physiology

premed 2018 - JU

Sheet ☑ Slides ☐

Number

21

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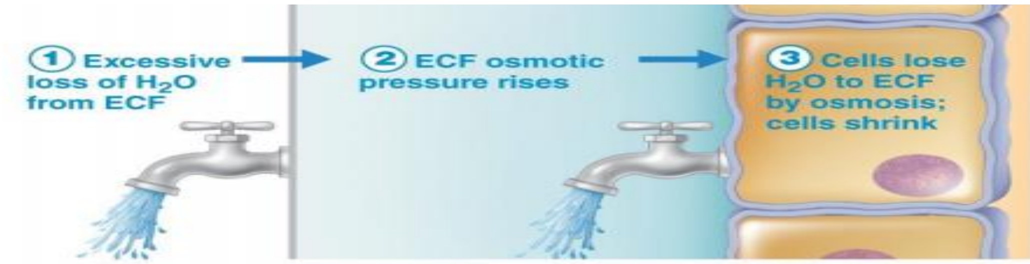
We took in the previous lecture, that:

1. Fluids are continuously moving between the extracellular(ECF) and intracellular(ICF) compartments by the effect of :
   a. Osmotic pressure
   b. Hydrostatic pressure
2. These forces are established by regulation of:
   a. Osmolality “Na^+ and Cl^- are its main determinates”
   b. Volume of ECF
   *** overlapping between those two is important too and we'll go through that in this sheet.
3. There are 4 systems involved in regulating water and electrolytes homeostasis:
   a. Kidneys
   b. Cardiovascular
   c. Endocrine hormones
   d. Lungs
4. Some aspects of responses to difference in concentration of water and electrolytes:
   a. If more water than solutes is lost from the extracellular fluid (hypotonic solution is lost) → cell shrinks.
   b. If more water than solutes is gained by the extracellular fluid (hypotonic solution is gained) → cell swells.
   In neural cells, swelling (water entrance to the cell) might lead to convulsion, coma, it could even lead to death, [disturbance of homeostasis = disease].



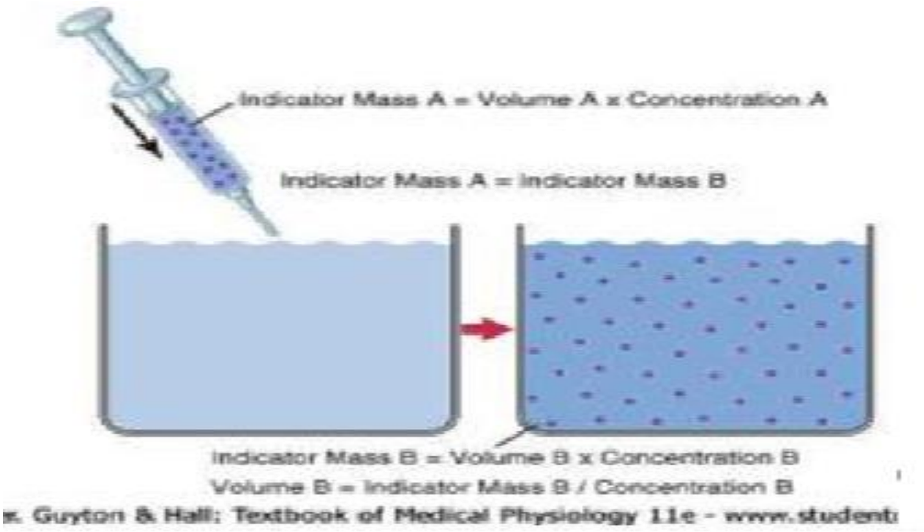
(a) Consequences of dehydration. If more water than solutes is lost, cells shrink.

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

Measurements of body fluids

*How are we measuring **total** body fluids?*

Simply by using " Dilution principle" in order to calculate the fluid **volume(**which represents fluid amount in our bodies).



- Suppose you have a specefic concentrated solution, take some of it(**in which you know it's volume and concentration)** and inject it in an **unknown** volume-of the body-,then take a sample after this injection is distributed through out your body, calculate the sample's concentration, now using the equation $C_1V_1=C_2V_2$

you can determine V2(total body's fluid volume).

V1=initial volume, V2=final volume, C1= initial concentration, C2= final concentration.

Example: →

$$\text{Volume B} = \frac{\text{Volume A} \times \text{Concentration A}}{\text{Concentration B}}$$

If 1ml of a 10mg/ml solution is injected into a fluid compartment, and the final concentration is 0.01mg/ml, the volume of the fluid compartment is,

$$\text{Volume B} = \frac{1\ \text{ml} \times 10\ \text{mg/ml}}{0.01\ \text{mg/ml}} = 1000\ \text{ml}$$

**Remember, C2 will be less than C1 due to the dilution method..*

- Tracer:(substance added to body fluid to help us follow- trace- its way through out it's distribution.)

Clarifyng definition- NOT required-: an element or compound containing atoms that can be ditinguished from their normal counterparts by physical means like radioactivity.

Properties of tracers*(used in dilution for example)***:**

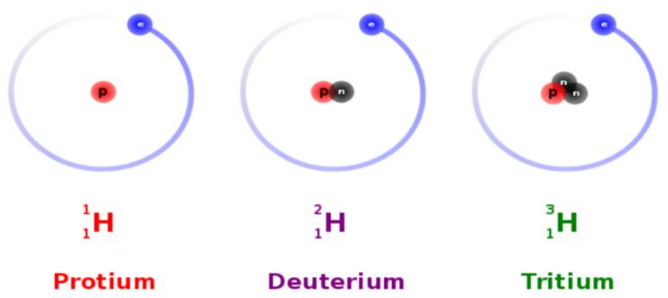
1. **Nontoxic** (remember we are dealing with human's body!).
2. Be rapidly and **evenly** distributed throughout the **nominated** (appointed) compartment and not any other compartment (e.g. You would like to measure total body fluid.. so it must be distributed to total body fluid but if you are interested with intravascular fluid it must be restricted to intravascular only and so on).
3. Not be metabolized fast. (it may take hours, but at least in the 1st hour it mustn't be metabolized so fast.
4. Not be excreted (or lost from body, with urine for example), as if its lost immediately then there is no benefit of using this trace ☺.
5. Be easy to measure
6. Not interfere with body fluid distribution

****Tracers(substances) used to measure total body fluid's volume (water):***

Think about it, you need a substance that can be found and distributed to total body fluid?

Simply, It's **WATER** :D!..

1. Radioactive water (Tritiated water) : (^3H_2O , T_2O , Tritium)
2. Heavy water : (^2H_2O , D_2O , Deuterium)



The three most stable isotopes of hydrogen: protium (*A* = 1), deuterium (*A* = 2), and tritium (*A* = 3).

3. Antipyrine (chemical compound):
   it can distribute **evenly** in all over body fluids, so when we measure it we can estimate the total volume of body fluid.

***for 1 and 2 → these will mix with the total body water in just a few hours and the dilution method for calculation can be used then.

***for example: add 1ml of substance with known radioactivity to plasma, in 1 hour it will distribute. Later, take a sample from the plasma and calculate the difference in radioactivity,, so that you will get the volume you are seeking for ^^.

Radioactivity-→ Concentration-→ Volume.

Measurement of ECF volumes:

Common feature that exists in all these materials is that they can't inter inside the cell, it makes sense because it is used to measure the volume of the ECF.

1. $^{22}Na^{+}$ → (sodium space)
2. ^{125}I-iothalamate
3. Thiosulfate
4. Inulin → (inulin space)

(Measured in 30-60 minutes)

Some notes regarding previous substances:

*One researcher used inulin in one experiment, and repeated the same conditions of that experiment but using **radioactive** sodium instead of inulin, he got different results, what's your explanation for that?*

If you are using sodium, it will distribute to ECM(mainly) but some of it may enter toward ICM, and that's why the term SODIUM SPACE is mentioned {i.e. the space that is occupied by sodium (thus this small amount inside ICM is included)}.

On the other hand, if inulin is used, it won't enter the ICM like sodium, and here the difference appears.

**one disadvantage about inulin that large amount of it is lost by urine.*

Calculation of ICF:

ICF = TOTAL BODY VOLUME – ECF.

plasma of blood

-it is the liquid part of the blood that carries cells and proteins throughout the body. It makes up about 55% of the body's total blood volume, It is the intravascular fluid part of extracellular fluid.

Plasma composition:

1. **Water**: > 90%
2. **Small molecule**: 2%, is electrolytes, nutriment, metabolic products, hormone, enzymes, etc.
3. **Protein**: 60-80 g/L, plasma protein include
    a. Albumin (dominant protein type) (40-50 g/L) (54%), its importance appears through regulating oncotic pressure.
    b. Globulins (20-30 g/L, α1 -, α2, β-, γ-(antibodies)) (38%)
    c. Fibrinogen (for coagulation, this is the stable form, after activation by thrombin it would be transferred into fibrin and finally to form a blood clot) (7%).

   Most of albumin and globulin are formed by liver –except for γ-globulin which is synthesized by white blood cells.

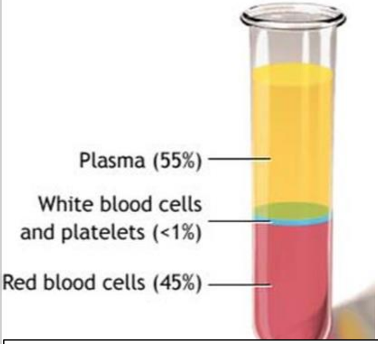
Note : formation of a blood clot is made by coagulation of blood contents

-we have soluble fibrinogen circulating normally in the blood, but in the case of injury it won't be soluble as usual, it wil be transformed to fibrin and the process proceeds^^.

- **Centrifugation is used to separate contents of blood from each other(cells, plasma or serum,..)**

Suppose we used a flat end tube in centrifugation-as in the figure aside- the surface area of each separated compartment is equal but they differ in their heights in the tube → different heights represent different percentage of each compartment in the tube.

Note/If the tube hadn't a flat end we put a paste like material at the bottom of it ☺.



slide 26, have a look on the figure exhibit there

- **Serum:** part of blood which lack clotting factors = [plasma-coagulation factors]
- **Plasma:** is composed of serum and clotting factors

***It is difficult to separate serum in comparison to plasma.

Measurement of Plasma volumes

1. ^{125}I-**Albumin** (RISA) (it will only distribute intravascular-plasma) → by measuring the difference in radioactivity before and after giving the tracer.
2. Evans Blue (Dye (T1824)) (it will only distribute in plasma) → by measuring the concentration of the dye using colorimetric method.

Measurement of total blood volume

1. ^{51}Cr-Labeled red blood cells.
2. or Calculated as = $$\frac{\text{Plasma Volume}}{\text{1-Hematocrit}}$$

***Hematocrit –also known as PCV= packed cell volume-: (the ratio-**percentage**- of the volume of red blood cells to the total volume of blood)

E.g.: to say hematocrit is 45%, that means we have 45% of the volume you have is cells, and remaining 55% is plasma.

So suppose you have 3 liters of plasma→ 0.55 of total volume, the rest is hematocrit= 0.45 of total volume

Applying the eq. above: 3/(1-0.45)=nearly 6 L is total blood volume ^^.

{Regulation of fluid volumes and osmolality}

***Fluids in our body are highly regulated with overlapping mechanisms: eg:((change in osmolality = change in the volume of ECF)))

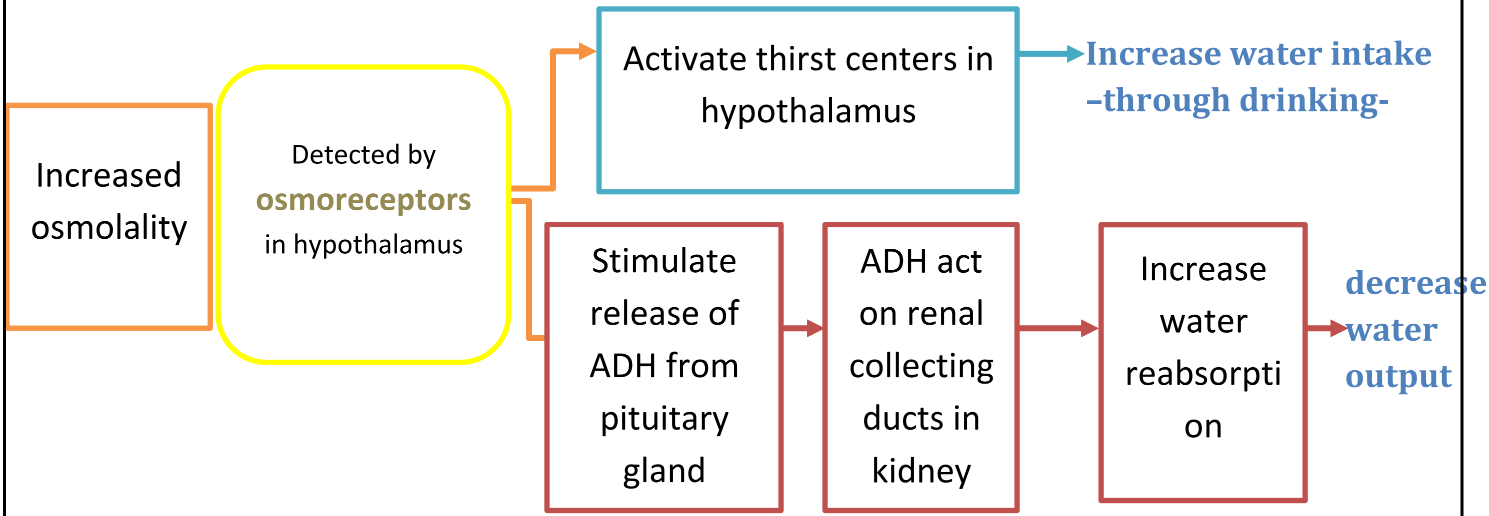
Regulation of Na+ and water:

***Involves regulation of:

1. Osmolality (by regulation of salts)
2. Volume of ECF.

*different regulations with many overlapping mechanisms

Osmolality (osmoregulation):



ADH: [Antidiuretic Hormone] is acting over kidney to prevent water excretion with urine(helping in water retention).

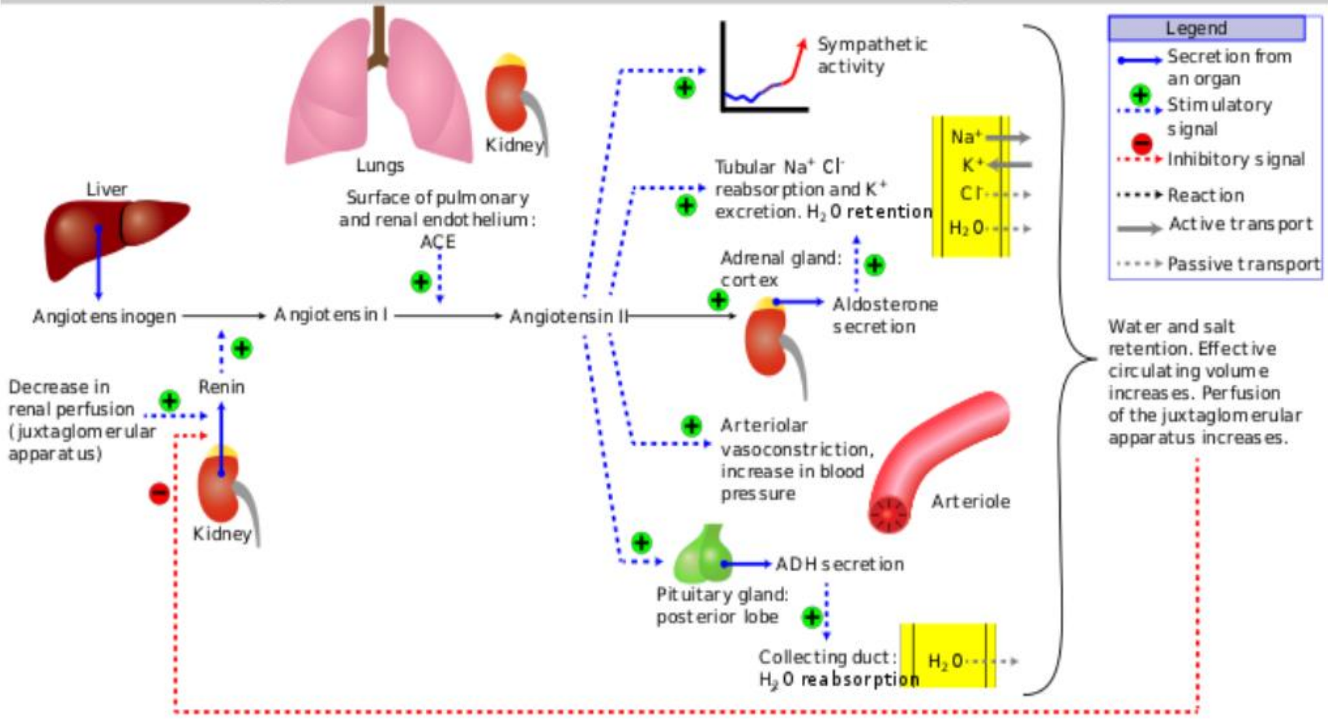
-any change in osmolality is detected by **Osmoreceptors**

Regulation of body water:

1. ***Regulation of intake***
   1)Regulated by: hypothalamic "thirst center"
   ***Thirst center" responds to osmoreceptor impulses, angiotensin II
   2)Working over kidney → increase water resorption
2. ***Regulation of output*** :
   Regulated by: hypothalamus
   ADH release from posterior pituitary
   ***2 regulations of output:

Regulated by renin-angiotensin mechanism	Regulated by atrial natriuretic peptide (ANP)-will be discussed in the next sheet.
Angiotensin II stimulates aldosterone secretion	Effects: a. reduces BP, salts and water by effects over vessels b. decrease Angiotensin II c. Aldosterone secretions

Renin-angiotensin-aldosterone system



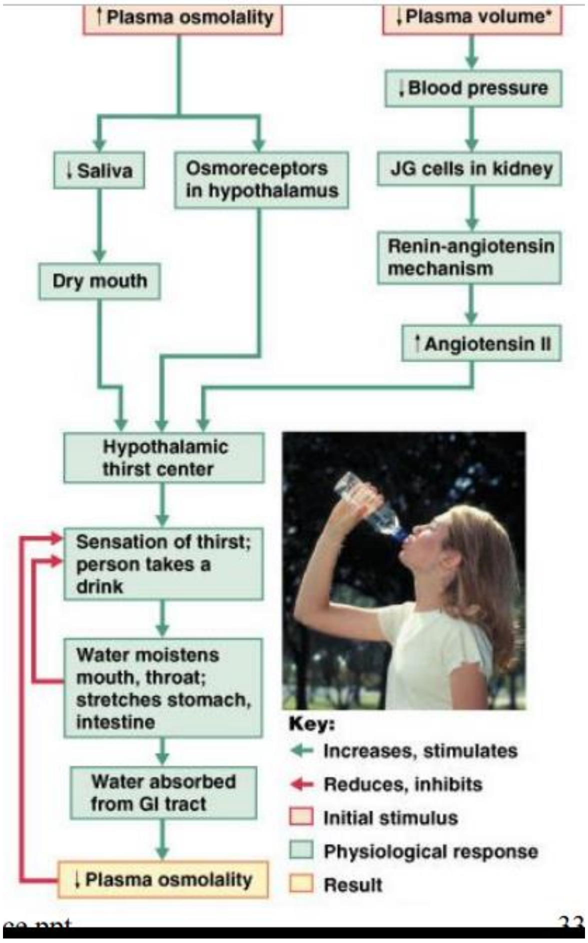
**both mechanisms are negative feedback mechanism.

Look at the figure above to overview the mechanism of [renin angiotensin aldosterone system].

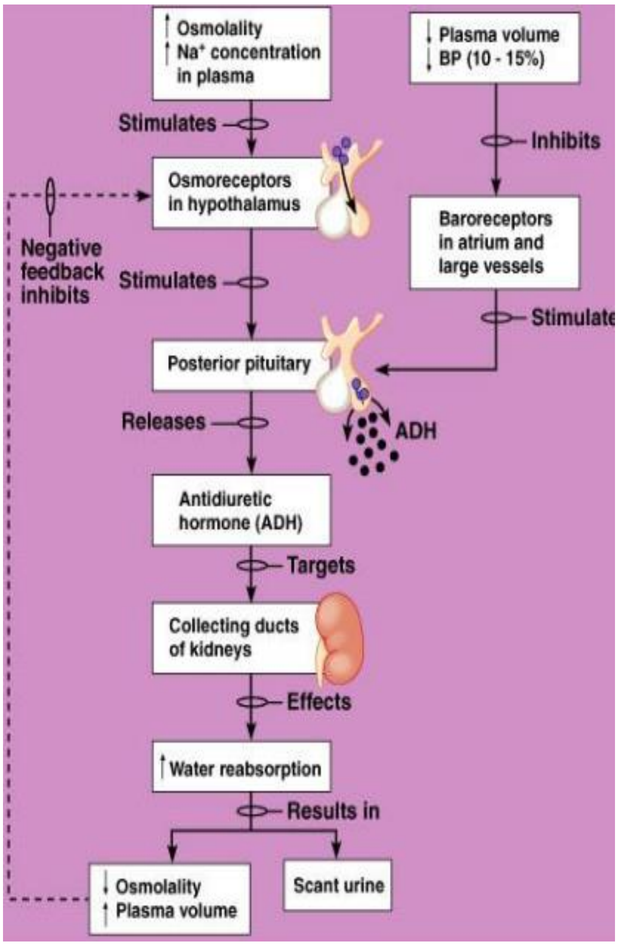
*fine details are not required.

- note: **Diabetes insipidus** is a medical case (condition) characterized by large amount of dilute urine.

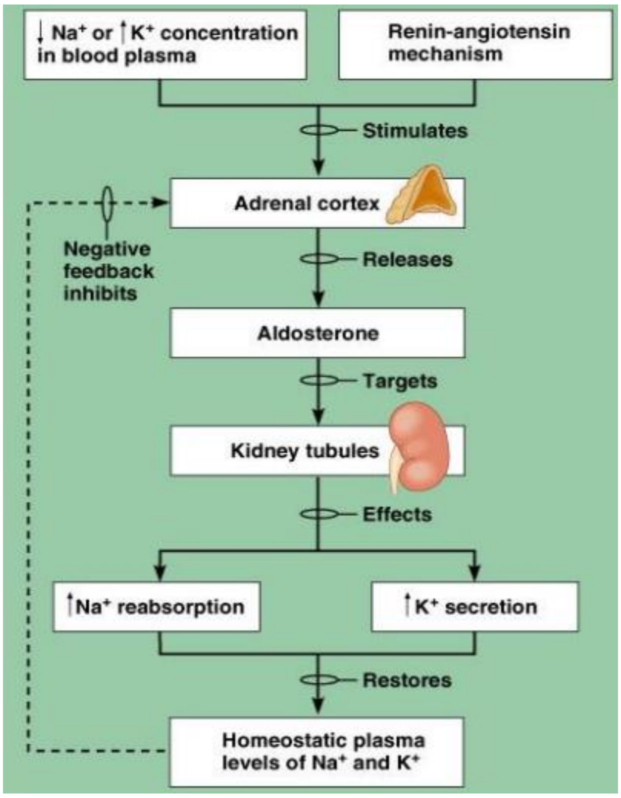
If ADH level is decreased → it will cause large amounts of dilute urine to be secreted and increased thirst feeling (due to high loss of hypotonic water from body) → osmolality will increase, volume will decrease and other body fluids will be affected.



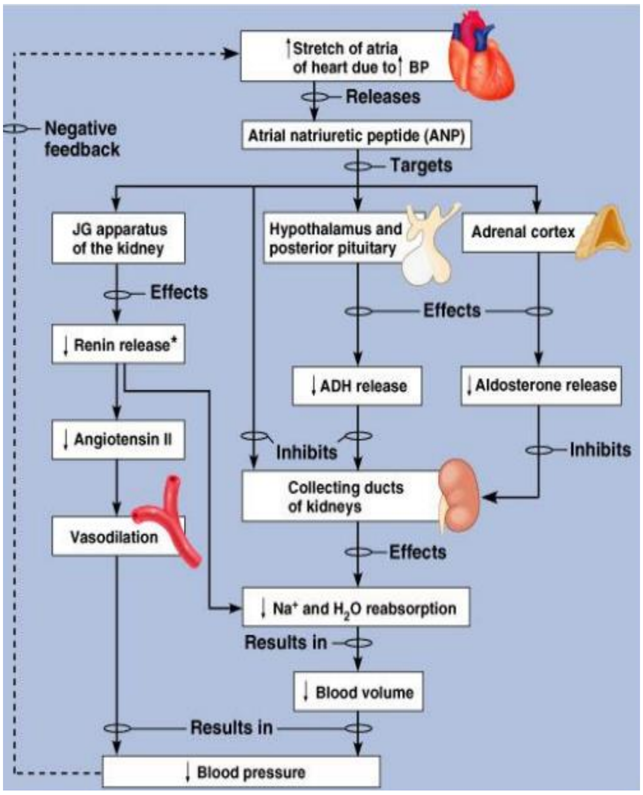
Regulation of input



Regulation of output



Output regulated by renin-angiotensin



Output regulated by ANP

volume of ECF

Depends on Na+ excretion in urine
Controlled by renin-angiotensin aldosterone system
*****reduced volume** of ECM (low flow of fluids to the kidney): This will cause Juxtaglomerular Cells (Kidney) to release Renin → Angiotensinogen (from liver) → (by renin-enzyme) →converted to Angiotensin I → (by ACE secreted by endothelium cells from the lung and some from the kidney) →converted to Angiotensin II (Lung) → act over adrenal gland → to stimulate the release of Aldosterone (increase reabsorption of sodium) → increase osmolality → ***and will complete the first mechanism of increase in osmolality.***
Notice the *overlap of two mechanisms*

*** Aldosterone secretion can also be stimulated by increasing potassium concentration {hyperkalemia} in our body fluid to get red of this potassium but in the same time we are getting the sodium reabsorbed too.

*** In hyperaldosteronism (high aldosterone content) → increase sodium absorption → increase osmolality→ increase in volume.

Disorders of volumes and osmolality(briefly):

Disorders of volume | **Disorders of osmolality**

Hypovolemia	**Hypervolemia**	**Hyponatremia**	**Hypernatremia**
Results by excessive loss of fluids	Results by excessive intake or administration of fluids	Results by excessive loss of Na+ or administration of hypotonic fluids	Results by excessive intake of Na+ or administration of hypertonic fluids
Dehydration	Over hydration	Dehydration	Over hydration

Summary:

Antidiuretic hormone (**ADH) and aldosterone** are hormones that tell your kidney to put water back in the blood....both work in the collecting duct - **ADH** causes it to take up water, whereas **aldosterone** causes it to take up salt and, in turn, causes water to follow.

Note: check out the figures mentioned in this sheet(taken from slides), their details are not required but you need to overveiw the whle story to pick up the idea ^^.

"احْرِصْ عَلَى مَا يَنْفَعُكَ ، وَاسْتَعِنْ بِاللَّهِ وَلَا تَعْجَزْ!"

-النّبيّ ﷺ ✿❤