
بسم الله الرحمن الرحيم


Renal Physiology
Water handling by the renal tubules
Urinary concentration & dilution.

وَفَوْقَ كُلِّ

ذِي عِلْمٍ

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يوسف(٧٦)

Water reabsorption

Water reabsorption is a passive process that occurs through the whole nephron.

It is of 2 types:

1- Obligatory.

2- Facultative.

1 - Obligatory water reabsorption

87% of filtered water is reabsorbed by osmosis.

Independent of ADH

2- Facultative water reabsorption

- 13%
- Under control of ADH.
- Occurs In Late DCT& Cortical CD

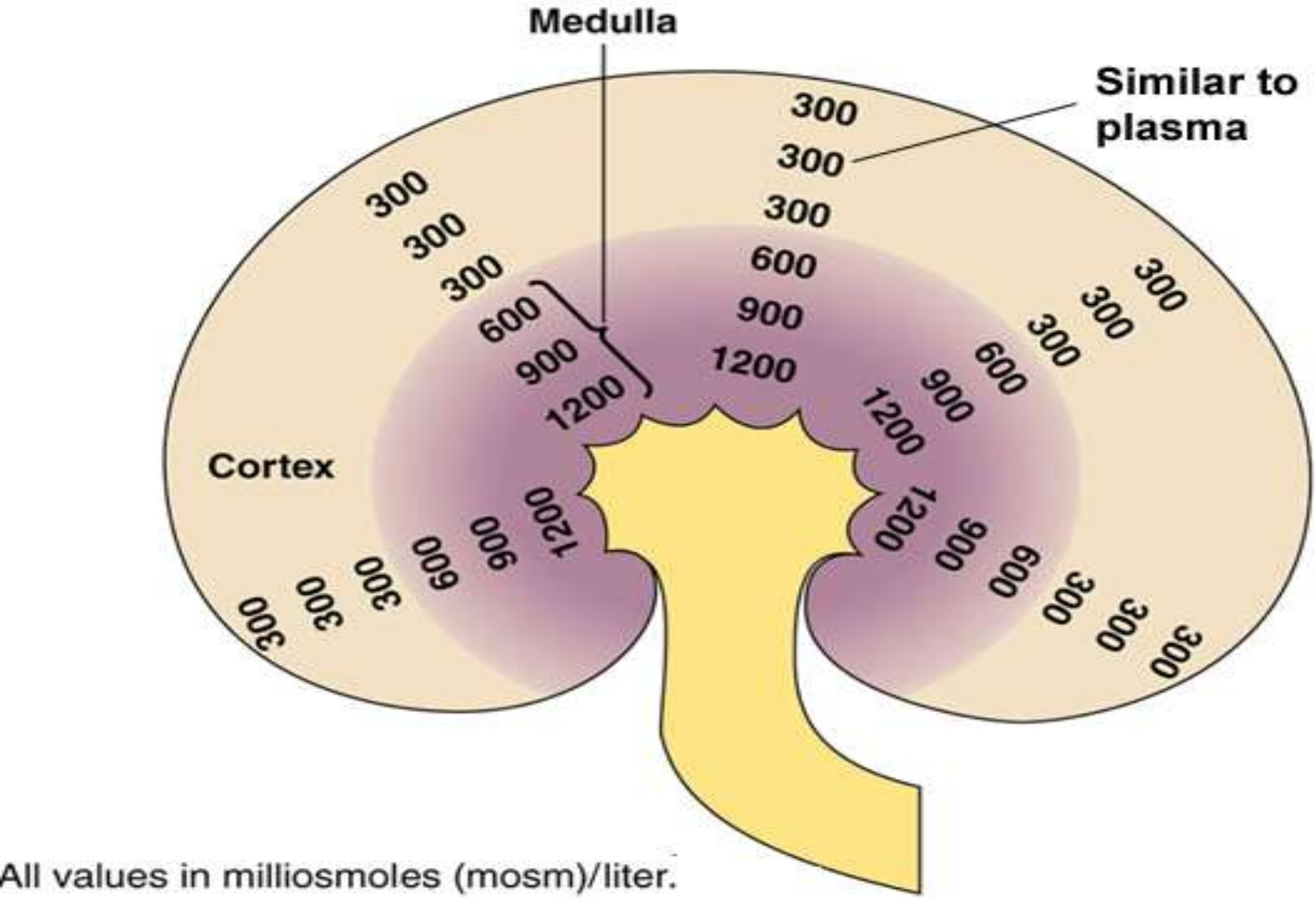
Water transport along the nephron

Segment	% filtered load reabsorbed	Mechanism of H_2O reabsorption	Hormones that regulate H_2O permeability
Proximal tubule	65	Passive	None
Descending loop of Henle – Early DCT	15 - 20	Passive	None
Ascending loop of Henle & Early Distal tubule	0	No water reabsorption	None
Late distal tubule & collecting duct	~5-14	Passive	ADH

Water Reabsorption in PCT

- 65% of filtered water is reabsorbed in PCT
- Extrusion of Na^+ from the renal cell to peritubular space → Increases osmolality of peritubular space → Drags water by osmosis
- Filtrate remains iso-osmotic (Equal quantity of water & solute are absorbed)

Hyperosmotic medullary interstitium



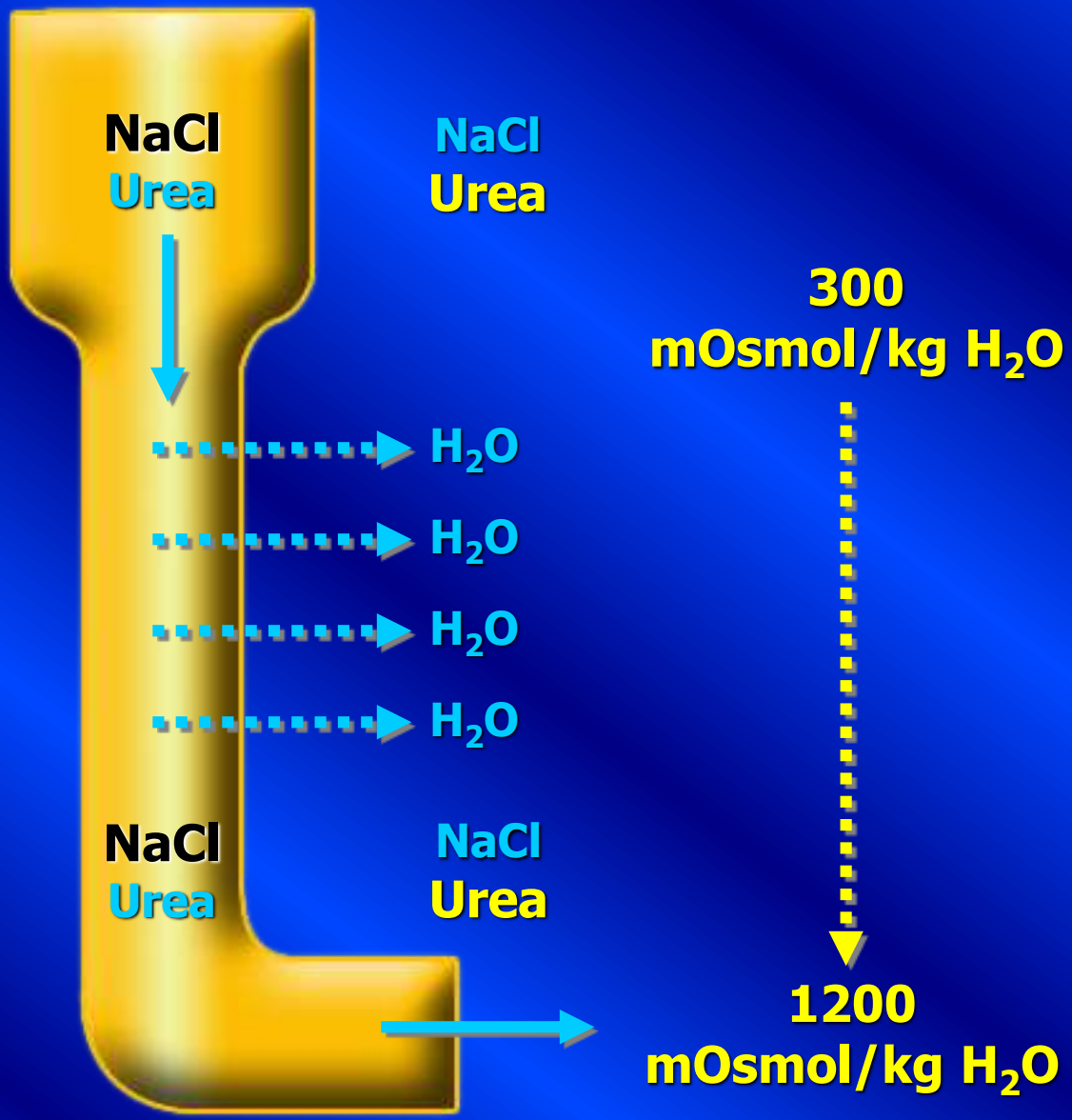
The Loop of Henle

Thin descending loop

Major function = H_2O reabsorption

- At start of descending loop osmolarity is same as plasma (~300 mOsm)
- At end of descending loop osmolarity = 1200 mOsm
- Not permeable to solutes reabsorption

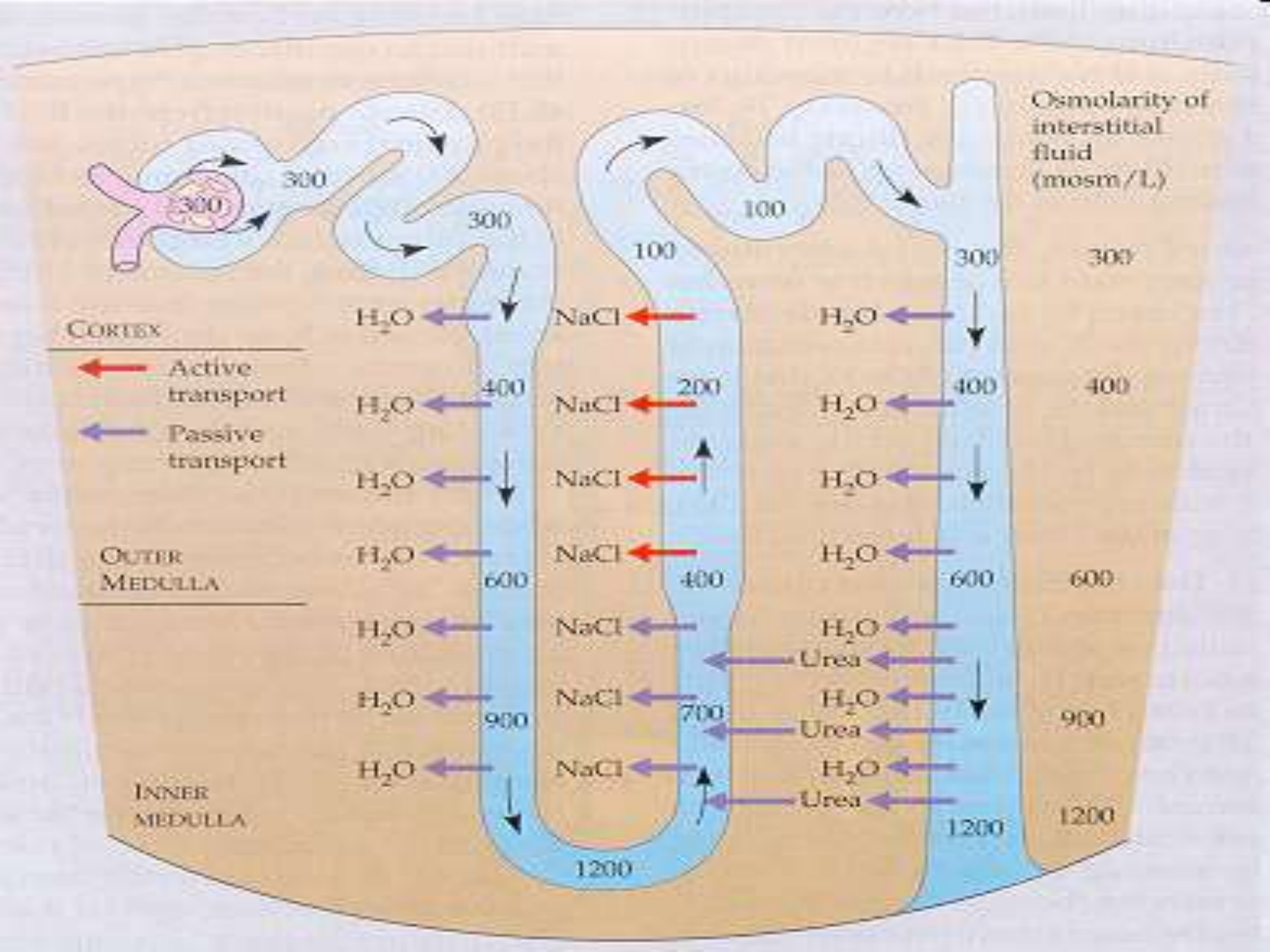
Concentrating segment



Diluting segments (LoH + DCT)

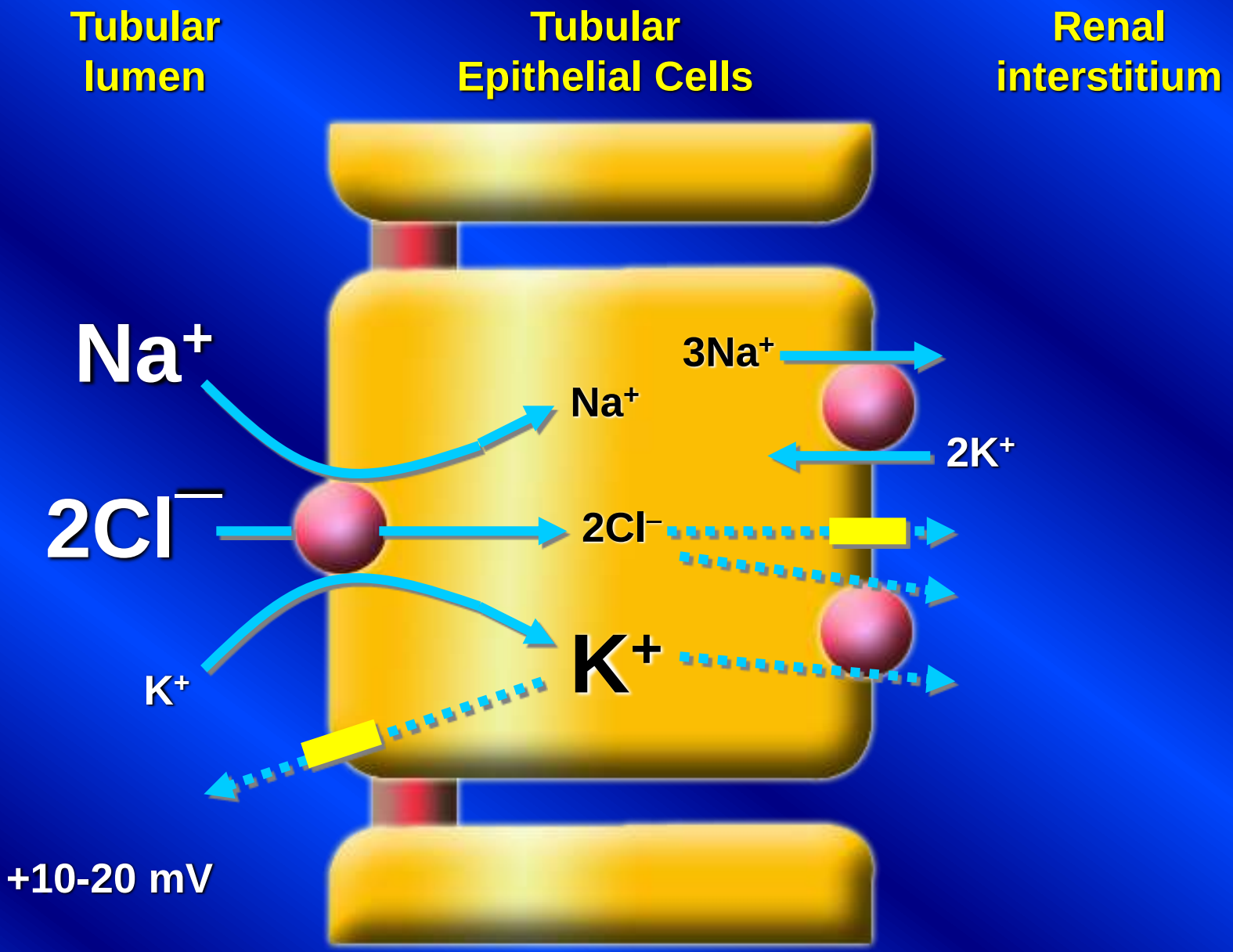
Thin ascending loop

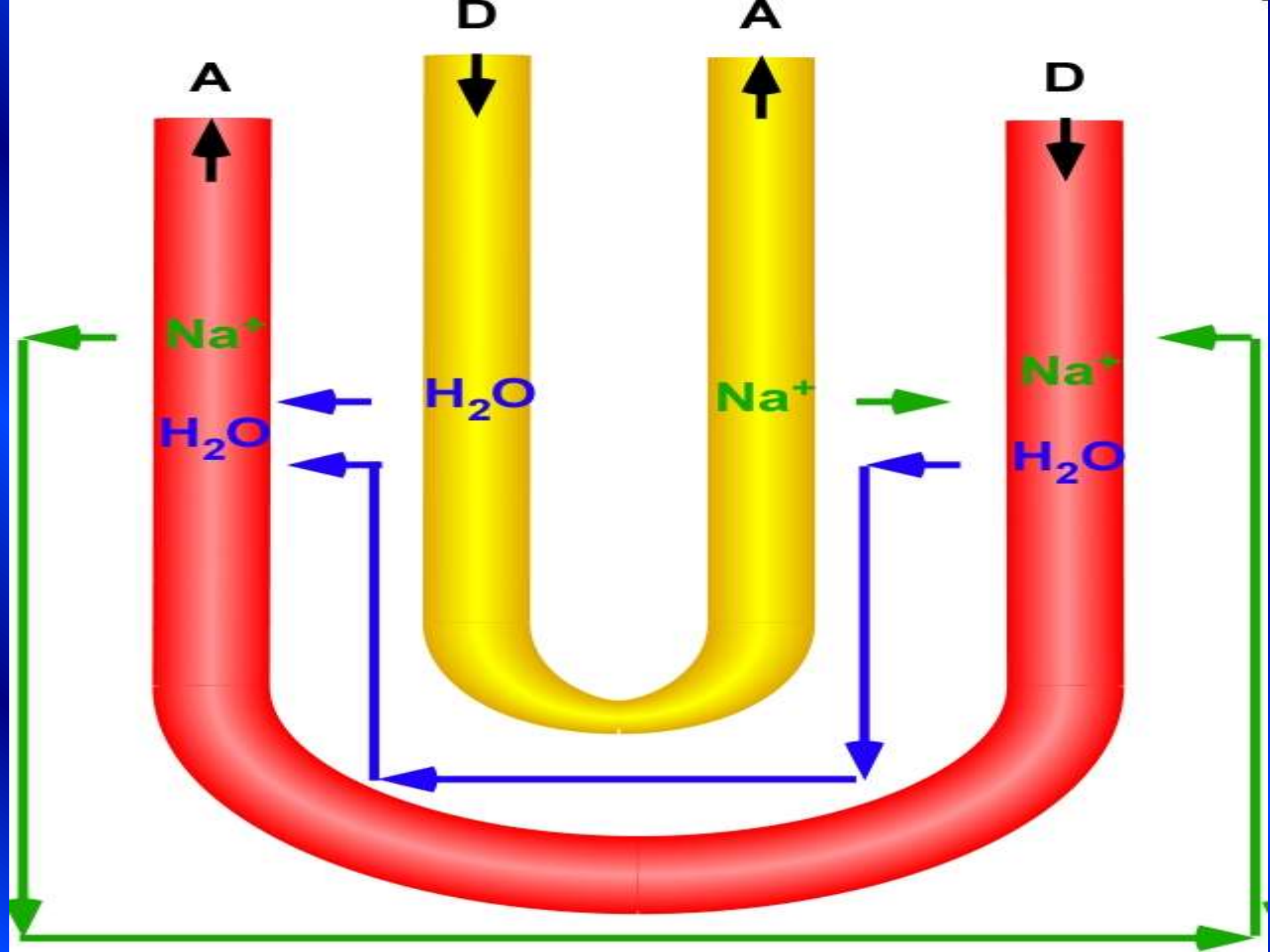
- No H_2O reabsorption
- Increases solute reabsorption (mainly NaCl)
- This part of the loop is very permeable to Na^+ and Cl^-
  - Passive diffusion out of tubule
  - As NaCl diffuses out of the tubule, the fluid becomes more dilute due to the movement of only solutes and not the H_2O.


Osmolarity of interstitial fluid (mosm/L)
300
300
300
100
100
300
300
400
200
400
400
600
400
600
600
900
700
900
1200
1200
CORTEX
Active transport
Passive transport
OUTER MEDULLA
INNER MEDULLA
H2O
NaCl
Urea

Thick ascending limb

- Reabsorption of NaCl from tubule to interstitial fluid is active (requiring energy).
- Na^+-K^+-$2Cl^-$ cotransport causes movement of these ions into cells from tubular lumen
- Na^+ is actively transported out of cell via Na^+-K^+ ATPase activity.
- Cl^- increases in cell due to the cotransporter (Na^+-K^+-$2Cl^-$ cotransport). Therefore Cl^- moves out of cell passively through Cl^- channels and K^+ - Cl^- cotransport.
- NaCl reabsorption acts to dilute urine
- Osmolarity at the end of thick ascending limb is near 100 mOsm and is dilute compared to plasma, which is ~300 mOsm


Tubular lumen
Tubular Epithelial Cells
Renal interstitium
Na+
2Cl−
K+
Na+
2Cl−
K+
3Na+
2K+
+10-20 mV


D
A
A
D
Na+
H2O
H2O
Na+
Na+
H2O

Distal Tubule and Collecting Duct

Same function as proximal tubule but absorbs less and has a smaller capacity:

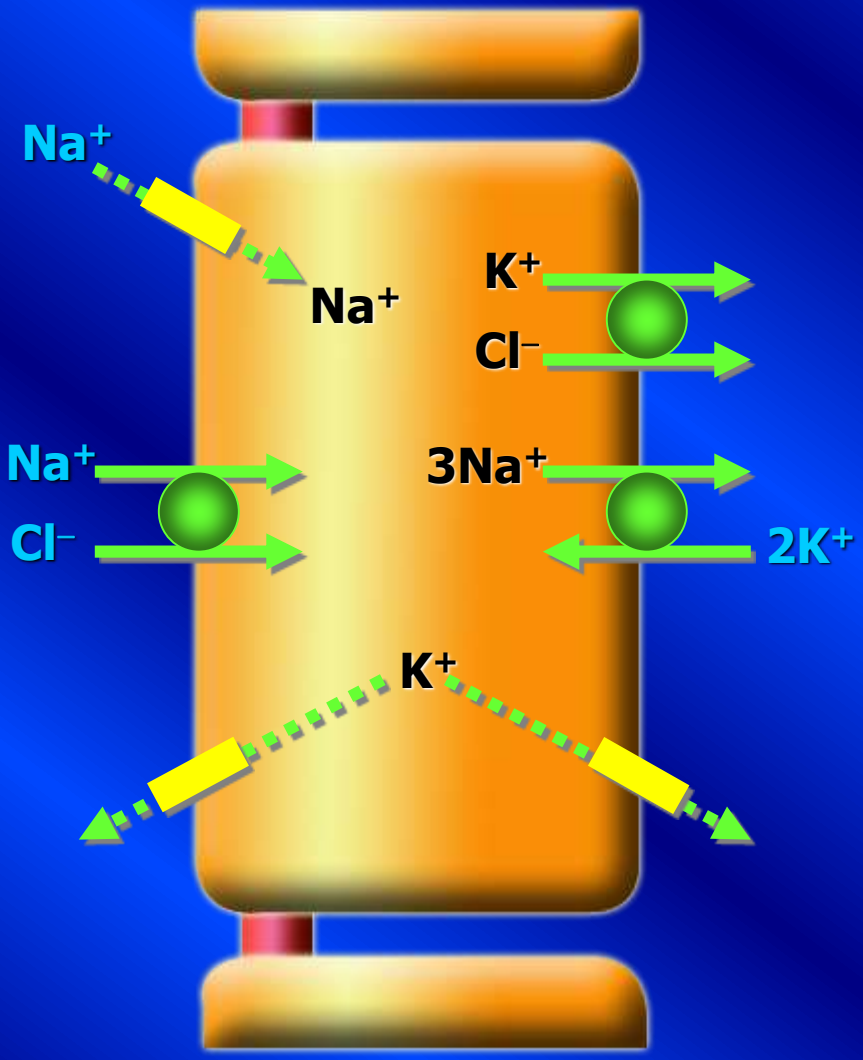
- Thoughout distal tubule Na^+ is actively reabsorbed and K^+ secreted
- Cl^- also reabsorbed

In distal tubule, Na^+- Cl^- cotransporter is responsible for Na^+ reabsorption along with Cl^-. This co-transport mechanism is different from the co-transport mechanism in the loop of Henle (Na-K-2Cl).

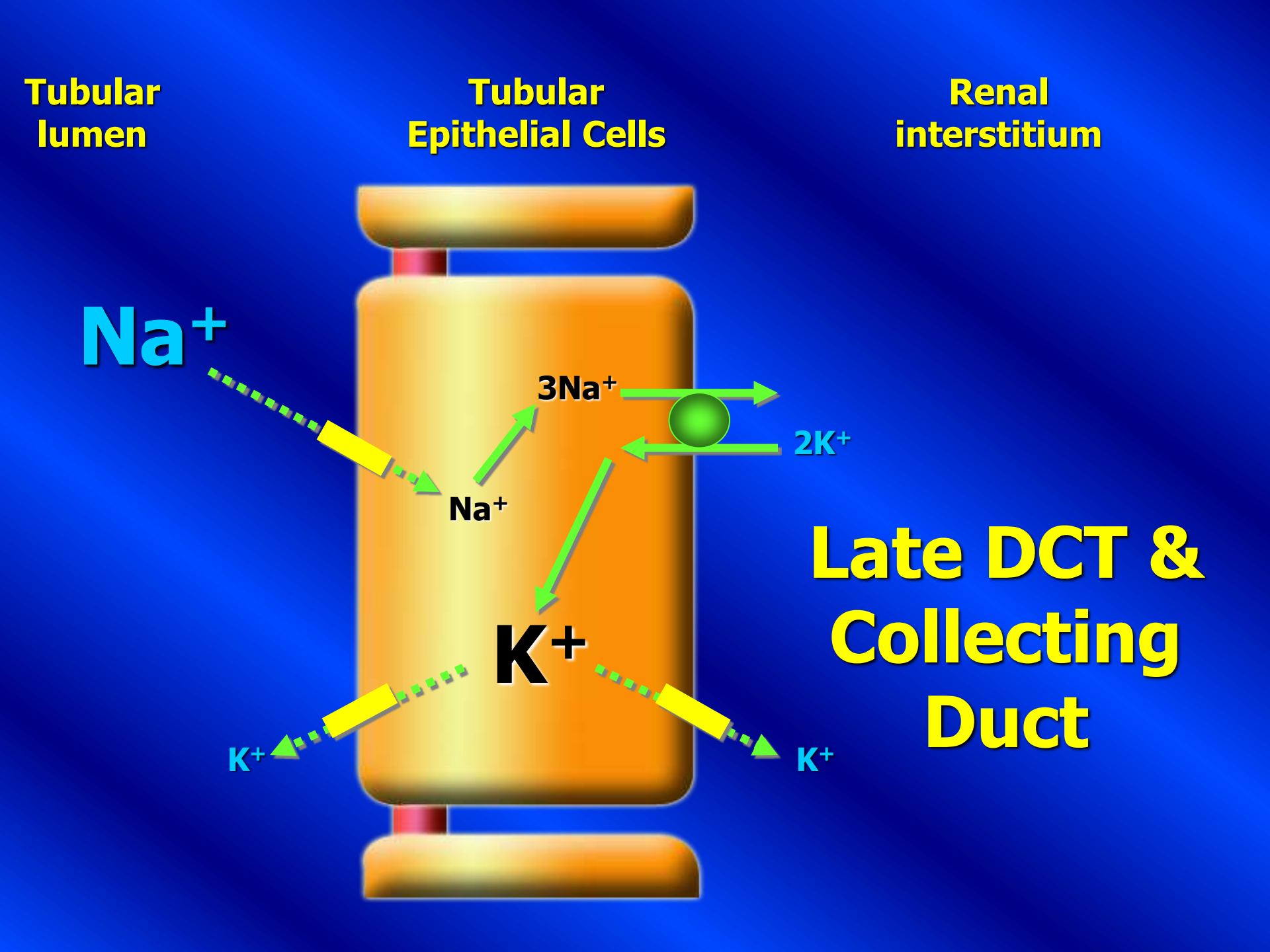
Tubular lumen

Tubular Epithelial Cells

Renal interstitium



Early Distal Tubule


Tubular lumen
Tubular Epithelial Cells
Renal interstitium
Na+
3Na+
2K+
Na+
K+
K+
K+
Late DCT & Collecting Duct

Diuresis

An increase in the rate of urine output.

Types:

1- Water diuresis.

2- Osmotic diuresis.

3- Pressure diuresis.

1- Water diuresis:

Drinking large amounts of water.

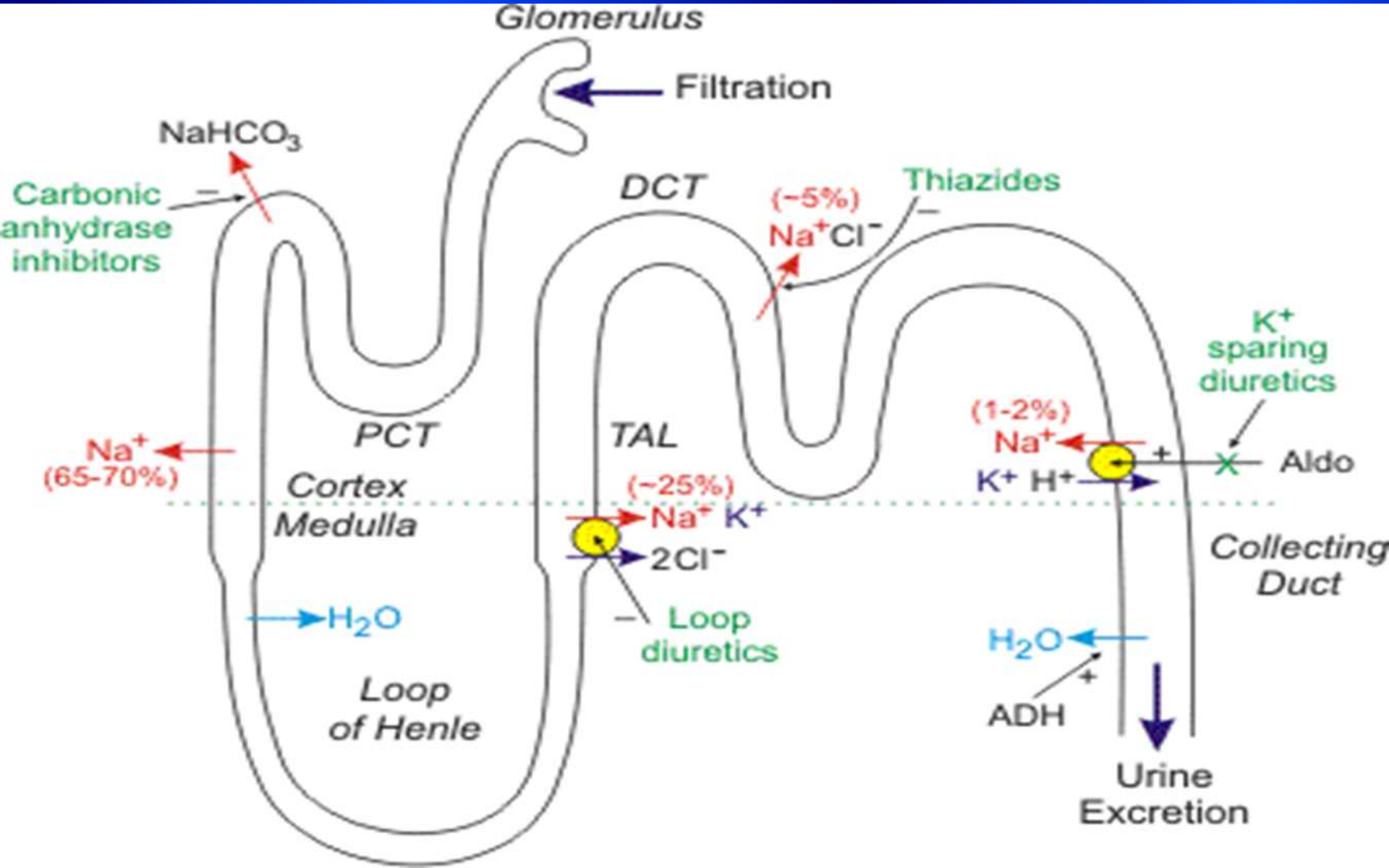
Begins after about 15 min. & reaches max. in about 40 min.

2- Osmotic diuresis:

Presence of large quantities of unabsorbed solutes . As is diabetes mellitus

3 – Medically induced diuresis (Diuretics).

Diuretics


Glomerulus
Filtration
NaHCO3
Carbonic anhydrase inhibitors
DCT
(~5%)
Na+Cl−
Thiazides
K+ sparing diuretics
(1-2%)
Na+
K+ H+
Aldo
Na+ (65-70%)
PCT
TAL
Cortex
Medulla
(~25%)
Na+ K+
2Cl−
Loop diuretics
Collecting Duct
H2O
Loop of Henle
H2O
ADH
Urine Excretion

Urine Concentration

Maximum urine concentration is 1200 mOsmol/L

Urine concentrating mechanisms are important for survival – saves H_2O

Changes in urine Osmolality are brought about by changes in ADH → mainly collecting ducts

- ADH – "antidiuretic hormone" is produced in the hypothalamus of brain and stored in the posterior pituitary gland
  - change in blood or plasma Osmolality affect ADH release
  - ↑ Osmolality → ↑ ADH release and ↑ H_2O reabsorption in collecting ducts
  - ↓ Osmolality → ↓ ADH release and ↓ H2O reabsorption in collecting ducts

Concentration Mechanism

Aim: Excess solute excretion

REQUIREMENT:

- Anatomical arrangement of Loop of Henle, Collecting Ducts and Vasa Recta.
- Parallel, adjacent / close to each other, with opposite flow “countercurrent”
- Different permeabilities

MECHANISM:

- Countercurrent multiplier (Loop of henle)
- Countercurrent exchanger (Vasa recta)
- Hyperosmotic medullary interstitium (Sodium and urea)
- Role of ADH

Countercurrent Multiplier Mechanism

- Active reabsorption of Na^+ in the thick ascending Loop of Henle (LoH) is responsible for initiation of this mechanism.
- Remember that the thin ascending LoH is totally impermeable to water, so water will not follow Na^+ in this part of the nephron. So, the tubular fluid will become dilute.

Countercurrent Multiplier Mechanism (Continued……)

- Now the situation is that the fluids in the interstitium and descending LoH are concentrated while the fluid in the thick ascending LoH is dilute and the concentration difference between these fluids is 200 mOsm.
- As the tubular fluid continues to flow forward, isosmotic fluid (300 mOsm) from PCT enters the descending LoH and dilute fluid from thick ascending LoH moves out to DCT.
- Active reabsorption of Na+ will continue in the thick ascending LoH without reabsorption of water, making the tubular fluid more dilute in this segment.

Function of Vasa recta

- Blood flow is very sluggish (1 – 2%)
- Important to give nutrients and oxygen to the medulla
- Works as countercurrent exchanger to maintain Medullary vertical osmotic gradient.

Diabetes Insipidus (*Disorders of urinary concentration*)

1. **Central diabetes insipidus**:

- Deficiency of ADH secretion due to lesion of the hypothalamus, hypothalamo-hypophyseal tract or posterior pituitary.

2. **Nephrogenic diabetes insipidus**:

- Inability of the kidney to respond to ADH e.g. congenital defect in the V_2 receptors in the collecting duct.

Diabetes Insipidus (Symptoms)

1) **Polyuria** : Passage of large amounts of dilute urine. (with NO glucose in urine)

2) **Polydipsia** : Drinking of large amounts of fluid.

It is the polydepsia that keeps these patients healthy. If the sense of thirst is depressed by loss of consciousness, these patients develop fatal dehydration.

	Central DI	Neprogenic DI
ADH level	Low	Normal or high
Treatment	ADH (Desmopressin)	Drugs to increase ADH sensitivity (Thiazide diuretics)

Thank you