PHYSIOLOGY TEAM 432

LECTURE : 7

Dilution and Concentration of Urine

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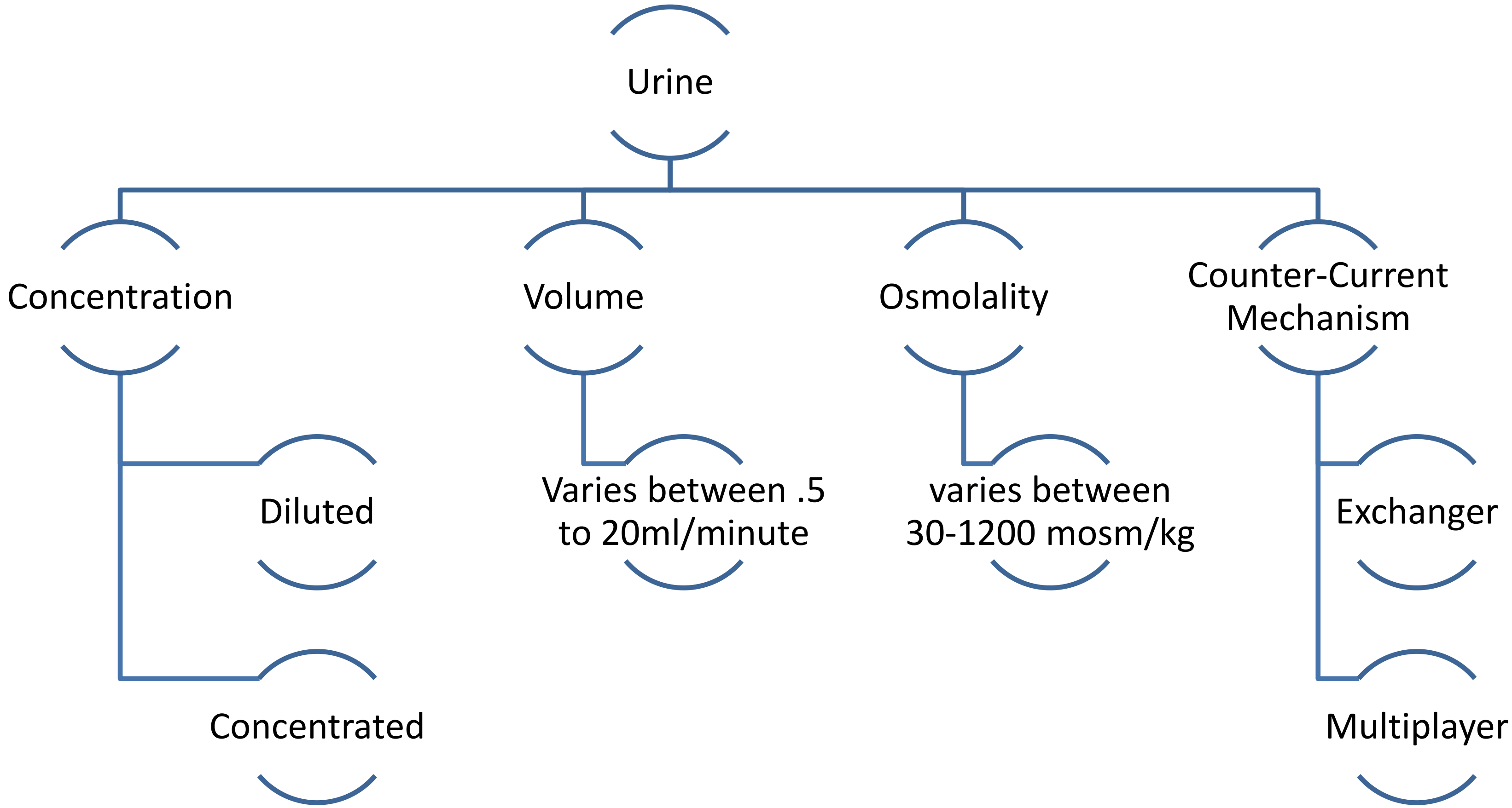
OBJECTIVES

At the end of this lecture student should be able to describe:

- **The loop of Henle is referred to as countercurrent multiplier and vasa recta as countercurrent exchange systems in concentrating and diluting urine.**
- **To describe the concentrating and diluting mechanisms of urine.**
- **To list the factors affecting concentration and dilution of urine.**
- **Differentiate between water diuresis and osmotic diuresis.**

MIND MAP



Slides are in Black color

The important points are in Red color

The doctor's notes are in Green color

Other colors are for design

Urine concentration

The ability of the kidney to concentrate urine (conserve water) is important function in regulating Extracellular volume (ECV),Extracellular Fluid osmolality .(If we don't have urine concentration mechanism, fasting people will get dehydrated) .. "the more water in ECV the less the osmolality will be".

- When there is excess water in the body and body fluid osmolarity is reduced "there is too much water with less solutes", the kidney can excrete urine with an Osmolarity as low as 50 mOsm/liter for a period of time and when every things go back to normal, volume will be normal.
- When there is a deficiency of water and extracellular fluids osmolarity is high "less water and too much solutes" e.g. during fasting, the kidney can excrete urine with a concentration of about 1200 to 1400 mOsm/liter "concentrated" to keep the water inside the body.

إذا كانت كمية الماء بالجسم كبيرة يتم استخراجها في البول فيقل تركيزه (osmolality) لأن زيادة الماء تخفف من تركيز الاملاح فيكون المقدار (volume) في هذه الحالة كبير. والعكس صحيح

Osmolarity, is the measure of solute concentration, defined as the number of osmoles (Osm) of solute per litre (L) of solution (osmol/L or Osm/L)

Urine volume and concentration

Diluted urine: the excreted urine has more water and less solutes «مخفف»
concentrated urine: the excreted urine has less water and more solutes «مركز»

- When water intake is normal:

*Urine flow is 1 -2 ml/min

*Urine osmolality is between 500-700 mOsm/kg.

(Higher than plasma osmolarity = 300mOsm/kg)

- Obligatory urine volume:

*It is the minimum urine volume in which the excreted solute can be dissolved and excreted = 0.5 L/min

* lower than this indicates renal function problem

Urine volume and concentration

Range of volume and osmolality regulated by the kidney:

* **Urine Osmolality varies between 30-1200 mosm/kg.**

(“30” is due to diuretics or high intake of water, “1200” is due to fasting)

* **Urine volume varies between 0.5-20 ml/minute.**

(“0.5” very concentrated urine, “20” is a diluted urine due to diuresis or ↑ water intake)

“These ranges show what the kidney can perform in the normal and the abnormal conditions”

The basic requirements for forming a concentrated or diluted urine

1. Controlled secretion of antidiuretic hormone (ADH), which regulates the permeability of the distal tubules and collecting ducts to water.

"High ADH causes high reabsorption of water, and there will be less amount of it in the urine".

2. A high osmolarity of the renal medullary interstitial fluid, which provides the osmotic gradient necessary for water reabsorption to occur in the presence of high level of ADH.

"water osmotic gradient will move water from low to high osmolarity which is necessary for water reabsorption"

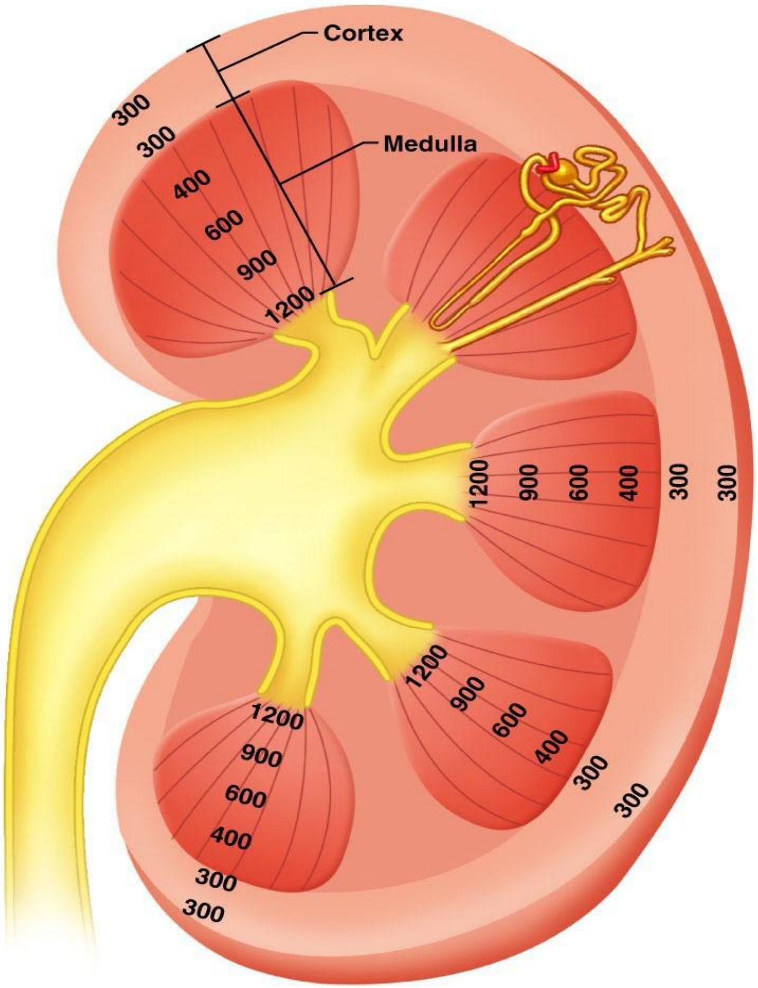
(The absence of any one of them prevents urine concentration)

water is reabsorbed from collecting duct to peritubular tissue (mainly in medulla) So we need high osmolar peritubular tissue to allow water reabsorption → that means medullary tissue should be hyperosmolar so that "in the presence of ADH" we can reabsorb water by osmosis.

Loop of henle

Ascending loop	Descending loop
impermeable to water	highly permeable to water
permeable to Na+(mediated by Na+/K+/2Cl-apical carrier -inhibited by furosemide (Lasix))	impermeable to Na+
Na+/K+-ATPase actively pumps out sodium of cell into interstitium	water exit promoted

The graded hyper-osmolar medulla



- If I take a sample from the cortex and I measure the osmolarity I find it equal to 300 mosm/kg.
- But if I take a sample from the medulla I notice that the osmolarity will increase in tissues (not fluid) and it will range between 400-1200 mosm/kg.
- The Cause: reabsorbed salts "NaCl" in the thick ascending loop of Henle will deposit in medulla to make it hyperosmolar

* As you go deep in the medulla the, osmolarity increase

Counter-Current Mechanism

(counter current **multiplayer** + counter current **exchanger**)

The hyperosmotic Renal Medullary Interstitium:

- Produced by **Counter-Current Multiplayer** .
- Maintained by **Counter current Exchanger** .
- Provides the osmotic gradient necessary for water reabsorption.
- Formed by the **Thick Ascending limb** of loop of Henle and **Collecting Ducts**.
- Is formed mainly by **Juxta-medullary nephrons** while **cortical nephron function is filtration**.

There are two types of nephron:

* cortical

***Juxta-medullary nephrons (forming concentrated urine)**

Counter-Current Mechanism

1. Counter current multiplayer (found in the nephrons)

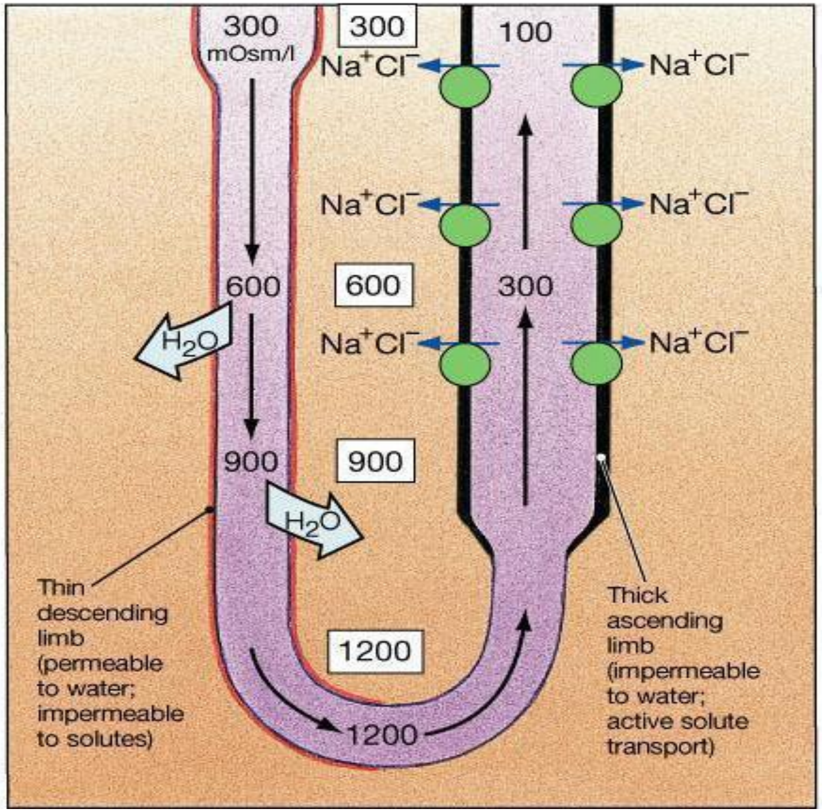
- Produces the hyperosmotic Medullary Interstitium

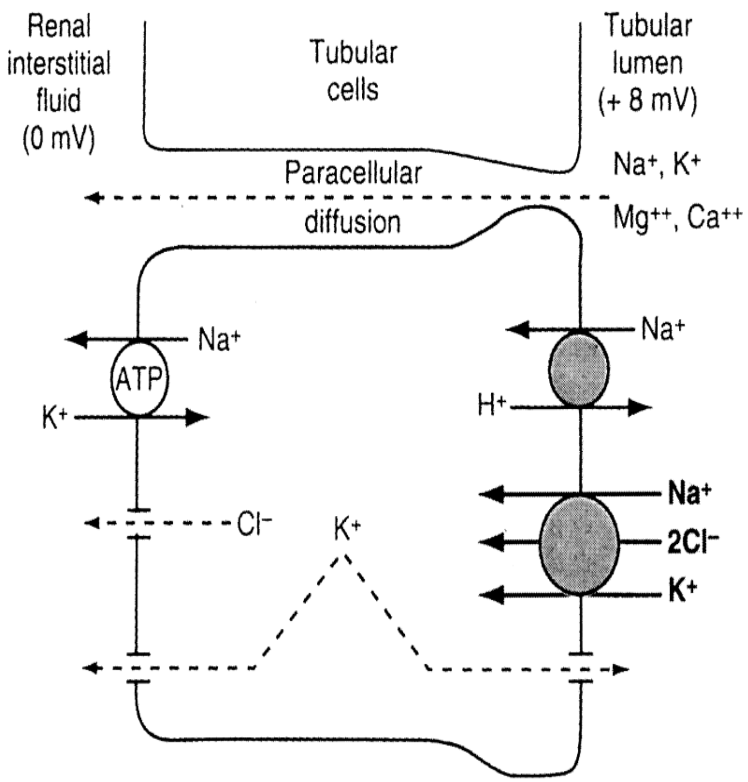
- Medullary hyper osmolality is due to solute deposition on medullary interstitium.

* **NaCl** reabsorbed from the **thick ascending limb** of loop of henle is deposited on medullary interstitium **(medullary blood supply is limited therefore these salts will remains in medulla)**

* **Urea** reabsorbed from **collecting duct (ADH)** to medullary interstitium also contribute to medullary hyperosmolality. **(Urea contributes for about 40 to 50 percent of the osmolalrity (500-600 mOsm/L) of the renal medullary interstitium when the kidney is forming a maximally concentrated urine)**

- **Water will be absorbed from the collecting duct to peritubular capillaries in the presence of ADH due to osmotic gradient. " Fact "**





Active transport of NaCl along thick ascending loop results in the movement of water from the descending limb

1. Counter current multiplayer

Thiazide (diuretics) block NaCl reabsorption on thick ascending loop → Diuresis

- By Two Mechanisms:

* **Remained Salt in filtrate will drag water** (no salt "NaCl" reabsorption) → **Osmotic diuresis**

  If the patient takes it for while →no hyperosmotic medulla → no water reabsorption

* **Decreases medullary osmolality** (If the patient takes it for while) → **Therefore water cannot be reabsorbed from collecting duct →No osmotic gradient →diuresis** (HTN)

Counter-Current Mechanism

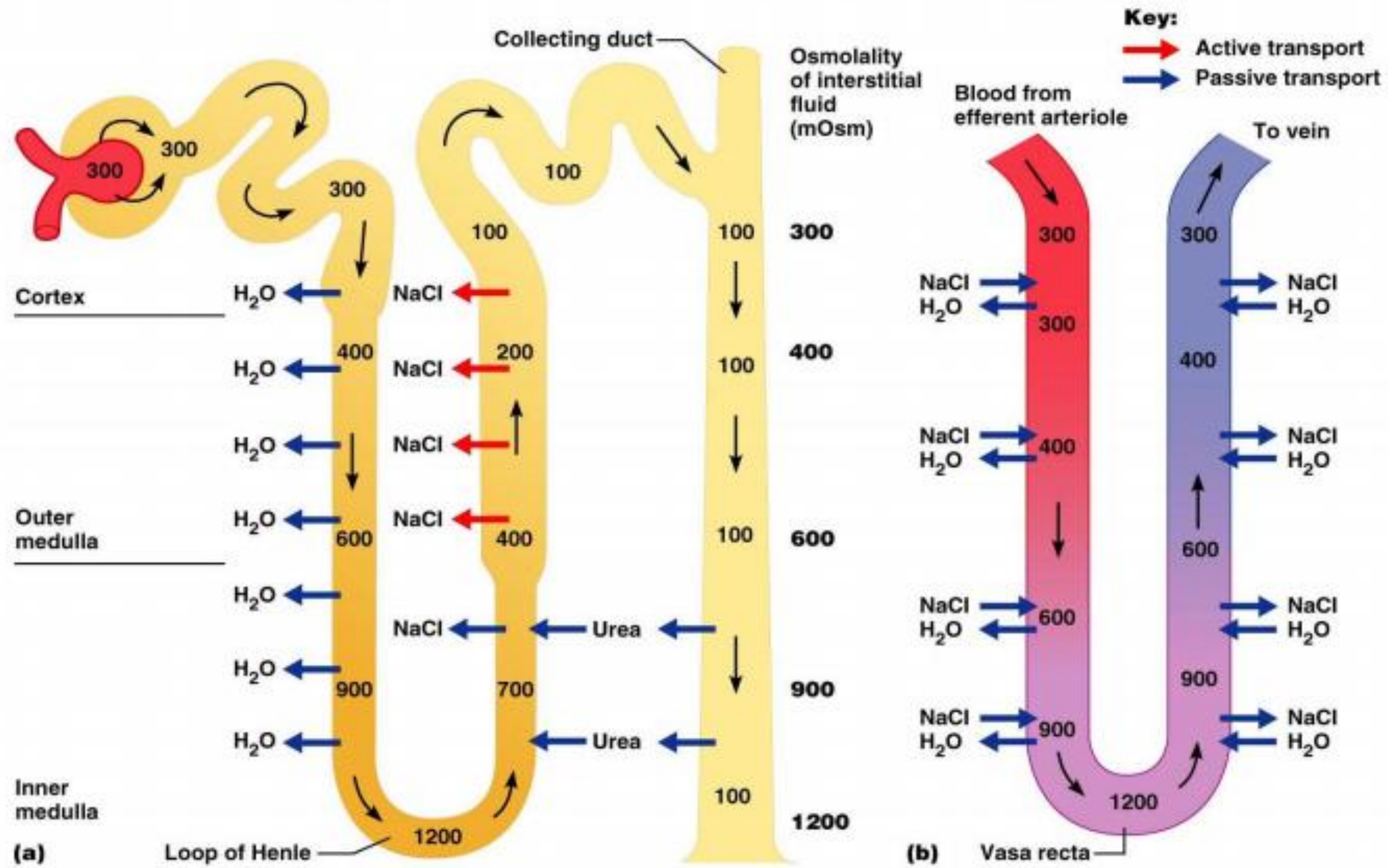
2. Counter Current <u>Exchanger</u> (found in the vasa recta" blood")

- **Maintains hyperosmolar medulla (Passive Process)**
- **Blood supply to medulla is** by **Vasa recta** (vasa recta enters the hyperosmolar medulla → water will move out from the blood with nutrient and o2, and salt enters the blood, making the blood hyperosmolar until it reaches 1200 then the vasa recta do a **U tern** and while going out of medulla the reverse will happen (water, co2 and wastes enter the blood and the salts go out). Blood leave the medulla with osmolarity=300 and leaving the medulla as it is HYPEROSMOLAR.

Descending limb of Vasa recta	Ascending limb of vasa recta
• Water pass out into hyperosmolar medulla carrying O_2 & nutrient • NaCl will enter the blood increasing its osmolality.	• Water will be reabsorbed back to the hyperosmolar blood carrying water, CO_2 and waste product • NaCl will leave the blood and become deposited in the medulla.

- Therefore blood leave the hyperosmolar medulla **undisturbed**.

Countercurrent mechanism



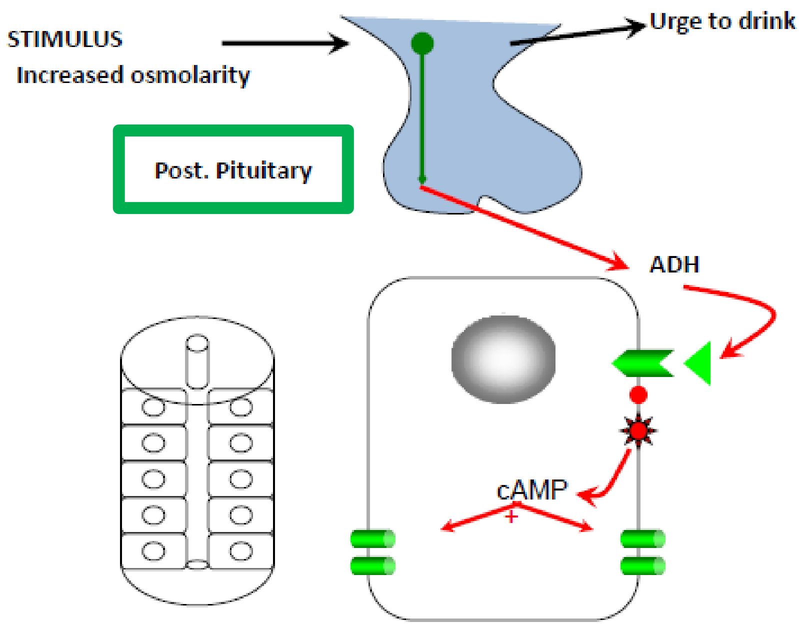
A) Counter current multiplayer
Nephron

B) Counter current exchanger
Vasa recta

The Role of ADH

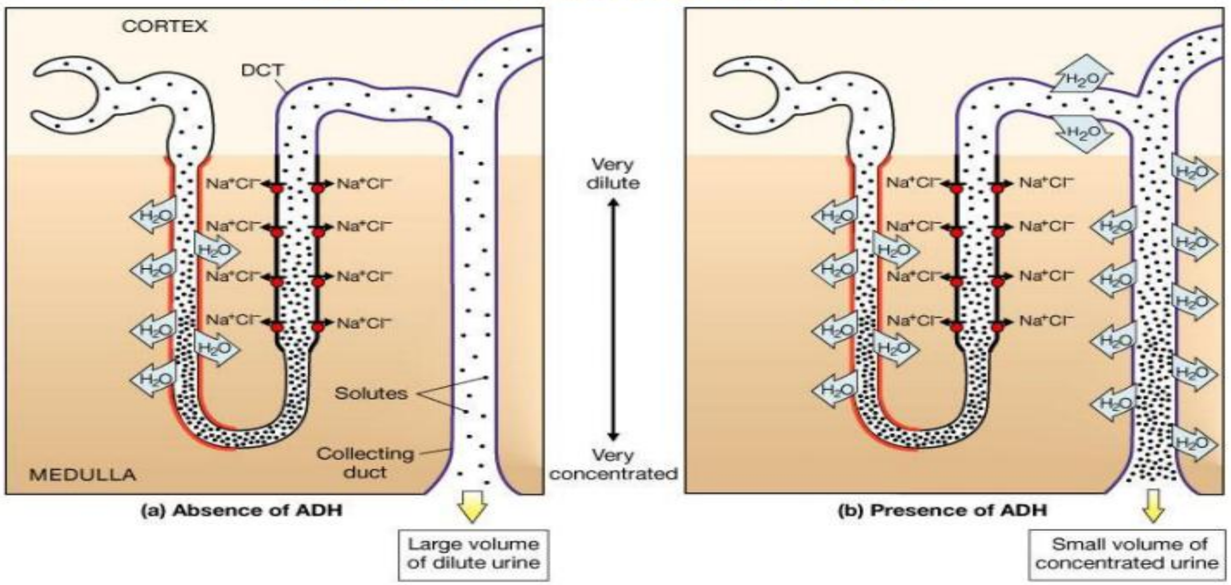
- Water reabsorbed from collecting duct **(by osmosis)** is determined by the hormone ADH (anti-diuretic hormone)
- **Osmoreceptors** in the hypothalamus detect the low levels of water (high osmolarity), so the hypothalamus sends an impulse to the pituitary gland which releases ADH into the bloodstream.
- **ADH makes the wall of the collecting duct more permeable to water.**
- In the present of ADH more water is reabsorbed and less is excreted.

Secretion of ADH



The pic shows that in the presence of ADH there's water reabsorption in the level of collecting duct and vise versa

The Effects of ADH on the distal collecting duct and Collecting Ducts



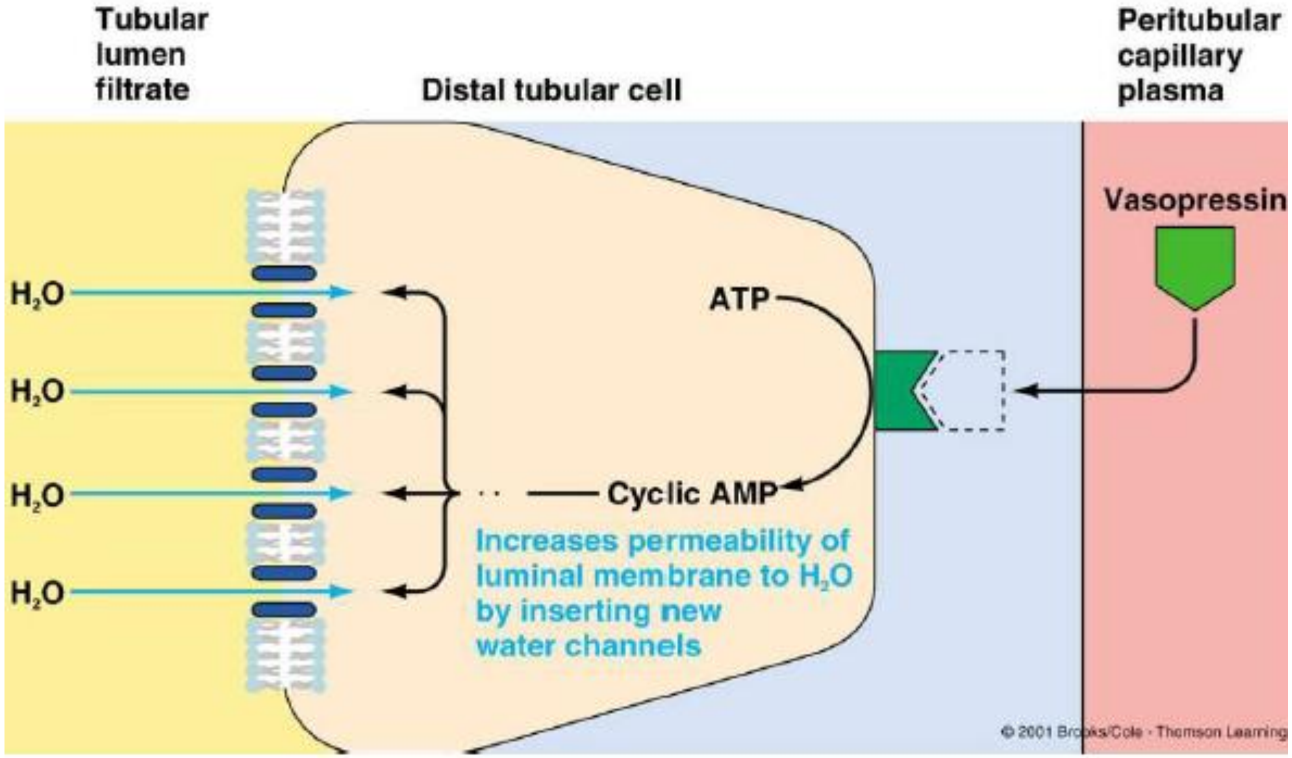
A

- No ADH
- No water reabsorption
- Diluted urine

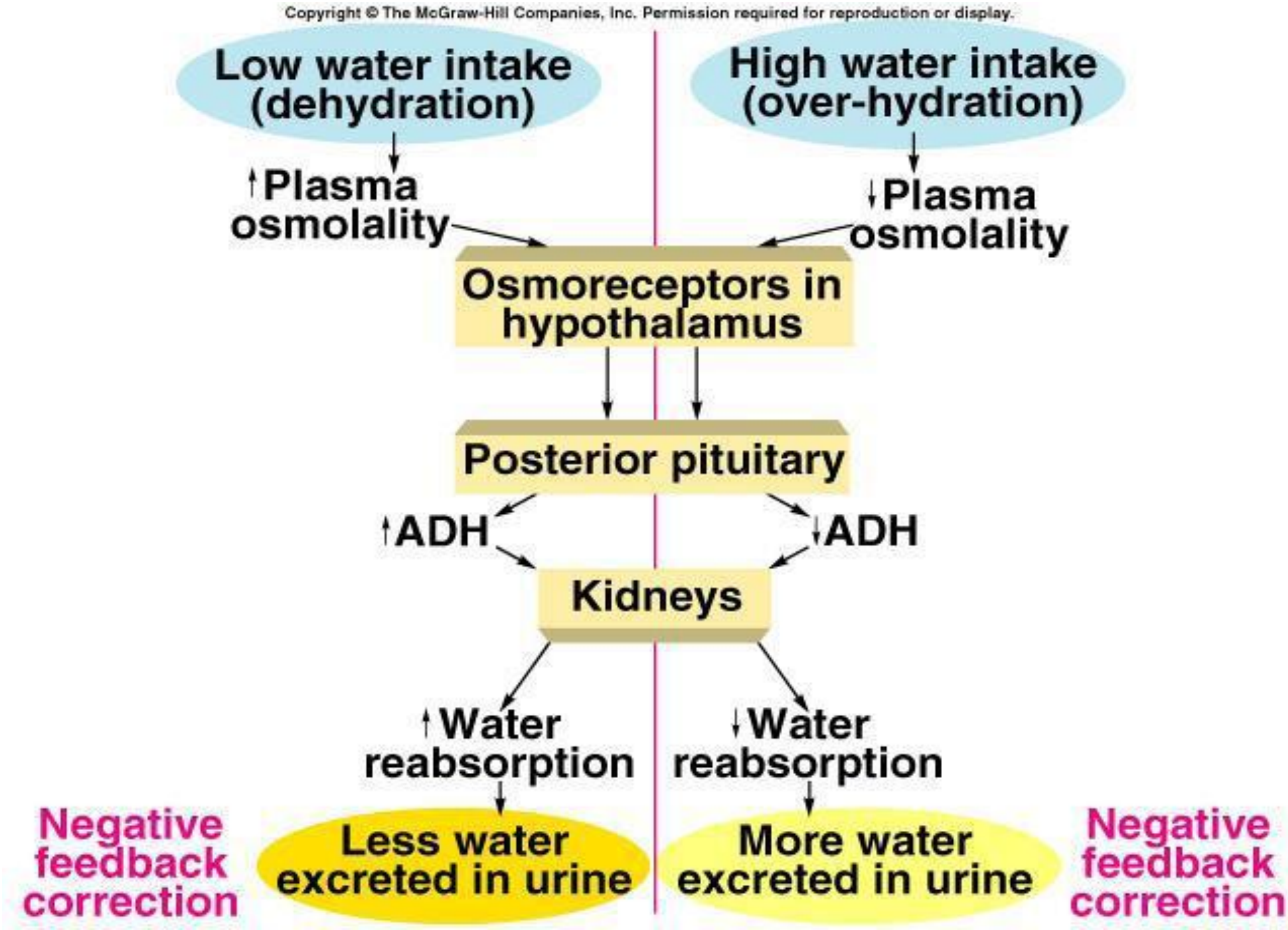
B

- Presence of ADH
- Water reabsorption
- Concentrated urine

The Role of ADH



The picture shows water channels on tubular and luminal membrane of collecting duct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Low water intake (dehydration)
↑Plasma osmolality
High water intake (over-hydration)
↓Plasma osmolality
Osmoreceptors in hypothalamus
Posterior pituitary
↑ADH
↓ADH
Kidneys
↑Water reabsorption
↓Water reabsorption
Negative feedback correction
Less water excreted in urine
More water excreted in urine
Negative feedback correction

Diuresis

Definition

- Is an increase of urine output. It has two types :

- o Water diuresis:

 *Drinking large quantity of water → dilute ECF→↓ADH→ no water reabsorption in collecting duct→ large volume of **"diluted"** urine.

- o Osmotic diuresis:

 *Diabetes → **Filtration of excessive osmotic active substances** (glucose in Diabetes , mannitol is an IV diuretic drug) → Drag water with it → Large volume of hyperosmolar **"concentrated "** urine "concentrated urine is the different between osmotic diuresis and water diuresis"

Polyurea: in Diabetes inspidus (Not a real diabetes but it's due to absence of ADH receptors or hyposecretion of it. Polyurea means excretion of water continuously and the patient with polyurea is more likely to be dehydrated)

Diabetes insipidus: is a condition characterized by excessive thirst and excretion of large amounts of severely diluted urine.
it is either a problem with the production of ADH (cranial diabetes inspidus) or kidney's response to ADH (nephrogenic diabetes insipidus).

Explanation of Countercurrent mechanism

For Knowledge

- **Countercurrent multiplier system is a system that expends energy to create a concentration gradient.**
- **Water flows from the tubular fluid of the descending limb of the loop of Henle into the medullary space.**
- **The ascending limb is impermeable to water (because of a lack of aquaporin, a common transporter protein for water channels in all cells except the walls of the ascending limb of the loop of Henle), but here Na+, Cl-, and K+ are actively transported into the medullary space, making the filtrate (in lumen) hypotonic (with a higher water potential). This constitutes the single effect of the countercurrent multiplication process.**
- **Active transport of these ions from the thick ascending limb creates an osmotic pressure drawing water from the descending limb into the hyperosmolar medullary space, making the filtrate hypertonic (with a lower water potential).**
- **The countercurrent flow within the descending and ascending limb thus increases, or multiplies the osmotic gradient between tubular fluid and interstitial space.**
- **Urea diffuses into the thin loop of Henle, and then passes through the distal tubules, and finally passes back into the collecting duct. The recirculation of urea helps to trap urea in the renal medulla and contributes to the hyperosmolarity of the renal medulla".**

Videos:

1- http://www.youtube.com/watch?v=ws-hQEXbT6U&feature=related

2- http://www.youtube.com/watch?v=XbI8eY-BeXY&feature=related

Summary

- Normal kidneys have tremendous capability to vary the relative proportions of solutes and water in the urine in response to various challenges.
- When there is excess water in the body and body fluid osmolarity is reduced, the kidney can excrete urine with an osmolarity as low as 50 mOsm/L.
- When there is a deficit of water and extracellular fluid osmolarity is high, the kidney can excrete urine with a concentration of 1200 to 1400 mOsm/L.
- There is a powerful feedback system for regulating plasma osmolarity and sodium concentration that operates by altering renal excretion of water independently of the rate of solute excretion. A primary effector of this feedback is *antidiuretic hormone (ADH),* also called *vasopressin*.
- Excess body water → excess urine production for a short while → when water volume is going back to normal, urine volume will retain to normal.
- Without ADH or medullary hyperosmolarity, the kidney can’t concentrate urine.
- Counter current multiplayer is a mechanism by which the kidney builds (forms) hyper osmolar medulla. It occurs in thick ascending limb and collecting duct.
- Counter current exchanger is for blood supplying to the medulla and for maintaining hyperosmolar medulla.
- Osmotic diuresis produces concentrated urine but water diuresis= diluted urine.

SUMMARY

- **LOOPS OF HENLE OF JUXTA MEDULLARY NEPHRONS establish hyperosmolarity of interstitium of medulla. They are called COUNTER CURRENT MULTIPLIERS.**
- **VASA RECTA maintain hyperosmolarity established by counter current multipliers. They are called COUNTER CURRENT EXCHANGERS.**
- **The medullary blood flow is low, accounting for less than 5 percent of the total renal blood flow. This sluggish blood flow (limited) is not sufficient to supply the metabolic needs of the tissues but helps to minimize solute loss from the medullary interstitium.**
- **The vasa recta serve as countercurrent exchangers, minimizing washout of solutes from the medullary interstitium unlike the cortical nephrons.**
- **Urea has a major role in the concentration of urine.**
- **ADH is present in situations of needing water to be inside the body like during fasting.**
- **U-shaped blood supply is important to maintain the hyperosmolarity, unless the salts will be washed out from the blood.**
- **The most animal species that can produce concentrated urine is the desert rat (dry urine) while camels conserve the water inside the body.**

THE END

If there are any problems or suggestions
Feel free to contact:

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THANK YOU