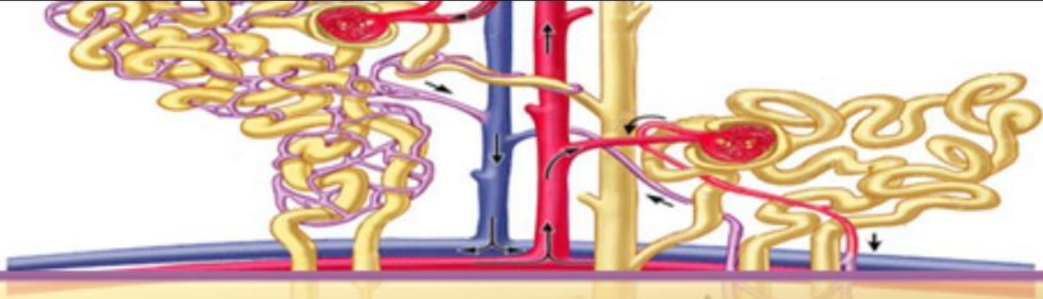
Renal concentration & dilution of urine

By

Dr. Nour A. Mohammed
MUTAH SCHOOL OF MEDICINE



Renal handling of water

- From 180 litres plasma filtered/day in both kidneys, only **1.5** litres of urine are excreted which means that about **99%** of water is **reabsorbed**. This occurs as follows:-

A- Water reabsorption in PCT

- About **65- 70%** of water is reabsorbed in **PCT** and this reabsorption **is passive** i.e., secondary to active transport of other solutes (NaCL , glucose and amino acids) which create a high osmotic pressure in the renal interstitium.
- It is **obligatory water reabsorption** because it is independent of ADH effect.
- It is helped by water channels "**aquaporin.1**" which are located in the luminal border of tubular epithelium of PCT.

B. Water reabsorption in the loop of Henle(15%)

A. At thin descending part: (not permeable to Na^+ but permeable to H_2O)

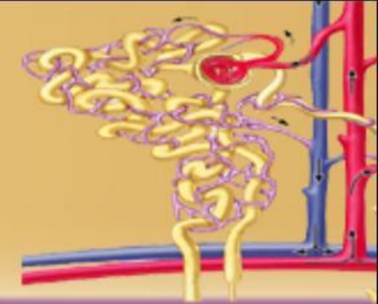
- It is the only part in the nephron in which Na^+ is not reabsorbed.
- Descending part is freely permeable to H_2O.
- This result in that the fluid reaching medulla is hypertonic.

***B.* At thick ascending part:** (permeable to Na^+ but not permeable to H_2O)

- Na^+ is reabsorbed by active co-transport protein carrier.
- It is called ($1Na^+$, $1K^+$, $2Cl^-$) active pump.
- Thick ascending part is poorly permeable to H_2O.
- This result in that the fluid leaving this thick part is hypotonic.

C. Water reabsorption in the DCT and collecting tubules:

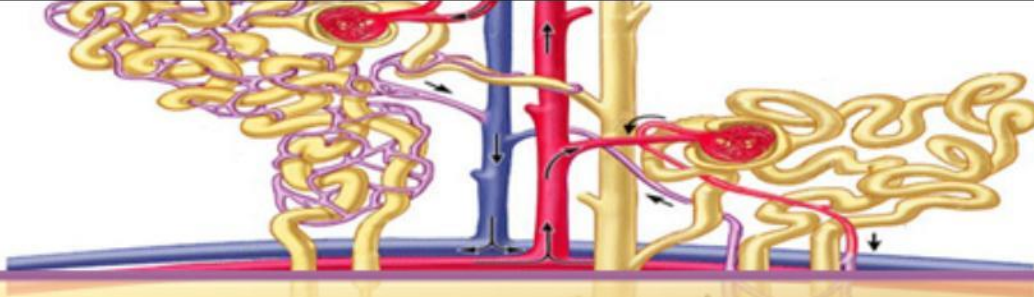
1. In the **first portion of DCT** a little amount of filtered water is reabsorbed. This segment is considered as continuation of thick ascending limb of Henel's loop i.e., **relatively impermeable to water** and here there is continuation of removal of solutes.

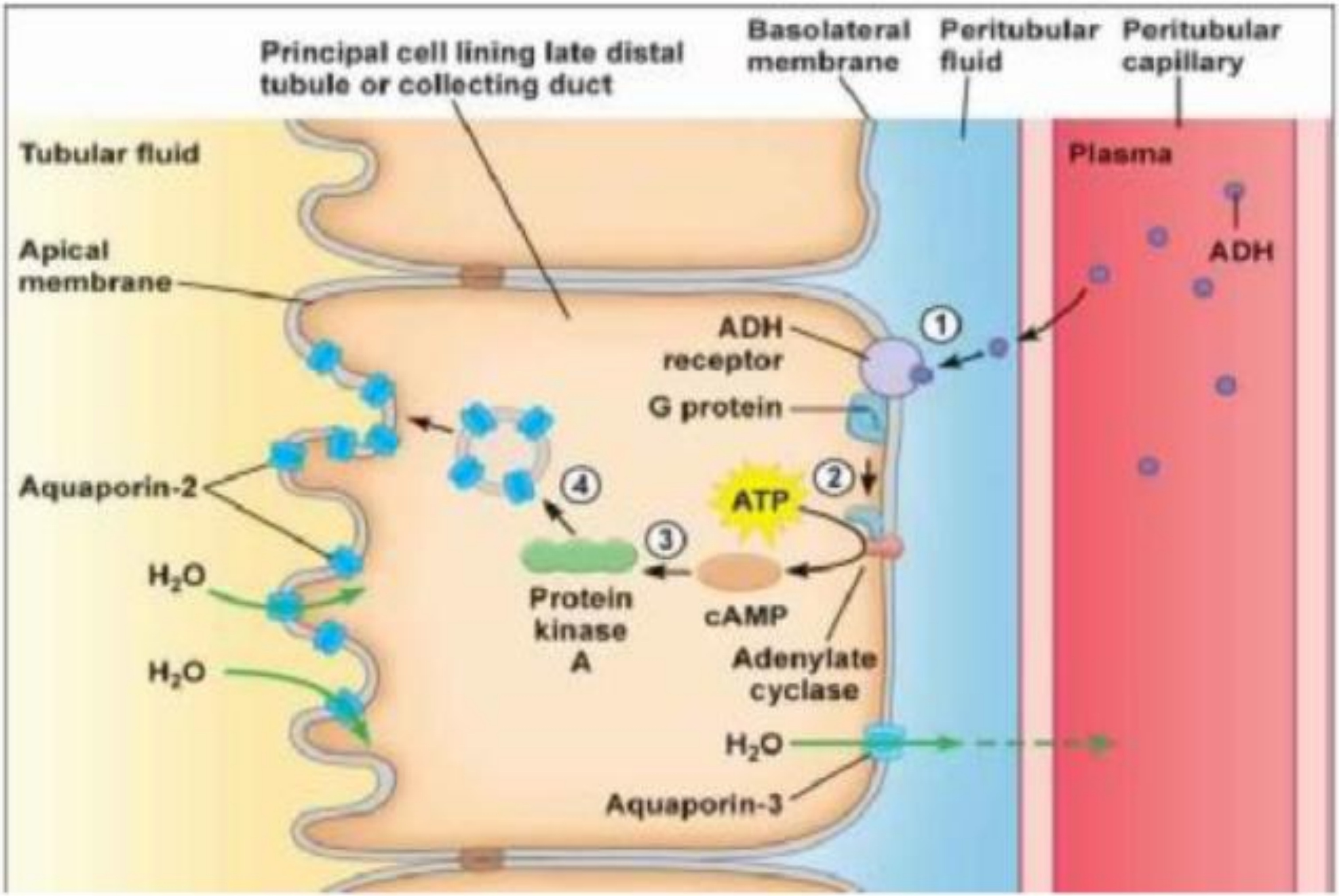


2. In late portion of DCT and collecting ducts:

In this part, about **(10- 14.2 %)** of water is reabsorbed by what is called **'facultative water reabsorption"** i.e., depends on circulating ADH.

- The hormone acts through water channels called "**aquaporine –2**" located in the principal cells of the collecting tubules leading to increase luminal membrane permeability to water.




Principal cell lining late distal tubule or collecting duct
Basolateral membrane
Peritubular fluid
Peritubular capillary
Tubular fluid
Plasma
ADH
Apical membrane
ADH receptor
G protein
Aquaporin-2
ATP
Protein kinase A
cAMP
Adenylate cyclase
H_2O
H_2O
H_2O
Aquaporin-3
1
2
3
4

Auto-regulation of the water content in urine output

- it is the ability of the kidney to excrete either concentrated or dilute urine
- in cases of marked water diuresis urine volume may reach up to **14 L/day** with urine osmolarity

50 mosmol / L ,**while** in water deficit urine volume may be reduced to **500ml/day** with urine osmolarity **1400 mosmol / L**

- This function is determined by the amount of water reabsorption in the renal tubules. Since water reabsorption is **obligatory in the PCTs** & **Loop of Henle**, final adjustment of the urine volume & osmolality (concentration) depends only on the extent of **facultative water reabsorption in the CDs**, which is determined by

two main factors:

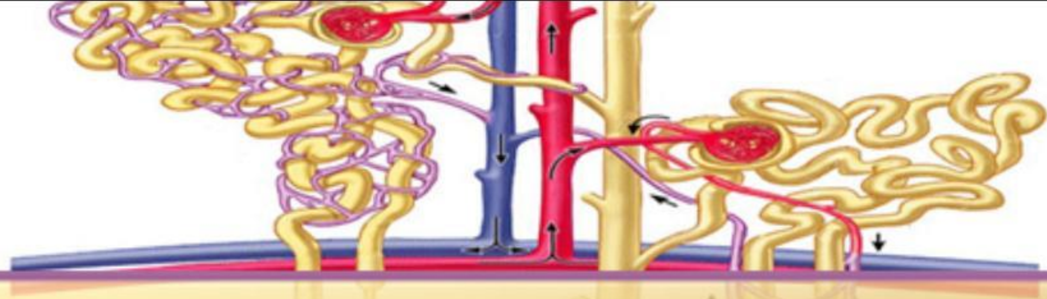
- **ADH**
- **hyper- osmolarity of the medullary interstitium**

1. The ADH blood level: This hormone renders the CDs (and the DCTs to little extent) highly water permeable

2. The hyper-osmolality of the medullary interstitium : This is developed by the renal counter current mechanism, and it is the force that cause passive water reabsorption from the CDs into the renal medulla.

- At normal level of ADH urine volume is about 1.5 litres daily with an osmolality about 400 mosmol/litre
- At high rate of ADH secretion there is more water reabsorption and consequently, more urine concentration, this results in excretion of concentrated urine with high osmolarity.

- At the low rate of ADH secretion the urine dilution occurs.
- 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 osmolarity than normal).



Counter current mechanisms

It is the (**Power of the kidney to concentrate urine**).

- The aim of this mechanism is to **create & maintain hyperosmolarity** of renal medullary interstitium → this increases the water reabsorption from CD

- By this mechanism, there are **4 folds** multiplication of tonicity across the renal medulla:

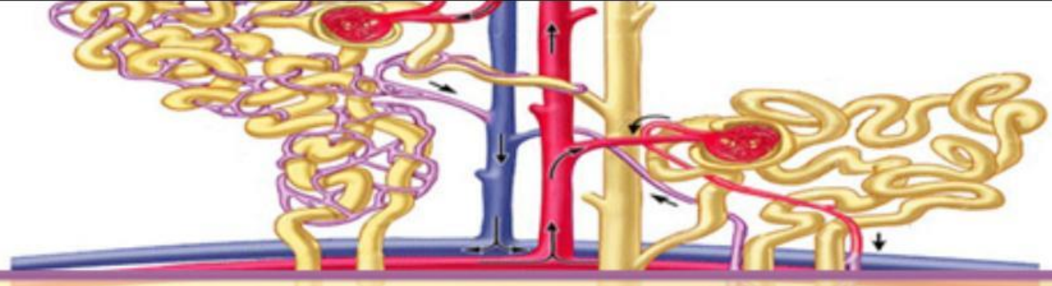
➢ In superficial layers of renal medulla = 300 mosmol/L.

➢ In deep layers of renal medulla = 1200 - 1400 mosmol/L.

- Two **synergistic** mechanisms work together at the same time:

I) Countercurrent **multiplier** mechanism. (***create*** the hypertonicity).

II) Countercurrent **exchanger** mechanism. (***maintain*** the hypertonicity).



Countercurrent multiplier mechanism:

- **It is the function of:** Loop of Henle

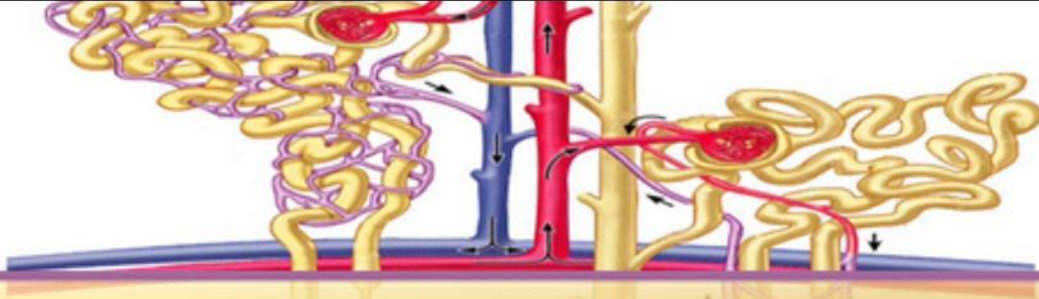
Aim: Creation of hypertonicity in deep renal medullary interstitium.

- This leads to shift of water **from** the CD **to** the renal medullary interstitium and **then to** the blood flow of vasa recta.
- **Steps of countercurrent multiplier:**

1. In thick ascending loop of Henle:

- Active transport of Na^+ followed by cotransport of K^+ & Cl^-

- It is called ($1Na^+$, $1K^+$, $2Cl^-$) active pump
- This shift of ions to renal medullary interstitium is **not followed** by water reabsorption because thick ascending limb is impermeable to water.



2. In descending loop of Henle:

- The water of the tubular fluid is continuously moved to the interstitium (by osmosis).

- Na+ & other ions remain inside lumen with **progressive** increasing of their concentration because the descending limb is permeable to water only.

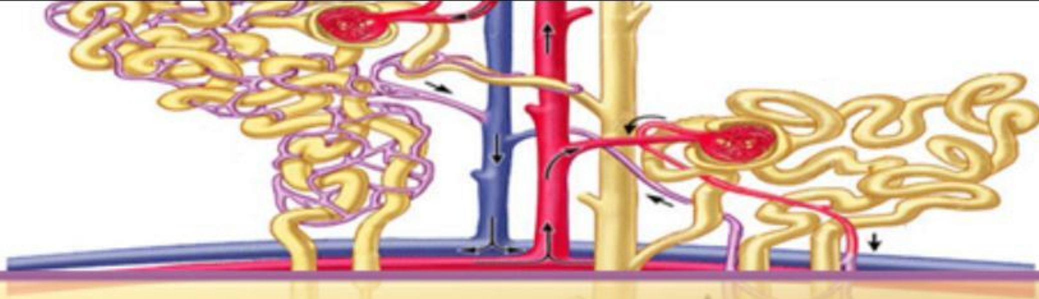
3. In thin part of ascending loop of Henle:

- Some of NaCl diffuses passively out to the medullary interstitium.

- This leads to:

a) ⇧ Osmolarity of medulla.

b) ⇩ NaCl in the ascending limb.



4. Repetition:

- Repetition of the first step and so on.

Unique characters of loop of Henle:

1) Two currents of fluids run in opposite direction: parallel and near to each other

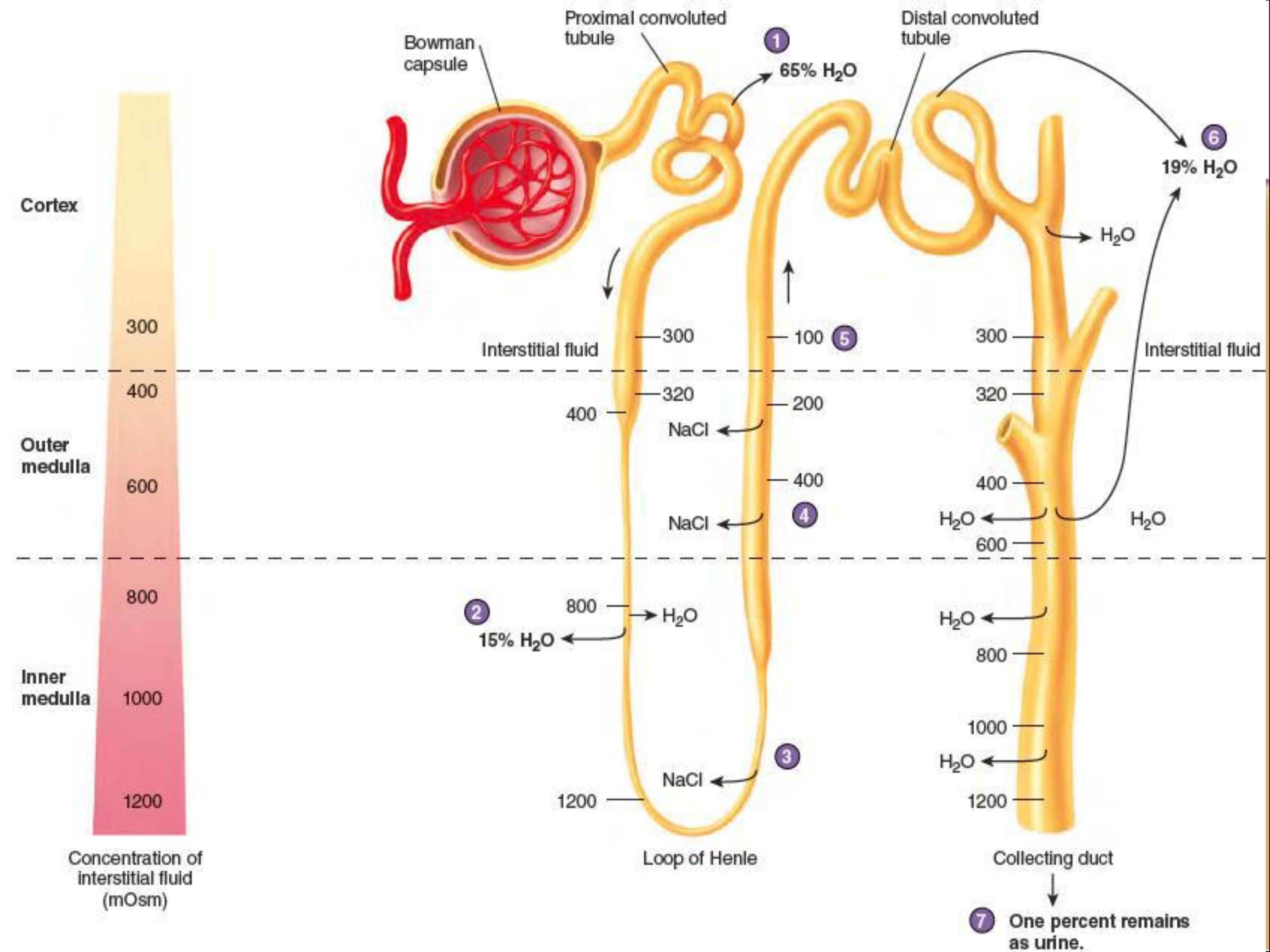
(descending & ascending limbs).

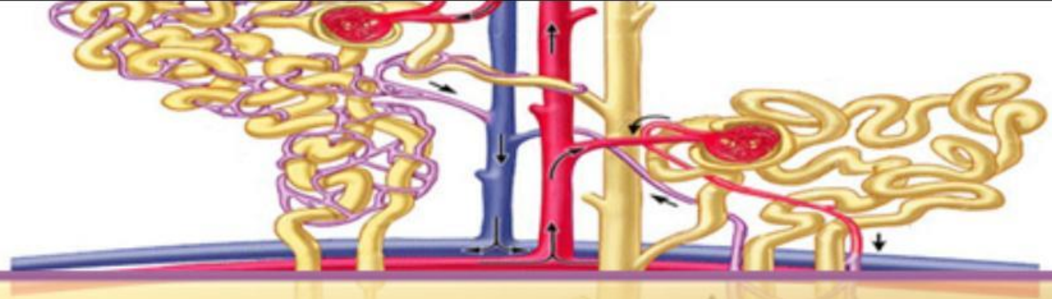
2) Difference in permeability of two limbs:

a) **Ascending limb:** permeable to Na+ but impermeable to water.

b) **Descending limb:** permeable to water but impermeable to Na+.

3) Source of energy: derived from ATP (for sodium pump) in the thick ascending part of the loop of Henle.


Proximal convoluted tubule
Bowman capsule
1
65% H_2O
Distal convoluted tubule
6
19% H_2O
Cortex
H_2O
300
Interstitial fluid
300
100
5
300
Interstitial fluid
400
320
400
200
320
NaCl
Outer medulla
600
400
NaCl
4
400
H_2O
H_2O
600
800
2
800
H_2O
15% H_2O
H_2O
800
Inner medulla
1000
1000
3
H_2O
NaCl
1200
1200
1200
Concentration of interstitial fluid (mOsm)
Loop of Henle
Collecting duct
7
One percent remains as urine.



2) Countercurrent exchanger mechanism:

- **It is the function of** Vasa recta .

Aim: **Maintenance** of hypertonicity of renal medullary interstitium by:

a) Removal of excess water from renal medullary interstitium.

b) Trapping of solutes (NaCl & urea) in renal medullary interstitium.

Steps of counter current exchanger:

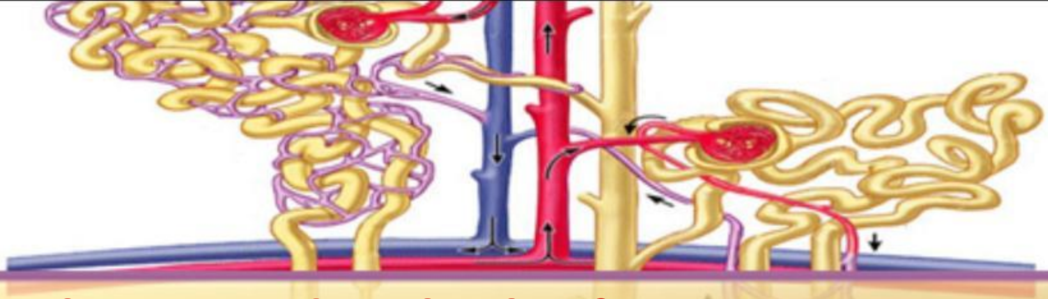
1. In the descending limb of vasa recta:

- Both **NaCl & urea** diffuse from renal medulla to the blood.

Due to their high concentration in renal medulla.

- **Water** leaves the descending limb to the hypertonic medulla.

Due to the hydrostatic pressure in the descending limb is more than osmotic pressure of plasma proteins.



2. In the ascending limb of vasa recta:

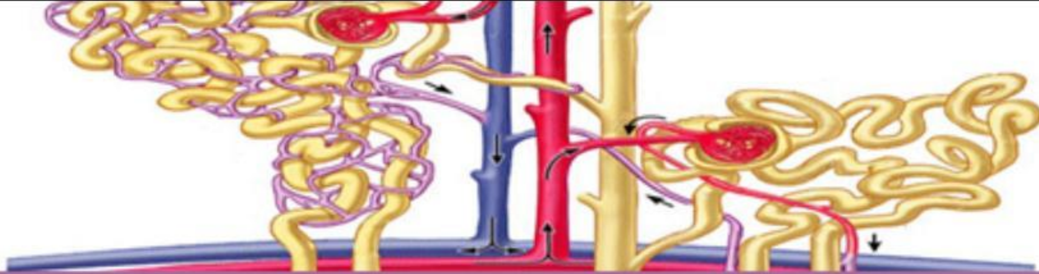
- Some of **NaCl & urea** diffuse out into the medullary interstitium
- ***Due to their high concentration in the ascending limb of vasa recta.***
- **Water** is reabsorbed into the ascending limb.
- ***Due to increased concentration of plasma proteins.***

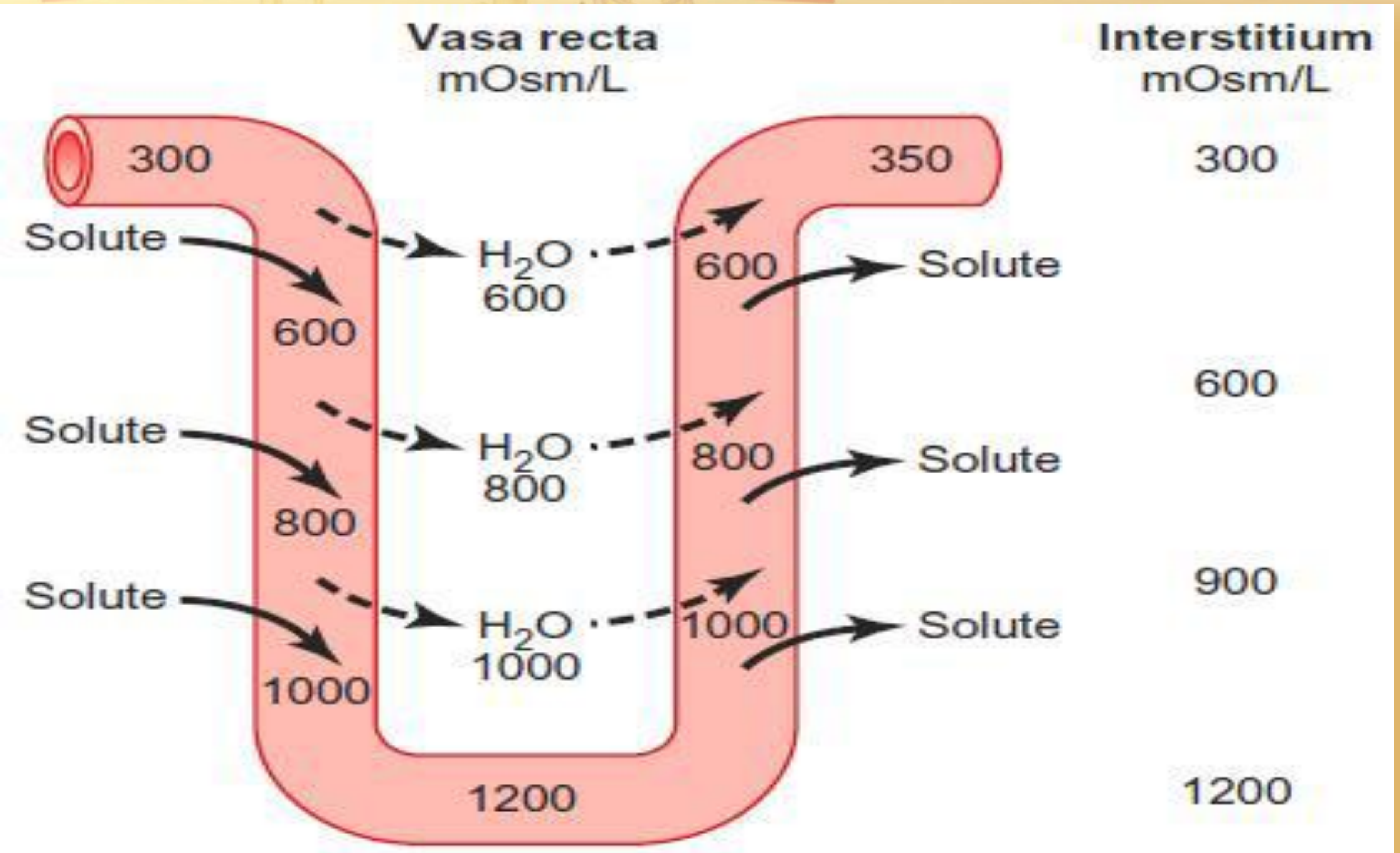
Reabsorbed water represents the water that leaves the descending loop of Henle & the collecting ducts.

- So, water absorbed in the vasa recta > water leaves the vasa recta.

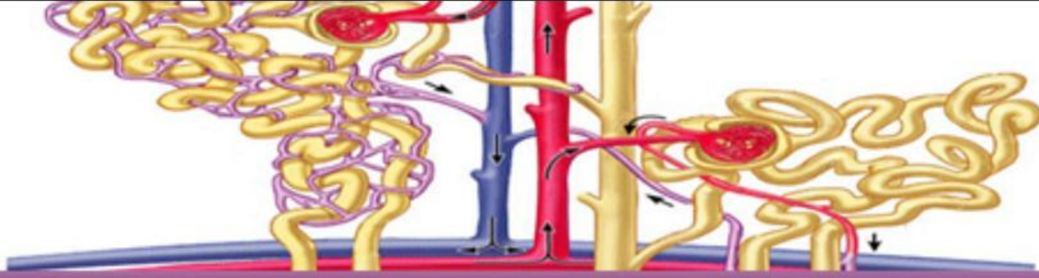
Unique characters of vasa recta:

1) **S**ame **high** permeability in both limbs.
2) **S**luggish circulation to allow exchange.
3) Low pressure. (slow & Low)





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



Unique characters present in the medulla

1. Medullary interstitial fluid is **hyperosmotic**.

- The hyper-osmolality of renal medulla is important to produce concentrated urine, because without this mechanism even large doses of ADH cannot produce such concentrated urine.

2. Many of fluids run in opposite directions, parallel to and near to reach other(**countercurrents**).

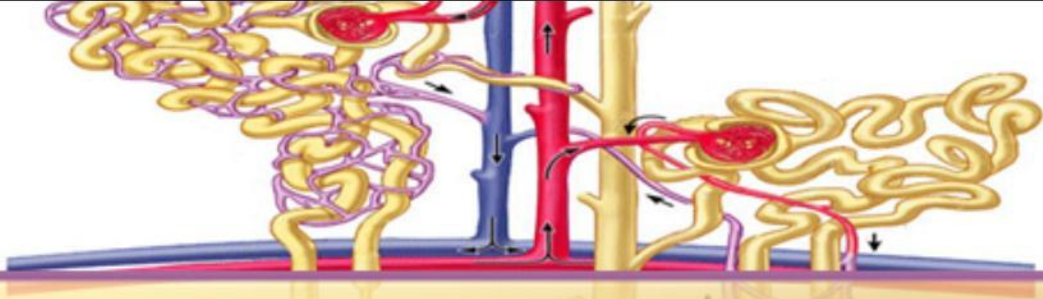
3. Difference in permeability of both two limbs of the loop.

4. Source of energy mostly derived from ATP (for sodium pump).

➢ **N.B. Causes of hyperosmolarity of renal medullary interstitium:**

1) Countercurrent mechanisms (**60%** of hyperosmolarity).

2) Urea cycle (**40%** of hyperosmolarity).



Urea cycle (Re circulation of urea)

Definition: Passive diffusion of **urea** following **water** from the medullary collecting ducts into the medullary interstitium due to its concentration gradient.

Steps:

1. Water reabsorption from the medullary CD by the high osmolarity of renal medulla ⇨ ⇧ concentration of urea in CD.

2. Urea diffuses from **CD to renal medullary interstitium** (following water reabsorption helped by ADH).

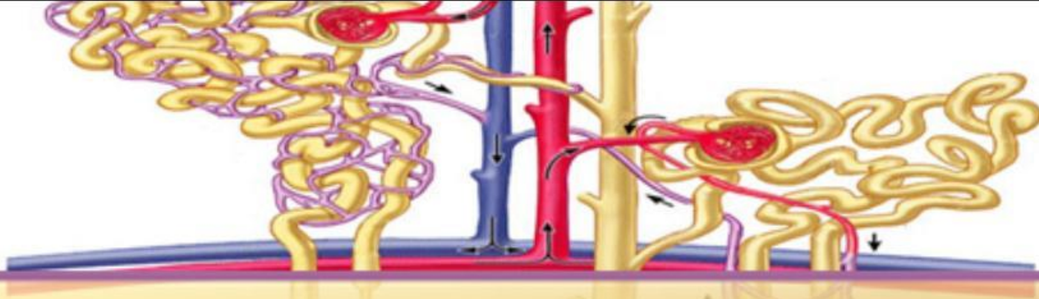
This increase the osmolarity in renal medulla.

3. Then, urea enters from renal medullary interstitium to the lumen of the *descending and thin ascending parts of loop of Henle.*

4. Then, urea is **trapped** inside the lumen of **thick ascending limb.**

This part is **impermeable** to H_2O & urea.

5. Urea **re-circulation** again till it reaches the *medullary collecting ducts* to start a new cycle and so on.



Importance:

1) It is responsible for **40%** of hypertonicity of renal medulla *(add 500 mosmol/liter to renal medulla).*

2) It plays important role in **urine concentration**

N.B. The only parts that are **permeable** to urea are **medullary collecting duct**,

descending & **thin ascending limb** of Henle's loop & **PCT** (partial permeable).

But **Thick ascending** part of loop of Henle, **DCT** & **cortical** collecting tubules are all **impermeable** **to urea**.