Renal Block

Physiology Team

7th Lecture

Dilution and Concentration of Urine

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Urine concentration :

The ability of the kidney to concentrate urine (by reabsorption of water to conserve it and increase ECV) or dilute urine (by excretion of water to reduce ECV) is an important function in the regulation of extracellular volume (ECV) and extracellular fluid osmolality (the more water in ECV the less the osmolality will be).

This happens in two situations:

1) When there is excess water in the body the extracellular fluid osmolality is reduced (there is so much water with less salts) the kidney will regulate the extracellular fluid osmolarity by excreting urine with an osmolarity as low as 50 mOsm/liter (excrete larger amount of water and less amount of salts) then the body fluid osmolarity will increase due to reduction of water in it.

2) When there is a deficiency of water or excess salts, and extracellular fluids osmolarity is high (there is less water and so much salts) the kidney will regulate the extracellular fluid osmolarity by excreting urine with a concentration of about 1200 to 1400 mOsm/liter (excrete salts more than water) then the extracellular fluid osmolarity will decrease due to the excretion of the excess salts.

> **Note:**
> Urine flow and osmolarity will be normal if the water intake is normal.

When water intake is normal urine flow is 1 -2 ml/min.

Obligatory urine volume: أقل كمية من البول ممكن تخرجه الكلية

Is equal to 0.5 liter and it is the minimum urine volume in which the excreted solute can be dissolved and excreted.

Range of volume and osmolality regulated by the kidney:

- Urine Osmolality varies between 50 -1400 or(30 -1200) mosm/kg.
- 50 mosm/kg (when the extracellular fluid osmolality is very low, e.g., when the individual drinks a lot of water), 1400 mosm/kg (when the extracellular fluid osmolality is very high, e.g., when the individual is fasting).

Notice that :

- these values are not the normal osmolality.
- there is no reference interval ("normal range") for urine osmolality as the interpretation depends on the clinical condition of the individual to determine an appropriate response but the doctor said "**urine osmolality is between 500-700 mOsm/kg".**

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

Note:

Secretion means tubular secretion which is the transfer of materials from peritubular capillaries to renal tubular lumen, but excretion means into urine.

The basic requirements for forming a concentrated(مركز) or diluted(مخفف) 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 and less water 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).

Notice that:

Low osmolarity = more water.
High osmolarity = more salts.

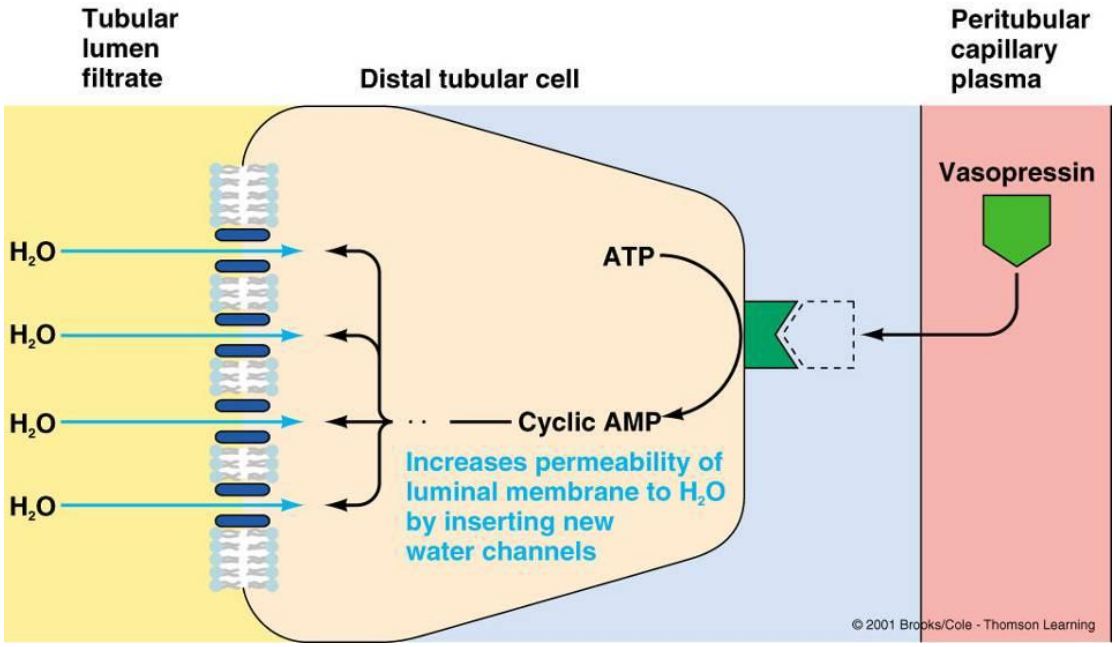
The graded hyperosmolar medulla: the deeper in the medulla the higher the osmolarity.

The Role of ADH

•Water reabsorbed from distal tubule and 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 posterior pituitary gland which releases ADH into the bloodstream (vasopressin).

•ADH makes the wall of the collecting duct more permeable to water.



Notice:

In the presence of ADH more water is reabsorbed and less is excreted. Increase of osmolarity in extracellular fluid will stimulate the ADH, this will decrease urine output.

For explanation:

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.

Countercurrent Mechanism

• The hyperosmotic renal medullary interstitium is produced by counter-current multiplier. (Important)

• The hyperosmolar medullary interstitium provides the osmotic gradient necessary for water reabsorption.

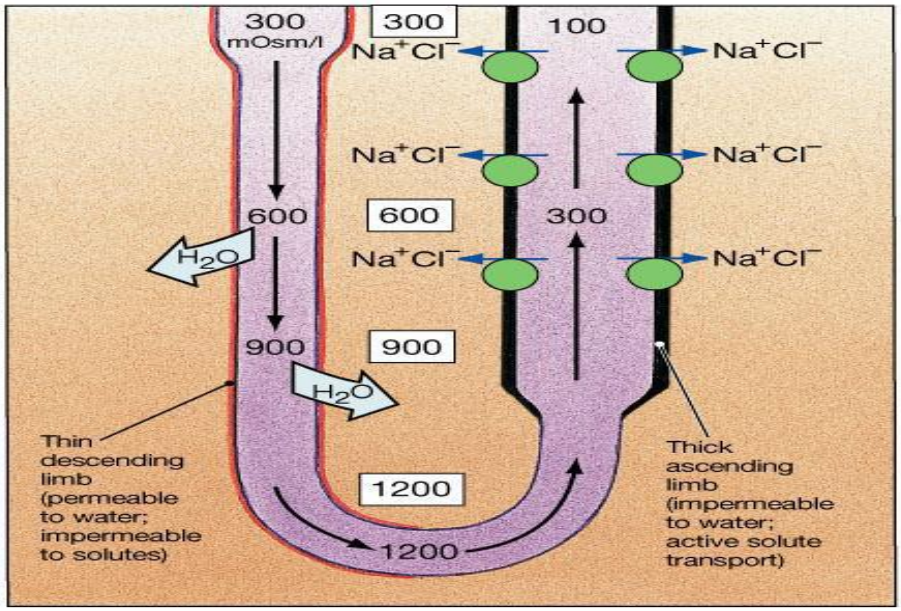
• The hyperosmolar medulla is formed by the thick Ascending limb of loop of Henle and Collecting Ducts

• Is formed mainly by Juxta-medullary nephrons.

Notice:
Without the hypreosmolarity in the medulla the kidney cannot reabsorb water and cannot control of the urine concentration (no osmotic gradient, no osmosis).

Countercurrent multiplayer:

- Medullary hyper-osmolality is due to solute deposition on medullary interstitium.
- NaCl reabsorbed from the thick ascending limb of loop is deposited on medullary interstitium. As we know, the descending limb of loop of henle is permeable to water and impermeable to salts (solutes) while the ascending limb of loop of henle is permeable to solute and impermeable to water, that means the ascending and descending limbs are working in a counter-current mechanism (عكس بعض) . This will help the ascending limb in the reabsorption of the NaCl or the descending limb in the reabsorption of water.
- Urea reabsorbed from collecting duct (ADH) to medullary interstitium also contributes to medullary hyper-osmolality.
- Water will be absorbed from the collecting duct to peritubular capillaries in the presence of ADH due to osmotic gradient.



(b) Active transport of NaCl along the ascending thick limb results in the movement of water from the descending limb.

Thiazide (diuretic) block NaCl reabsorption on thick ascending loop then causes diuresis.

Mechanism:

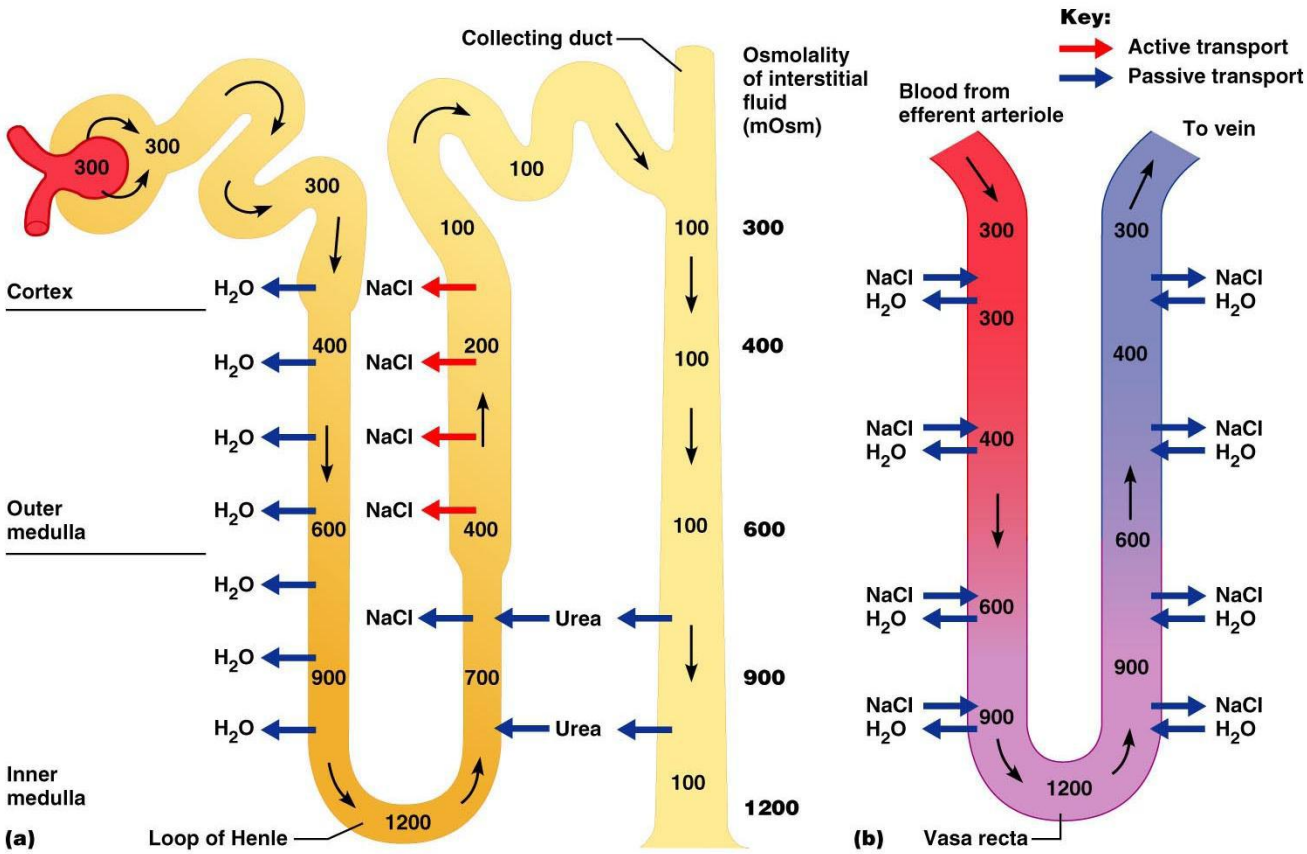
- Salt remains in filtrate and drags water causing osmotic diuresis.
- Decreases medullary osmolality therefore water cannot be reabsorbed from collecting duct (No osmotic gradient) leading to diuresis. (Osmotic gradient will work (reabsorption of water) only if the osmolarity is high in the medullary interstitium).

Countercurrent exchange (the action):

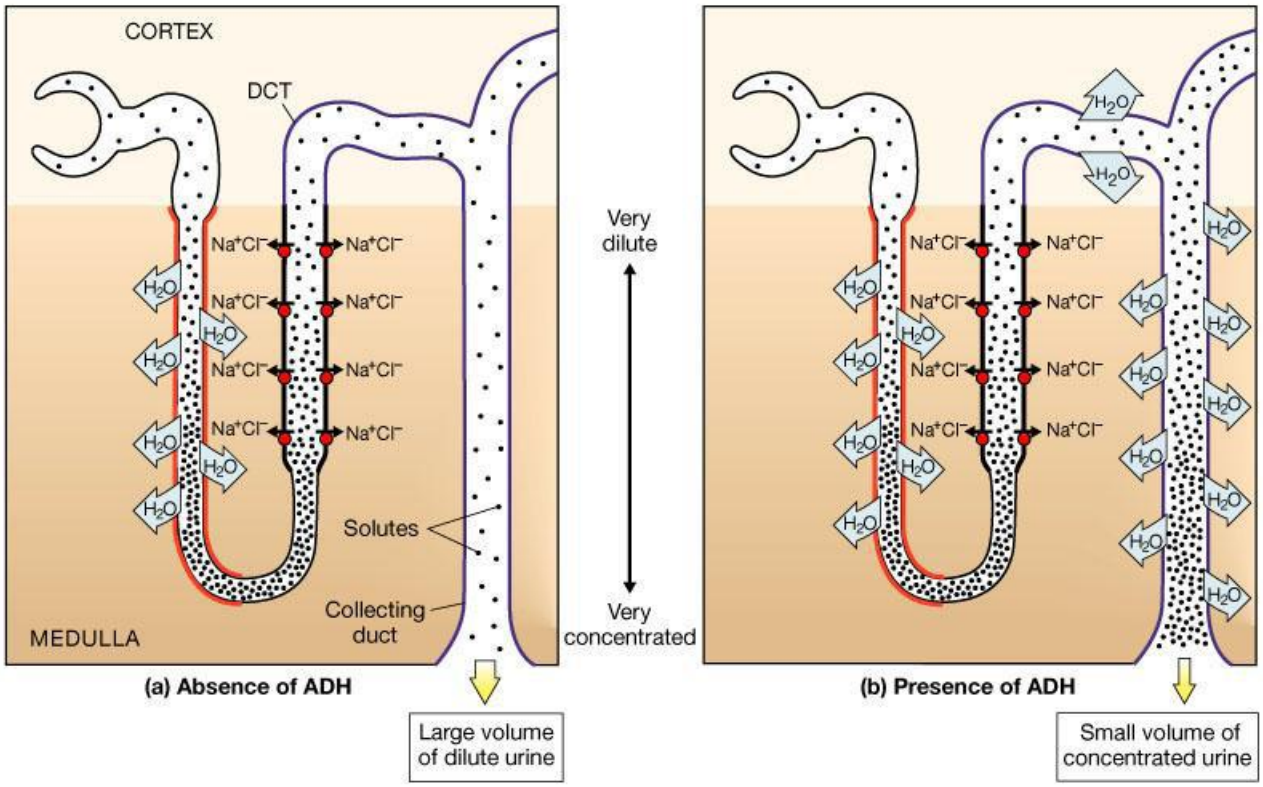
- Maintains hyper-osmolar medulla important
- Blood supply to medulla is by Vasa recta.
- Descending limb: water passes out into hyperosmolar medulla (from blood) carrying O2 & nutrient, NaCl will enter the blood increasing its osmolarity. (Exchange)

•Ascending limb: water will be absorbed back to the hyperosmolar blood carrying CO2, waste product & NaCl will leave the blood deposited as it is in the medulla. (Exchange again).

•Therefore blood leaves the hyperosmolar medulla undisturbed (same amount of water will leave and enter again).



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



Diuresis:

The increase of urine output.

- **Water diuresis:**
  - Drinking large quantity of water
  - Dilute ECF
  - Decrease both ADH and osmolarity.
  - No water reabsorption in collecting duct.
  - Large volume of diluted urine.

- **Osmotic diuresis:**
  - –Diabetes
  - Filtration of excessive osmotic active substances (glucose, mannitol) (hyperosmotic filtrate).
  - –Drags water with it.
  - –Large volume of hyperosmolar urine.

- **Polyuria:**

Diabetes insipidus (just a name, has nothing to do with diabetes but the high amount of urine)

- **It is due one of the following:**

1) ADH deficiency.

2) Kidney ADH insensitivity.