Renal system

PHYSIOLOGY

Very important

Extra information

References :

- GUYTON AND HALL 12th edition
- LINDA 5th edition

* Guyton corners, anything that is colored with grey is EXTRA explanation

Renal Regulation of Body Fluid

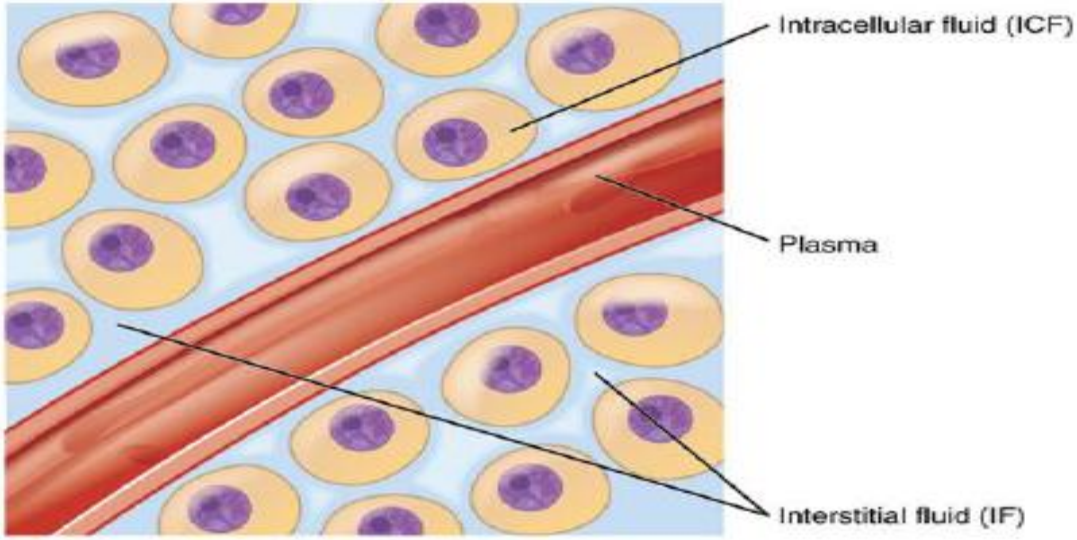
Objectives :

- Identify and describe the role of the Sensors and Effectors in the renal regulation of body fluid volume & osmolality.
- Describe the role of the kidney in regulation of body fluid volume & osmolality.
- Understand the role of ADH in the reabsorption of water and urea.
- Identify the site and describe the influence of aldosterone on reabsorption of Na+ in the late distal tubules.

Contact us : Physiology435@gmail.com

Recall from foundation block : Body fluids

- Fluid Compartments
  - Extracellular fluid (ECF)
    - plasma
    - Interstitial Fluid
    - Transcellular Fluid
      - pericardial "surrounding the heart"
      - peritoneal "in abdominal cavity"
      - Intraocular " in the eye "
      - CSF " In the brain"
      - Synovial "in joints"
      - Digestive Secretions
      - Pleural
  - Intracellular fluid (ICF)



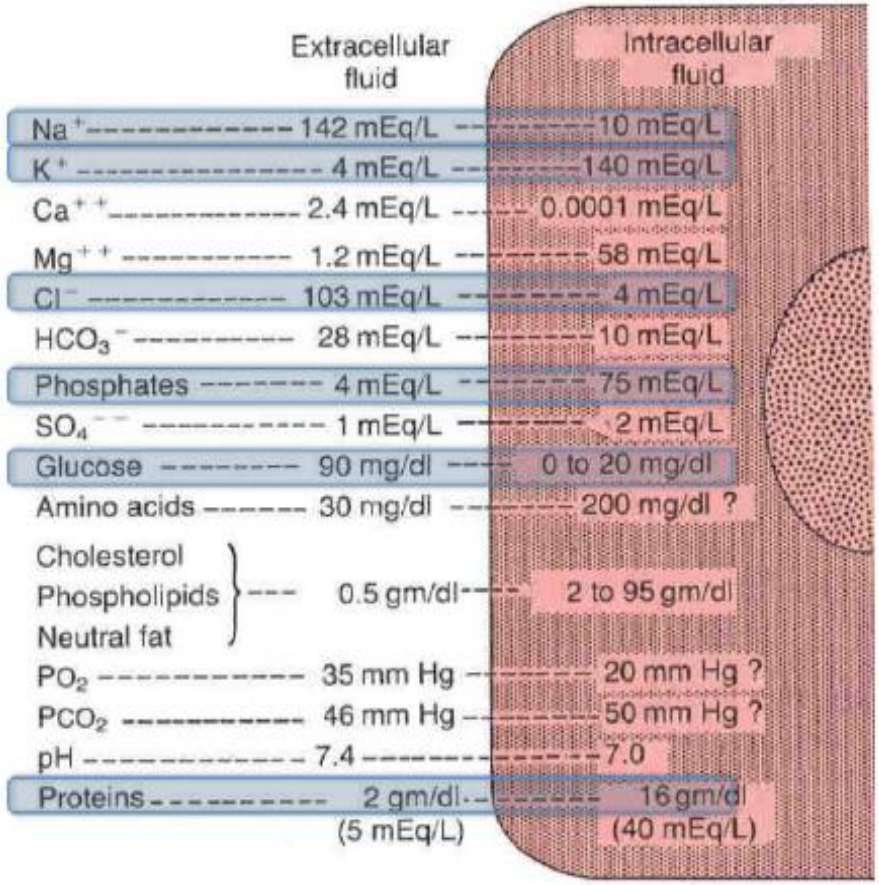
Recall from foundation block : Body fluid

Extracellular fluids :

- Sodium is the chief cation(+) "Na"
- Chloride is the chief anion (-) "Cl"

Intracellular fluids :

- Potassium is the chief cation(+) "K"
- Phosphate is the chief anion(-)



Solute Overview: Intracellular vs. Extracellular

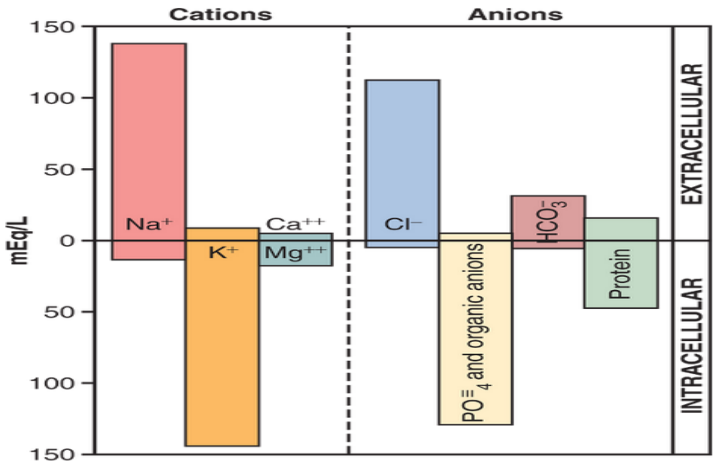
- Ionic composition is very different between extracellular and intracellular.
  (Means the balance or the amount of Na+ and K+ in extra-intra-cellular, but not the charge).

- Total ionic concentration is very similar
  (means the amount of the positive charges of K should be equal or nearly equal to the amount of positive charge of Na+).

- Total osmotic concentrations virtually identical.
  (means the balance between extra-intra-cellular are maintained by the permeability of the cell membrane).

• Guyton corner :

The intracellular fluid is separated from the extracellular fluid by a cell membrane that is highly permeable to water but not to most of the electrolytes in the body. In contrast to the extracellular fluid, the intracellular fluid contains only small quantities of sodium and chloride ions and almost no calcium ions. Instead, it contains large amounts of potassium and phosphate ions plus moderate quantities of magnesium and sulfate ions, all of which have low concentrations in the extracellular fluid. Also, cells contain large amounts of protein, almost four times as much as in the plasma.



- The major EC Cation is Na+ e while the major EC anions is Chloride.
- The major intracellular cation is potassium while the major anions are phosphate, proteins.
- Ion = cation + anion

EXTRA

	Plasma (mOsm/L H_2O)	Interstitial (mOsm/L H_2O)	Intracellular (mOsm/L H_2O)
Na^+	142	139	14
K^+	4.2	4.0	140
Ca^{++}	1.3	1.2	0
Mg^{++}	0.8	0.7	20
Cl^-	108	108	4
HCO_3^-	24	28.3	10
$HPO_4^=$, $H_2PO_4^-$	2	2	11
$SO_4^=$	0.5	0.5	1
Phosphocreatine			45
Carnosine			14
Amino acids	2	2	8
Creatine	0.2	0.2	9
Lactate	1.2	1.2	1.5
Adenosine triphosphate			5
Hexose monophosphate			3.7
Glucose	5.6	5.6	
Protein	1.2	0.2	4
Urea	4	4	4
Others	4.8	3.9	10
Total mOsm/L	301.8	300.8	301.2
Corrected osmolar activity (mOsm/L)	282.0	281.0	281.0
Total osmotic pressure at 37 °C (mm Hg)	5443	5423	5423

Table 25-2

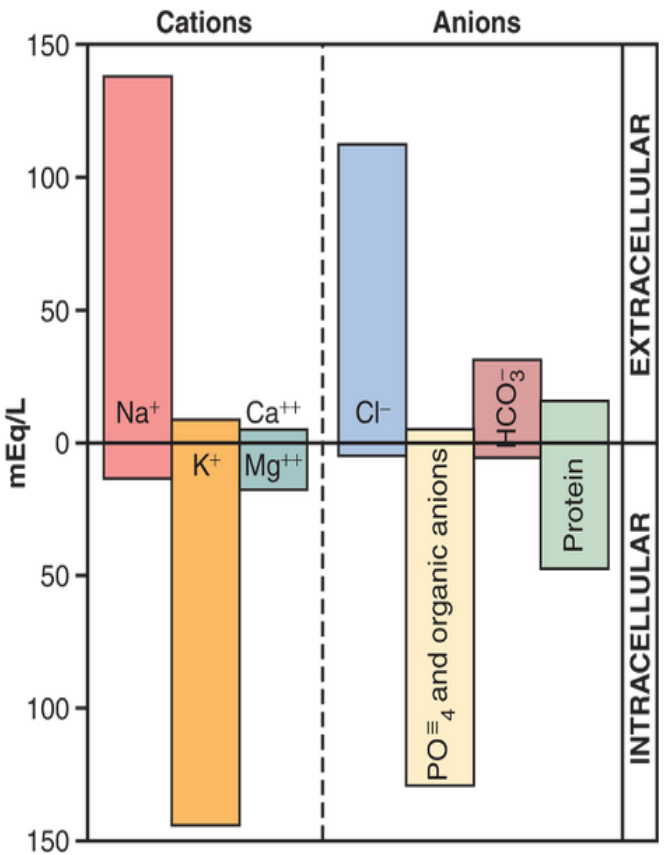


Figure 25-2

- **Guyton corner :**

Comparisons of the composition of the extracellular fluid, including the plasma and interstitial fluid, and the intracellular fluid are shown in Figure 25-2 and in Table 25-2.

If you forgot the basics, go back to foundation physiology :)

EXTRA

- ECF is composed of 2 parts interstitial fluid and plasma component .
- Balance between intake and output should be maintained and the output is regulated mainly by kidney.

- **Guyton corner :**

Body Fluid Compartments

The total body fluid is distributed mainly between two compartments: the *extracellular fluid* and the *intracellular fluid* (Figure 25-1). The extracellular fluid is divided into the *interstitial fluid* and the blood *plasma*.

There is another small compartment of fluid that is referred to as *transcellular fluid*. This compartment includes fluid in the synovial, peritoneal, pericardial, and intraocular spaces, as well as the cerebrospinal fluid; it is usually considered to be a specialized type of extracellular fluid, although in some cases its composition may differ markedly from that of the plasma or interstitial fluid. All the transcellular fluids together constitute about 1 to 2 liters.

In the average 70-kilogram adult man, the total body water is about 60 percent of the body weight, or about 42 liters. This percentage can change, depending on age, gender, and degree of obesity. As a person grows older, the percentage of total body weight that is fluid gradually decreases. This is due in part to the fact that aging is usually associated with an increased percentage of the body weight being fat, which decreases the percentage of water in the body.

Because women normally have more body fat than men, their total body water averages about 50 percent of the body weight. In premature and newborn babies, the total body water ranges from 70 to 75 percent of body weight. Therefore, when discussing the “average” body fluid compartments, we should realize that variations exist, depending on age, gender, and percentage of body fat.

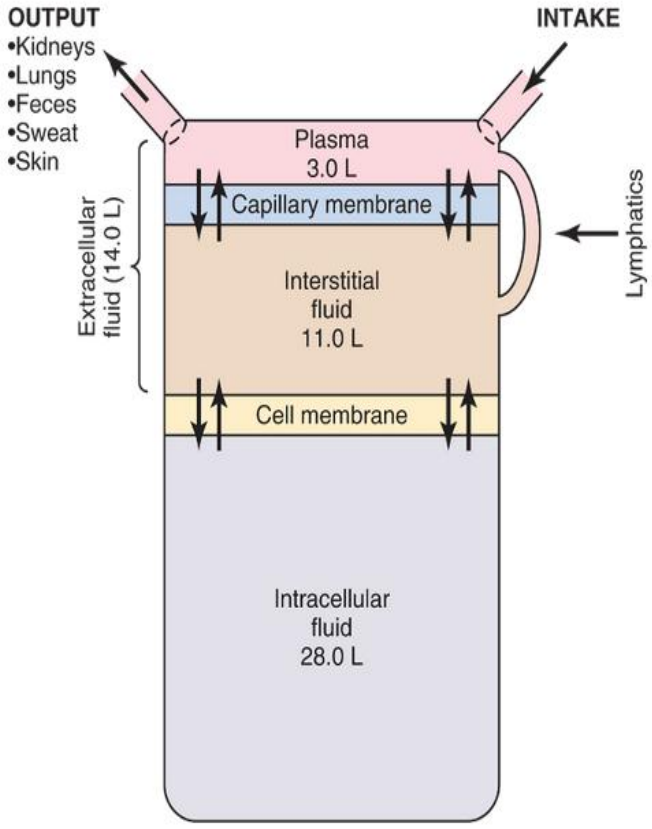


Figure 25-1

EXTRA

It is something interesting to know!

- **Guyton corner :**

Vascular Control by Ions and Other Chemical Factors :

1. Many different ions and other chemical factors can either dilate or constrict local blood vessels. Most of them have little function in overall regulation of the circulation, but some specific effects are:
2. An increase in calcium ion concentration causes vasoconstriction. This results from the general effect of calcium to stimulate smooth muscle contraction,.
3. An increase in potassium ion concentration, within the physiological range, causes vasodilation. This results from the ability of potassium ions to inhibit smooth muscle contraction.
4. An increase in magnesium ion concentration causes powerful vasodilation because magnesium ions inhibit smooth muscle contraction.
5. An increase in hydrogen ion concentration (decrease in pH) causes dilation of the arterioles. Conversely, slight decrease in hydrogen ion concentration causes arteriolar constriction.
6. Anions that have significant effects on blood vessels are acetate and citrate, both of which cause mild degrees of vasodilation.
7. An increase in carbon dioxide concentration causes moderate vasodilation in most tissues but marked vasodilation in the brain. Also, carbon dioxide in the blood, acting on the brain vasomotor center, has an extremely powerful indirect effect, transmitted through the sympathetic nervous vasoconstrictor system, to cause widespread vasoconstriction throughout the body.

Regulation of volume & osmolality

- Body water balance must be maintained.
- Kidneys *concentrate* or *dilute* urine. (as a response for any change of the fluid volume).
- To remain properly hydrated, water intake must equal water output.
- **Increases** in plasma osmolality trigger thirst and release of antidiuretic hormone *(ADH).*

The volume of the body fluid *don't have certain receptor* to detect the change of the fluid volume *but it has sensors* which will be explained in next slide.

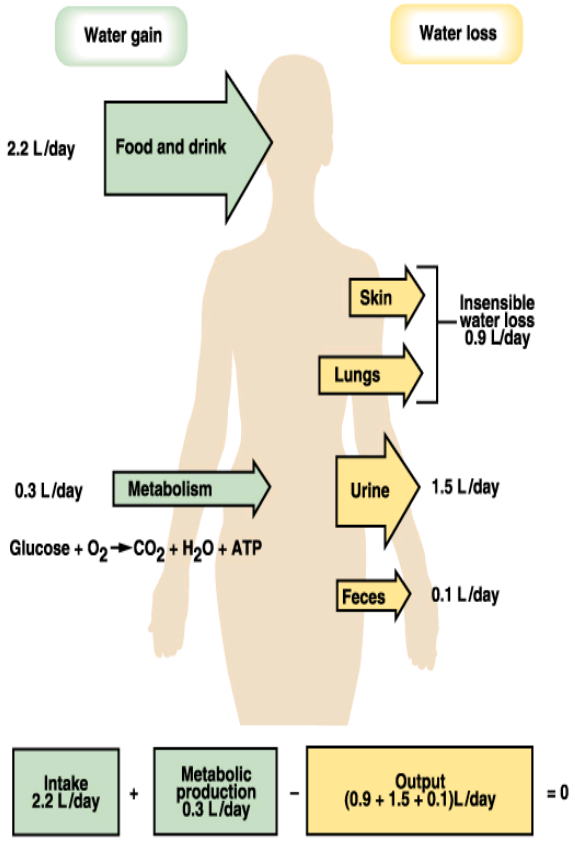
- Water balance between ICF and ECF must be maintained .The kidneys play an important role in regulation of fluids by regulating the volume of urine and its composition either its *concentrated* urine or *diluted* urine.
- *concentrated* urine = more ions / *diluted* urine = more water.
- Once the plasma becomes concentrated (increased osmolality) it will stimulate thirst center in the brain and the thirst triggers drinking to supply enough water that the body need.
- If the stores of water are decreased the body release *ADH* that will act on the kidney to reabsorb more water

Water steady state

- Amount ingested = amount eliminated.
- **Pathological losses:**

Pathological losses of the fluid

- Vascular bleeding
- Vomiting
- Diarrhea



Control of Circulating Volume

- All down to Na^+ balance i.e. absorption & excretion.

Absorption or excretion of Na will facilitate the reabsorption and excretion for other electrolyte e.g.; water

- **Volume sensors:** *(Effectively pressure receptors)*

  - **Vascular:**

    1) Low pressure sensors: Sensors that are found in the low pressure area such as atria (right atrium > venous blood)

    Cardiac atria (ANP), pulmonary vasculature.

    2) High pressure: Sensors that are found in the high pressure area

    Carotid sinus, aortic arch and juxtaglomerular apparatus of the kidney.

  - **Central nervous system.**

  - **Hepatic.**

- **Guyton corner :**

Even small increases in arterial pressure can cause marked increases in urinary excretion of sodium and water, phenomena that are referred to as *pressure natriuresis* and *pressure diuresis.* Because of the autoregulatory mechanisms increasing the arterial pressure between the limits of 75 and 160 mm Hg usually has only a small effect on renal blood flow and GFR. The slight increase in GFR that does occur contributes in part to the effect of increased arterial pressure on urine output.

Control of Circulating Volume

Volume sensor signals/Mediators:

1.Neural

- If the pressure decreased↓ , Renal sympathetic will be stimulated and causes :

a) Afferent & Efferent arterioles constrict:

- GFR decreased.
- Less Na^+ filtered.
- More Na^+ absorbed by PCT. *(Proximal convoluted tubule)*

b) Renin released :

- increase Aldosterone secretion. *(to increase the Na+ reabsorption)*
- increase angiotensin II formation. *(vasoconstriction)*

1. vascular sensors will sense the pressure changes and these changes reflects the change in body volume.
2. Neural sensor if the BP decrease this will stimulate neural sensors these neural sensors will act causing stimulation in renal sympathetic system → sympathetic act on A.A & E.A → constriction

- if the renal arterioles are constricted this will decrease the GFR → the total amount of Na is decreased → leading to more Na absorption as compensatory mechanism for the decrease total amount delivered to the kidney .
- If there is change in the Blood volume it will stimulate the renin to be secreted →AngII is a vasoconstrictor and it stimulate the release of aldosterone →this will stimulate Na and water reabsorption → this will correct the decrease in BV and BP .

- **Guyton corner :**

Sympathetic Nervous System Activation Decreases GFR :

Essentially all the blood vessels of the kidneys, including the afferent and the efferent arterioles, are richly innervated by sympathetic nerve fibers. Strong activation of the renal sympathetic nerves can constrict the renal arterioles and decrease renal blood flow and GFR. Moderate or mild sympathetic stimulation has little influence on renal blood flow and GFR. For example, reflex activation of the sympathetic nervous system resulting from moderate decreases in pressure at the carotid sinus baroreceptors or cardiopulmonary receptors has little influence on renal blood flow or GFR.

The renal sympathetic nerves seem to be most important in reducing GFR during severe, acute disturbances lasting for a few minutes to a few hours, such as those elicited by the defense reaction, brain ischemia, or severe hemorrhage. In the healthy resting person, sympathetic tone appears to have little influence on renal blood flow.

Angiotensin II Preferentially Constricts Efferent Arterioles in Most Physiologic Conditions :

A powerful renal vasoconstrictor, *angiotensin II,* can be considered a circulating hormone, as well as a locally produced autacoid because it is formed in the kidneys and in the systemic circulation. Receptors for angiotensin II are present in virtually all blood vessels of the kidneys. However, the preglomerular blood vessels, especially the afferent arterioles, appear to be relatively protected from angiotensin II–mediated constriction in most physiologic conditions associated with activation of the renin-angiotensin system such as during a low-sodium diet or reduced renal perfusion pressure due to renal artery stenosis. This protection is due to release of vasodilators, especially *nitric oxide* and *prostaglandins,* which counteract the vasoconstrictor effects of angiotensin II in these blood vessels.

The efferent arterioles, however, are highly sensitive to angiotensin II. Because angiotensin II preferentially constricts efferent arterioles in most physiologic conditions, increased angiotensin II levels raise glomerular hydrostatic pressure while reducing renal blood flow. It should be kept in mind that increased angiotensin II formation usually occurs in circumstances associated with decreased arterial pressure or volume depletion, which tend to decrease GFR. In these circumstances, the increased level of angiotensin II, by constricting efferent arterioles, helps *prevent* decreases in glomerular hydrostatic pressure and GFR; at the same time, though, the reduction in renal blood flow caused by efferent arteriolar constriction contributes to decreased flow through the peritubular capillaries, which in turn increases reabsorption of sodium and water.

Thus, increased angiotensin II levels that occur with a low-sodium diet or volume depletion help maintain GFR and normal excretion of metabolic waste products such as urea and creatinine that depend on glomerular filtration for their excretion; at the same time, the angiotensin II-induced constriction of efferent arterioles increases tubular reabsorption of sodium and water, which helps restore blood volume and blood pressure.

Extra

- **Guyton corner :** page 346

Aldosterone Increases Sodium Reabsorption and Potassium Secretion.

The most important stimuli for aldosterone are (1) increased extracellular potassium concentration and (2) increased angiotensin II levels, which typically occur in conditions associated with sodium and volume depletion or low blood pressure. The increased secretion of aldosterone associated with these conditions causes renal sodium and water retention, helping to increase extracellular fluid volume and restore blood pressure toward normal.

- **Guyton corner :** page 346

Angiotensin II Increases Sodium and Water Reabsorption.

Angiotensin II is perhaps the body's most powerful sodium-retaining hormone. angiotensin II formation increases in circumstances associated with low blood pressure and/or low extracellular fluid volume, such as during hemorrhage or loss of salt and water from the body fluids by excessive sweating or severe diarrhea. The increased formation of angiotensin II helps to return blood pressure and extracellular volume toward normal by increasing sodium and water reabsorption from the renal tubules through three main effects: 1. Angiotensin II stimulates aldosterone secretion, which in turn increases sodium reabsorption. 2. *Angiotensin II constricts the efferent arterioles. 3. Angiotensin II directly stimulates sodium reabsorption in the proximal tubules, the loops of Henle, the distal tubules, and the collecting tubules.*

Control of Circulating Volume

2.Hormonal :

1

Renin-angiotensin-aldosterone system (↓ pressure):

- **Renin secreted by:**
  a) Sympathetic stimulation
  b) ↓ perfusion pressure
  c) ↓ Na+ reaching *macula densa*.

- **Angiotensin II:**
  a) **Aldosterone** release by *adrenal cortex.*
  b) Increase Na^+ reabsorption in TAL, DT, CD.
  c) Vasoconstriction.
  d) **ADH** release.
  e) ↑ Na^+ reabsorption in PCT.

2

ANP : *(Atrial natriuretic peptide)*

Released from **atrial** myocytes by stretch of atrium, thus *increase NaCl & water excretion*.

Antagonist of renin-angiotensin:

- Vasodilation of afferent arteriole, Vasoconstriction of efferent ;i.e. ↑ GFR
- ↓ Renin release.
- Direct ↓ aldosterone release.
- ↓ Na^+ reabsorption in CD *(collecting duct)*
- ↓ ADH release.

- The trigger for release of RAAS is the drop in blood pressure.
- It will be secreted by sympathetic stimulation to correct this situation.

- TAL : Thick ascending limb
- DT : distal tubule
- CD : collecting duct
- PCT : Proximal convoluted tubule

Actions of Angiotensin II

First action:

- **Angiotensin II** receptors are found on the *zona glomerulosa cells of the adrenal cortex*.
- Activation of these receptors leads to an immediate and rapid increase in *Aldosterone secretion.*
- **Aldosterone** acts on the *distal tubule* and *collecting duct* to cause ***sodium* retention**.
- This is likely to be an important mechanism for determining long-term sodium balance.

Second action: *(Vascular actions)*

- Angiotensin II is one of the most potent vasoconstrictors known.
- Constriction of vascular smooth muscle leads to a prompt rise in blood pressure.
- It plays an important role in maintaining vascular tone and blood pressure in volume depleted states, for example haemorrhage and fluid depletion.

- Adrenal gland is the suprarenal gland and its composed of cortex and medulla so the receptors of AngII are located in the zona glomerulosa cells in the cortex of adrenal gland
- long term because it will stimulate aldosterone and after that aldosterone will regulate sodium balance .
- Aldosterone Action : DT & CD > sodium retention = sodium reabsorption.

Regulation of volume & osmolality

Large water intake	**Low** water intake
Hypoosmotic urine	Hyperosmotic urine
Diluted urine (~ 50 mOsm/kg)	**concentrated** urine (up to 1200 mOsm/kg)
Large volume (up to 18 L/day)	small volume (0.5 L/d)

- Renal water excretion mechanisms *independent* of solute excretion mechanisms which allows water balance maintenance without damaging solute homeostasis *(e.g. Na+, K+)*.

- Increase water intake = Decreased osmolality = Diluted urine = Hypoosmotic.
- Dehydration contributes to concentrated urine = Hyperosmotic.
- we need to keep the balance of the main solute of the body with normal range as well as water balance (constant osmolality of blood) .

Antidiuretic hormone (ADH)/ Vasopressin

Antidiuretic hormone (ADH):

- It is synthesized in neuroendocrine cells located within the supraoptic and paraventricular nuclei of the *hypothalamus*.

Dr ahmed mentioned that: ADH is synthesized by the hypothalamus and secreted by the posterior lobe of pituitary gland, that's why we mentioned it's synthesized in neuroendocrine cells.

- The synthesized hormone is packaged in granules that are transported down the axon of the cell and stored in nerve terminals located in the neurohypophysis in the *posterior lobe of pituitary gland*.

Characters of ADH:

- Prevents water loss.
- Small protein hormone (formed only by 9 amino acids).
- Fast acting, short half life in the circulation.
- Stimulates thirst center, also *thirst will stimulate secretion of ADH*.

- ADH is synthesized in hypothalamus and secreted by posterior pituitary gland .Its main action is to stimulate water reabsorption.
- Its structure is protein hormone (small amino acid number)
- short half life means once it release it will produce action and metabolized
- one of triggers of ADH → thirst
- If we have hyperosmotic plasma → increase release of ADH.
- If we have hypoosmotic plasma → decrease ADH release.
- hemodynamic indicates changes in BP and BV
- ANP is stimulated by increased BV→ stretch the wall of atrium → release of ANP that decrease BV → so it will inhibit ADH release .

Antidiuretic hormone (ADH) / Vasopressin

Factors influencing ADH release:

- Osmolality.

Increased osmolality will stimulate secretion of ADH, also low osmolality will suppress secretions of ADH.

- Haemodynamic factors.

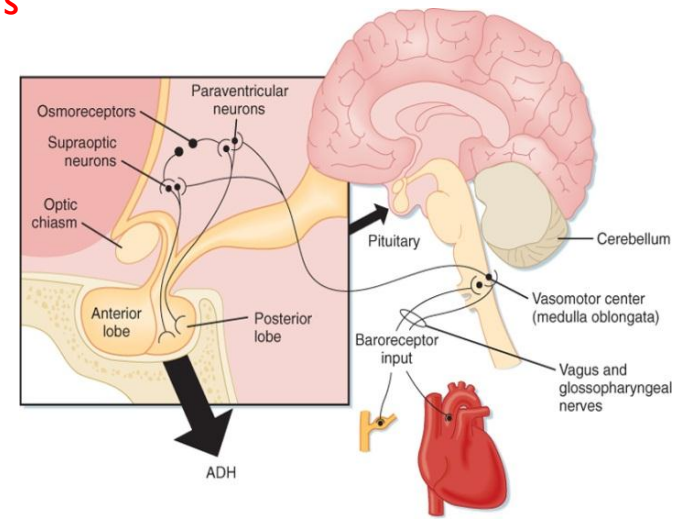
What meant by factors either hypovolemia or hypervolemia

- Nausea → will *stimulate* ADH release.
- Atrial nitric peptide (ANP) → will *inhibit* ADH release.
- Angiotensin II → will *stimulate ADH release*.

*Colored with red are the Main physiological factors

Explanation of the diagram:

Baroreceptors detect pressure changes → send signals to the vasometer center in medulla oblongata → which will send signals to the supraoptic and paraventricular nuclei of the hypothalamus to synthesize the hormone.



EXTRA

- **Guyton corner :** page 347

ADH Increases Water Reabsorption.

The most important renal action of ADH is to increase the water permeability of the distal tubule, collecting tubule, and collecting duct epithelia. This effect helps the body to conserve water in circumstances such as dehydration. In the absence of ADH, the permeability of the distal tubules and collecting ducts to water is low, causing the kidneys to excrete large amounts of dilute urine, a condition called *diabetes insipidus*. Thus, the actions of ADH play a key role in controlling the degree of dilution or concentration of the urine.

- **Guyton corner :** page 347

Atrial Natriuretic Peptide Decreases Sodium and Water Reabsorption.

When specific cells of the cardiac atria are stretched because of plasma volume expansion and increased atrial blood pressure, they secrete a peptide called *atrial natriuretic peptide (ANP)*. Increased levels of this peptide in turn directly inhibit the reabsorption of sodium and water by the renal tubules, especially in the collecting ducts. ANP also inhibits renin secretion and therefore angiotensin II formation, which in turn reduces renal tubular reabsorption. This decreased sodium and water reabsorption increases urinary excretion, which helps to return blood volume back toward normal.

ADH renal target

- **ADH doesn't effect all parts of the nephron, it effects:**

  - *Collecting duct cells only permeable to water in presence of ADH.*

  - ADH causes in increased **urea** permeability *in inner medullary collecting ducts.*

  - ADH stimulates reabsorption of NaCl by the *thick ascending limb* of Henle's loop and by the *distal convoluted tubules* and cortical segment of collecting ducts.

- In the previous lecture we said that the collecting duct & DCT are permeable to water only in the presence of ADH which mean that they are hormone-dependent.

EXTRA "ADH"

- **Guyton corner :**

ADH Synthesis in Supraoptic and Paraventricular Nuclei of the Hypothalamus and ADH Release from the Posterior Pituitary

Figure 28-10 shows the neuroanatomy of the hypothalamus and the pituitary gland, where ADH is synthesized and released. The hypothalamus contains two types of *magnocellular (large) neurons that synthesize ADH in the supraoptic and paraventricular nuclei of the hypothalamus,* about five sixths in the supraoptic nuclei and about one sixth in the paraventricular nuclei. Both of these nuclei have axonal extensions to the posterior pituitary. Once ADH is synthesized, it is transported down the axons of the neurons to their tips, terminating in the posterior pituitary gland. When the supraoptic and paraventricular nuclei are stimulated by increased osmolarity or other factors, nerve impulses pass down these nerve endings, changing their membrane permeability and increasing calcium entry. ADH stored in the secretory granules (also called vesicles) of the nerve endings is released in response to increased calcium entry. The released ADH is then carried away in the capillary blood of the posterior pituitary into the systemic circulation.Secretion of ADH in response to an osmotic stimulus is rapid, so plasma ADH levels can increase severalfold within minutes, thereby providing a rapid means for altering renal excretion of water.A second neuronal area important in controlling osmolarity and ADH secretion is located along the *anteroventral region of the third ventricle,* called the *AV3V region.* At the upper part of this region is a structure called the *subfornical organ,* and at the inferior part is another structure called the *organum vasculosum* of the *lamina terminalis.* Between these two organs is the *median preoptic nucleus,* which has multiple nerve connections with the two organs, as well as with the supraoptic nuclei and the blood pressure control centers in the medulla of the brain. Lesions of the AV3V region cause multiple deficits in the control of ADH secretion, thirst, sodium appetite, and blood pressure. Electrical stimulation of this region or stimulation by angiotensin II can increase ADH secretion, thirst, and sodium appetite.

In the vicinity of the AV3V region and the supraoptic nuclei are neuronal cells that are excited by small increases in extracellular fluid osmolarity; hence, the term *osmoreceptors* has been used to describe these neurons. These cells send nerve signals to the supraoptic nuclei to control their firing and secretion of ADH. It is also likely that they induce thirst in response to increased extracellular fluid osmolarity.

Both the subfornical organ and the organum vasculosum of the lamina terminalis have vascular supplies that lack the typical blood-brain barrier that impedes the diffusion of most ions from the blood into the brain tissue. This makes it possible for ions and other solutes to cross between the blood and the local interstitial fluid in this region. As a result, the osmoreceptors rapidly respond to changes in osmolarity of the extracellular fluid, exerting powerful control over the secretion of ADH and over thirst.

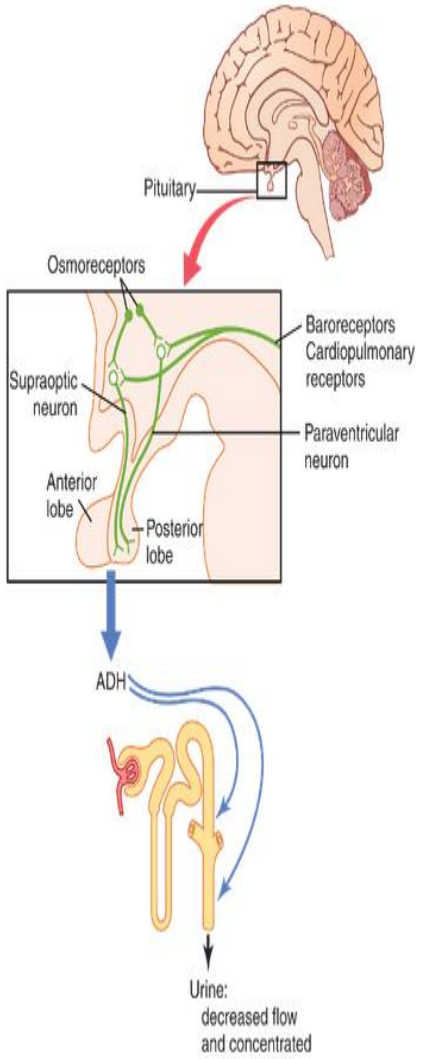


Figure 28-10

EXTRA "ADH"

- **Guyton corner :**

Osmoreceptor-ADH Feedback System

Figure 28-9 shows the basic components of the osmoreceptor-ADH feedback system for control of extracellular fluid sodium concentration and osmolarity. When osmolarity (plasma sodium concentration) increases above normal because of water deficit, for example, this feedback system operates as follows:

- An increase in extracellular fluid osmolarity (which in practical terms means an increase in plasma sodium concentration) causes the special nerve cells called osmoreceptor cells, located in the anterior hypothalamus near the supraoptic nuclei, to shrink.
- Shrinkage of the osmoreceptor cells causes them to fire, sending nerve signals to additional nerve cells in the supraoptic nuclei, which then relay these signals down the stalk of the pituitary gland to the posterior pituitary.
- These action potentials conducted to the posterior pituitary stimulate the release of ADH, which is stored in secretory granules (or vesicles) in the nerve endings.
- ADH enters the blood stream and is transported to the kidneys, where it increases the water permeability of the late distal tubules, cortical collecting tubules, and medullary collecting ducts.
- The increased water permeability in the distal nephron segments causes increased water reabsorption and excretion of a small volume of concentrated urine.

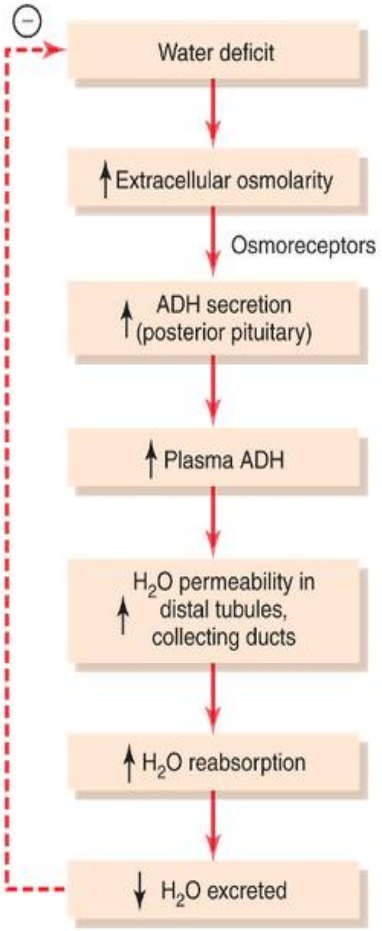


Figure 28-9

EXTRA "ADH"

- **Guyton corner :**

stimuli increase ADH secretion: (1) decreased arterial pressure and (2) decreased blood volume. Whenever blood pressure and blood volume are reduced, such as occurs during hemorrhage, increased ADH secretion causes increased fluid reabsorption by the kidneys, helping to restore blood pressure and blood volume toward normal.

Low Blood Volume and Low Blood Pressure Stimulate ADH Secretion—Vasoconstrictor Effects of ADH :

Low Blood Volume and Low Blood Pressure Stimulate ADH Secretion—Vasoconstrictor Effects of ADH
Whereas minute concentrations of ADH cause increased water conservation by the kidneys, higher concentrations of ADH have a potent effect of constricting the arterioles throughout the body and therefore increasing the arterial pressure. For this reason, ADH has another name, vasopressin.
One of the stimuli for causing intense ADH secretion is decreased blood volume. This occurs strongly when the blood volume decreases 15 to 25 percent or more; the secretory rate then sometimes rises to as high as 50 times normal. The cause of this is the following.

The atria have stretch receptors that are excited by overfilling. When excited, they send signals to the brain to inhibit ADH secretion. Conversely, when the receptors are unexcited as a result of underfilling, the opposite occurs, with greatly increased ADH secretion. Decreased stretch of the baroreceptors of the carotid, aortic, and pulmonary regions also stimulates ADH secretion.

Osmolality

Osmolality estimation:

A rough estimate of ECF osmolality can be obtained by *doubling* Plasma sodium concentration.

Example:

{ 145 mEq/l X 2 = 290 *(Normal 285-295 mOsm/kg H2O)* }

- Sodium concentration gives best estimate of *effective osmolality of ECF*.
- **Above** 295 → increased osmolality → increased ADH secretion.
- **Under** 285 → decreased osmolality → decreased ADH secretion.\

Clinically:

- In clinical situations glucose & urea concentrations (mmols) are also taken into account, useful in cases of patients with diabetes mellitus or chronic renal failure.
- Neither glucose or urea are effective osmoles ,they *do not* shift fluid between ECF & ICF.
- **Non-absorbed glucose** in kidney tubule can however prevent fluid absorption generating an *osmotic diuresis*.* الجلوكوز يسحب الماء معاه

*Osmotic diuresis is increased urination due to the presence of certain substances in the fluid filtered by the kidneys. This fluid eventually becomes urine. These substances cause additional water to come into the urine, increasing its amount.

- Also potassium levels are important but we have to consider if the patient is dehydrated or not.

- If you double the amount of Na+ , this equals the plasma osmolality (290).
- glucose and urea account for plasma osmolality but they will not cause fluid shift *(fluid shift = reabsorption of water).*

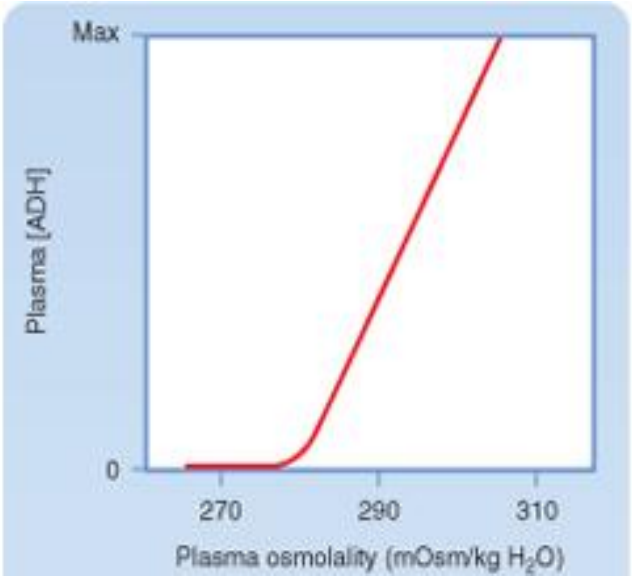
Osmolality

Osmoreceptors :

- Are usually found in *hypothalamus* outside blood-brain barrier.
- It will detect changes in osmolality and stimulate the secretion of ADH.
- **Set point** : ~ 280 – 285 mOsm/kg H2O

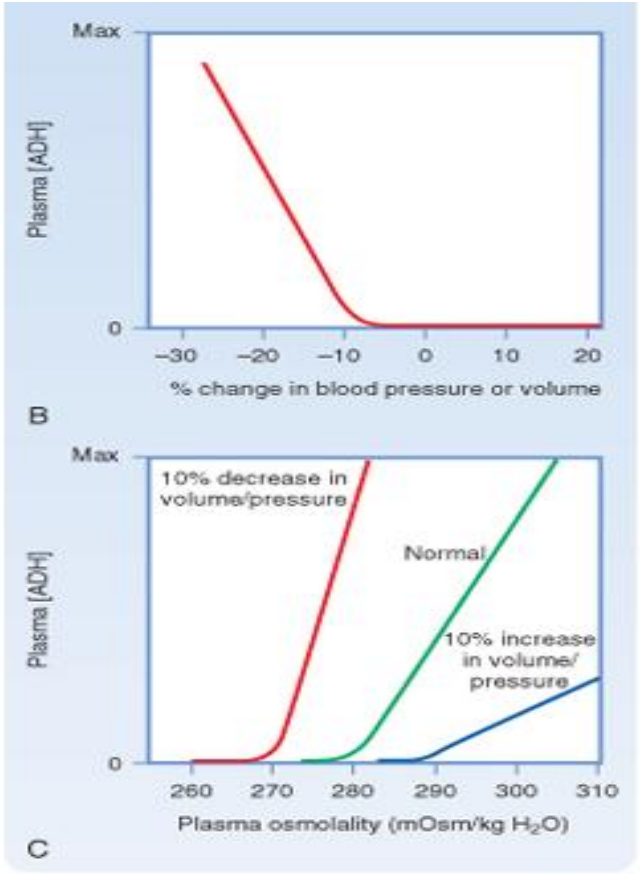
  "At this range the osmoreceptors won't stimulate the secretion of ADH"

- Osmoreceptors sense any changes in plasma osmolality and they are located in hypothalamus.
- Set point : The point at which increase in the plasma osmolality will stimulate ADH to be released. ***(Exceeding normal plasma osmolality).***
- **Diagram explanation:** When it increase above the normal range this stimulate release of ADH. As the plasma osmolality increases the ADH release increases. *(Directly proportional)*



Blood volume

- **Decreased blood volume** will *stimulate ADH release.*
- It's **less sensitive** than osmolality.
- To stimulate ADH secretion you'll need a significant amount of blood to be lost. *(5%-10% of the blood).*
- **Changes in blood volume/pressure** affect *osmolality* so any change in the osmolality *above* or *lower* than the *set point* would either stimulate or suppress the secretion of *ADH*.
- ↓ volume/BP ⇒ ↓ set point steeper "sharp" curve.



- If the blood volume decreases (drop blood pressure) I need ADH to preserve the blood volume and correct the BP
- **Osmolality is more potent stimulant of ADH than blood volume.**
- We need 5-10% drop in Blood volume in order to start stimulating ADH.
- *Decreased Blood volume = Increased osmolality.*

Regulation of water intake

The hypothalamic thirst center is stimulated by:

1- a *decline* in plasma volume of 10%–15%

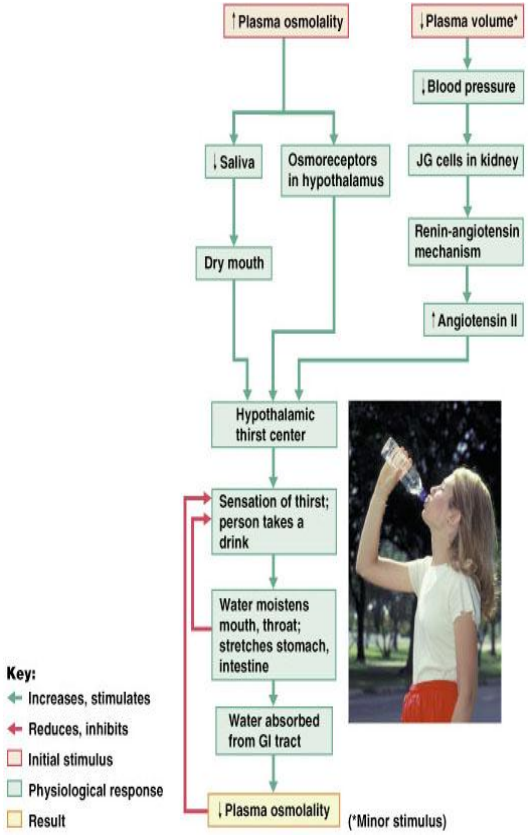
2- *increases* in plasma osmolality of 1–2%

Baroreceptor

input will be stimulated by sympathetic division, angiotensin II will be secreted, and other stimuli and *all of the previously mentioned will stimulate secretion of ADH*.

Thirst is quenched as soon as we begin to drink water, feedback signals that inhibit the thirst center include: "Quenched : overcome"

- Moistening of the mucosa of the mouth and throat.
- Activation of stomach and intestinal stretch receptors.



- Baroreceptors sense the drop in BP it will stimulate thirst center → blood volume correction as well as blood pressure.
- Once you sense the thirst and drink water the feedback mechanism will be inhibited – when water reaches the stomach will inhibit the thirst center.

Physiology Leaders :

Khawla Alammari
Meshal Alhazmy

Girls team :

- Alhanouf Aljlaoud
- Afnan Almalki
- Asrar Batarfi
- Amal alomran
- Alanoud AlOmair
- Deema AlFaris
- Elham Alzahrani
- Hissah almuzini
- Johara Almalki
- Jwaher alHarbi
- Lojain alsiwat
- Munerah AlOmari
- Munira Alhussaini
- Malak alshareef
- Mai Alageel
- Nojood alhaidri
- Nora Alsomali
- Noura Alkharraz
- Noura alTawil
- Norah Alakeel
- Reem AlAgeel
- Renad alkhtani
- Raghad alnafisah
- Ruba Alselaimy
- Reema Allhuidan
- Razan Alsabti
- Wadha Alotaibi
- Nurah Alqahtani

Boys team :

- Abdullah Aljaafar
- Omar Alotaibi
- Abdulrahman Albarakah
- Adel Alshehri
- Abdulaziz Alghanaym
- Abdulmajeed Alotaibi
- Khalil Alduraibi
- Hassan Albeladi
- Omar Alshehri
- Saleh Alshawi
- Abdulaziz Alhammad
- Faisal Alabdulatif
- Abdulnasser Alwabel
- Saad Almutairy