Counter-Current Mechanisms and Renal Control of Acid-Base Balance and Nitrogenous wastes

ZCT 434- PG SEM 4, Comparative Animal Physiology

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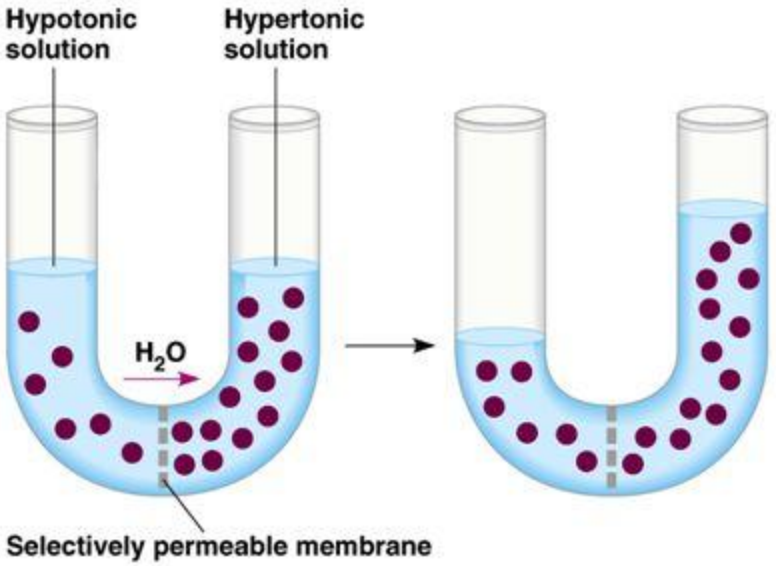
About Counter Current Mechanism

- The mechanism that the kidneys use to concentrate urine is called the counter current mechanism.
- The counter current mechanism takes place in Juxtamedullary nephron.
- The ADH promotes water reabsorption through the walls of the distal convoluted tubule and collecting duct.
- Urea reabsorbed from collecting duct to medullary interstitum produces the hyperosmotic Medullary interstitium. Reabsorption of urea will occur in the presence of ADH.
- Nephrogenic diabetes insipidus patients will have no response from the kidney to ADH.
- The function of the Countercurrent exchanger"vasa recta" is to maintain hyperosmolar medulla.
- Solutes are the particles that are dissolved in a solvent, and together they form a **solution**. ... A **hypotonic solution** is one in which the concentration of solutes is greater inside the cell than outside of it, and a **hypertonic solution** is one where the concentration of solutes is greater outside the cell than inside it.

Osmotic Concentration

- The concentration of all solutes in a solution.
- When a selectively permeable membrane separates 2 solutions, each solution can be identified as either:
  - **Hypotonic** or **Hypoosmotic**
    - The solution with the lower solute concentration.
  - **Hypertonic** or **Hyperosmotic**
    - The solution with the higher solute concentration.
  - **Isotonic** or **Isoosmotic**
    - The solute concentrations in both solutions are the same.



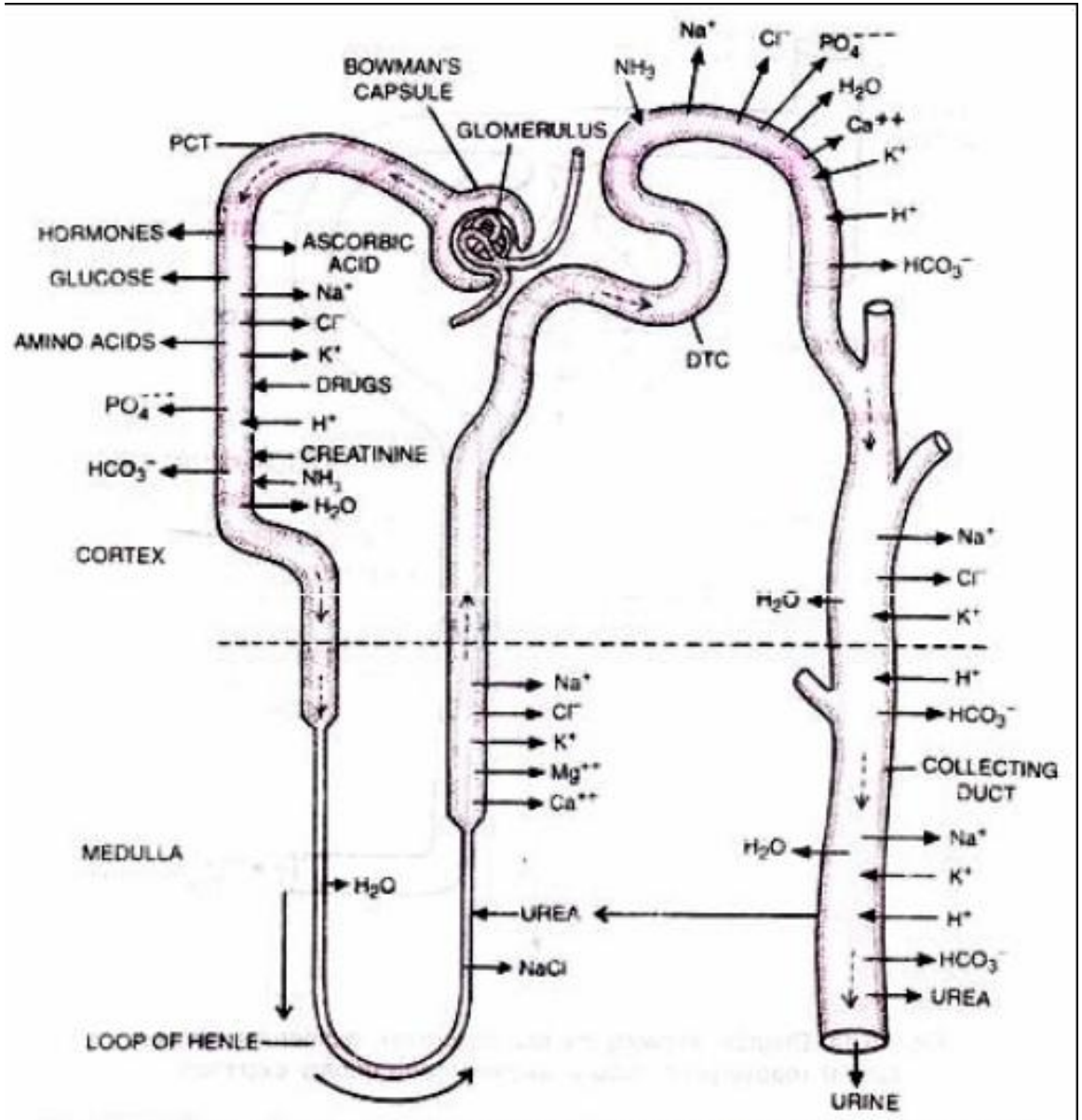
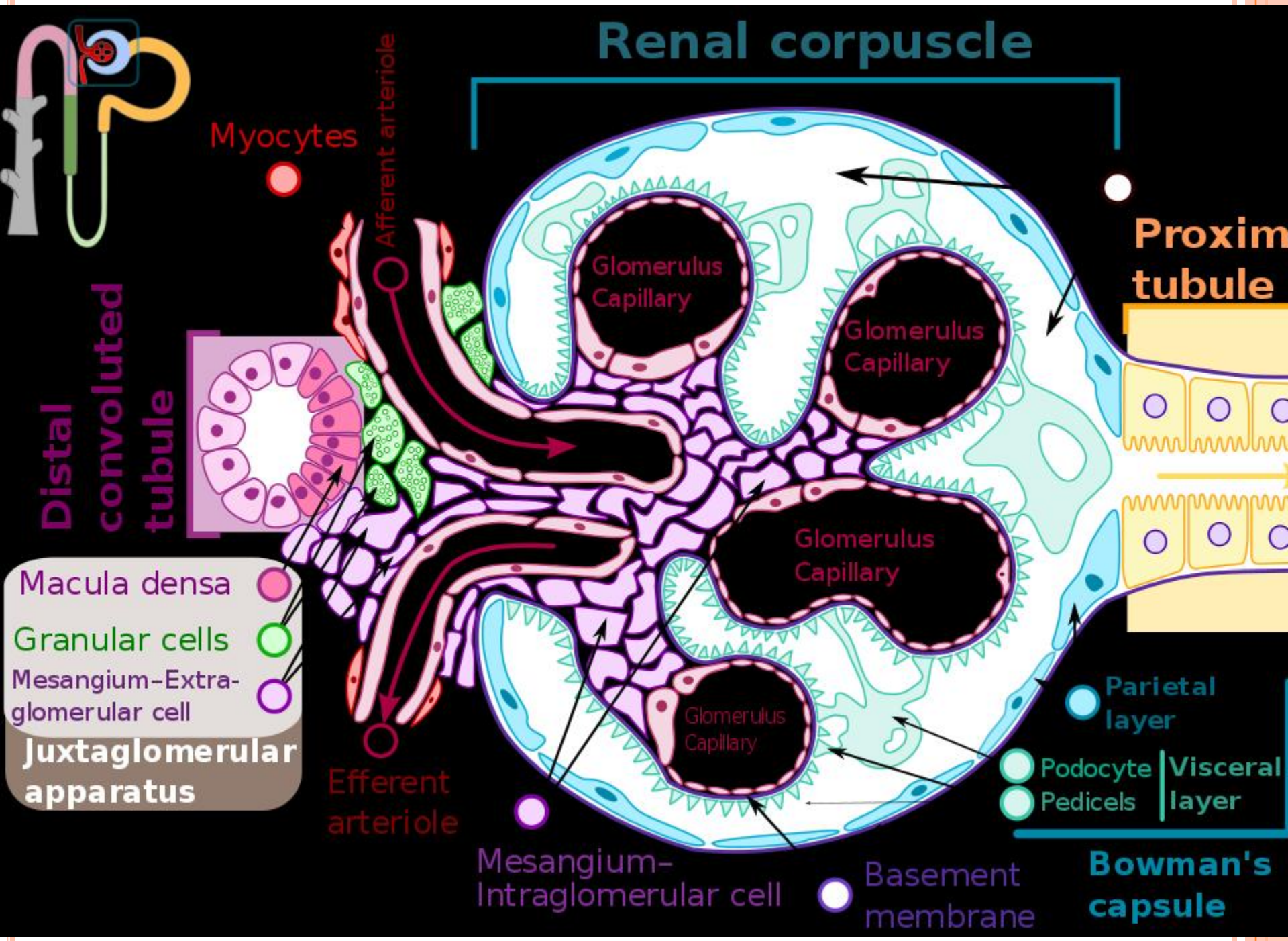
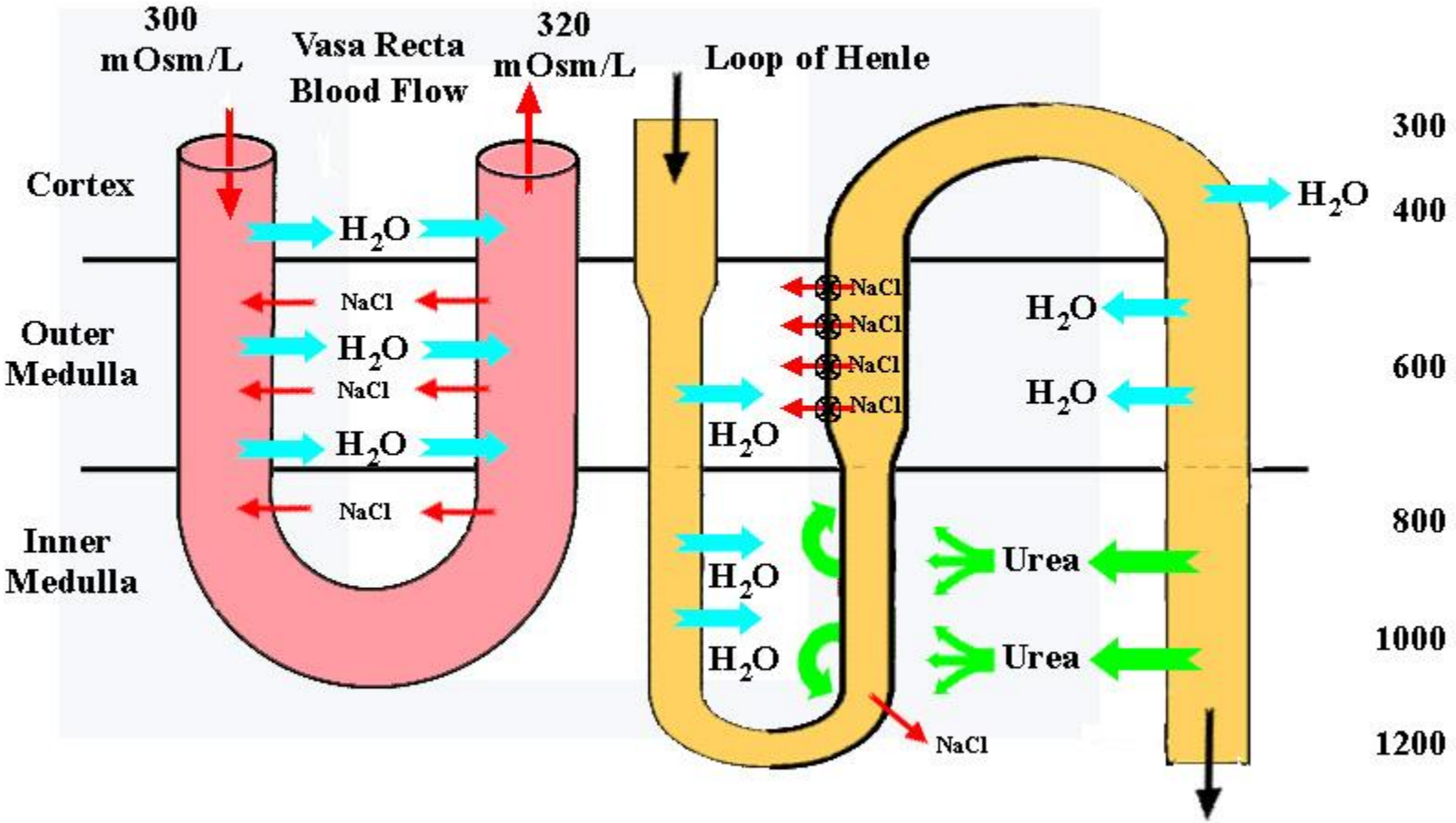


Fig. 19.15. Figure showing tubular reabsorption and secretion of major substances (Arrows indicate direction of movement of materials) in a mammalian nephron.


Renal corpuscle
Myocytes
Afferent arteriole
Glomerulus Capillary
Glomerulus Capillary
Glomerulus Capillary
Glomerulus Capillary
Proxim tubule
Distal convoluted tubule
Macula densa
Granular cells
Mesangium–Extra-glomerular cell
Juxtaglomerular apparatus
Efferent arteriole
Mesangium–Intraglomerular cell
Basement membrane
Parietal layer
Podocyte Pedicels
Visceral layer
Bowman's capsule

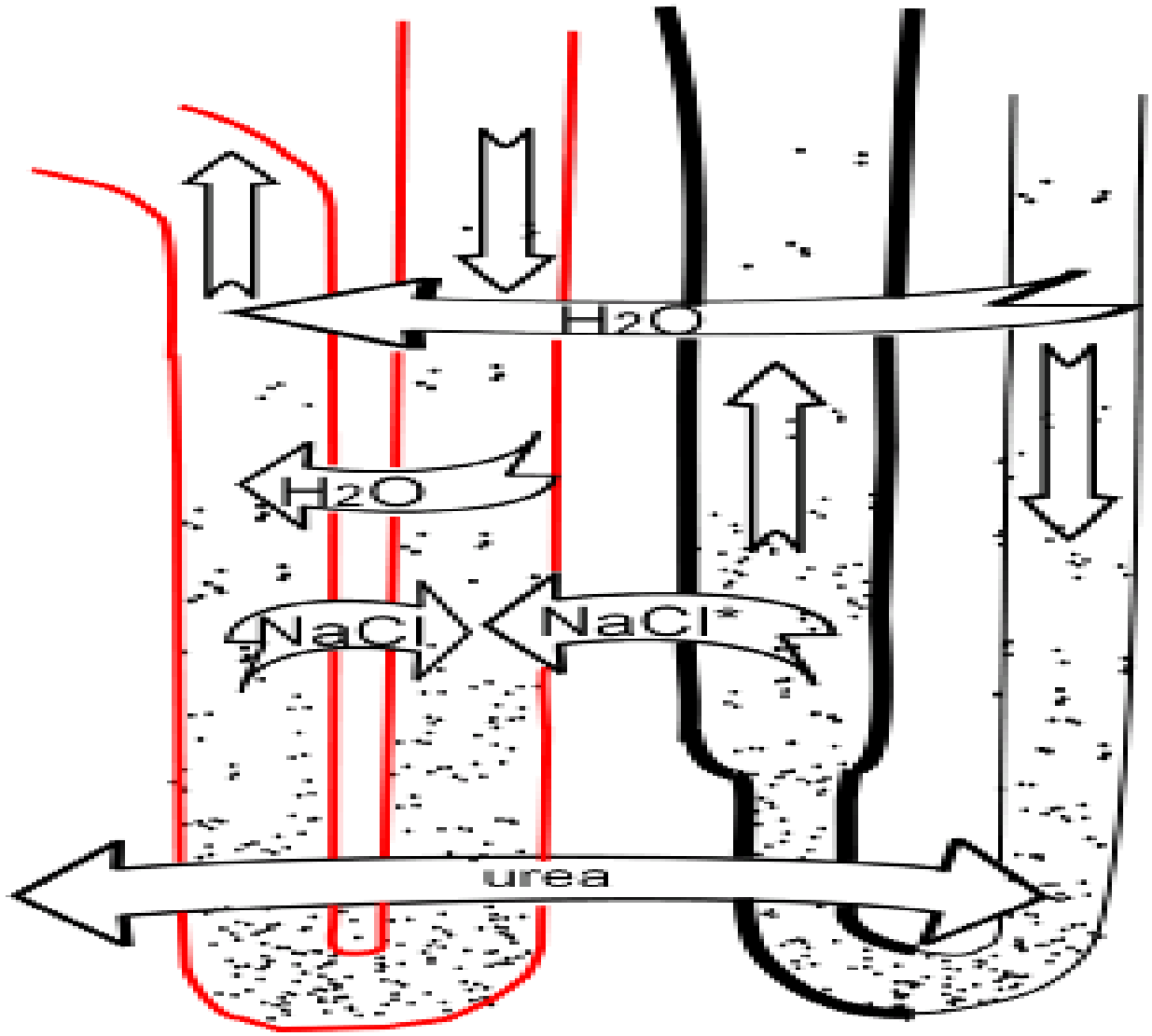
Mechanism

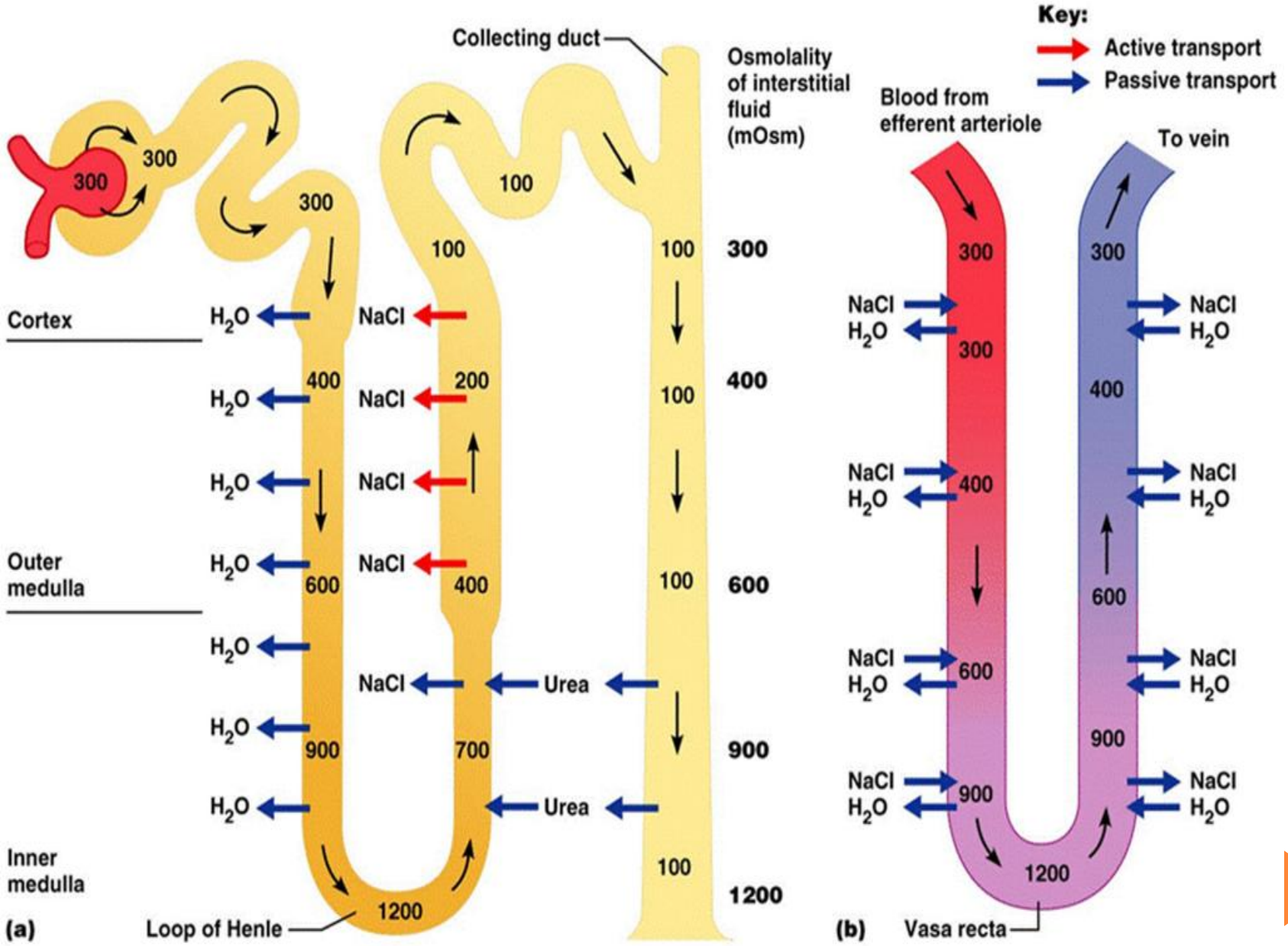
- **Step 1:** Assume that the loop of Henle is filled with a concentration of 300mOsm/L the same as that leaving the proximal tubules.
- **Step 2:** The active ion pump of the thick ascending limb on the loop of Henle reduces the concentration inside the tubule and raises the interstitial concentration.
- **Step 3:** The tubular fluid in the descending limb and the interstitial fluid quickly reach osmotic equilibrium because of osmosis of water out of the descending limb.
- **Step 4:** The Additional flow of the fluid into the loop of Henle from the proximal tubule, which causes the hyperosmotic fluid previously formed in the descending limb to flow into the ascending limb.


300
mOsm/L
Vasa Recta
Blood Flow
320
mOsm/L
Loop of Henle
Cortex
Outer
Medulla
Inner
Medulla
H2O
NaCl
H2O
NaCl
H2O
NaCl
H2O
NaCl
NaCl
NaCl
NaCl
H2O
H2O
H2O
H2O
H2O
Urea
Urea
NaCl
300
400
600
800
1000
1200

Mechanism

- **Step 5:** Additional ions pumped into the interstitium with water remaining in the tubular fluid, until a 200-mOsm/L osmotic gradient is established.
- **Step 6:** Again, the fluid in the descending limb reaches equilibrium with the hyperosmotic medullary interstitial fluid and as the hyperosmotic tubular fluid from the descending limb flows into the ascending limb, still more solute is continuously pumped out of the tubules and deposited into the medullary interstitium.
- **Step 7:** These steps are repeated over and over, with net effect of adding more and more solute to the medulla in excess of water, with sufficient time, this process gradually traps solutes in the medulla and multiplies the concentration gradient established by the active pumping of ions out of the thick ascending limb , eventually raising the interstitial fluid osmolarity to 1200- 1400 mOsm/L .


H2O
H2O
NaCl
NaCl*
urea

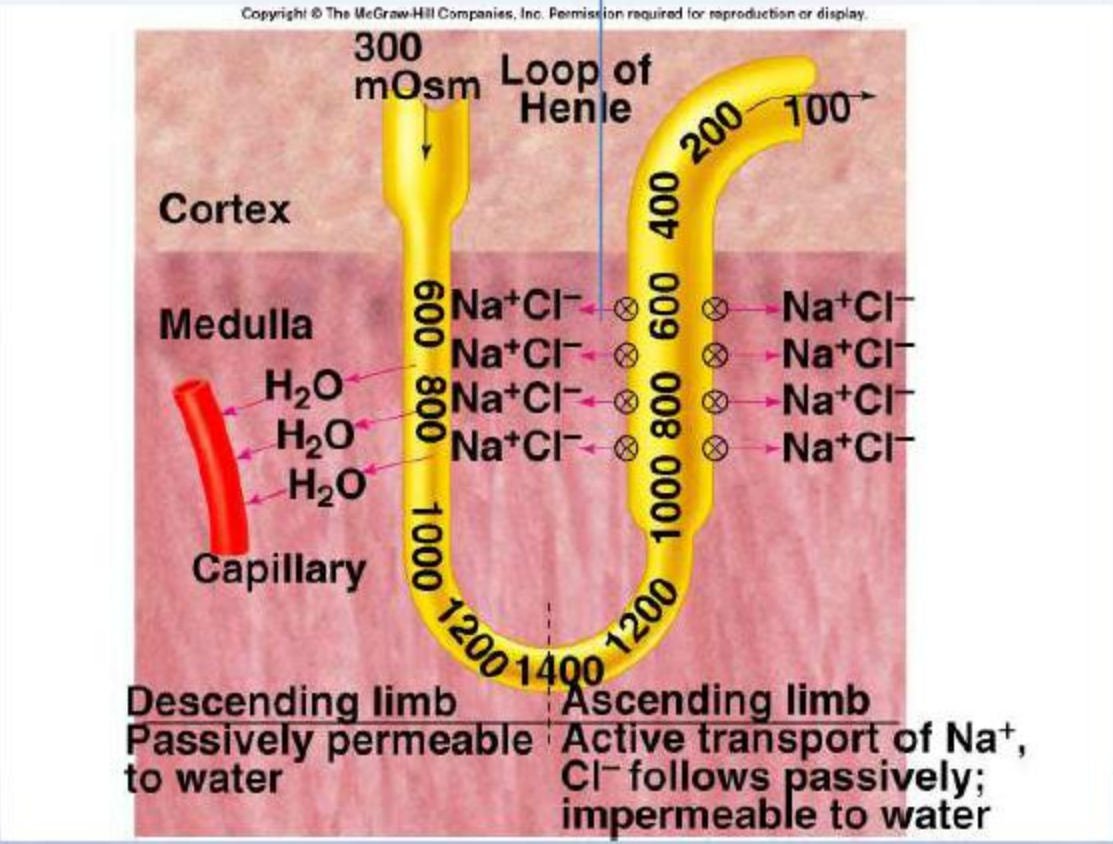

Collecting duct
Osmolality of interstitial fluid (mOsm)
300
300
300
100
100
100
300
Cortex
H_2O
NaCl
400
H_2O
NaCl
200
100
400
H_2O
NaCl
100
Outer medulla
H_2O
NaCl
600
400
100
600
H_2O
NaCl
Urea
H_2O
900
700
900
H_2O
Urea
Inner medulla
100
1200
(a)
Loop of Henle
1200
Key:
Active transport
Passive transport
Blood from efferent arteriole
To vein
300
300
NaCl
H_2O
NaCl
H_2O
300
400
NaCl
H_2O
400
NaCl
H_2O
600
NaCl
H_2O
600
NaCl
H_2O
900
NaCl
H_2O
900
NaCl
H_2O
1200
(b)
Vasa recta

- The existence of a steep osmotic gradient in the renal medullary interstitium is the most critical in the formation of concentrated urine. The architectural organization of the renal tubules and blood vessels in the medulla constitutes counterflow systems which are essential for both generating and maintaining a high osmotic pressure of the renal medulla.
- Active NaCl transport in the thick ascending limb of Henle's loop plays the most fundamental role in the operation of the countercurrent multiplication system in the renal medulla.

- Urea is absorbed from the inner medullary collecting duct and secreted into the thin ascending limb. Maximal concentrating ability is decreased in protein-deprived animals and restored by urea.
- Urea transport occurs by a vasopressin stimulated facilitated transport process in terminal inner medullary collecting ducts. As the urea concentration in the lumen of terminal inner medullary collecting ducts exceeds that in vasa recta.

Counter current Multiplier

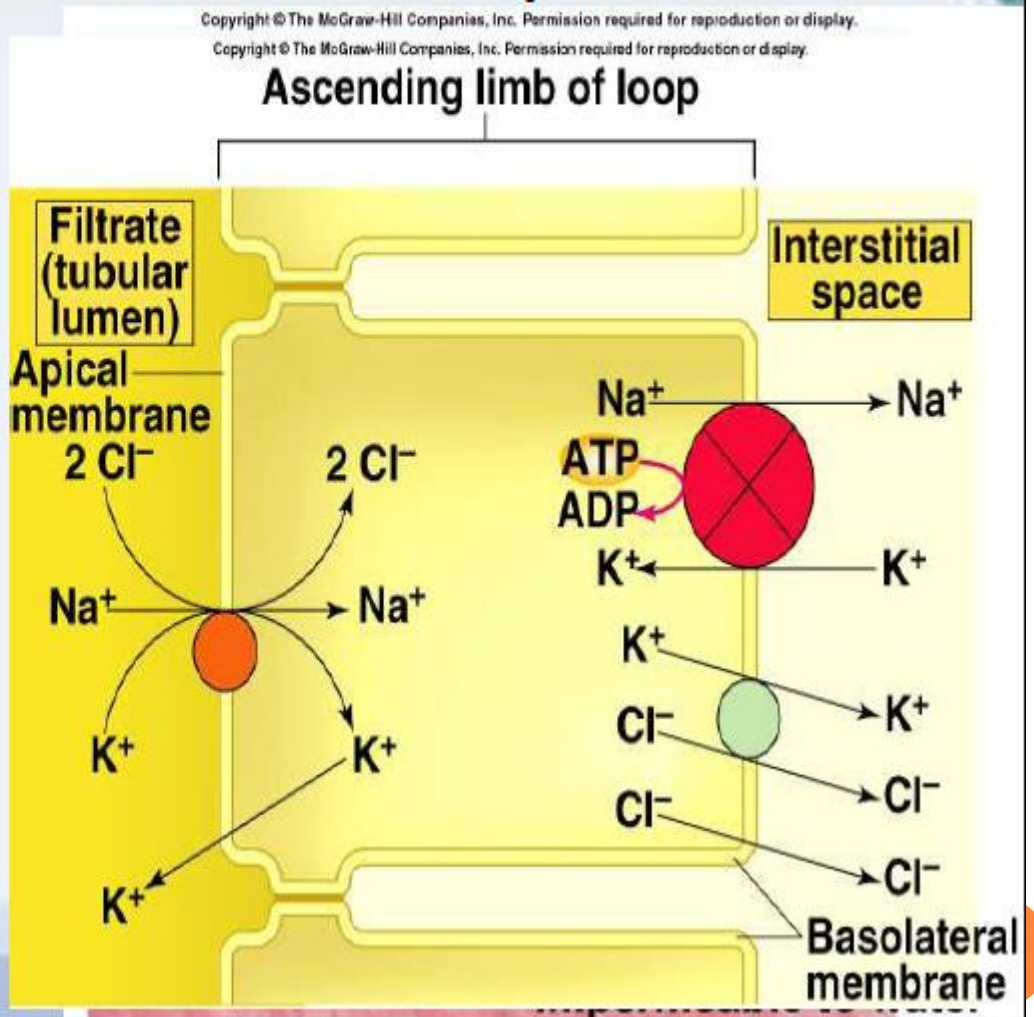
Interstitial fluid should be hypertonic for water to be reabsorbed



Counter current multiplier

Na+ is actively pumped out of the ascending limb into the interstitial fluid.

- Cl- follows Na+ passively
- Increases the Na+ and Cl- of interstitial fluid by about 4 times.
- Water seeps out of the of the descending limb into the interstitial fluid by osmosis



Counter current multipier

- Down the descending limb of the LOH, fluid becomes more concentrated due to loss of water.
- Na+ and Cl- concentration increase as fluid turns and heads on towards the ascending limb.
- All the way up osmotic pressure of fluid in LOH is almost equal to the osmotic pressure in interstitial fluid.
- The fluid again passes through hypertonic interstitial fluid loosing water again until into the collecting duct.
- The final product in the CD is urine.

Renal Control of Acid-Base Balance

Renal Control of Acid-Base Balance

- The kidneys control acid-base balance by excreting either acidic or basic urine
- Excreting acidic urine reduces the amount of acid in extracellular fluid
- Excreting basic urine removes base from the extracellular fluid

The kidneys regulate extracellular fluid H+ concentration through three fundamental

mechanisms:

(1)secretion of H+

(2) reabsorption of filtered HCO3

(3) production of new HCO3

- In acidosis, the kidneys do not excrete HCO3 into the urine but reabsorb all the filtered
- HCO3 and produce new HCO3 which is added back to the extracellular fluid
- This reduces the extracellular fluid H+ concentration back toward normal

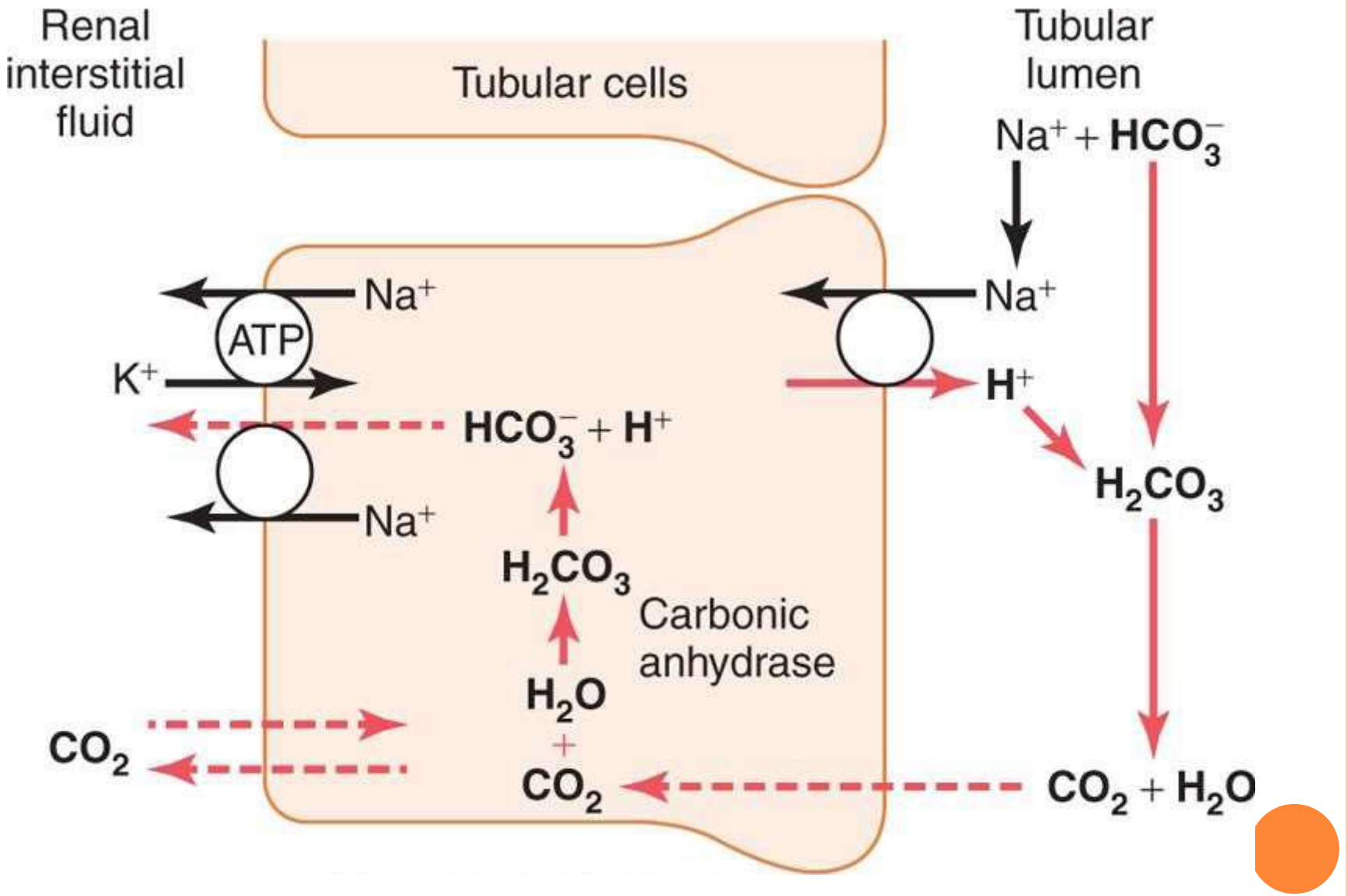
In alkalosis the kidneys fail to reabsorb all the filtered HCO_3 thus increasing the excretion of HCO_3

- Because HCO_3 normally buffers H^+ in the extracellular fluid, this loss of HCO_3 is the same as adding H^+ to the extracellular fluid.
- In alkalosis the removal of HCO_3 raises the extracellular fluid H^+ concentration back towards normal

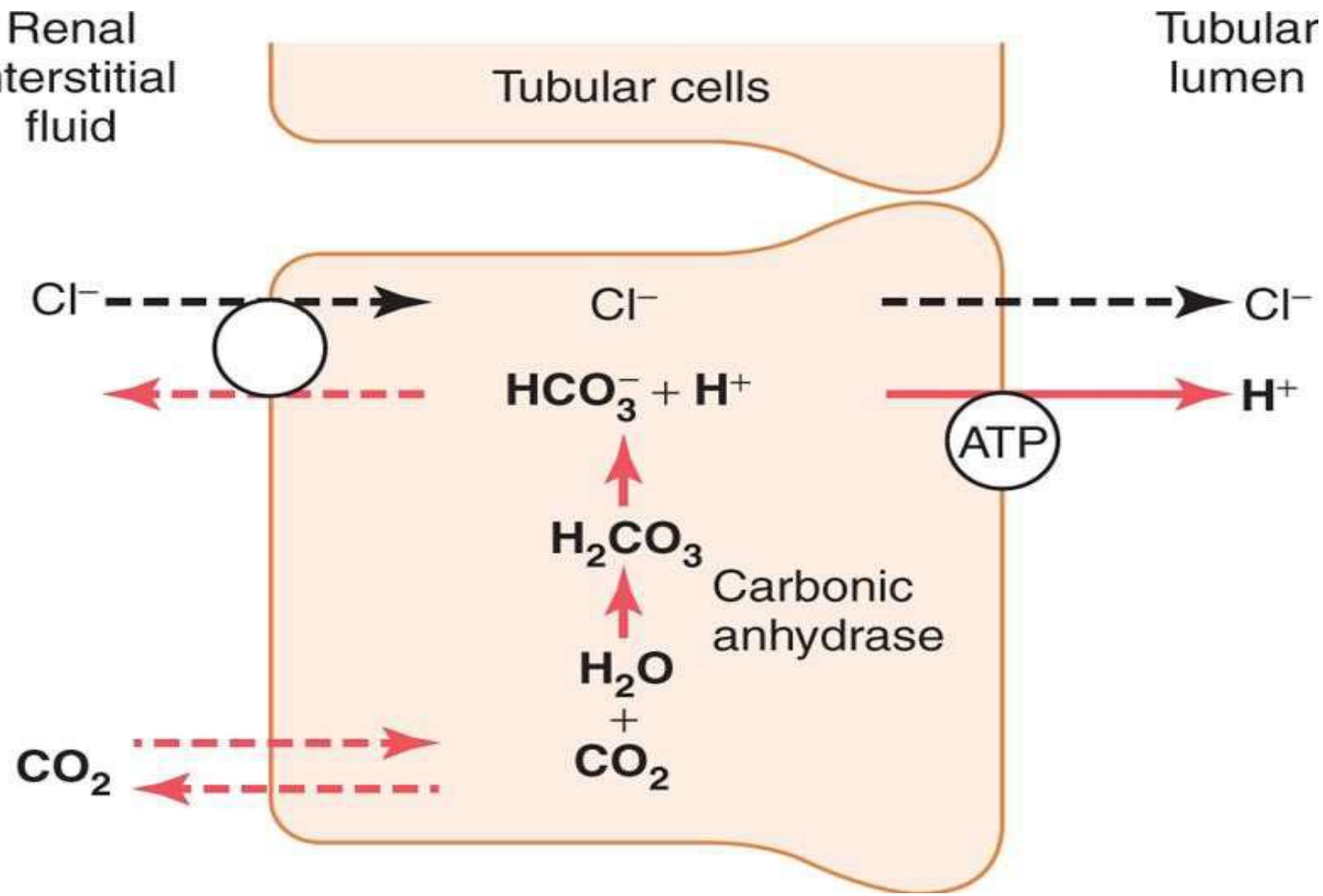
Secretion of H+ and Reabsorption of Bicarbonate by the Renal Tubules

- About 80 to 90 percent of the bicarbonate reabsorption and H^+ secretion occurs in the proximal tubule

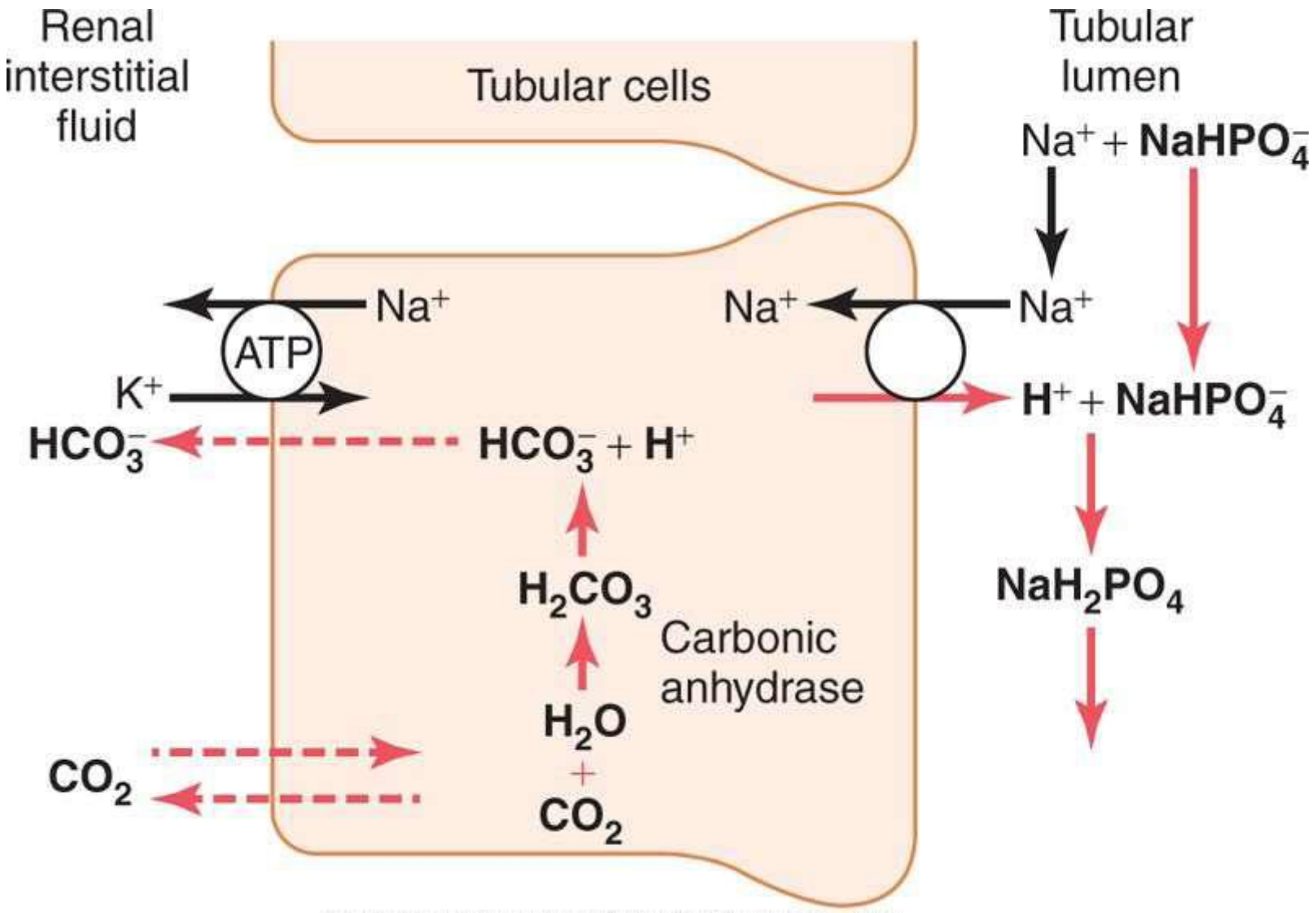
Mechanism of Hydrogen ion secretion and Bicarbonate Reabsorption



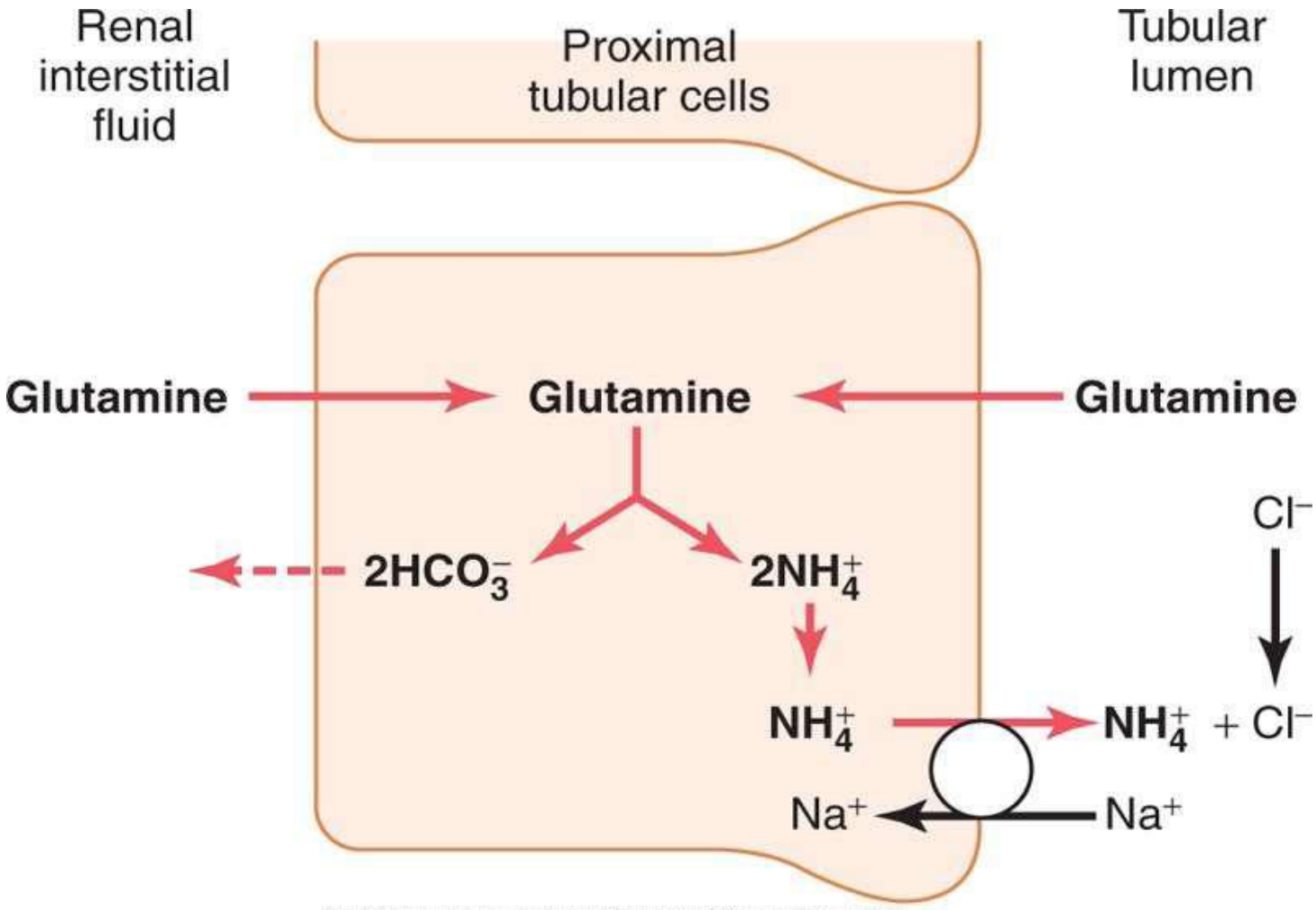
Primary Active Secretion of H+ in the Intercalated Cells of Late Distal and Collecting Tubules



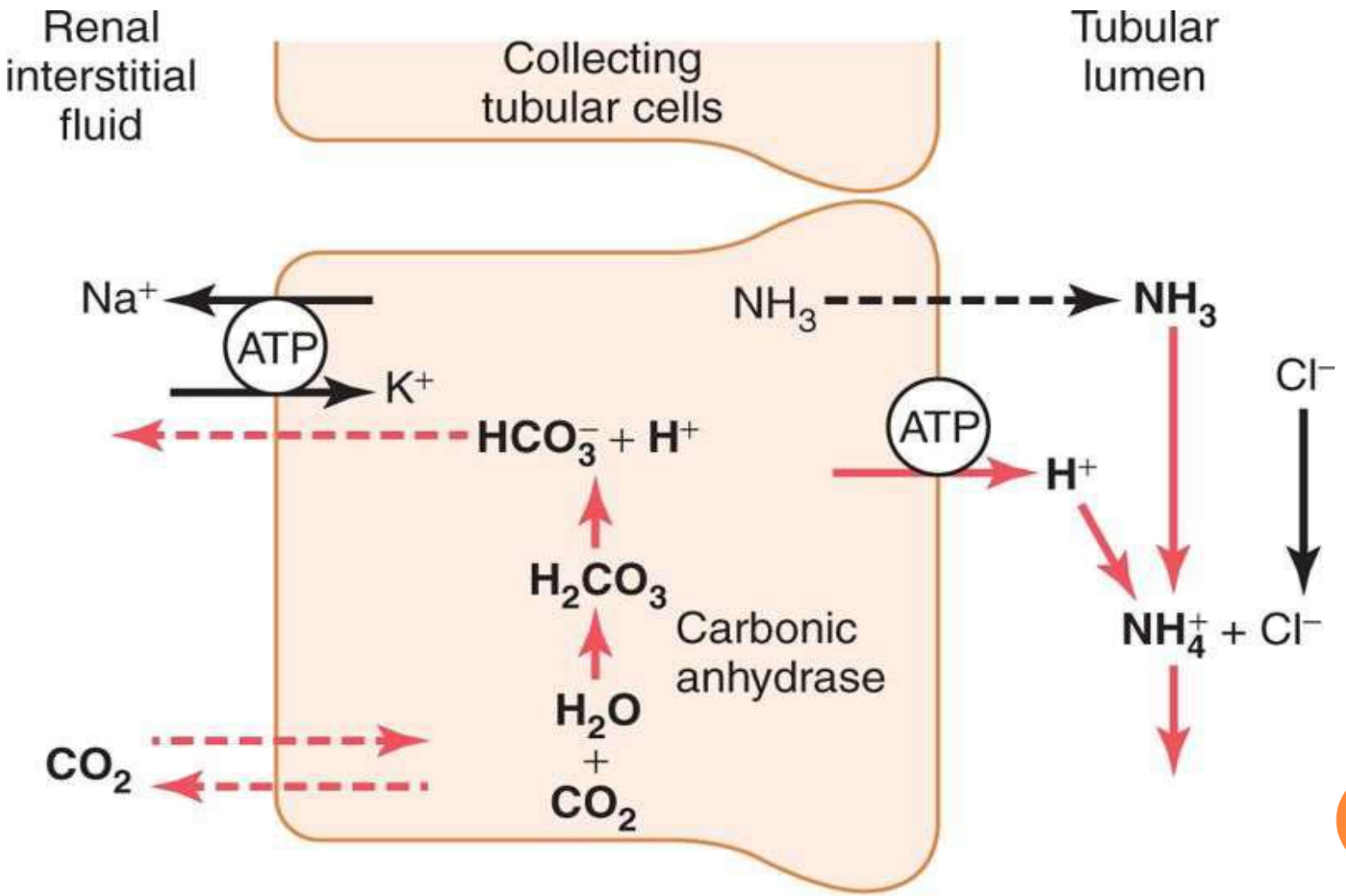
Buffering of Secreted Hydrogen Ions by Filtered Phosphate



Excretion of Excess H+ and Generation of New Bicarbonate by the Ammonia Buffer System



Buffering of hydrogen ion secretion by ammonia (NH3) in the collecting tubules



Renal Correction of Acidosis-Increased Excretion of H+ and Addition of Bicarbonate to the ECF

- Acidosis decreases the ratio of Bicarbonate/Hydrogen ion in Renal Tubular Fluid
- As a result, there is excess H+ in the renal tubules, causing complete reabsorption of bicarbonate and still leaving additional H+ available to combine with the urinary buffers (phosphate and ammonia)
- Thus, in acidosis, the kidneys reabsorb all the filtered bicarbonate and contribute new bicarbonate through the formation of ammonium ions and titratable acid

Renal Correction of Alkalosis-Decreased Tubular Secretion of H+ and Increased Excretion of Bicarbonate

Alkalosis increases the ratio of bicarbonate/hydrogen ion in renal tubular fluid

- The compensatory response to a primary reduction in PCO_2 in respiratory alkalosis is a reduction in plasma concentration, caused by increased renal excretion of bicarbonate
- In metabolic alkalosis, there is also an increase in plasma pH and decrease in H^+ concentration
- The cause of metabolic alkalosis is a rise in the extracellular fluid bicarbonate concentration
- This is partly compensated for by a reduction in the respiration rate, which increases PCO_2 and helps return the extracellular fluid pH toward normal
- In addition, the increase in bicarbonate concentration in the extracellular fluid leads to an increase in the filtered load of bicarbonate which in turn causes an excess of bicarbonate over H^+ secreted in the renal tubular fluid
- The excess bicarbonate in the tubular fluid fails to be reabsorbed because there is no H^+ to react with, and it is excreted in the urine
- In metabolic alkalosis, the primary compensations are decreased ventilation, which raises PCO_2, and increased renal excretion of bicarbonate which helps to compensate for the initial rise in extracellular fluid bicarbonate concentration

NITROGENOUS WASTE

- Nitrogenous wastes are synthesized by animals from excess amino acids
- Unlike lipids and carbohydrates amino acids are not stored in the body
- They are deaminated by the liver tissues and the amino group has to be excreted.

Deamination

- NH2.CHR.COOH + H2O $\xrightarrow{\text{Transaminase}}$ NH3 + O CHR.COOH

Amino acid **Water** **Ammonia** **Keto acid**

Toxic, it must be excreted

Can be converted into glucose and recycled

Three types of nitrogenous wastes are used by the vertebrates

- Ammonia
- Urea
- Uric acid

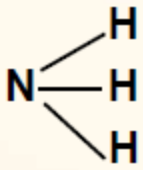
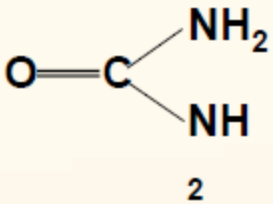
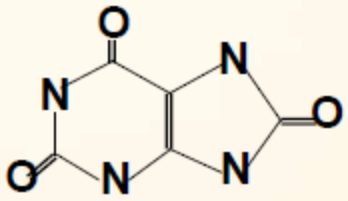
Ammonia is a direct product of deamination. In the liver

Urea is produced from ammonia. This also takes place in the liver tissues

$$2NH_3 + CO_2 \rightarrow CO(NH_2)_2 + H_2O$$

Uric acid is formed directly from amino acids in a series of reactions that produces its complex ring structure.

The use of these three forms of nitrogenous wastes follows a pattern in animals

AMMONIA	UREA	URIC ACID
NH_3	$CO(NH_2)_2$	$C_5H_4O_3N_4$
		
Highly toxic	Moderately toxic	Not very toxic
Highly soluble	Moderately soluble	Insoluble
Excreted mainly by aquatic invertebrates, osteichthyes (bony fish) and tadpoles	Excreted by chondricthyes (sharks and rays), terrestrial amphibians and mammals	Excreted by insects, most reptiles and all birds


THANK YOU!