Renal Regulation of Body Fluids

Red: very important.
Green: Doctor's notes.
Pink: formulas.
Yellow: numbers.
Gray: notes and explanation.

Physiology Team 436 – Renal Block Lecture 7

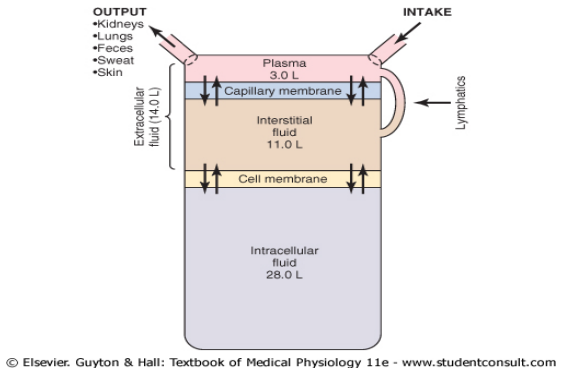
For further understanding please check our "Extra Notes" file which contains extra explanation from reference books.

Objectives

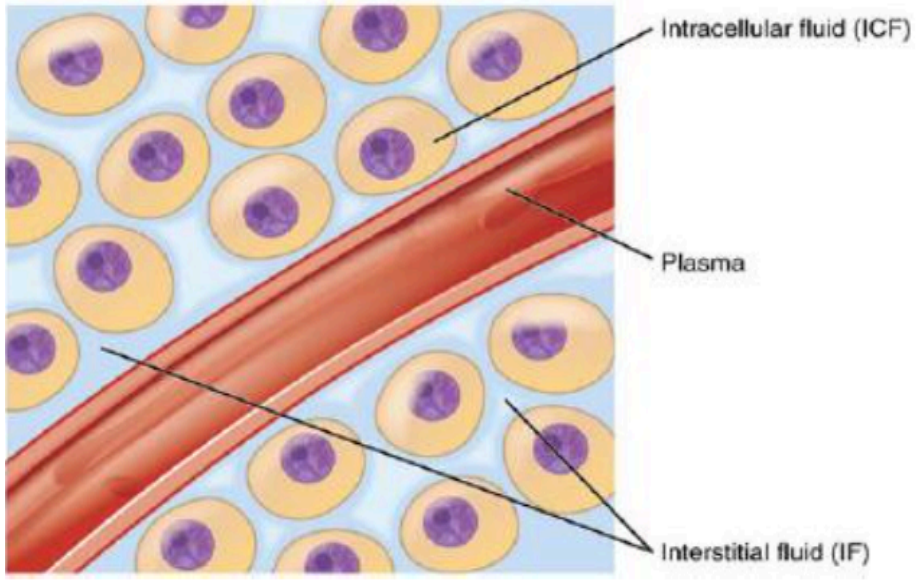
- Identify and describe the role of the Sensors and Effectors in the renal regulation of body fluid volume & osmolality
- Describe the role of the kidney in regulation of body fluid volume & osmolality
- Understand the role of ADH in the reabsorption of water and urea
- Identify the site and describe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

Recall from Foundation: Body Fluids

Major Body Fluid Compartments



- Fluid Compartments
  - Extracellular fluid
    - Plasma
    - Interstitial fluid
  - Intracellular Fluid
    - Transcellular fluid
      - Pericardial "around heart"
      - Peritoneal "in abdominal cavity"
      - CSF "in brain"
      - Synovial "in joints"
      - Digestive Secretions
      - Pleural



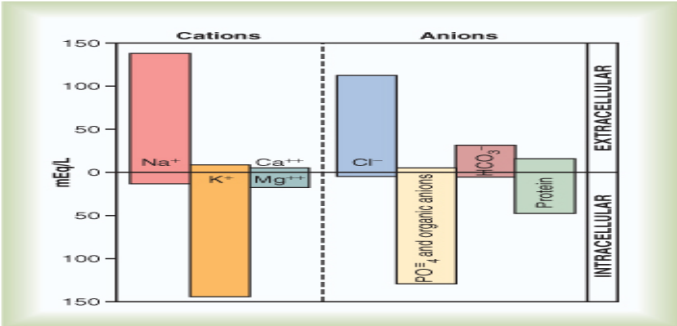
Recall From Foundation: Body Fluids IC vs EC

Intracellular Fluid

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

Extracellular Fluid

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



- 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).

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

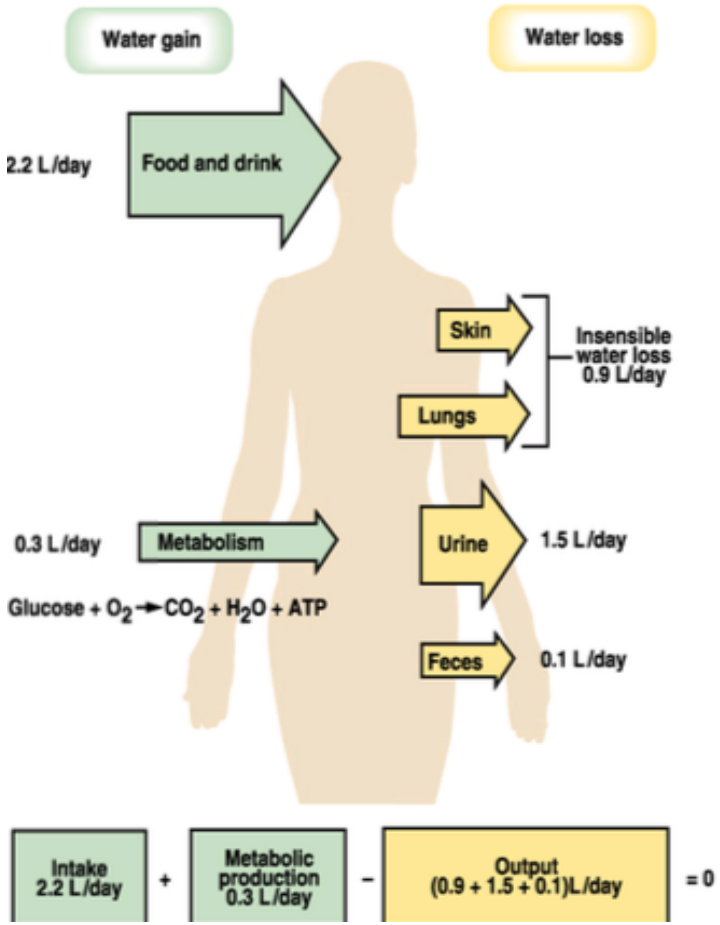
- Water balance between ICF and ECF must be maintained .The kidneys play an important role in regulation of fluids by regulating the volume of urine and its composition either its *concentrated* urine or *diluted* urine.
- *concentrated* urine = more ions / *diluted* urine = more water.
- Once the plasma 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:

Vascular bleeding | vomiting | diarrhea

if those pathological conditions occur we need to increase input to maintain steady state



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: (Effective pressure receptors)

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

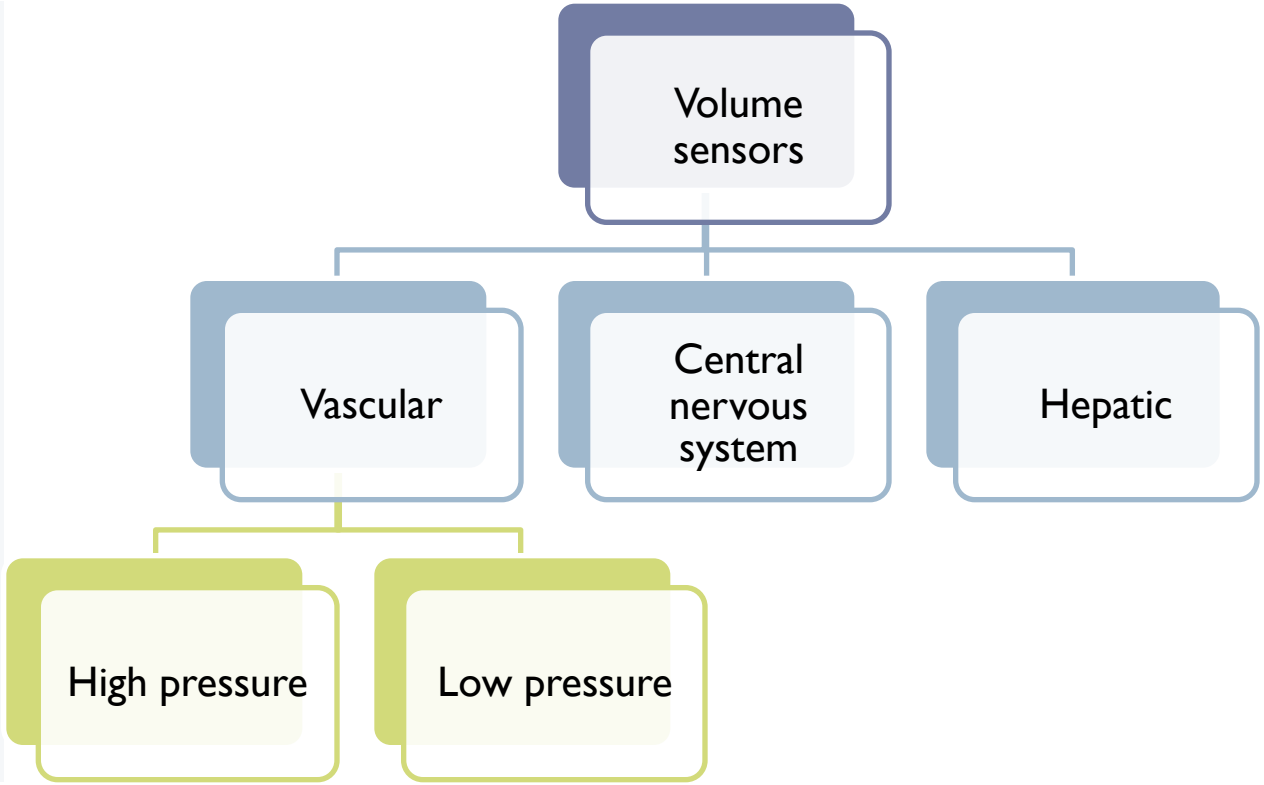
Cardiac atria (ANP), pulmonary vasculature.

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.

High and low pressure is due to their location; High pressure is found in places where pressure is high and vice versa

Volume Sensor Signals: Neural

- Volume sensor signals/Mediators:
- 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 .

Control of Circulating Volume: Hormonal

1. Renin-angiotensin-aldosterone system (decrease pressure):

- Renin secreted by:
  - a) Sympathetic stimulation
  - b) decrease perfusion pressure
  - c) decrease Na+ reaching macula densa.
- Angiotensin II:
  - a) Aldosterone release by adrenal cortex. Aldosterone increase Na+ reabsorption in TAL, DT, CD.
  - c) Vasoconstriction.
  - d) ADH release.
  - e) increase 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. increase GFR
- Decrease Renin release.
- Direct decrease aldosterone release.
- Decrease Na+ reabsorption in CD (collecting duct)
- Decrease ADH release.

Low pressure → RAAS
High pressure → ANP
ANP opposite to Aldosterone

- 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:

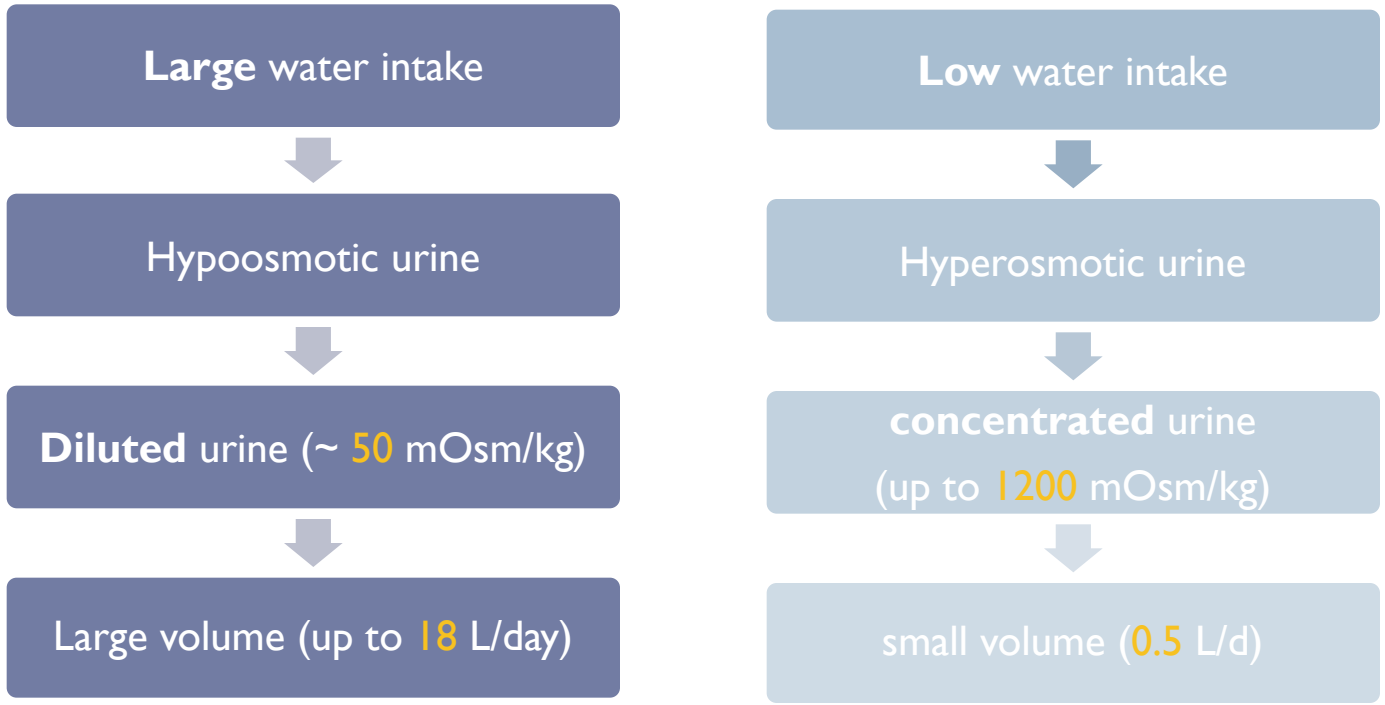
- **Angiotensin II** receptors are found on the *zona glomerulosa cells of the adrenal cortex*.
- Activation of these receptors leads to an immediate and rapid increase in *Aldosterone secretion.*
- **Aldosterone** acts on the *distal tubule* and *collecting duct* to cause ***sodium* retention**.
- This 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



- 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) .

- Renal water excretion mechanisms *independent* of solute excretion

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

Antidiuretic hormone (ADH)/ Vasopressin

➢ Antidiuretic hormone (ADH):

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

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.

➢ 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.(BP – V)

What meant by factors either hypovolemia or hypervolemia

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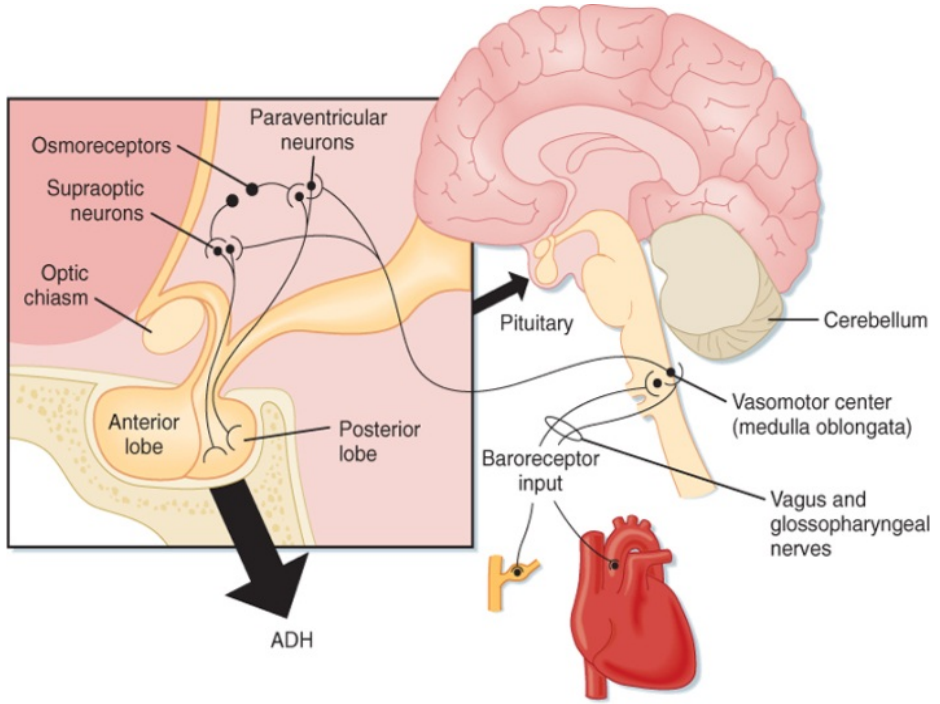
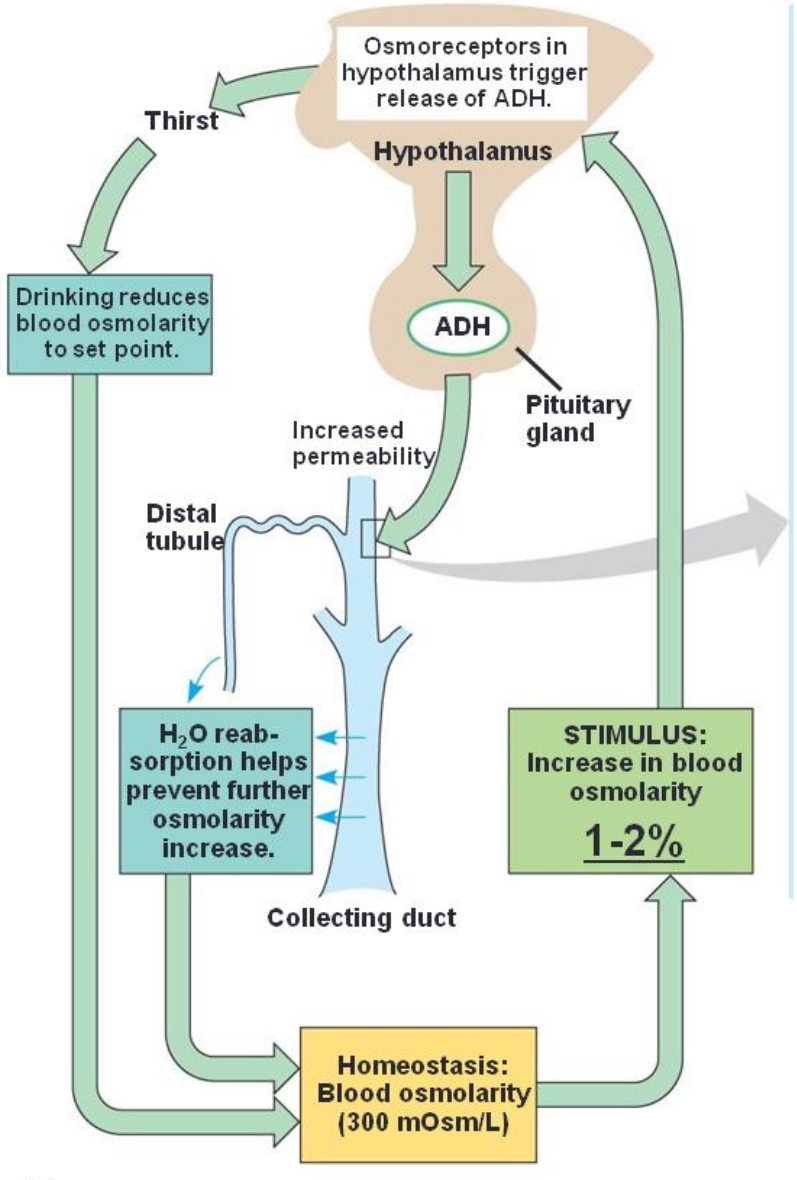
- Nausea → will *stimulate* ADH release.
- Atrial nitric peptide (ANP) → will *inhibit* ADH release.
- Angiotensin II → will *stimulate ADH release*.



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.

*Colored with red are the Main physiological factors



In normal situations: osmolarity = 300
A 1-2 % increase in osmolarity (even if it's the osmolarity in the hypothalamus interstitium) will trigger the release of ADH --> will increase permeability of distal portion of the nephron
→ Increase reabsorption of water + stimulation of thirst center→ osmolarity isback to normal

Osmolality

➢ Osmolality estimation:

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

↑ osmolality ⇒ ADH release
↓ blood volume ⇒ ADH release

➢ 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.

- 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)*.

➢ 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.

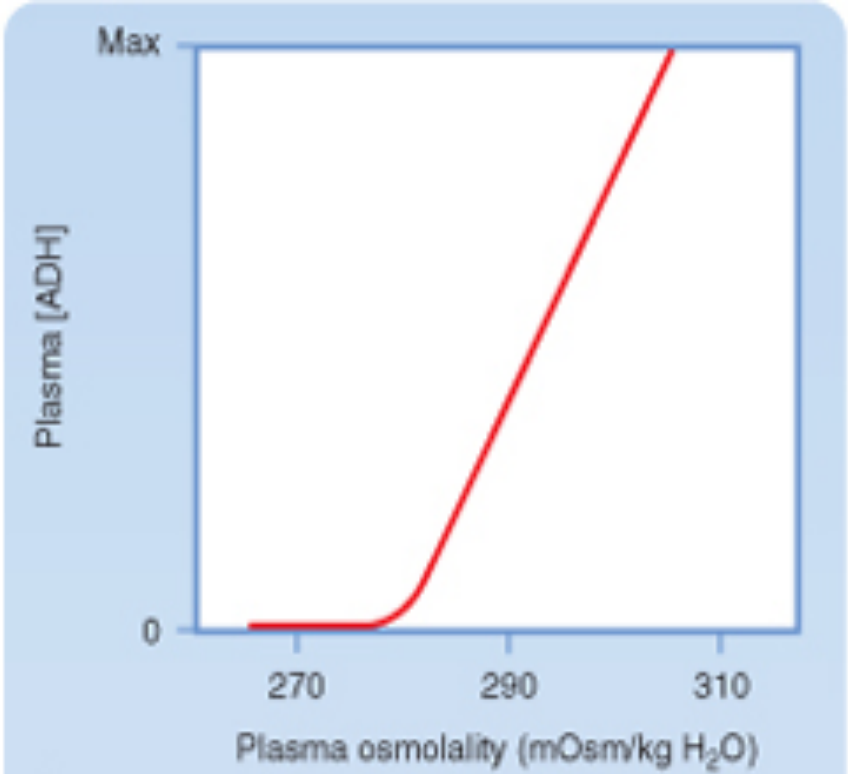
Osmolality

➢ **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 as the osmolality is still considered low and therefore your body will not see the need to secrete ADH to balance out the osmolality"

- 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)*



If there's a slight increase in osmolality (shift in the set point) → ADH release

Blood volume

➢ **Decreased blood volume**

will *stimulate ADH release.*

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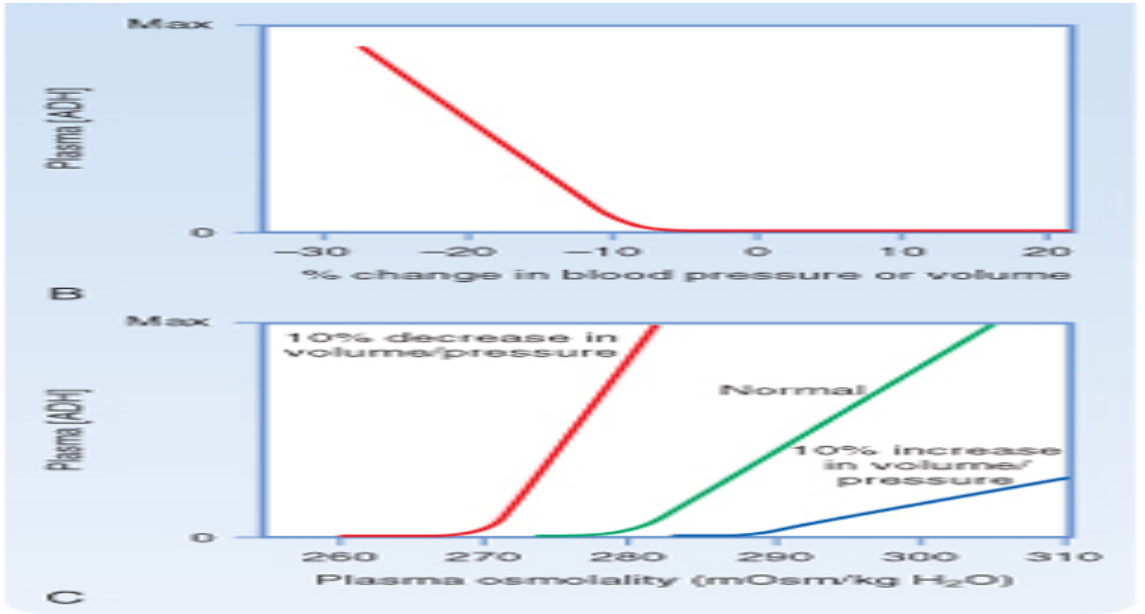
- It's **less sensitive** than osmolality.
- To stimulate ADH secretion you'll need a significant amount of blood to be lost.

(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.

1-2% increase in osmolarity → ADH

5-10% decrease in volume → ADH

- 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.*

ONLY IN MALES' SLIDES

Control of ADH secretion

NOT IMPORTANT

Increase ADH	Decrease ADH
↑ Plasma osmolarity	↓ Plasma osmolarity
↓ Blood volume	↑ Blood volume
↓ Blood pressure	↑ Blood pressure
Nausea	
Hypoxia	
Drugs: Morphine	Drugs: Alcohol

Increase Thirst	Decrease Thirst
↑ Plasma osmolarity	↓ Plasma osmolarity
↓ Blood volume	↑ Blood volume
↓ Blood pressure	↑ Blood pressure
↑ Angiotensin II	↓ Angiotensin II
Dry mouth	Gastric distention

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.* (مهم جدًا)

مايشتغل الا بجهاز الي اهو CD
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. (هذي الجمله د. منى حذفتها عشان مانتلخبط)

- 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.

Regulation of water intake

The hypothalamic thirst center is stimulated by:

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

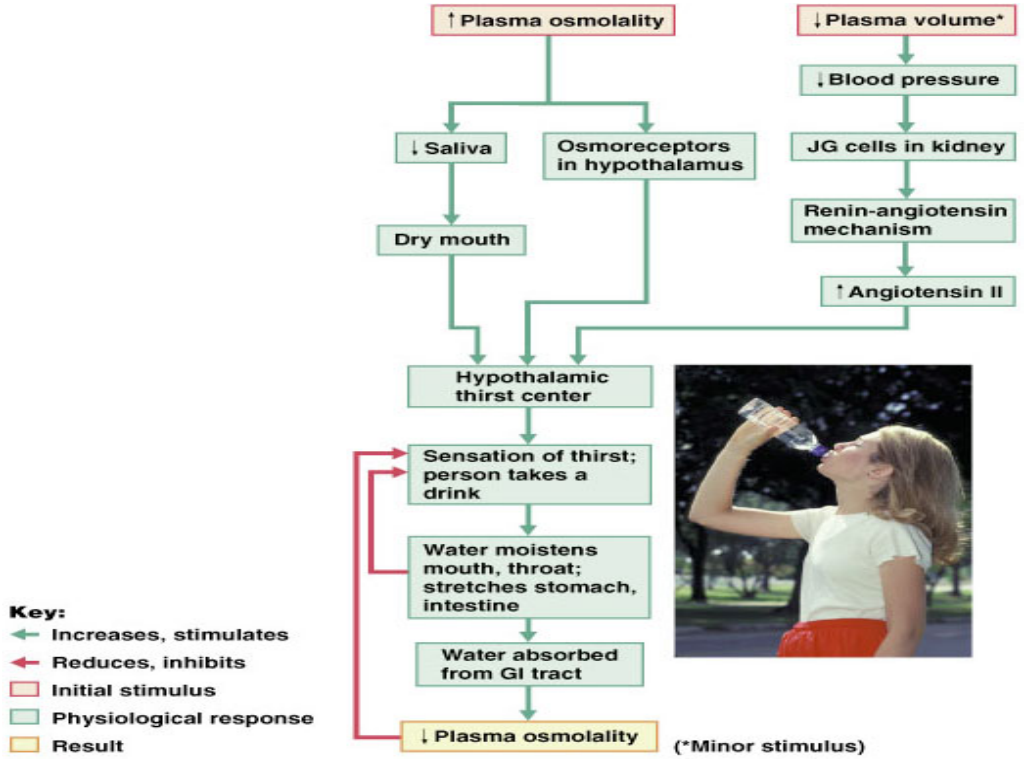
2- *increases* in plasma osmolality of 1–2%

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:

- 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.

"Quenched : overcome"

Thank you!

اعمل لترسم بسمة، اعمل لتمسح دمعة، اعمل و أنت تعلم أن الله لا يضيع أجر من أحسن عملا.

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Link to Editing File

References:

- Girls' and boys' slides.
- 435 Team.
- Guyton and Hall Textbook of Medical Physiology (13th Edition).
- Linda (5th Edition).

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