UG MODULE
PHYSIOLOGY(LECTURE 4)
Renal Concentration and Dilution of Urine

BY

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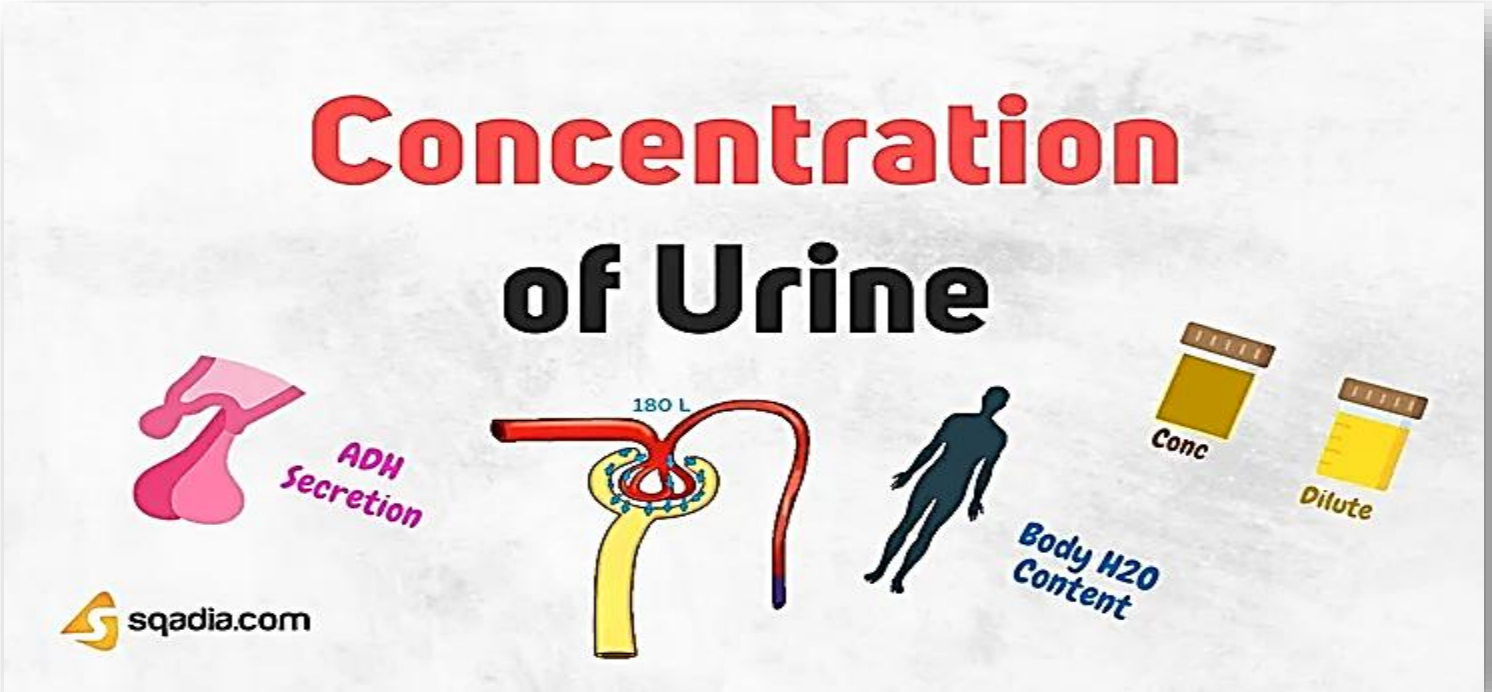
2023-2024



Renal Concentration and Dilution of Urine

-The kidneys can excrete either **concentrated or dilute urine** according to **the water balance of the body**.

-In dehydration, water is conserved in the body and concentrated urine having high osmolality is excreted.

-While in hydration, excess water is eliminated from the body and dilute urine having low osmolality is excreted.

-This function is determined by the amount of water reabsorption in renal tubules:

Since water reabsorption is **obligatory in the PCTs (65 %) and LH (15 %) (about 80 %)**, it is clear that the **final adjustment of the urine volume and osmolality** depends only on the extent of **facultative water reabsorption in CDs**, which is determined by 2 main factors:

1) **The ADH blood level:** This hormone renders the CDs (and late DCTs to some extent) highly water permeable and the higher its blood level, the greater the area of CDs that becomes water permeable (and vice versa).
2) **The hyperosmolarity of medullary interstitium (MI):** This is developed by the renal countercurrent multiplier system (LH of juxtamedullary nephrons), and is the force that causes passive water reabsorption from the MCDs into the renal medulla.

Loop of Henle and Renal Countercurrent Mechanism

Countercurrent system

- It is a system in which the inflow of a current runs parallel, opposite and close to its outflow for some distance.
- So, LH acts as countercurrent system.

Renal countercurrent mechanism:

- It is the **mechanism by which urine is concentrated in the kidney**.
- It **depends on the production and maintenance of a state of hyperosmolarity (hypertonicity) in the renal medullary interstitium (MI)** by the action of the structures that pass in the renal medulla which are:

1. **LH of juxtamedullary nephrons (countercurrent multiplier system)**.
2. **Vasa Recta (countercurrent exchanger system)**.
3. **Medullary collecting ducts (MCDs).**

1. **LH of juxtamedullary nephrons:**

These constitute a **countercurrent multiplier system** that operates actively to **construct an osmotic stratification in the renal medulla (i.e. a progressively increasing hyperosmolality in the renal medulla)**.
So that the osmolality of the MI gradually increases from 300 mOsm/L in the renal cortex to **1200-1400 mOsm/L** at the renal papillae.

2. **Vasa Recta (VR):**

These constitute a **countercurrent exchanger system** that operates passively to **maintain the hyperosmolality of the MI**.

3. **Medullary collecting ducts (MCDs).**

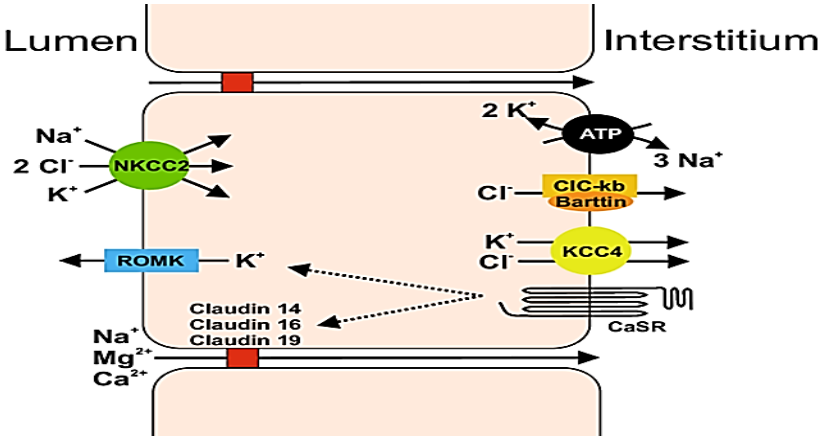
Countercurrent multiplier system

This system consists of **LH of juxtamedullary nephrons** which dip deeply in renal medulla, and is concerned with **production of graded hyperosmolality in MI** by the following mechanism:

Steps involved in causing hyperosmotic renal medullary interstitium:

Step (1): First assume that the LH is filled with fluid with a concentration of 300mOsmol/L, the same as that leaving PCT.

Step (2): There is a carrier in thick ascending LH which actively transported one Na^+, one K^+, and 2 Cl^- from the tubular lumen into the cells. Na^+ is actively pumped out by the ATPase in exchange for K^+ (which enters the cells then passively diffuses into tubular fluid) and one Cl^- is co-transported with the absorbed K^+ into the MI while the other Cl^- diffuses passively. Active transport of these solutes raises the interstitial concentration.



Step (3): Osmosis of water out of the descending limb of LH raising osmolarity inside it gradually to about 1200 mOsmol/L.

Step (4): Additional flow of fluid in LH from PCT, which causes the hyperosmotic fluid previously formed in the descending limb to flow into the ascending limb.

Step (5): Active transport in the ascending limb repeated over and over with the net effect of adding more and more solutes to the medullary interstitium in excess of water.

Countercurrent Multiplier System in the Loop of Henle

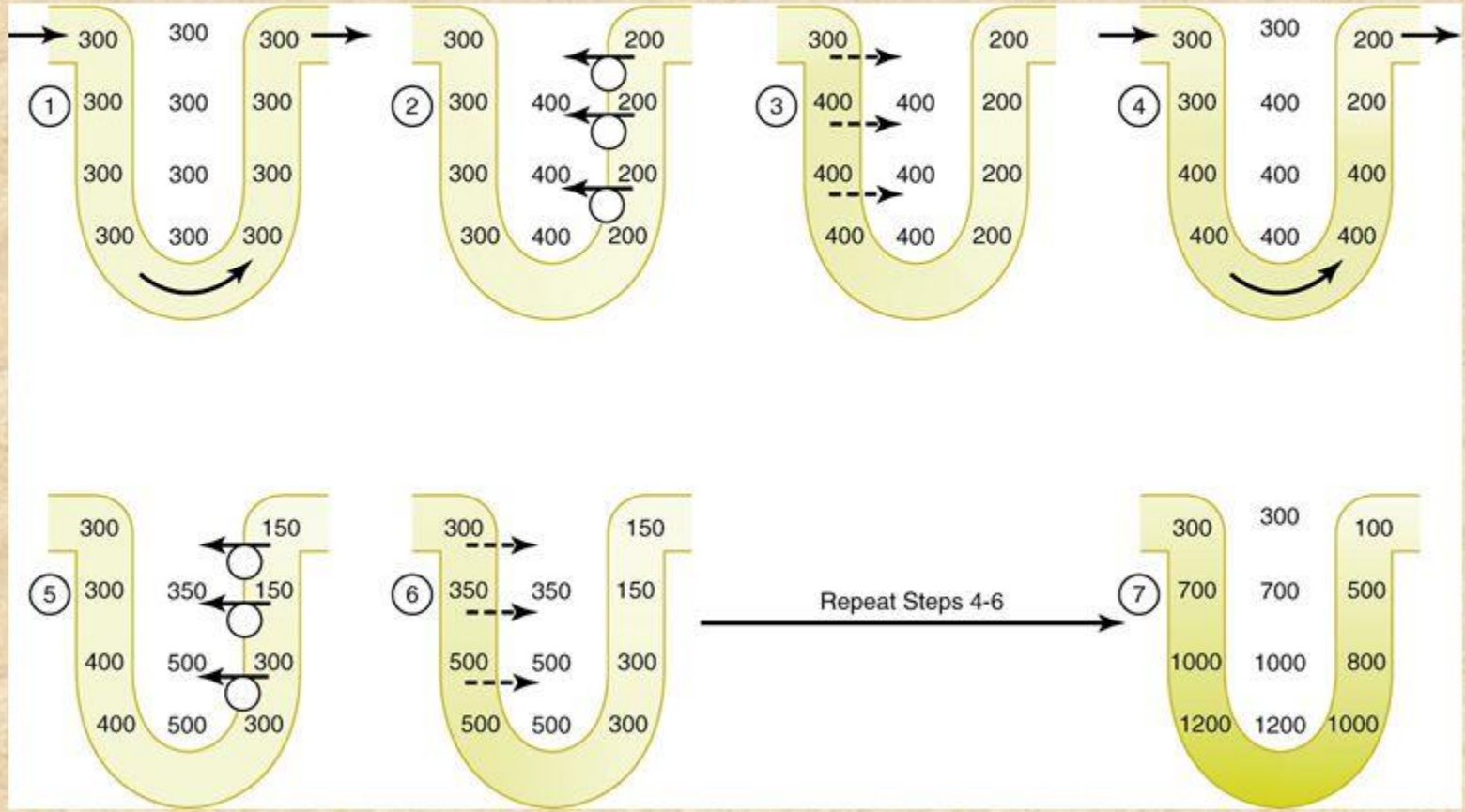


Figure 28-3; Guyton and Hall

The ascending limbs of LH:

Are the segments responsible for creating graded hyperosmolality in MI.

The distal thick part:

It is impermeable to water and poorly-permeable to all solutes.
However, **both Na^+ and Cl^-** are actively transported from the tubular lumen into the MI. This produces hyperosmolality in the MI and at the same time, the tubular fluid becomes more hypotonic with an osmolality about **100 mOsm/L when delivered to the DCTs**.
The transport mechanism depends on **a carrier that transports one Na^+, one K^+ & 2 Cl^-** from the tubular lumen into the cells.

The initial thin part:
It is impermeable to water but highly permeable to Na^+ and Cl^-.
Na^+ and Cl^- diffuse passively down their concentration gradients into MI.
Therefore, the tonicity of tubular fluid progressively decreases as it moves up while hyperosmolality is developed in MI.

The descending limbs of LH:

- Receive **isotonic (iso-osmotic) fluid** from the **PCTs**.
- Their walls are:
- Highly permeable to water.
- Poorly permeable to solutes (namely Na^+, Cl^- and urea).
- Accordingly water passively diffuses outward down an osmotic gradient into the MI (which is hypertonic by the countercurrent multiplier effect of the ascending limb).
- As a result, the tubular fluid becomes hypertonic, and its hypertonicity increases gradually as it flows downwards reaching 1200 (up to 1400) mOsm/L at the tips of the renal pyramids.
- The amount of reabsorbed water in the LH is about 15% of the filtered water in the glomeruli, and it is also an obligatory reabsorption as that occurring in the PCTs.

Causes of MI hyperosmolality:

1. The thick ascending limb of LH: Active reabsorption of Na^+, K^+, and Cl^- (by common carrier protein that transports one Na^+, one K^+ & 2 Cl^-) with passive reabsorption of +ve ions.

2. The medullary collecting tubule (MCD):

- Active reabsorption of Na^+ with passive reabsorption of Cl^- ions.
- **ADH** increases permeability very much to water → water reabsorption →↑ concentration of **urea** in the tubular fluid→ diffuses to medullary interstitium.

3. Transport of additional Na^+ and Cl^- into the medullary interstitium from the **thin ascending limb of the LH.**

Countercurrent exchanger system of the vasa recta

Without a special medullary vascular system, the flow of blood in the medulla will wash out excess solutes and prevent the previous mechanisms from increase the osmolality of the medullary interstitium.

Fortunately, the medullary blood flow has 2 characteristics:

1. It is very sluggish representing 1-2% of the total RBF. So, removal of solutes is minimized.
2. **The vasa recta function as a countercurrent exchanger** that prevents wash out of solutes from the medulla. How?

- Fluid flows through along U tubule, with its arms lying very close to each other so that fluid and solutes can exchange readily between the 2 arms (countercurrent exchanger).

- Thus, as the blood flows down the descending limb, NaCl and urea diffuse into the blood from the highly concentrated interstitium while water diffuses outward into the interstitium. Both effects cause the blood osmotic concentration to raise progressively higher to a maximum of **1200 mOsmol/L** at the tips of vasa recta.

- As the blood flows back up the ascending limb, all the NaCl and urea diffuses back out the blood into the interstitial fluid while water diffuses back into blood.
- Therefore, by the time the blood leaves the medulla with osmolarity slightly greater than that of the blood that had initially enter the vasa recta. As a result, blood flowing through the vasa recta carries only minute amounts of medullary interstitial solutes away from the medulla.

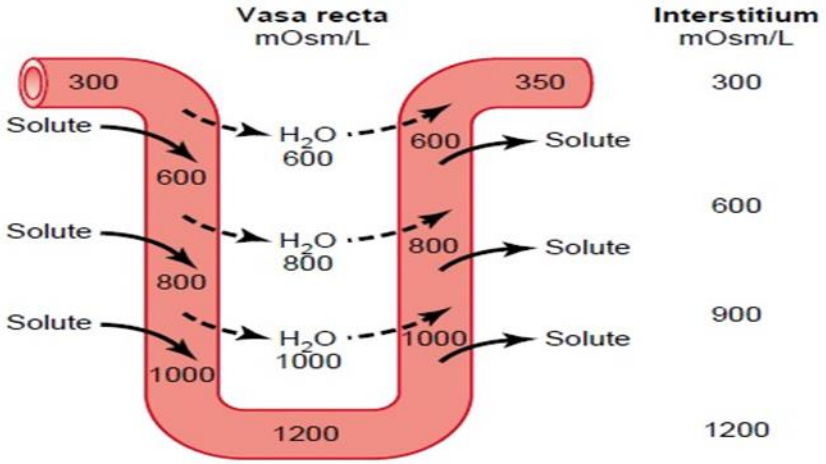
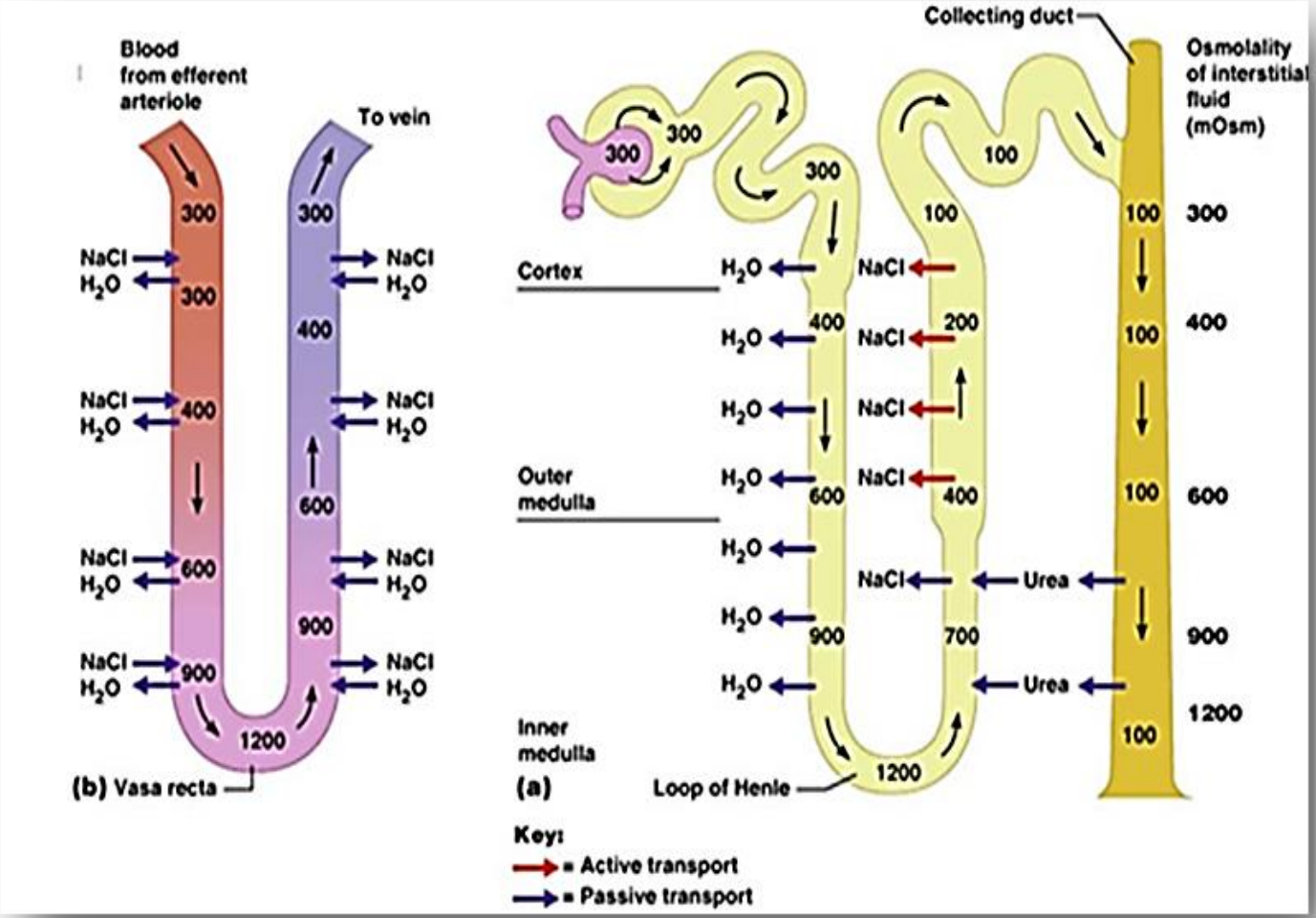


Figure 28–6

Countercurrent exchange in the vasa recta. Plasma flowing down the descending limb of the vasa recta becomes more hyperosmotic because of diffusion of water out of the blood and diffusion of solutes from the renal interstitial fluid into the blood. In the ascending limb of the vasa recta, solutes diffuse back into the interstitial fluid and water diffuses back into the vasa recta. Large amounts of solutes would be lost from the renal medulla without the U shape of the vasa recta capillaries. (Numerical values are in milliosmoles per liter.)

- In this way, solutes are trapped in the MI while excess water is removed from it, and both effects help **maintenance of MI hyperosmolality**.
- The excess water comes from 2 sources:
  - Water that diffuses from the descending limbs of both VR and LH.
  - Water that is reabsorbed from the MCDs.
- The countercurrent exchanger function of VR is helped by:
  - They are highly permeable to both solutes and water.
  - Blood flow is sluggish and small (about 2% of total RBF).
- **Thus, the main function of VR is to maintain the MI hyperosmolality**.


Blood from efferent arteriole
To vein
300
300
NaCl
H2O
300
400
NaCl
H2O
400
600
NaCl
H2O
600
900
NaCl
H2O
900
1200
(b) Vasa recta
Collecting duct
Osmolality of interstitial fluid (mOsm)
300
100
300
100
100
300
Cortex
H2O
NaCl
400
200
100
400
Outer medulla
600
400
100
600
Urea
900
700
900
Urea
1200
100
Inner medulla
(a)
Loop of Henle
Key:
= Active transport
= Passive transport

Mechanism of Urine Concentration

- At the normal rate of ADH secretion, about **10 % of water is reabsorbed in the CCD and 4.2 % is reabsorbed in the MCDs**, leading to a total water reabsorption of about 99.2% and a urine volume about 1.5 liters daily with an osmolality about 400 mOsm/liter.

- However, more water reabsorption (and consequently, more urine concentration) is required in cases of hypovolemia (e.g. dehydration and hemorrhage) and blood hypertonicity. In such cases, ADH secretion is stimulated, thus larger parts of the MCDs become water-permeable and accordingly, more water is reabsorbed, resulting in excretion of concentrated urine with high osmolality.

- In cases of maximal anti-diuresis (maximal ADH) e.g. severe hemorrhage, the whole length of the MCDs becomes water-permeable, and **4.7%** of water is reabsorbed there (instead of the normal 4.2%) leading to a total water reabsorption of 99.7% and a urine volume about 0.5 liter daily with an osmolality of about 1400 mOsm/liter.

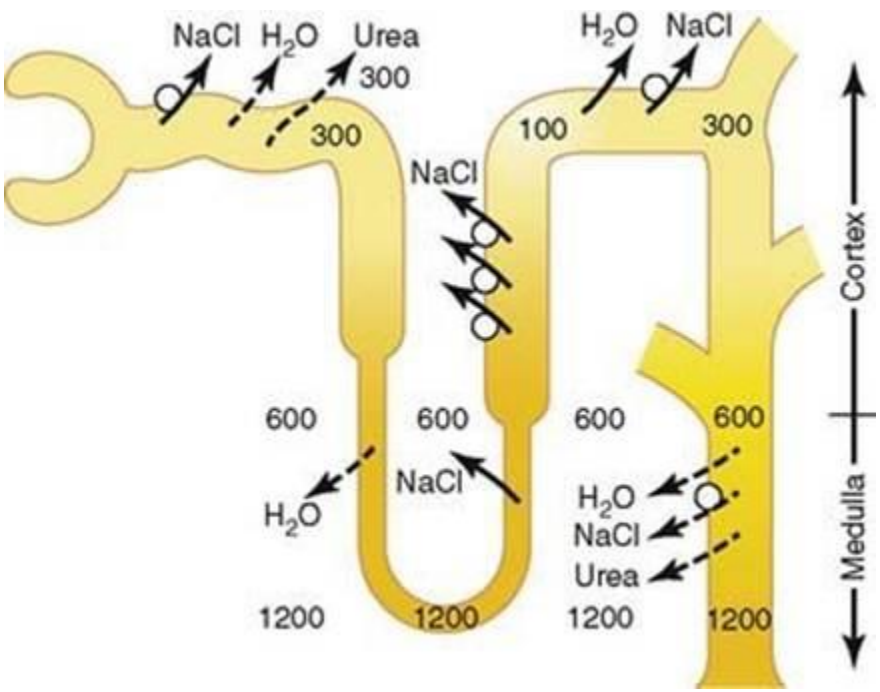
Mechanism of Urine Dilution

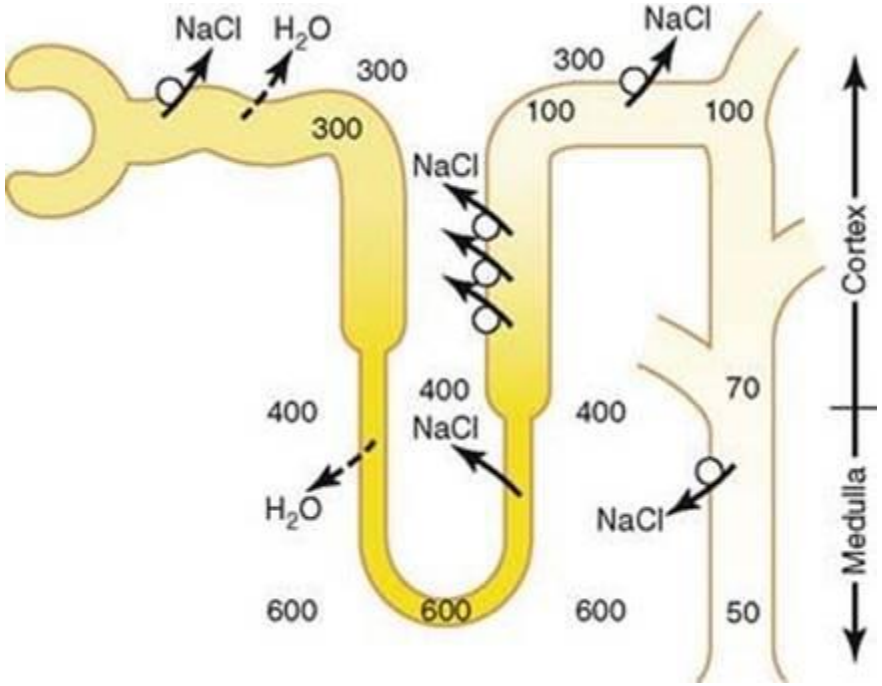
This occurs in cases of hydration and after drinking large amounts of water.
It is produced secondary to decreased secretion of ADH (as a result of both hypervolemia and blood hypotonicity). This decreases the water-permeable area in the CDs (thus the reabsorbed amount of water is decreased leading to excretion of a large volume of urine with a lower osmolality than normal; dilute urine).

In severe cases of diabetes insipidus (= a disease in which ADH secretion is greatly impaired), the late parts of DCTs and almost the whole length of the CDs become water-impermeable, thus water reabsorption is markedly decreased. In addition, there is continuous Na^+ reabsorption, so the osmolality of the tubular fluid in the CCDs decreases to about 90 mOsm/liter and is further decreased in the MCDs, leading to excretion of a large volume of dilute urine with an osmolality less than 80 mOsm/liter (about 50 mOsm/L).

In cases of complete absence of ADH, the urine osmolality becomes about 30 mOsm/liter, and its volume about 23.3 liters/day.

Mechanism of Urine Concentration and Dilution





THANK YOU