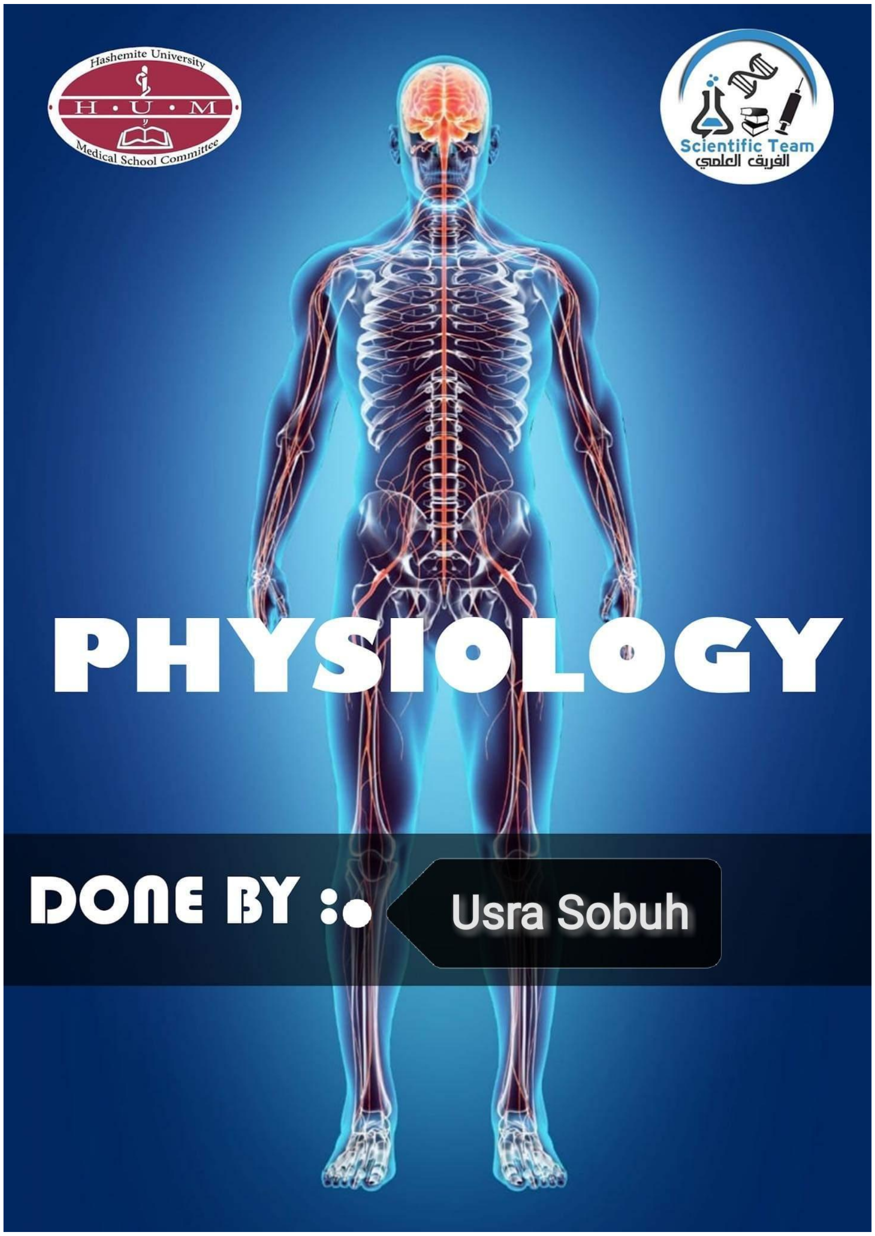

Hashemite University
H · U · M
Medical School Committee
Scientific Team
الفريق العلمي
PHYSIOLOGY
DONE BY :
Usra Sobuh

بسم الله الرحمن الرحيم

**In this lecture we will talk about the mechanisms of urine concentration & dilution as well as the regulation of extracellular fluid osmolarity and sodium concentration.**

The control of extracellular osmolarity is mainly directed to the NACL conc.

The extracellular osmolarity is determined by:

1- Amount of solutes mainly NACL
2- ECFV ( extracellular fluid volume

- Our body regulate the extracellular osmolarity by the adjustment of the **amount of extracellular water** which regulated by:

1- Water intake    2- water excretion

Water intake and excretion is regulated by **ADH-Thirst osmoreceptor system**

Mechanism: in case of ↑ extracellular osmolarity (NACL) → stimulate ADH release → ↑ water reabsorption and stimulate thirst (intake of water)

## Concentration and dilution of urine

- Kidneys dilute urine through excreting a lot of water relative to the solutes (too much water and less solutes)

Minimal urine concentration (high H2O) =50-70 mOsm/L

- Kidneys concentrate urine through excreting a lesser amount of water relative to the solutes (less water and too much solutes)

Maximal urine concentration (H2O deficit) =1200-1400

**Water diuresis in a human after ingestion of 1 Liter of H2O**

- **Plasma osmolarity** remains constant
- **Urine osmolarity** decreased

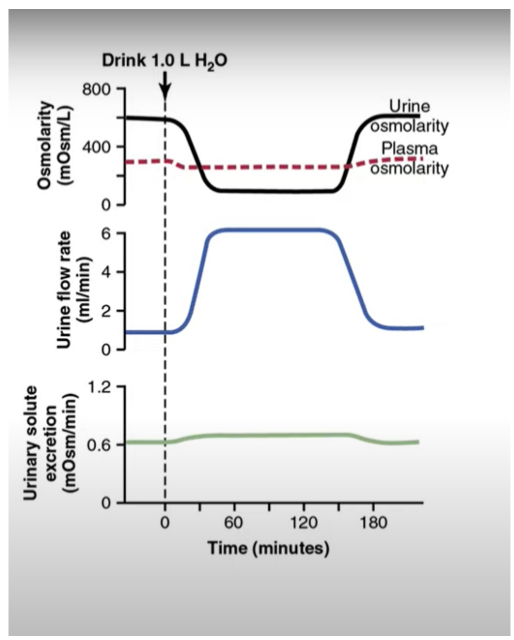
The ingestion of too much water is compensated by the kidney through excretion of that water so urine osmolarity is decreased

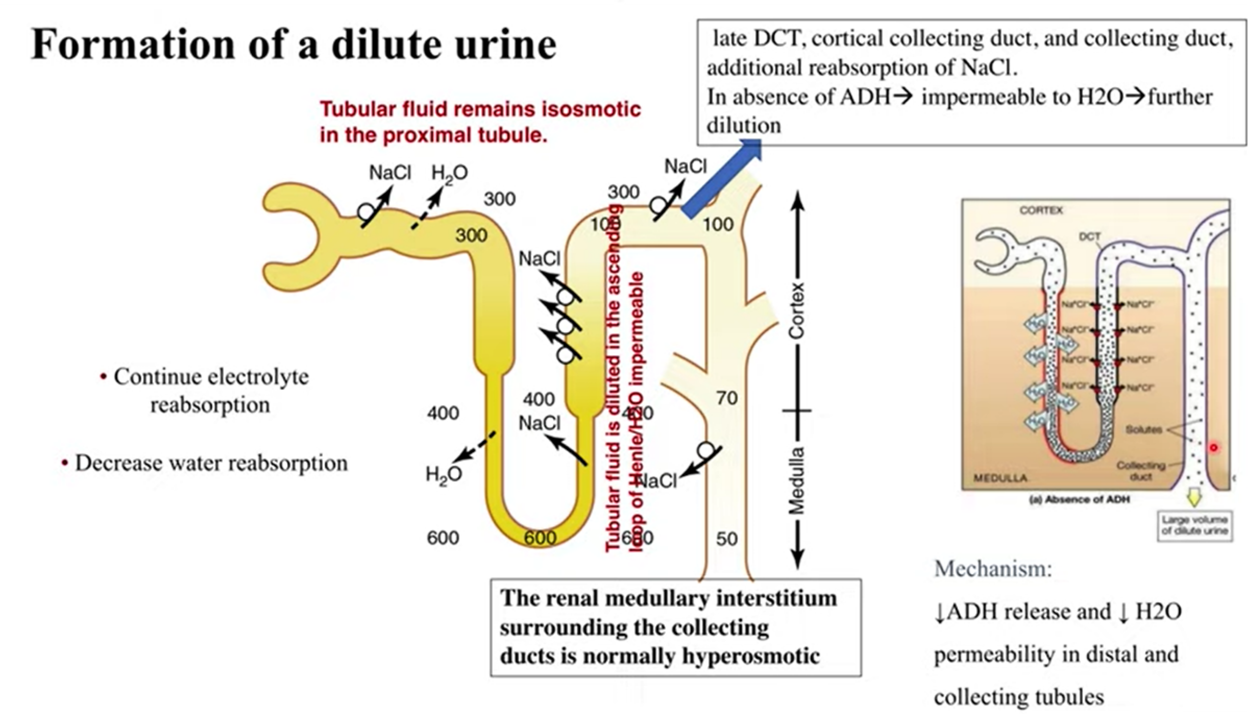
- **Urine flow rate** is increased

Because the urinary excretion is increased

- **Urinary solutes excretion** remains constant

This reflex the ability of the kidney to adjust the osmolarity through changing the amount of excreted water while the solutes which required by the body remains unchanged



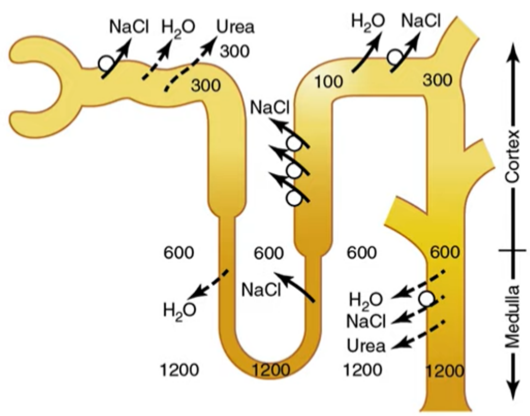


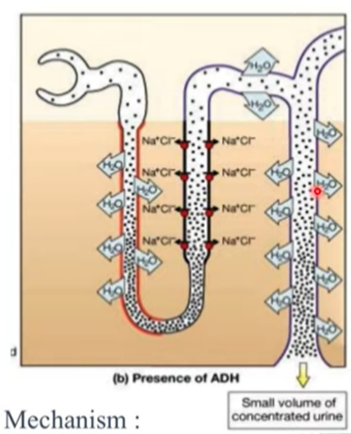

**The picture above shows the characteristics of each segment of the nephron which are mentioned in the previous lecture but remember that:**

1- The proximal tubule is permeable to both water & solutes at the same ratio so osmolarity remains constant =300
2- The descending tubule of Henle is permeable to water more than the solutes because of medullary interstitium hyperosmolarity
3- The ascending tubule of Henle is permeable to solutes only (impermeable to water) so more solutes is reabsorbed ( diluting segment )
4- The permeability of late distal tubule and collecting duct depends on the presence of ADH

- Kidneys form dilute urine through continuous solutes reabsorption and decreased water reabsorption

**Formation of a Concentrated Urine when**




- Continue electrolyte reabsorption
- Increase water reabsorption

Mechanism :

- Increased ADH release which increases water permeability in distal and collecting tubules
- High osmolarity of renal medulla
- Countercurrent flow of tubular fluid

In the formation of concentrated urine the kidneys still reabsorb the electrolytes which are needed to our body’s homeostasis, and increase water reabsorption through:

1- action of ADH
2- high osmolarity of renal medulla = 1200
3- countercurrent flow of tubular fluid ( explained later )

**Obligatory urine volume**: is the minimum urine volume in which the excreted solutes can be dissolved and excreted

Our body produce daily an amount of waste products that must be excreted outside through the kidney

But as we know the kidneys cannot excrete these products as a dry secretions

So it is require a minimal amount of water in order to dissolve theses wastes to be easily excreted that is called the obligatory urine volume

We can calculate this volume by dividing the minimal amount of waste products must be excreted daily over the maximal urine osmolarity

600 mOsm/day / 1200 mOsm/liter = 0.5 L/day

**Relationship between urine osmolarity and specific gravity**

**Urine specific gravity**: is a measure of weight of solutes in a given volume of urine and determined by the number and size of solute

Range from 1.002-1.28 g/ml

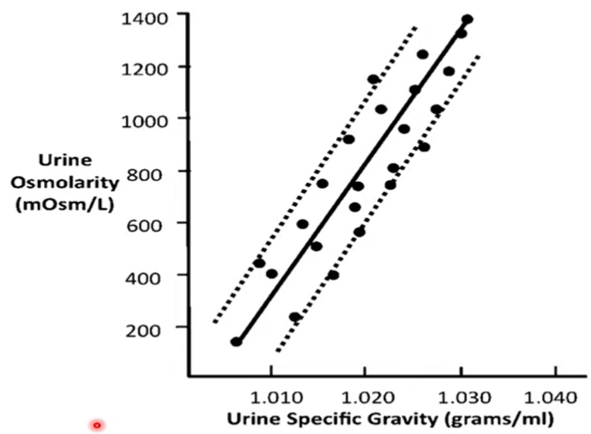
Osmolarity is determined by the number of solutes in a given volume

So, if the number of solutes is increased

the osmolarity will increase and specific gravity also increase

The relationship between osmolarity and specific gravity is **linear proportional**

Note: the relationship between osmolarity and specific gravity is altered when there are significant amounts of glucose, radiocontrast media and antibiotics

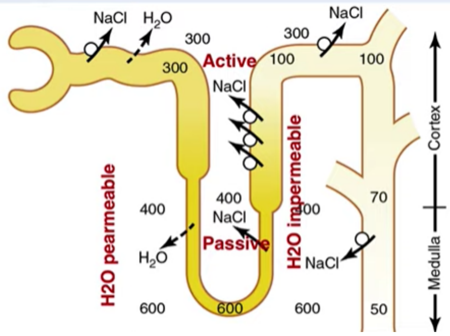


**Now we will talk about the factors that mediate and maintain the hyperosmolarity of renal medulla :**

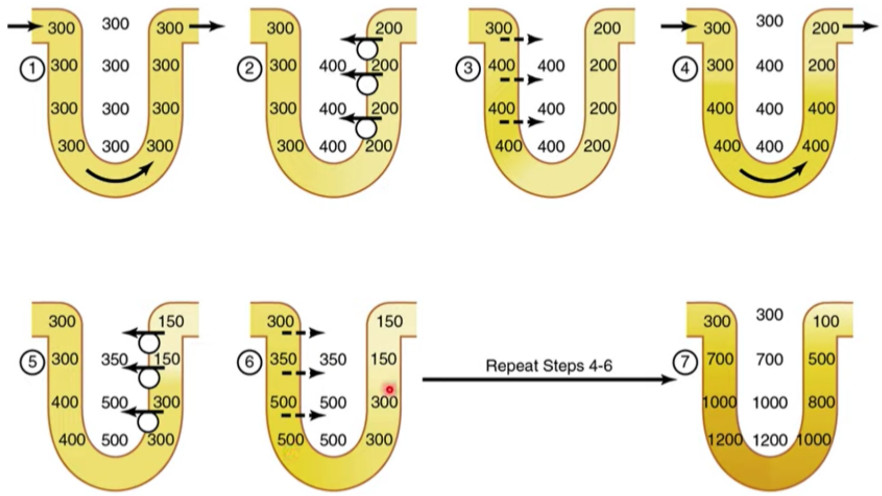
1- active transport of Na+, Cl-, K+ and other ions from thick ascending loop of Henle into medullary interstitium
2- active transport of ions from medullary collecting ducts into interstitium
3- passive diffusion of urea from terminal part of medullary collecting ducts into interstitium ( urea recirculation ) which stimulated by ADH
4- diffusion of only small amounts of water into medullary interstitium because the medullary blood flow is less than cortical blood flow
5- special anatomical arrangement of the loops of Henle ( countercurrent multiplier ) and vasa recta

**Table 29-1** Summary of Tubule Characteristics—Urine Concentration

| | Active NaCl Transport | *Permeability* $H_2O$ | *Permeability* NaCl | *Permeability* Urea |
|---|---|---|---|---|
| Proximal tubule | ++ | ++ | + | + |
| Thin descending limb | 0 | ++ | + | + |
| Thin ascending limb | 0 | 0 | + | + |
| Thick ascending limb | ++ | 0 | 0 | 0 |
| Distal tubule | + | +ADH | 0 | 0 |
| Cortical collecting tubule | + | +ADH | 0 | 0 |
| Inner medullary collecting duct | + | +ADH | 0 | +ADH |



# Countercurrent multiplier system in the loop of Henle.



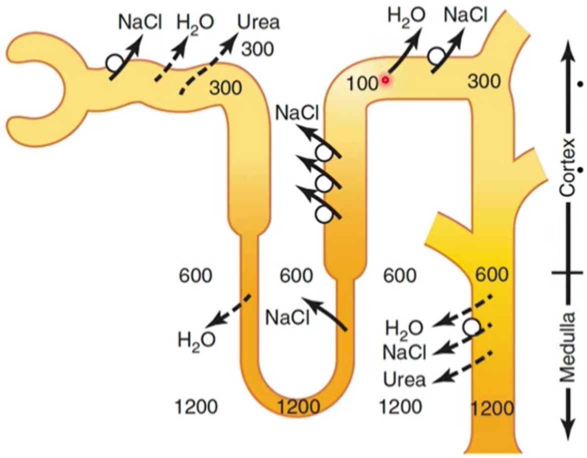

**Steps**:

1- when the urine leaves the proximal tubule remains isosmotic ( 300 ) until it reaches the ascending tubule
2- the ascending tubule (diluting segment) is water impermeable while the solutes undergo active transport to the interstitium which results in interstitial hyperosmolarity with difference 200 mOsm
(Lumen 200, interstitium 400)
3- when another cycle of filtration reaches the descending loop of Henle, reabsorption of water will occur until the lumen osmolarity become equal to the interstitial osmolarity
(Lumen 400, interstitium 400)
4- further concentrated urine will reach the ascending loop of Henle
5- more solute will actively transported to the interstitium with difference 200 mOsm

(Lumen 300, interstitium 500)

6- Another cycles will occur until the medullary interstitial osmolarity reach 1200 mOsm

**Hyperosmotic renal medulla**




- large amounts of water are reabsorbed into the cortex (ADH action), rather than into the renal medulla, helps to preserve the
- Diffusion of only small amounts of water into medullary interstitium→ high medullary interstitial fluid osmolarity
- The reabsorbed water absorbed to medullary interstitium is carried away by the vasa recta into the venous blood.

# Net Effects of Countercurrent Multiplier

1. More solute than water is added to the renal medulla.
   i.e solutes are "trapped" in the renal medulla
2. Fluid in the ascending loop is diluted
3. Most of the water reabsorption occurs in the cortex
   (i.e. in the proximal tubule and in the distal convoluted tubule) rather than in the medulla
4. Horizontal gradient of solute concentration established
   by the active pumping of NaCl is "multiplied"
   by countercurrent flow of fluid.

**Urea recirculation**

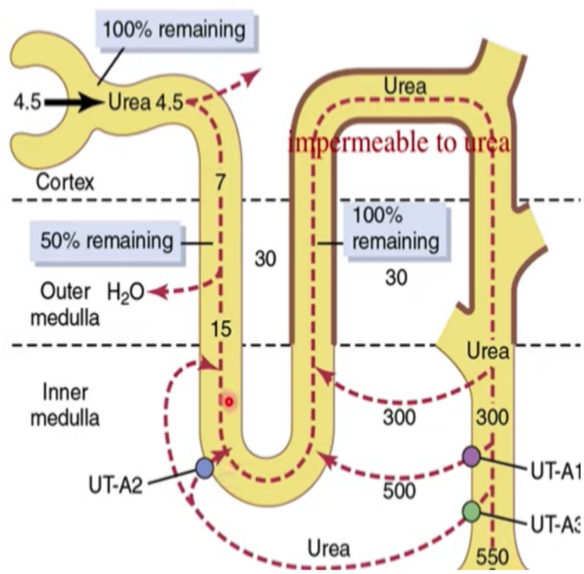
Plays an important role in the medullary interstitium hyperosmolarity

After filtration, approximately all the urea will filter to the proximal tubule, 50% remains in the renal tubules and 50% reabsorbed passively to the interstitium

All parts of nephron are impermeable to urea except the inner medullary part of collecting duct

ADH increase urea permeability of medullary collecting tubule by activating urea transporters A 1&3

Part of the diffused urea will diffuse back to the thin loop of Henle and then pass through distal tubules and finally to the collecting duct



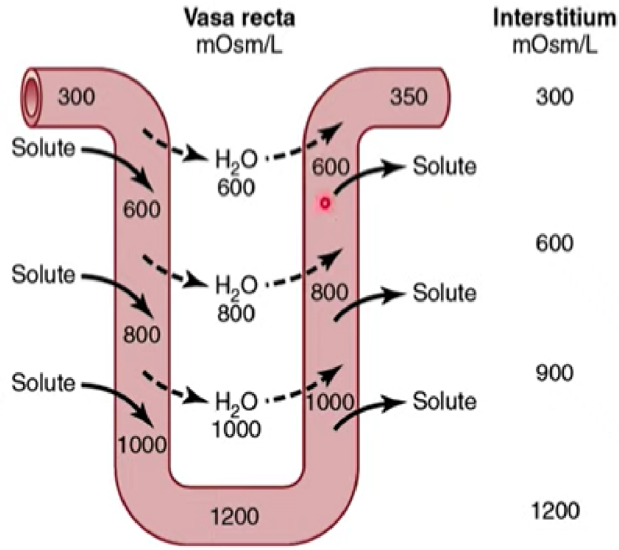

**Vasa recta**: is a capillaries network that supply blood to medulla and return back to the venous system

Vasa recta preserve hyperosmolarity of renal medulla by:

1-its blood flow is low (only 1-2% of total renal blood flow) in order to minimize the washing out of solutes from renal medullary interstitium

2- The vasa recta serves as countercurrent exchangers (blood pass through 2 opposite directions so the amount of solutes which diffused from the interstitium to the blood in the descending limb will return back to the interstitium through the ascending limb

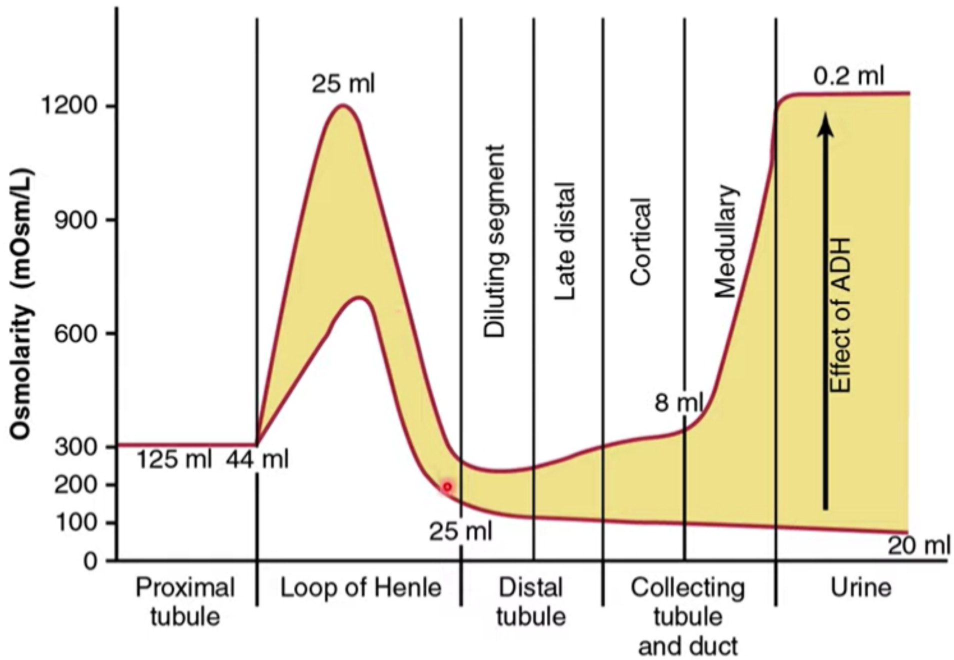
Note: large amount of solutes would be lost from the renal medulla without the U shape of the vasa recta capillaries


Vasa recta
mOsm/L
Interstitium
mOsm/L
300
350
300
Solute
H2O
600
600
Solute
600
600
Solute
H2O
800
800
Solute
800
900
Solute
H2O
1000
1000
Solute
1000
1200
1200

# Summary of water reabsorption and osmolarity in different parts of the tubule

| Tubular part | $H_2O$ Reabsorption (%) | Osmolarity |
|---|---|---|
| Proximal Tubule | 65 (water channel aquaporin 1 (AQP-1)) | isosmotic |
| Desc. loop | 15 | increases |
| Asc. loop | 0 | decreases |
| Early distal | 0 | decreases |
| Late distal and coll. tubules | ADH dependent | ADH dependent |
| Medullary coll. ducts | ADH dependent | ADH dependent |

# Changes in osmolarity of the tubular fluid




- Proximal tubule : 300 iso osmolarity with the interstitium
- Descending loop of Henle : hyperosmolarity of the tubular fluid
- Ascending loop of Henle (diluting segment) : hypo osmolarity
- Collecting tubule under the action of ADH : hyperosmolarity

## Control of extracellular osmolarity

Plasma sodium is the most abundant ion in the extracellular matrix so, its concentration is used to estimate the plasma osmolarity

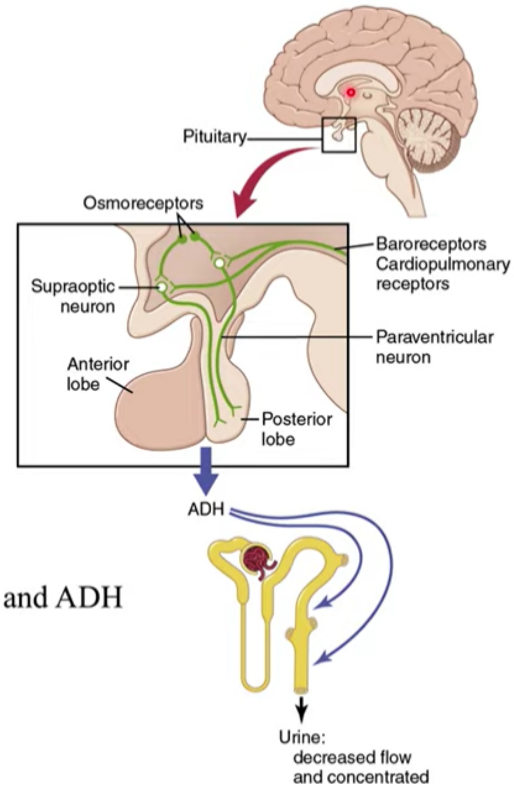
Plasma sodium is normally regulated within close limits (140-145 mEq/L) Avg 142

Plasma osmolarity Avg 300mOsm/L

$$P_{osm} = 2 \times [P_{Na^+}, \text{mmol/L}] + [P_{glucose}, \text{mmol/L}] + [P_{urea}, \text{mmol/L}]$$

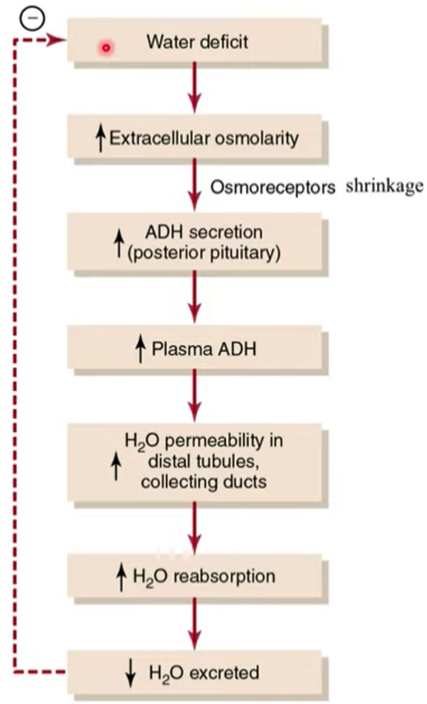
**As we said before the extracellular osmolarity is controlled by ADH-Thirst osmoreceptor system**

ADH synthesis in the magnocellular neurons of hypothalamus, release by the posterior pituitary, and action on the kidneys




AV3V region also controls osmolarity and ADH secretion

Osmoreceptor–antidiuretic hormone (ADH) feedback mechanism for regulating extracellular fluid osmolarity.



## ADH control of extracellular fluid sodium concentration and osmolarity

↓extracellular fluid osmolarity
↓
↓ ADH is formed
↓
↓ renal tubules permeability for water
↓
↓ water reabsorption
↓
↑volume of diluted urine
↓
concentrates body fluids and returns plasma osmolarity toward normal

**Stimuli for ADH secretion**

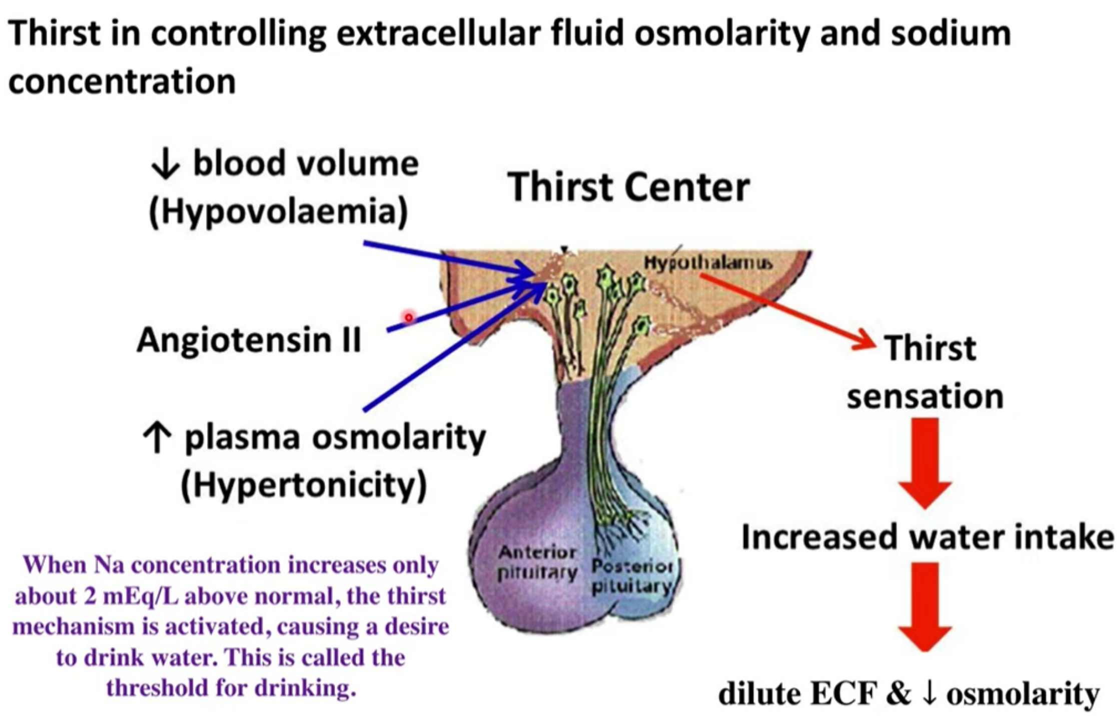
- Increased osmolarity
- Decreased blood volume (cardiopulmonary reflexes)
- Decreased blood pressure (arterial baroreceptors)
- Other stimuli
  - Input from cerebral cortex (e.g fear)
  - Angiotensin II
  - Nausea
  - Nicotine
  - Morphine

**Factors that decrease ADH release**

- Decreased osmolarity
- Increased blood volume (cardiopulmonary reflexes)
- Increased blood pressure (arterial baroreceptors)

- Other factors
  - Alcohol
  - Clonidine (antihypertensive drug)
  - Haloperidol (antipsychotic)

Note: ADH is more sensetive tosmall change in osmolarity than to similar percentage changes in blood volume




**Stimuli for thirst**

- Increased osmolarity
- Decreased blood volume (cardiopulmonary reflexes)
- Deceased blood pressure (arterial baroreceptor)
- Increased angitensin II
- Other stimuli
  - Dryness of mouth & mucous membranes of the esophagus

**Factors that decreased thirst**

- Decreased osmolarity
- Increased blood volume(cardiopulmonary reflexes)
- Increased blood pressure (arterial baroreceptor)
- Deceased angitensin II
- Other stimuli
    - Gastric distention

Osmoreceptor–antidiuretic hormone (ADH) feedback mechanism for regulating extracellular fluid osmolarity.