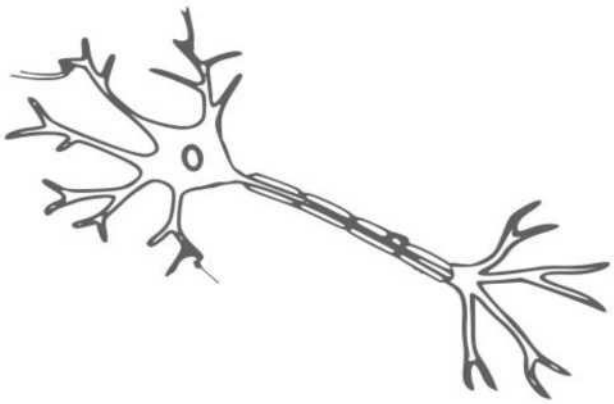
Sheet no16

Physiology



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Body fluids measurements continued.

1-Measurement of Plasma volumes.
2-Measurement of Total Blood Volume.

- A chart showing the differences between plasma and blood to help you understand.

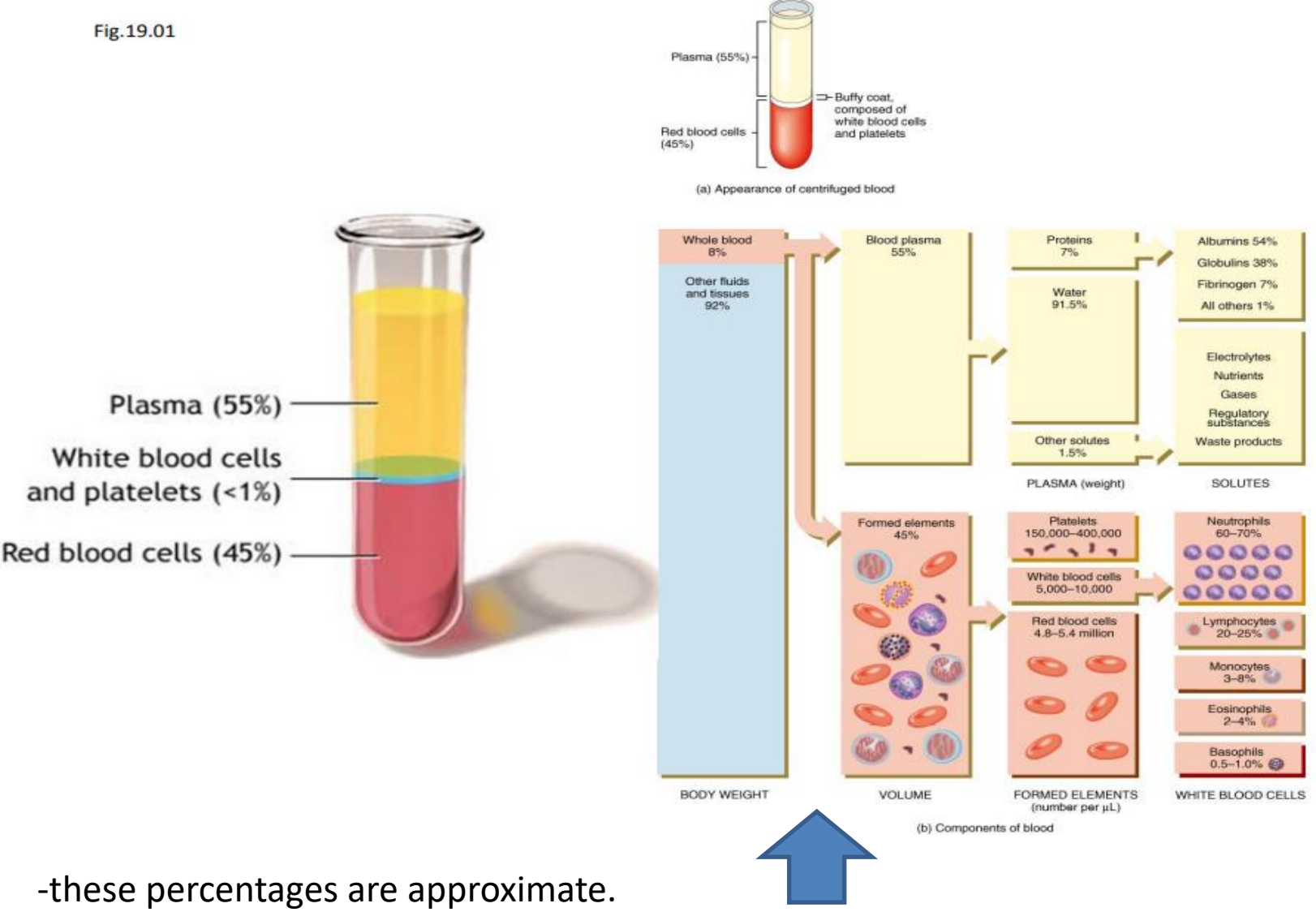
Edit	Blood	Plasma
Definition	Blood is the main bodily fluid and responsible for transporting important nutrients, oxygen, carbon dioxide and waste products to and away from the cells.	Plasma is the yellow liquid component of blood and constitutes 55% of the total blood volume.
Composition	Plasma, red 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 :
1.We have high amounts of proteins in plasma.
2. γ- globulins are antibodies.
3. Fibrinogen is important for the process of coagulation (تخثر الدم)

Fig.19.01



-these percentages are approximate.
-To measure plasma volume, a substance must be used that does not readily penetrate capillary membranes but remains in the vascular system after injection.
-Now we shall talk about Measurement of plasma volume.
We can use:
1. 125I-Albumin (RISA) (Radio iodide albumin) It can't be distributed out of the vascular fluid 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 said 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*

-Another method in the next slide-------→

-we can also measure the total blood volume using:

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

- 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 at the top).
-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

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-Now we shall continue talking about the regulation of body fluids.

-we said that we have different regulatory mechanisms in our bodies to regulate Na+ and water that are involved in the regulation of osmolality and volume of ECF. Remember that there is an overlapping in the regulatory mechanisms of water and Na+.

-before talking about osmoregulation I want you to know the following I took this info from the book and I think that you should also know them:

-The osmolal concentration of a solution is called osmolality when the concentration is expressed as osmoles per kilogram of water; it is called osmolarity when it is expressed as osmoles per liter of solution. In dilute solutions such as the body fluids, these two terms can be used almost synonymously because the differences are small. In most cases, it is easier to express body fluid quantities in liters of fluid rather than in kilograms of water.
-by regulating osmolarity you are regulating the volume and vice versa
So if you have high amounts of water from the kidney(reabsorbed) you will have less amount of water loss so in this case you have decreased osmolality and increased water content in the body.
- So in our bodies the process of regulation of osmolality is called osmoregulation.

-Now we are ready to talk about osmoregulation:

-Note that about 80 percent of the total osmolarity of the interstitial fluid and plasma is due to sodium and chloride ions, whereas for intracellular fluid, almost half the osmolarity is due to potassium ions and the remainder is divided among many other intracellular substances.

-We have in our bodies receptors that are called osmoreceptors (they sense changes in osmolarity).they send signals for example(when osmolarity increases) to thirst centers in the Hypothalamus which in return increase thirst sensation so you drink water.

-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.
In this case the volume of ECF 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.
-To sum it up If there is an increase in body fluid's 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
So you can think of these process as a negative feedback system because the end result is opposite to the initiating one.
-by osmoregulation we should regulate two important things:
1-Intake
2-Output

- Osmolality:

Osmoregulation

- **Increased osmolality → thirst (Increase water intake).**
- **Increased osmolality → stimulates release of ADH --> acts on renal collecting ducts → increased water reabsorption (Decrease water output)**

Regulation of Na+ and Water

Involves regulation of:

- Osmolality
- Volume of ECF

different regulations with many overlapping mechanisms.

• 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:

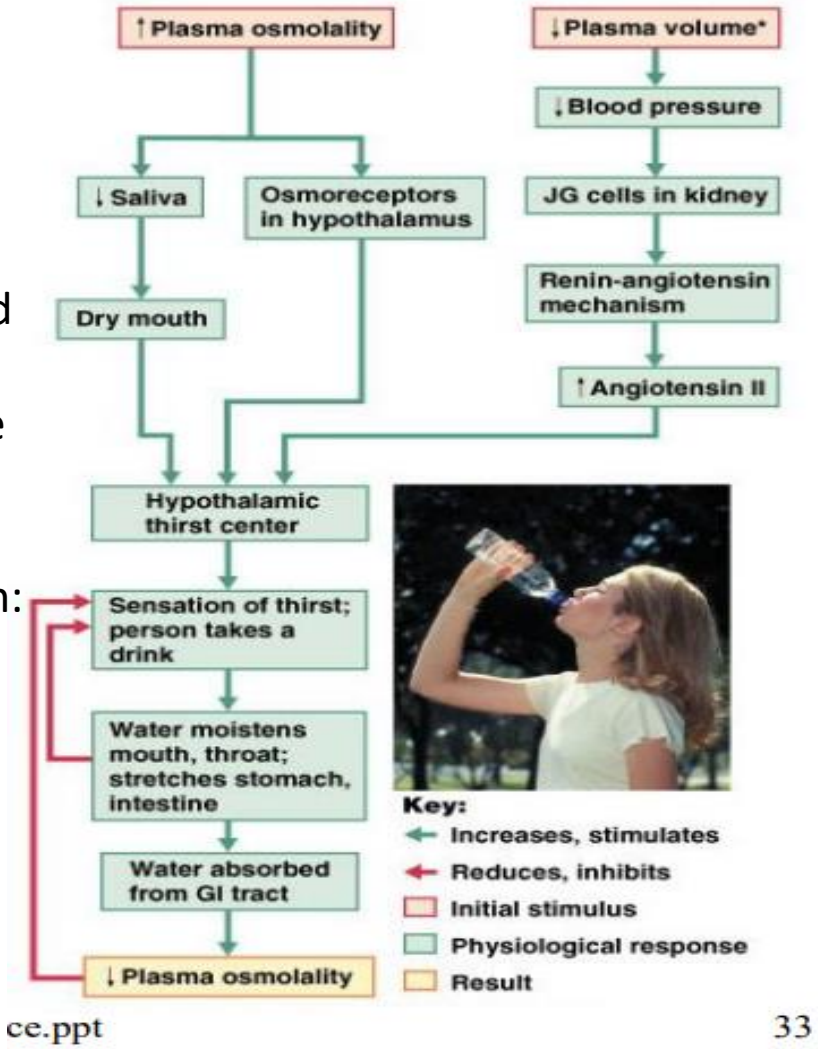
*You should know that hypothalamic thirst centers are activated by dry mouth.

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



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-notes:

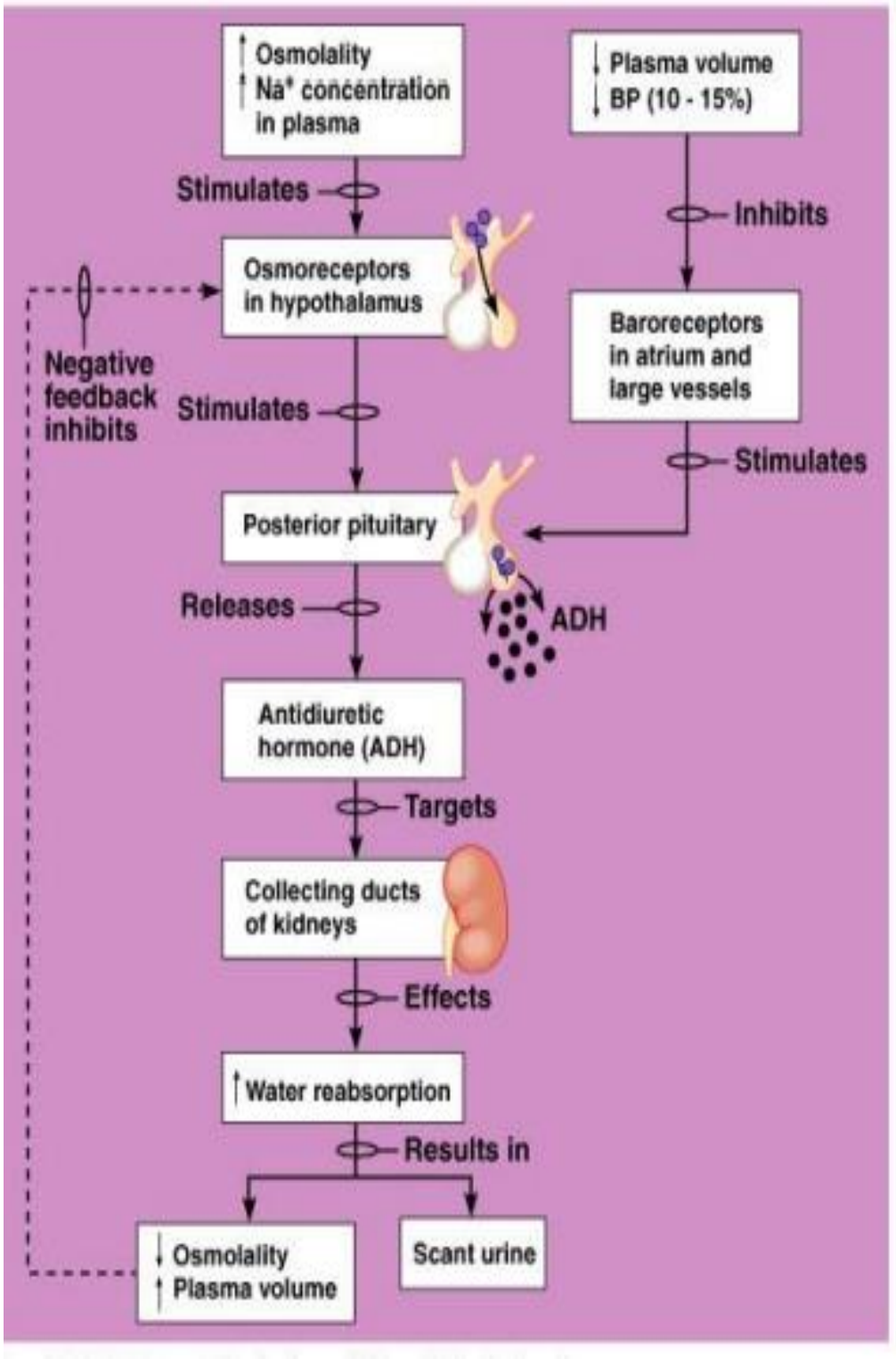
We have an enzyme at the level of the kidney which is the renin this enzyme converts angiotensinogen to angiotensin1 This enzyme(angiotensin1) is activated at the lung tissue to get angiotensin2 which acts over the suprarenal gland(adrenal gland) to get release of aldosterone which increases the absorption of sodium so we increase the osmolality by this we increase the volume by retention of water.

-from google: The juxtaglomerular apparatus (also known as the juxtaglomerular complex) is **a structure in the kidney that regulates the function of each nephron, the functional units of the kidney.**

-**Regulation of output**

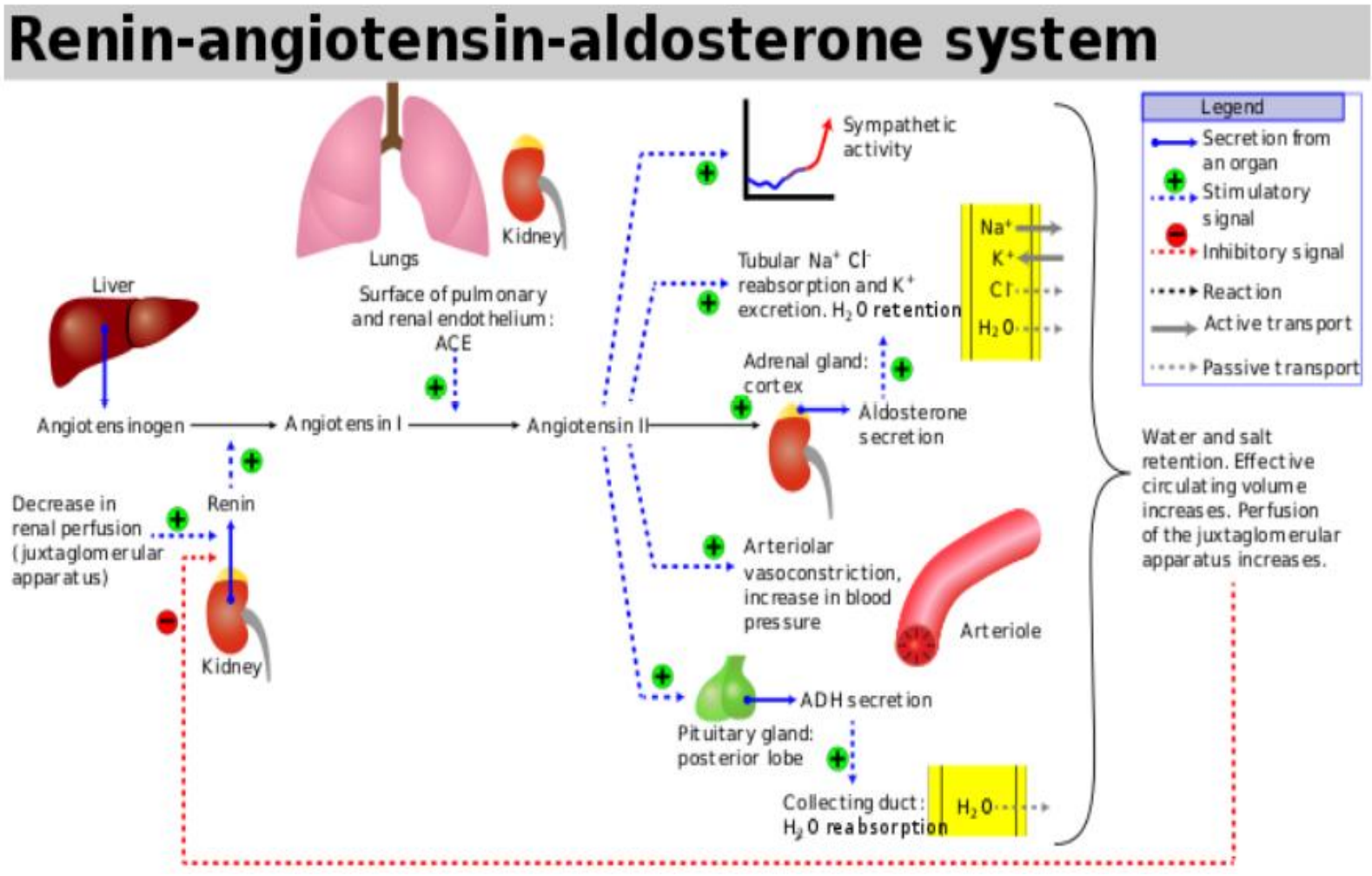
-Increased osmolarity stimulates the release of ADH (antidiuretic hormone) from posterior pituitary gland which acts on renal collecting ducts and increases water reabsorption. And this is how water output decreases

-The output is regulated by the hypothalamus.

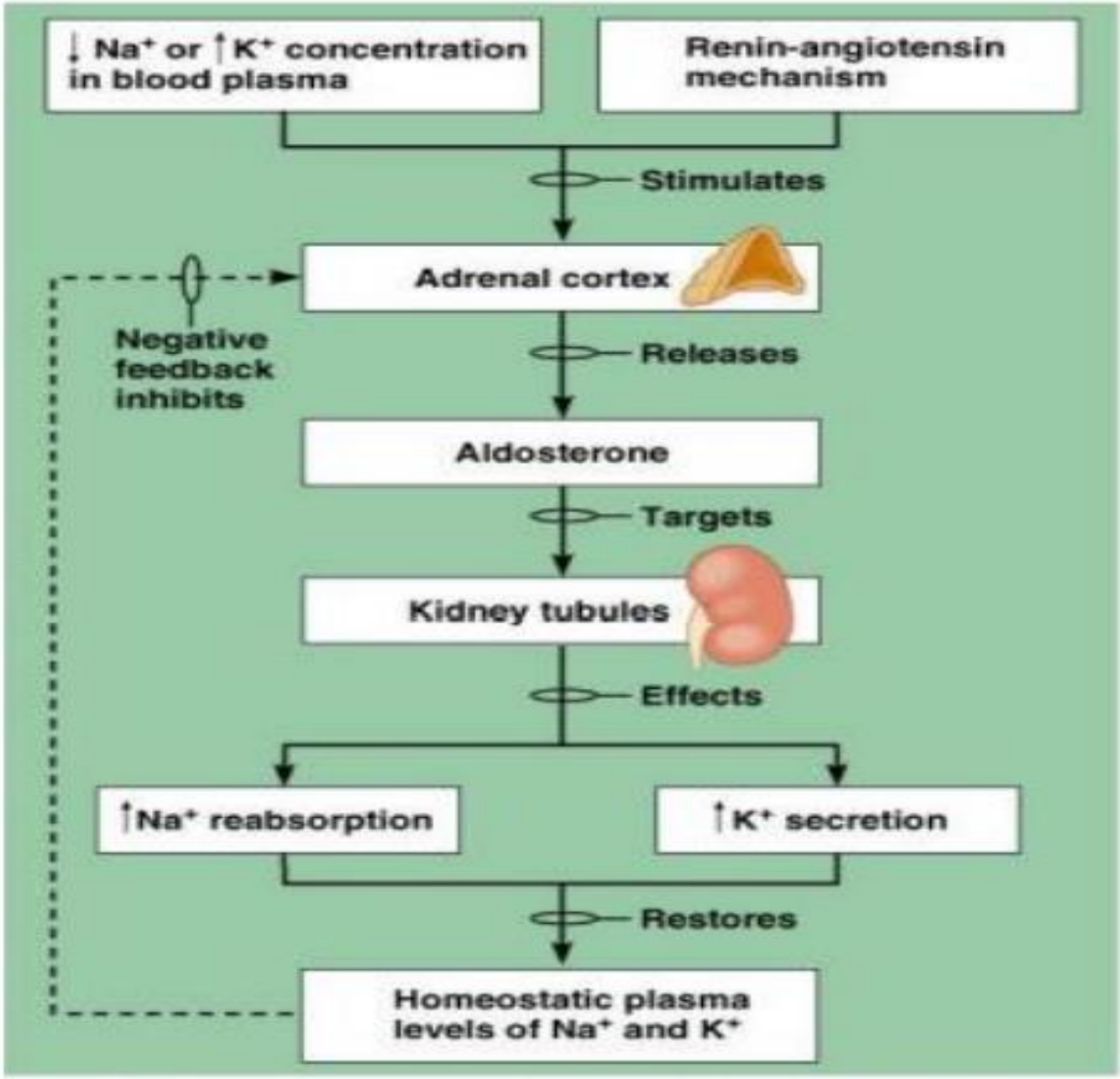


Regulation of ECF volume:

-The regulation of ECF volume depends on
Na+ excretion in urine and it is controlled by Renin-Angiotensin-Aldosterone 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.



-note the angiotensin has other effects which include effects over the vessels
It can cause contraction of smooth muscle cells of vessels to increase blood pressure.



-notice that Renin-Angiotensin-Aldosterone system is also involved in the homeostasis of Na+ and K

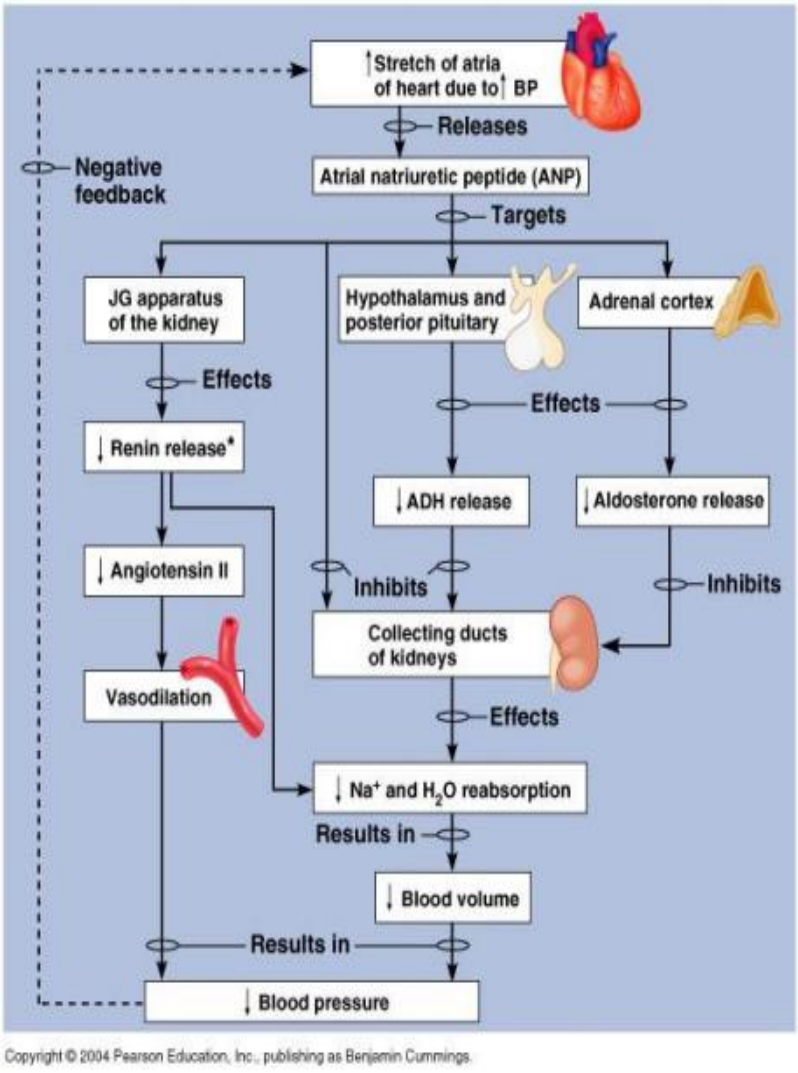
Note that the atrial natriuretic peptide increases the output from the body

-note:
Water intoxication, also known as water poisoning, hyperhydration, overhydration, or water toxemia, is a **potentially fatal disturbance in brain functions** that results when the normal balance of electrolytes in the body is pushed outside safe limits by excessive water intake.

Body Water

- **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



Atrial natriuretic peptide (ANP) effects:

1. Reduces BP, salts (Na+ from ECF) and water by effects over vessels (vasodilation).
2. Decrease Angiotensin II and Aldosterone secretions.

Notice that it's the opposite of Renin-Angiotensin-Aldosterone mechanism.

DISORDERS OF VOLUME

-Some of the different factors that can cause extracellular and intracellular volumes to change markedly are excess ingestion or renal retention of water, dehydration, intravenous infusion of different types of solutions, loss of large amounts of fluid from the gastrointestinal tract, and loss of abnormal amounts of fluid by sweating or through the kidneys.

-basic principles to keep in mind:
1-Water moves rapidly across cell membranes; therefore, the osmolarities of intracellular and extracellular fluids remain almost exactly equal to each other except for a few minutes after a change in one of the compartments.
2-Cell membranes are almost completely impermeable to many solutes, such as sodium and chloride; therefore, the number of osmoles in the extracellular or intracellular fluid generally remains constant unless solutes are added to or lost from the extracellular compartment.

-Now we are ready to talk about the disorders.

-**first disorders of volume**:

1-***Hypovolemia*** (decreased water volume) results include:
A-excessive loss of fluids. Caused by diarrhea, vomiting and blood loss.
B-Decreased ADH release can also cause hypovolemia (diabetes insipidus).

2- **Hypervolemia** (increased water volume) results include:
A- Results by excessive intake or administration of fluids.
-for example if you increase the secretion of ADH you will increase water volume but you will decrease the osmolarity. So you can see that there is an overlapping between mechanisms so by affecting one parameter by a certain mechanism you affect the other one by different mechanism.

-**Disorders of osmolality:**

-note You should know that osmolality is mainly determined by sodium.

A- Hyponatremia (decreased osmolality) causes include:

1- Results by excessive loss of Na+ or administration of hypotonic fluids.

2- Can be caused by excessive intake of potable water(ماء نقي)

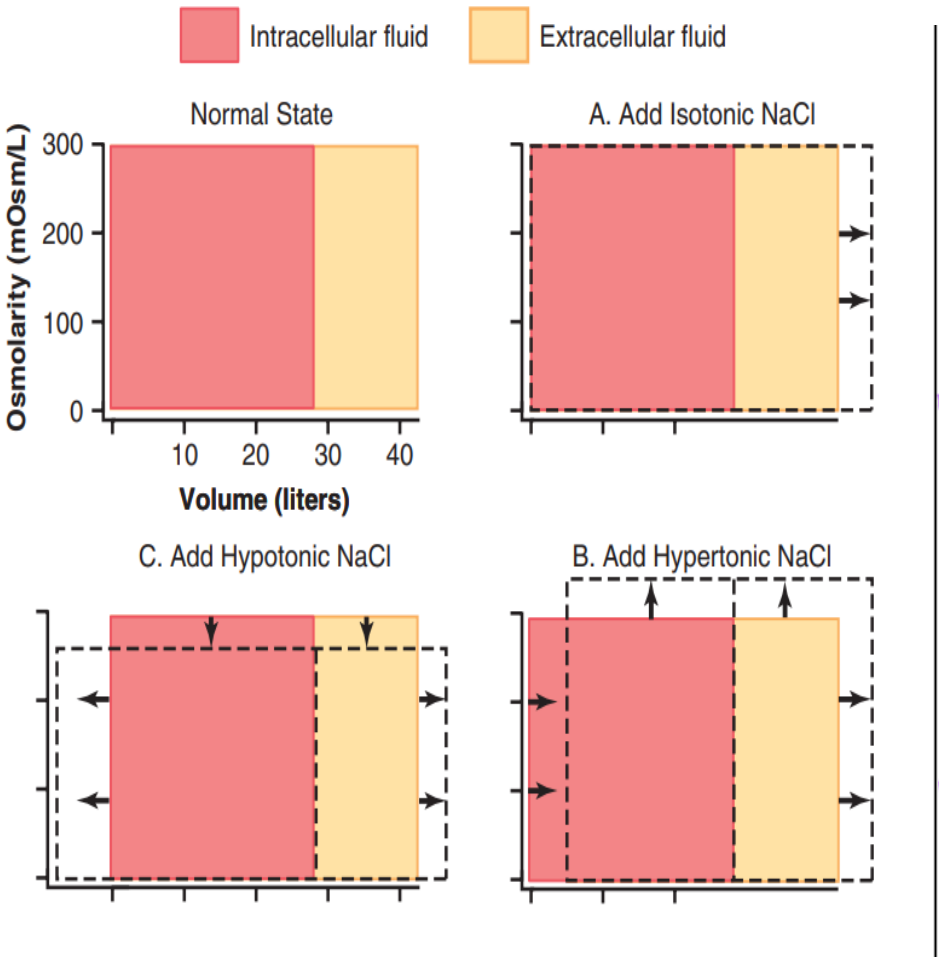
-decreased release in aldosterone also can cause it

B- Hypernatremia (increased osmolality) causes include:

1- Results by excessive intake of Na+ or administration of hypertonic fluids.

2- Results by excessive intake of Na+ or administration of hypertonic fluids.

-Notes from the book: 1-Addison's disease, which results from decreased secretion of the hormone aldosterone impairs the ability of the kidneys to reabsorb sodium and can cause a modest degree of hyponatremia.
2-excessive secretion of antidiuretic hormone, which causes the kidney tubules to reabsorb more water, can lead to hyponatremia and overhydration.



isotonic

A. No change in ICF volume.
ECF volume ↑
No change in osmolality.

Hypertonic

B. ECF volume ↑
ECF osmolality ↑
ICF volume ↓
ICF osmolality ↑

Hypotonic

C. ECF volume ↑
ECF osmolality ↓
ICF volume ↑
ICF osmolality ↓

A- If isotonic saline is added to the extracellular fluid compartment, the osmolarity of the extracellular fluid does not change; therefore, no osmosis occurs through the cell membranes. The only effect is an increase in extracellular fluid volume.

B- If a hypertonic solution is added to the extracellular fluid, the extracellular osmolarity increases and causes osmosis of water out of the cells into the extracellular compartment fluid diffuses from the cells into the extracellular space to achieve osmotic equilibrium. The net effect is an increase in extracellular volume (greater than the volume of fluid added), a decrease in intracellular volume, and a rise in osmolarity in both compartments.

C- If a hypotonic solution is added to the extracellular fluid, the osmolarity of the extracellular fluid decreases and some of the extracellular water diffuses into the cells until the intracellular and extracellular compartments have the same osmolarity.
-from the book: The sodium and chloride largely remain in the extracellular fluid because the cell membrane behaves as though it were virtually impermeable to the sodium chloride.

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 with only drinking hypotonic water.

- **Hyponatremia with overhydration**

High retention of water (administration).
Increased ADH.

High release of ADH increases the volume and decreases the osmolality.

- **Hypernatremia with dehydration**

Loss of hypotonic fluid.

- **Hypernatremia with overhydration**

High release of aldosterone (hyperaldosteronism) causes more Na+ retention and thus osmolality increases and volume increases.

Table 25-4 Abnormalities of Body Fluid Volume Regulation: Hyponatremia and Hypernatremia

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	↑	↑	↓

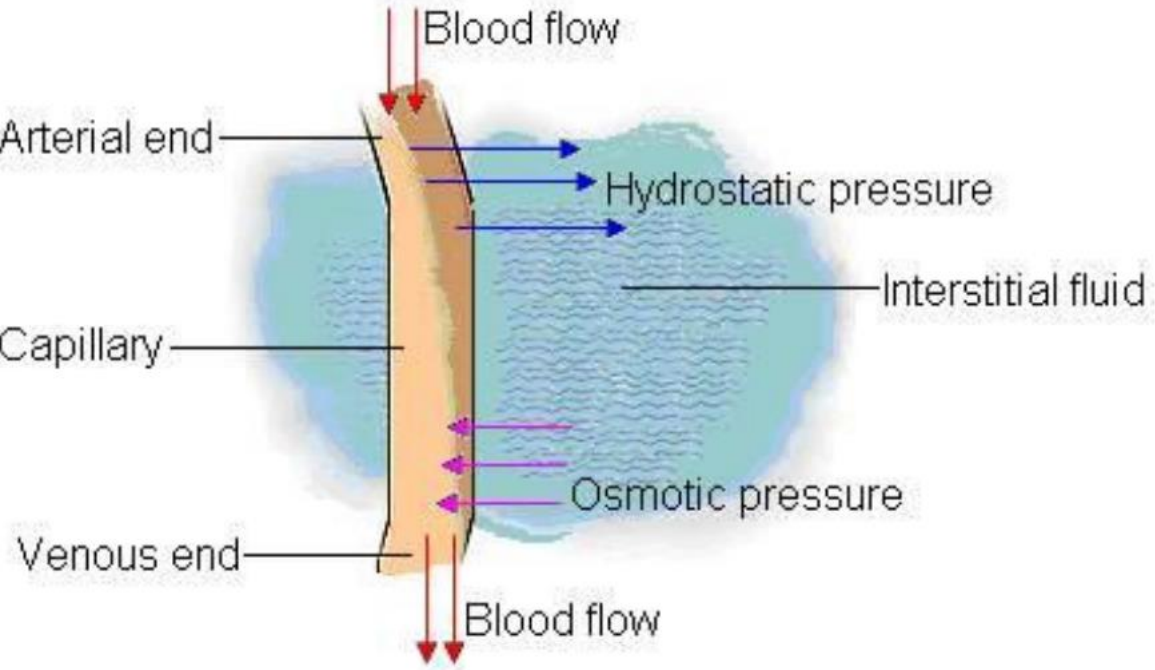
ADH, antidiuretic hormone; SIADH, syndrome of inappropriate ADH.

Oedema

-oedema is the same as edema
-now it is Localized retention of fluids at the interstitial compartment(which is a branch of the extracellular fluid).

-it usually happens in the lower limbs
-the causes of the Oedema:
1- increasing capillary filtration.
2-Decreased oncotic pressure.
3-Increase capillary permeability.
4-Decreased lymph drainage

-Osmotic pressure is also called colloid pressure.
-Onotic pressure : caused by high amount of protein in plasma and low amount in interstitial fluid



-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.

-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.

-the determinant for oncotic pressure at the level of capillaries is the presence of proteins such as albumin and this pressure is important to get reabsorption of water so if there is a decrease of protein content in the plasma this will result in decreasing the absorption so the net loss of water will be higher than the gain or absorption so this will cause edema.

- 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.

Explanation for the causes of the edema:

1- Increasing capillary filtration:
A- Increased capillary hydrostatic pressure:
-Kidney causes: more retention of water and salts *increased inside capillaries* (Renal failure).
-Excess of Mineralocorticoids (aldosterone). → Increasing Na+ and water.

B- High venous pressure: (in normal conditions it is very low).
Heart failure, decrease of Venous return (obstruction, decreased venous pump activity).

-notes from the book the heart fails to pump blood normally from the veins into the arteries, which raises venous pressure and capillary pressure, causing increased capillary filtration. In addition, the arterial pressure tends to fall, causing decreased excretion of salt and water by the kidneys, which causes still more edema.
Also, blood flow to the kidneys is reduced in persons with heart failure, and this reduced blood flow stimulates secretion of renin, causing increased formation of angiotensin II and increased secretion of aldosterone, both of which cause additional salt and water retention by the kidneys.

Decreased arteriolar resistance:

C- Vasodilation → More blood flow → More filtration

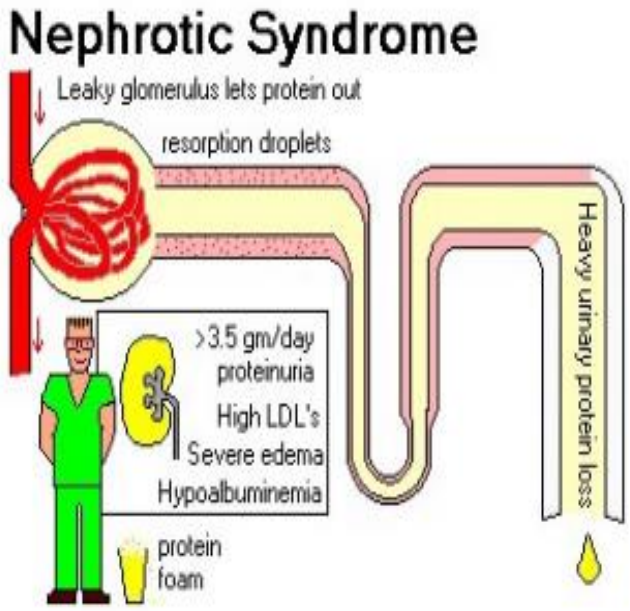
Vasodilation can be caused by 1- excessive body heat
2- insufficiency of SNS
3- vasodilators

B Decreased Oncotic pressure

Increased loss of proteins:

- From Kidney in nephrotic syndrome
Proteins are lost in urine. (خلل في عملية الارتشاح)

- from skin in burns and severe wounds



-notes from the book:
1-Failure to produce normal amounts of proteins or leakage of proteins from the plasma causes the plasma colloid osmotic pressure to fall. This leads to increased capillary filtration throughout the body and extracellular edema.

2-Cirrhosis of the liver is another condition that causes a reduction in plasma protein concentration.

Decreased production of proteins :

- Liver diseases (mostly the production of albumin)

- Decreased intake of proteins in malnutrition

Patients who suffer from kidney and liver problems develop oedema.

Increase capillary permeability

- During immune reactions by release of histamine
- Toxins
- Infections
- Vitamin C deficiency
- Ischemia
- Burns

Decreased lymph drainage:

- Cancer
- Infections
- Surgery
- Absence or abnormality of lymphatic vessels

Lymph drainage can get proteins back from interstitial fluid to general circulation.

-from the book:
When lymphatic function is greatly impaired as a result of blockage or loss of the lymph vessels, edema can become especially severe because plasma proteins that leak into the interstitium have no other way to be removed. The rise in protein concentration raises the colloid osmotic pressure of the interstitial fluid, which draws even more fluid out of the capillaries.

Safety factors for preventing oedema.

1.Low tissue compliance
2.Increased lymph flow
3.Increased protein wash-down from interstitial fluids

Low tissue compliance

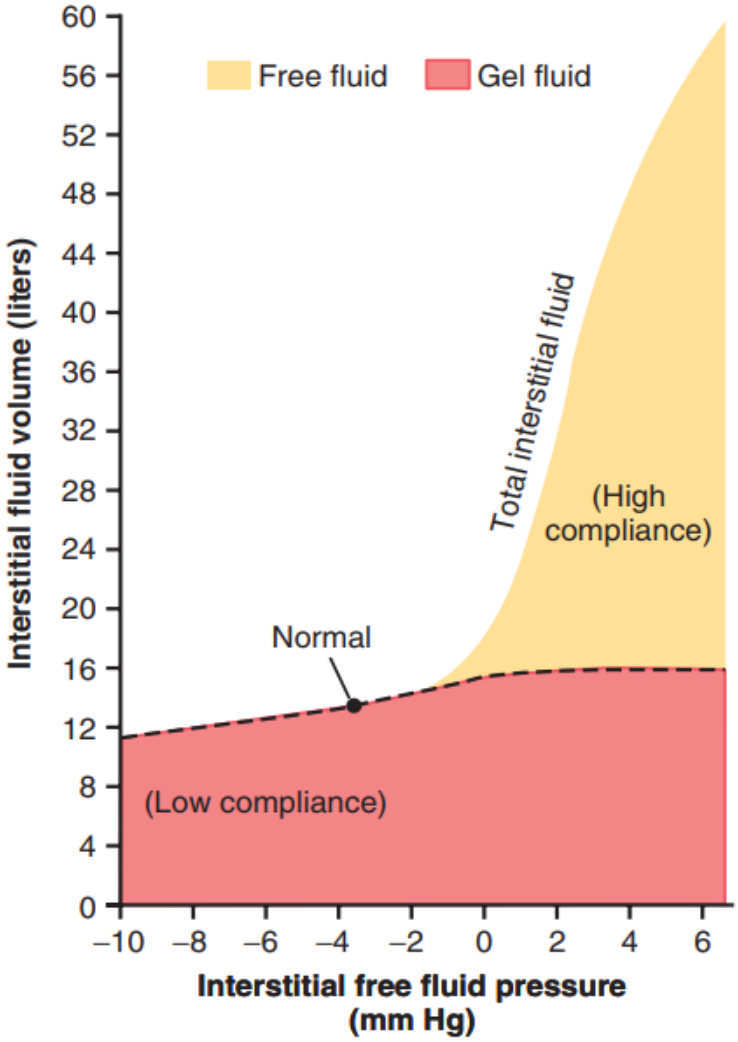


Figure 25-8. Relation between interstitial fluid hydrostatic pressure and interstitial fluid volumes, including total volume, free fluid volume, and gel fluid volume, for loose tissues such as skin. Note that significant amounts of free fluid occur only when the interstitial fluid pressure becomes positive. *(Modified from Guyton AC, Granger HJ, Taylor AE: Interstitial fluid pressure. Physiol Rev 51:527, 1971.)*

-In negative pressure ranges LOW compliance by presence of gel fluids results in relative increase in hydrostatic pressure to small changes in volume Prevents capillary filtration.

-In positive pressure ranges HIGH compliance by accumulation of free fluids results in smaller increase in hydrostatic pressure to high changes in volume Pitting oedema.

Increased lymph flow

Lymph flow can increase up to 10-50 folds → Carry away large amounts of fluids → prevents interstitial pressure from rising into POSITIVE ranges (where we have high compliance)

Increased protein wash-down from interstitial fluids

Increased lymph flow
→ Carry away large amounts of proteins (Protein washed out from interstitial fluids)
→ decrease Colloid osmotic pressure in interstitial fluid
→ Lowering net filtration forces
→ Prevents accumulation of fluids

-final things I highly recommend to you to read pages 317-319 in guyton 13edition book they will help you understand a lot

-Youtube links for videos that also will help you understand

https://youtu.be/rPWf43lYcBU
https://youtu.be/nJ44wZ5_TvA

Well now the sheet is finished it took a lot of work and time I hope it gives all of you the best experience and comprehensive explanation for the concepts.

“it’s the possibility of having a dream come true that makes life interesting.”

-Paulo Coelho

Well life isn’t all rainbows and sunshine you will always struggle but you need to be strong enough to handle that and keep going no matter how much it hurts.

Good look to all of you.

لا تنسونا من صالح دعائكم.