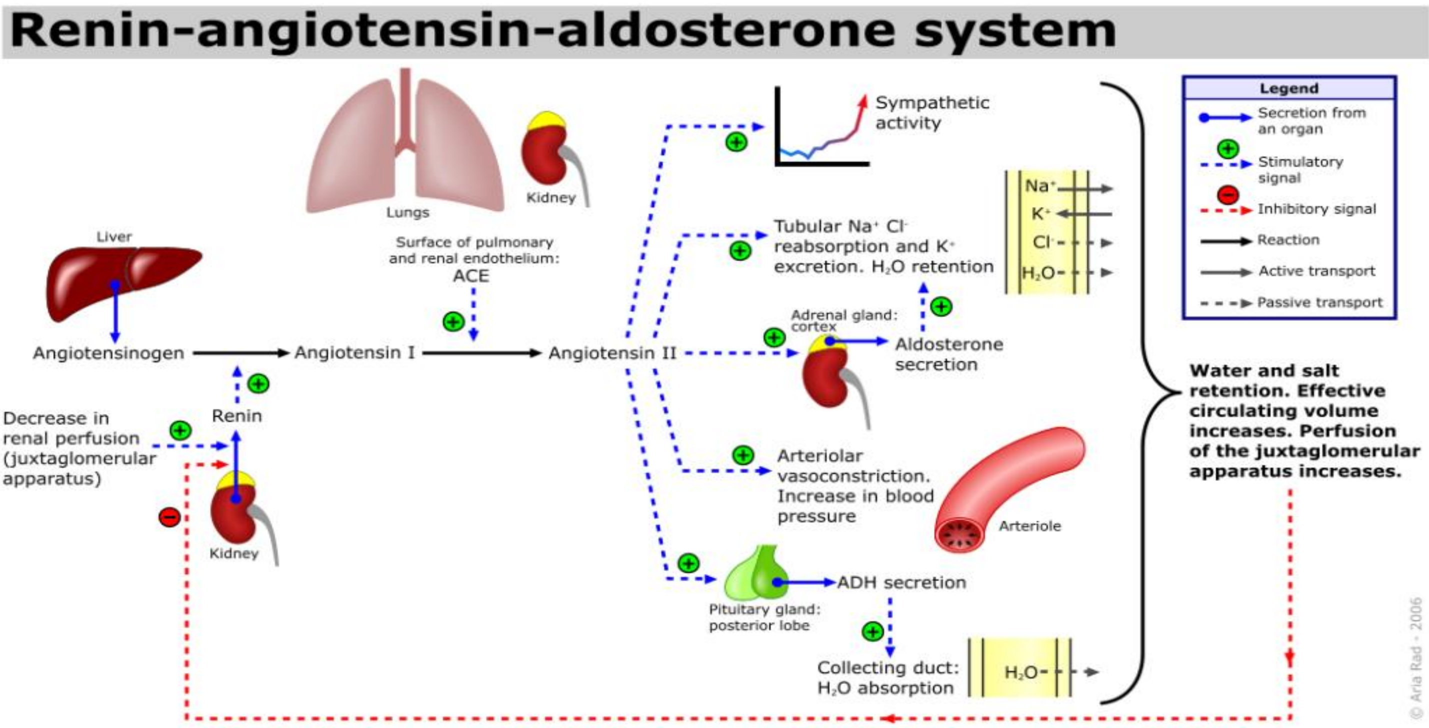
*Let's go deeper…

Regulation of input and output

- We have in our bodies receptors that are called osmoreceptors, (they sense changes in osmolarity), and then send signals, for example: when osmolarity increases, they send signals to thirst centers in the Hypothalamus, which in return increase thirst sensation so you drink water, in addition to that, the increase in osmolality will increase the release of ADH hormone which acts over the renal ducts or renal system (renal=kidneys), so we get (by this process) reabsorption of water.

**and please don't panic from the "so called: osmolality" it's very similar to osmolarity except that it's specifically osmole per Kg not per liter.

And you may remember now the renin-angiotensin-aldosterone system, which is related to the regulation of the decrease of the blood pressure (in other word: we want more water inside blood vessels) and this is a quick revision for it:-

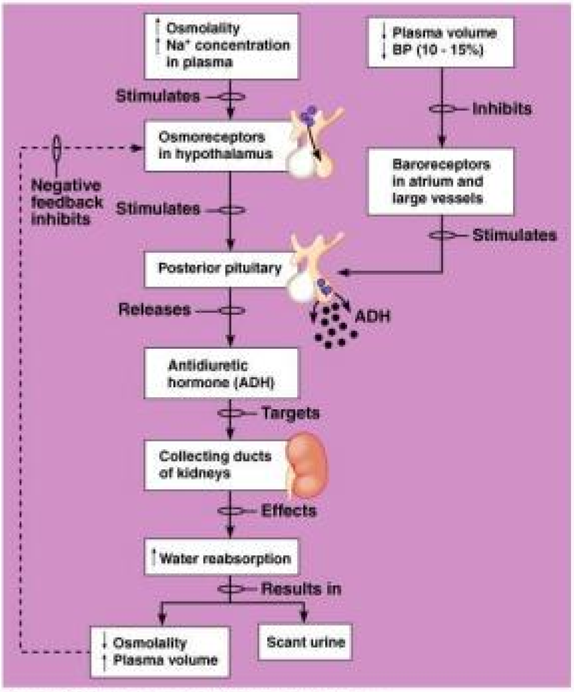


****The figure above is very important with it's all details.**

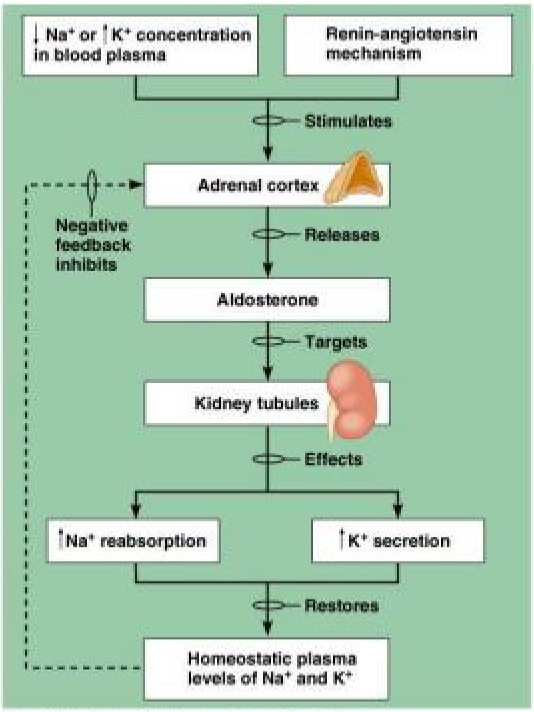
- In this case, the volume of extracellular fluid will increase, so in this way we will decrease the osmolality back to normal, and this will lead to decreasing the water output of the body, and yes, it's the negative feedback again.

****Consider this figures carefully: -**

- **Regulation of output**
  - Regulated by hypothalamus
    - ADH release from posterior pituitary



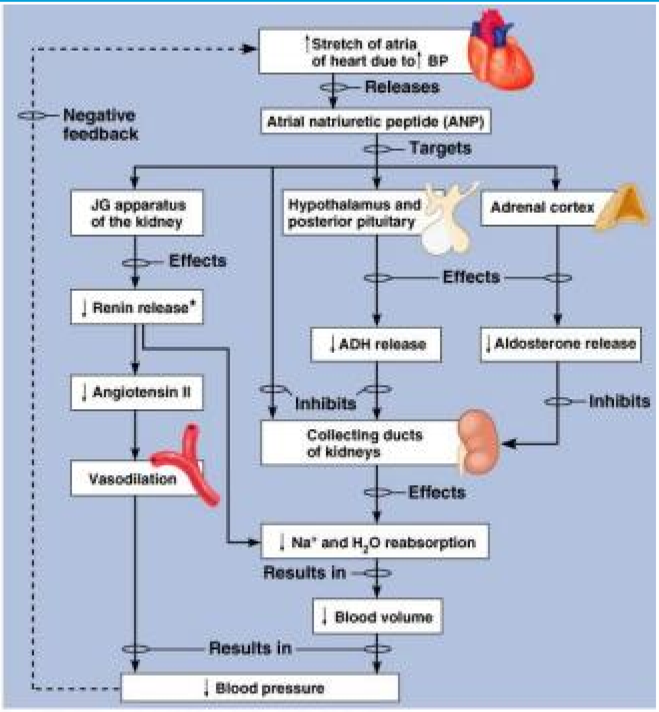
- **Regulation of output**
  - Regulated by renin-angiotensin mechanism
    - Angiotensin II stimulates aldosterone secretion



Regulation of output

– Regulated by atrial natriuretic peptide (ANP)

Effects: reduces BP, Salts and water by effects over vessels, decrease Angiotensin II, and Aldosterone secretions



Abnormalities

- Also known as water poisoning, water intoxication is a disruption of brain function caused by drinking too much water, doing so increases the amount of water in the blood, this can dilute the electrolytes, especially sodium, in the blood.
- The water loss in diarrhea and vomiting will never make any movement of water between the extracellular and intracellular, that's because it's a case of isotonic fluid loss, so osmolarity will stay the same in the extracellular with no change, and this is a situation of volume contraction without any change in osmolarity, (isoosmolar volume contraction)… (hypovolemia)

** the opposite situation (isoosmolar volume expansion) will happen in the case of isotonic water gain… (hypervolemia)

- Another case is the gain of hypertonic fluid, in the situation of eating salty chips for example, this will lead to (hyperosmolar volume expansion) … (hypervolemia).
- Or the another case of an abnormality in adrenal gland, let say it has been destroyed, this will lead to severe deficiency of aldosterone, then sodium will not be reabsorbed, and more sodium will be lost with urine, although water reabsorption is still good, this what we can call: (hypoosmolar volume contraction) … (hypovolemia)

- Another case if we add hypotonic solution, in this situation we will have: (hypoosmolar volume expansion)… (hypervolemia)
- We have also the case of decreased ADH release or in another case, when someone is sweating a lot without drinking any water (sweat is hypotionic), this can cause: hyperosmolar volume contraction… (hypovolemia) and it's called: diabetes insipidus.
****Diabetes insipidus is an uncommon disorder that causes an imbalance of fluids in the body, this imbalance leads you to produce large amounts of urine, it also makes you very thirsty even if you have something to drink.**
****notice that whenever we say "water loss", that's mean we are dealing with hypovolemia, and whenever we say "water gain", that's mean we are dealing with hypervolemia**
****Let's take another description: -**

-Hyponatremia (decreased osmolality) causes include:
Results by excessive loss of Na+ or administration (gain) of hypotonic fluids, and Can be caused by excessive intake of potable water or due to decreased release in aldosterone.

-Hypernatremia (increased osmolality) causes include:
Results by excessive intake of Na+ or administration of hypertonic fluids, or by excessive intake of Na+ or administration of hypertonic fluids.
****There can be a combination of disorders of volumes and osmolality:**
- Hyponatremia with dehydration: high loss of water (diarrhea, vomiting or blood loss) and solids, replaced only with drinking hypotonic water.
- Hyponatremia with over hydration: high retention of water (administration) or increased ADH.
- Hypernatremia with dehydration: loss of hypotonic fluid
- Hypernatremia with over hydration: high release of aldosterone causes more Na+ retention and thus osmolality and volume increases.

**** Now take a deep breath and consider the figure below:**

Abnormality	Cause	Plasma Na+ Concentration	Extracellular Fluid Volume	Intracellular Fluid Volume
Hyponatremia—dehydration	Adrenal insufficiency; overuse of diuretics	↓	↓	↑
Hyponatremia—overhydration	Excess ADH (SIADH); bronchogenic tumors	↓	↑	↑
Hypernatremia—dehydration	Diabetes insipidus; excessive sweating	↑	↓	↓
Hypernatremia—overhydration	Cushing's disease; primary aldosteronism	↑	↑	↓

edema

- edema: is a build-up of fluid in the body which causes the affected tissue to become swollen.

- Causes of edema: -

1- increasing capillary filtration.

****Filtration is the opposite of reabsorption.**

2- Decreased oncotic pressure.

****Oncotic pressure, or colloid osmotic-pressure, is a form of osmotic pressure induced by the proteins, notably albumin, in a blood vessel's plasma (blood/liquid) that causes a pull on fluid back into the capillary.**

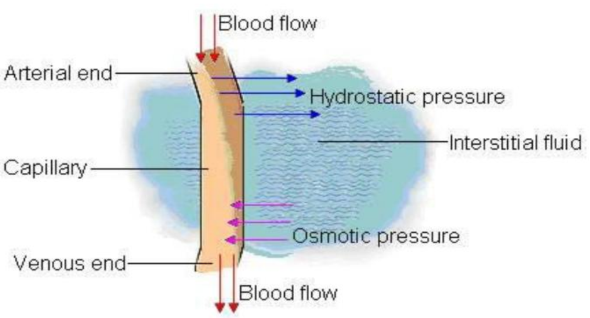
3- Increase capillary permeability.

4- Decreased lymph drainage.

**** Lymphatic drainage is the natural function of the lymphatic system, which is an essential part of immunity, if this function isn't working properly, it can cause a build-up of fluid in tissues.**

- Let's understand step by step:

1- Increasing capillary filtration and 2- decreasing oncotic pressure:



- In the normal condition, we have filtration of fluids at the arterial end, because of the hydrostatic pressure which cause the fluids to get out of the capillary to the interstitial fluids, we have reabsorption of these fluids at the venous end caused by the osmotic pressure, usually the amount of water filtrated is equal to the amount absorbed.

- Now in the abnormal condition which causes the edema: if we have more filtration (higher hydrostatic pressure at the arterial end), And less reabsorption, this will cause accumulation of the fluids at the interstitial compartment, and this happens due to a decrease in the protein content of the plasma, notably albumin, One of the most important causes of decreased plasma protein concentration is loss of proteins in the urine in certain kidney diseases, a condition referred to as nephrotic syndrome, now pay attention that in this case, hydrostatic pressure didn't changed, but oncotic pressure decreased instead, in another condition such as renal failure, an abnormality will cause more retention of water and salts (increased inside capillaries), and so hydrostatic pressure in this case will change (will increase), eventually, fluid will make a pressure on the capillary wall, and will move to the interstitial fluid causing edema, a similar condition will happen in another abnormality in the kidney function, which causes an excess of aldosterone.

- In some cases, high venous pressure will cause edema, due to an abnormality of the function of the heart (heart failure), this will lead to an increase in the hydrostatic pressure on the capillary wall.

3-* increasing capillary permeability: -

- This is due to many factors like: toxins, infections, vitamin C deficiency, ischemia, burns, and during immune reactions by release of histamine.

****Ischemia is a condition in which there is insufficient blood flow to one of the body's organs, often caused by an atherosclerotic plaque in the artery supplying that organ.**

4-* decreasing lymph drainage: it can be caused by cancer, infections, surgery, and absence or abnormality of lymphatic vessels.

Safety factors for preventing edema:

1. Low tissue compliance

**Compliance is the ability of a hollow organ (vessel) to distend and increase volume with increasing transmural pressure or the tendency of a hollow organ to resist recoil toward its original dimensions, and by making the tissue compliance low, this will prevent the existence of high amount of water in the tissue.

2. Increased lymph flow

**Lymph flow can increase up to 10-50 folds, carrying away a large amount of fluids, and preventing interstitial pressure from rising into positive ranges (where we have a high compliance).

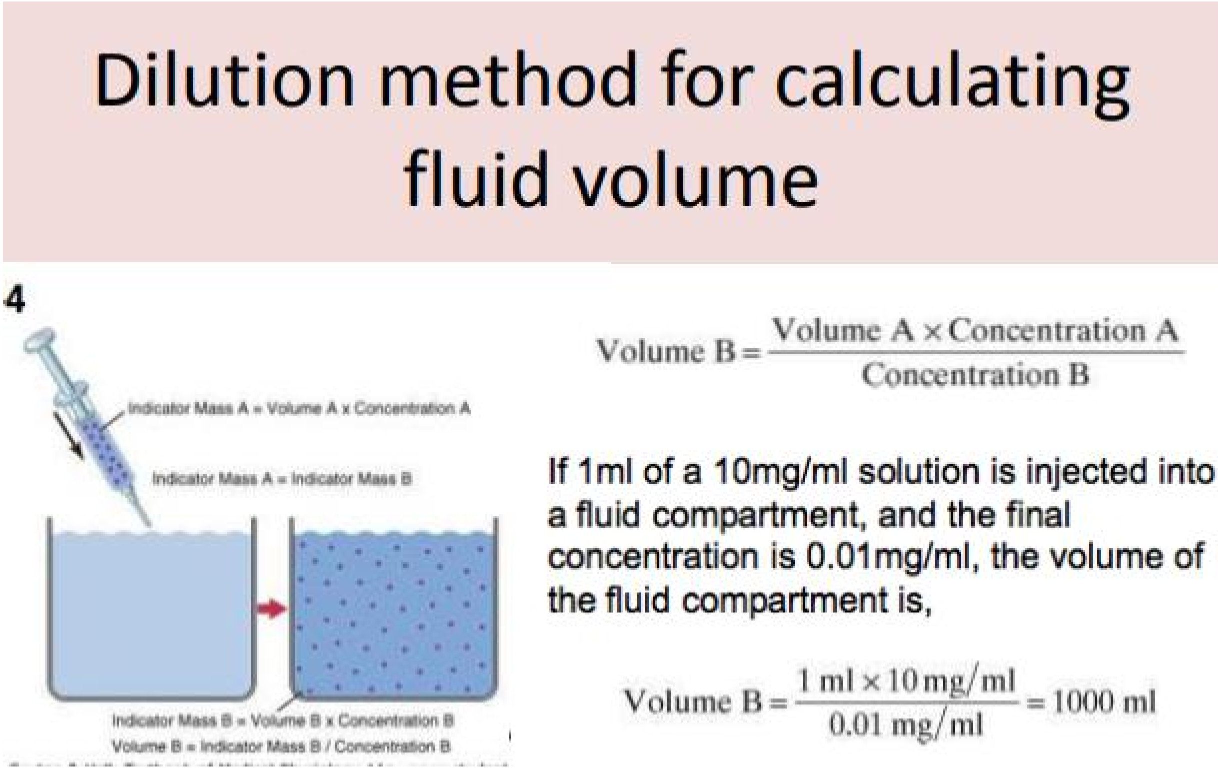
***interstitial pressure comes from substances that leak out of blood capillaries (the smallest type of blood vessel), and it is determined by a complex interplay between the fluid influx (blood capillary filtration), the fluid outflow (lymph flow), and the compartment's ability to expand (tissue compliance), if this interstitial pressure increase, it will lead to increasing in interstitial fluid, and will cause edema.

3. Increased protein wash-down from interstitial fluids: - by increased lymph flow, carrying a large amount of proteins (protein washed out from interstitial fluid), decrease colloid osmotic pressure (oncotic pressure), lowering net filtration forces, and preventing accumulation of fluids.

Boring subject: Measurements of body fluids

- The volume of a fluid compartment in the body can be measured by placing an indicator substance in the compartment, allowing it to disperse evenly throughout the compartment's fluid, and then analyzing the extent to which the substance becomes diluted.

- Dilution principle:-



- 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.

**** Properties of tracers used for calculation of volumes:**

Properties of tracers used for calculation of volumes

- Properties of an Ideal Tracer The tracer should:
- be nontoxic
- be rapidly and evenly distribute throughout the nominated compartment 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
- not interfere with body fluid distribution

- 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 these for total body measurement:
1-Radioactive water ($^{3}H_2O$, T_2O, Tritium) or heavy water ($^{2}H_2O$, 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.
***Radioactive water and heavy water are radioactive, but they differ in radioactivity, and we use these substances in tiny concentrations.**

- For 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 which isn't radioactive and is very lipid soluble and can rapidly penetrate cell membranes and distribute itself uniformly throughout the intracellular and extracellular compartments.

- Extracellular fluid (ECF) measurement:

- To measure ECF volume, we can use:

1. 22Na+ (Sodium space), it is radioactive, we can use sodium to measure ECF volume because sodium is mainly found in ECF.

2. 125I-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.

- **Plasma volume and Total blood volume: -**

***This chart showing the differences between plasma and blood:**

Edit	Blood	Plasma
Definition	Blood is the main bodily fluid and responsible for transporting important nutrients, oxygen, carbon dioxide and waste products to and away from the cells.	Plasma is the yellow liquid component of blood and constitutes 55% of the total blood volume.
Composition	Plasma, red blood cells (erythrocytes), white blood cells (leukocytes), and thromobocytes (platelets).	Water (90%), proteins (albumin, fibrinogen and globulins), nutrients (glucose, fatty acids, amino acids), waste products (urea, uric acid, lactic acid, creatinine), clotting factors, minerals, immunoglobulins, hormones and carbon dioxide
Color	Red	Straw-yellow
Cells (Red, white blood cells, thrombocytes)	Yes	No
Clotting factors	Yes	Yes
nature	Plasma is liquid component of blood.	After clotting, remaining fluid protein of plasma except clotting substance

- Now let's talk about plasma composition:

1-water >90%

2-small molecules: 2%, they are electrolytes, nutriments, metabolic products, hormones, enzymes, etc.

3-Protein: 60-80 g/L, plasma proteins include albumin (40-50 g/L) (54%), globulins (20-30 g/L, α1 -, α2, β-, γ-) (38%), and fibrinogen (7%), most of albumins and globulins are made from liver.

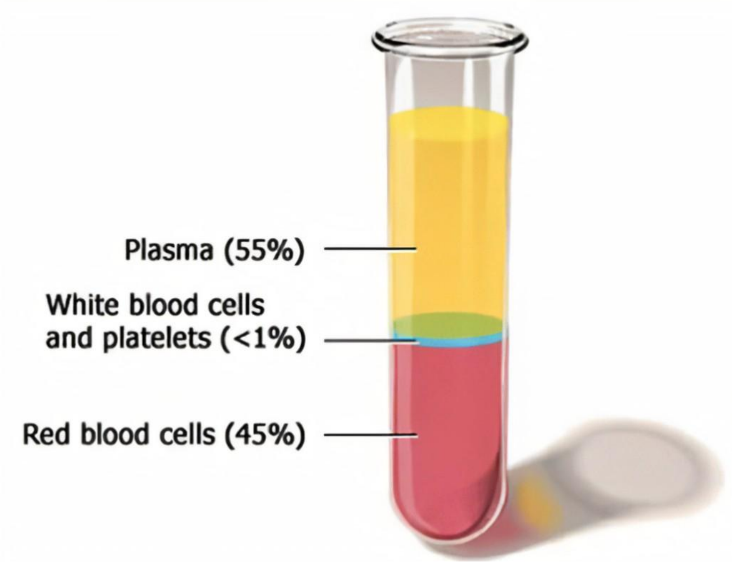
****Notes:**

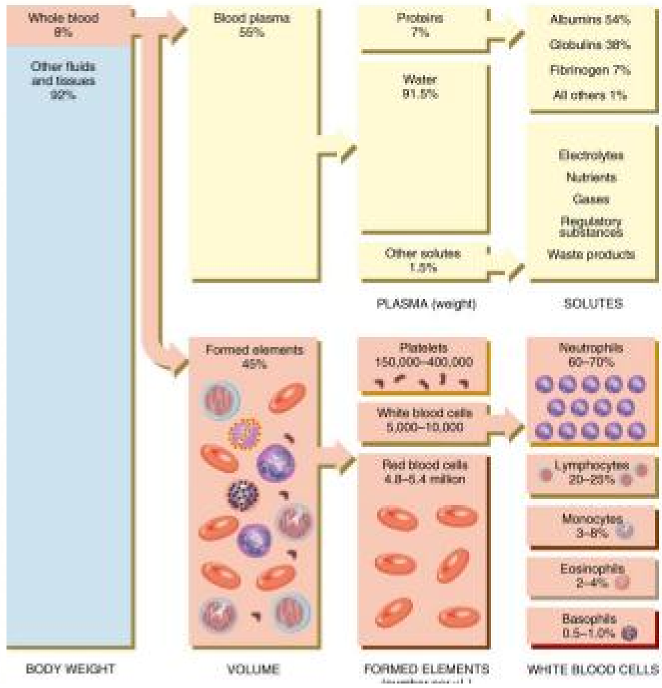
- We have high amounts of proteins in plasma.

- γ- globulins are antibodies.

- Fibrinogen is important for the process of coagulation.

- This figure represents some approximate percentages:





- To measure plasma volume, a substance must be used that does not readily penetrate capillary membranes but remains in the vascular system after injection.

- Measurement of plasma volume: -

- We can use: 1. 125I-Albumin (RISA) (Radio iodide albumin), It can't be distributed out of the vascular fluid, and it is radioactive (radioactive iodine).

2. Evans Blue (Dye (T1824)) which can be distributed only inside vessels.

-Now concerning the blood volume: we can measure it by:

1- using labeled red blood cells (We label RBCs with iodide chromium (51Cr), then we inject them in the blood), after that, we use dilution principle, the doctor said that: he hadn't placed information concerning the fluorescent tag, so it is enough to know that we can use labeled red blood cells, However, we can use fluorescent dyes rather than radioactive dyes.

2- We can use:

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

- If one measures plasma volume using the methods described earlier, blood volume can also be calculated if one knows the hematocrit, (using the equation shown earlier).
****Hematocrit: the fraction of the total blood volume composed of cells, for example, if plasma volume is 3 liters and hematocrit is 0.40, total blood volume would be calculated as 3 liters/(1-0.4) = 5 liters.**
……………………………………………

وَإِنّي لَمِن قَومٍ كَأَنَّ نُفوسَنا

بِها أَنَفٌ أَن تَسكُنَ اللَحمَ وَالعَظما

كَذا أَنا يا دُنيا إِذا شِئتِ فَاِذهَبي

وَيا نَفسُ زيدي في كَرائِهِها قُدما

فَلا عَبَرَت بي ساعَةٌ لا تُعِزُّني

وَلا صَحِبَتني مُهجَةٌ تَقبَلُ الظُلما