Renal tubular functions

The renal tubules receive about 125 ml of glomerular filtrate / min i.e about 180 liters / day = 125 X 60 min X 24 hours.

This amount is about 4 times as much as the total body water (40 – 45 liters)

Since the plasma volume is about 3 liters, it is evident that the plasma is filtered by the kidney about 60 times / daily.

The glomerular filtrate, during its flow in the renal tubules, it is changed into urine through 3 processes:

Reabsorption.

Secretion.

Synthesis of certain substances as ammonia.

Steps of tubular reabsorbtion:

The molecules pass from the tubular lumen to the capillaries in two steps.

1-From the lumen to interstitial fluid (ISF)either by.

a-Transcellular route.

From luminal border of tubular epithelium to the inside of the cell ,then through the basolateral membrane to (ISF)

b-Paracellular route , as molecules pass directly through the tight junctions to (ISF)

2-From ISF to the capillaries.

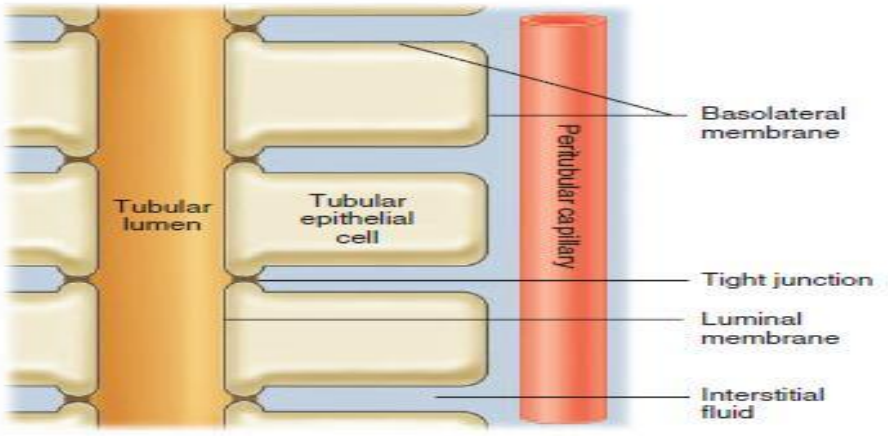


Figure (9): Diagrammatic representation of tubular epithelium.

Evidence of tubular Reabsorption:

1-Much smaller volume of urine (1 – 1.5 liters daily) compared with glomerular filtrate (180 liters / day)

2-disappearance of many substances present in glomerular filtrate from the urine e.g glucose and NaHCO3

Renal handling of sodium ions

Sodium ion is actively reabsorped at all tubular segments except the thin parts of loop of Henle.

The share of each segment in Na+ reabsorbtion is as follow:

I-Proximal tubule: 65 %

II-Ascending limb of loop of Henle: 27 %

III-Distal and collecting tubules: 6 - 8 %

I-Proximal convoluted tubules:

Na+ Reabsorption occurs in two steps

a-First step :

Through the luminal border.

1-Na+ ions first diffuse passively from the tubular lumen into the tubular epithelial cells down a concentration gradient ,because Na+ concentration in the tubular fluid is higher than its concentration in the tubular cells. There is a potential difference of about 66 mv across the luminal border (inside negative) which help diffusion of Na+ ions which is positive into the tubular cells.This passive Na+ ion transport needs a specific carrier (Facilitated diffusion).

2-This passive transport is accompanied by Co-transport of glucose and amino acids by secondary active transport, and by H+ transport (counter transport) i.e from the tubular cell to the lumen.

3- Na+ - H+ exchange is linked directly to HCO3 – Reabsorption (from tubular lumen to tubular cells), so that it acts as a feed back mechanism to regulate the acid –base balance

e.g

In acidosis there is secretion of increased amount of H+ into tubular fluid associated by increased amount of HCO3- Reabsorption to correct acidosis.

While in alkaloses the reverse occurs, as there is decreased H+ secretion and so decreased HCO3 reabsorption so is excreted in urine to correct alkaloses.

4-In the middle and late proximal tubule Na+ Reabsorption is accompanied by chloride transport from luminal fluid to tubular cells because all filtered glucose, amino acids, and bicarbonates have been already absorbed in early proximal tubule.

5-Na+ diffusion occurs both through transcellular and paracellular routes.

6-Carbonic anhydrase inhibitors (e.g acetazolamide) are diuretics that act on the early proximal tubules by inhibiting HCO3 reabsorption leading to its excretion driving water with it leading to diuresis.

b-Second step:

Through the basolateral border.

Na+ is actively transported through the basolateral border (membrane) via the Na+ - K+ ATP ase pump to interstitial fluid .This Na+ efflux creates a negative electrochemical gradient inside the cells which is responsiple for passive Na+ diffusion in step (1)

N.B

Na+ transport to the inside of the cells creates an osmotic gradient for water transport so that tubular fluid remains iso –osmolar along the proximal tubule.

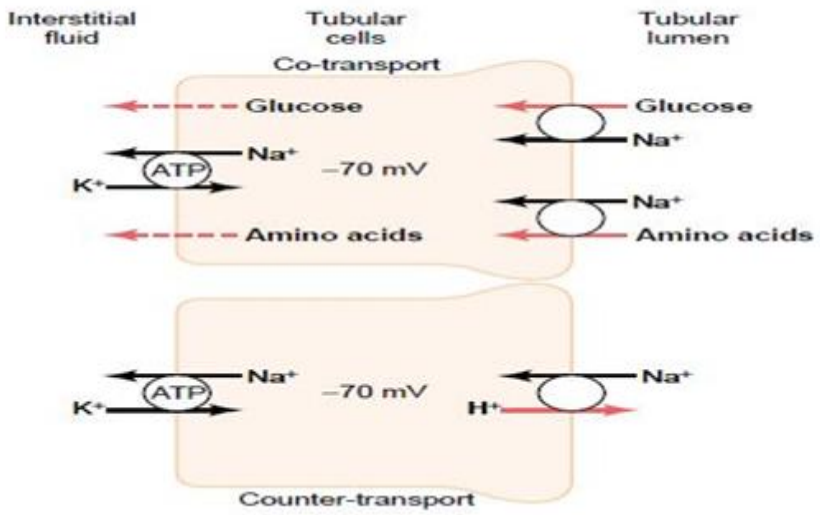


Figure (11): Na+ reabsorbtion at P.C.T The upper cell shows the *co-transport* of glucose and amino acids along with sodium ions The lower cell shows the *counter-transport* of hydrogen ions.

II-Ascending limb of loop of Henle:

a-Thin segment of the ascending limb of loop of Henle.

Na+ Reabsorption occur after CL- Reabsorption along the paracellular route.It is a passive transport.

b-Thick segment of the ascending limb of loop of Henle.

Na+ Reabsorption across the luminal membrane is mediated primarily by a

1-sodium, 2-chloride, 1-potassium co- transporter.

It is the site of action of loop diuretics (e.g furosemide , ethacrenic acid and butmetanide) which inhibit CO- Transport.

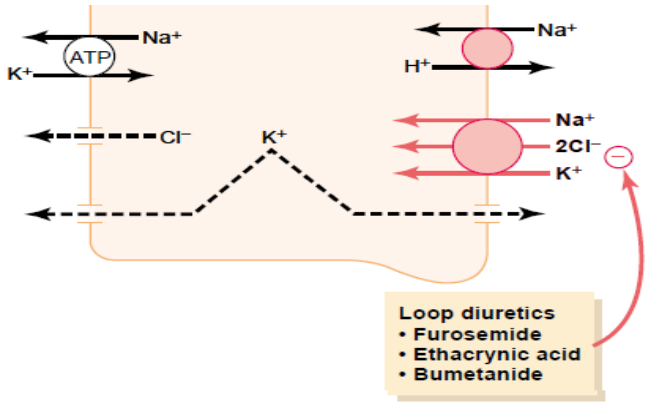


Figure (12): Na+ reabsorbtion at the thick ascending limb of L.H

III- Distal and collecting tubules:

a-At the early distal tubule:

The sodium-chloride co-transporter moves sodium chloride from the tubular lumen into the cell, and the sodium-potassium ATPase pump transports sodium out of the cell across the basolateral membrane. Chloride diffuses out of the cell into the renal interstitial fluid through chloride channels in the basolateral membrane.

The thiazide diuretics inhibit the sodium chloride co-transporter.

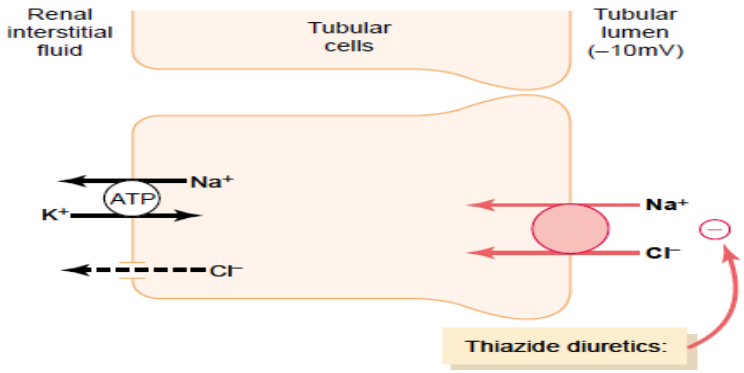


Figure (13): Na+ reabsorbtion at the early distal tubule.

b- At the late distal tubule and collecting ducts:
Na+ is transported at the luminal border either by.
Na+ - H+ exchange Or Na+ - K+ exchange.

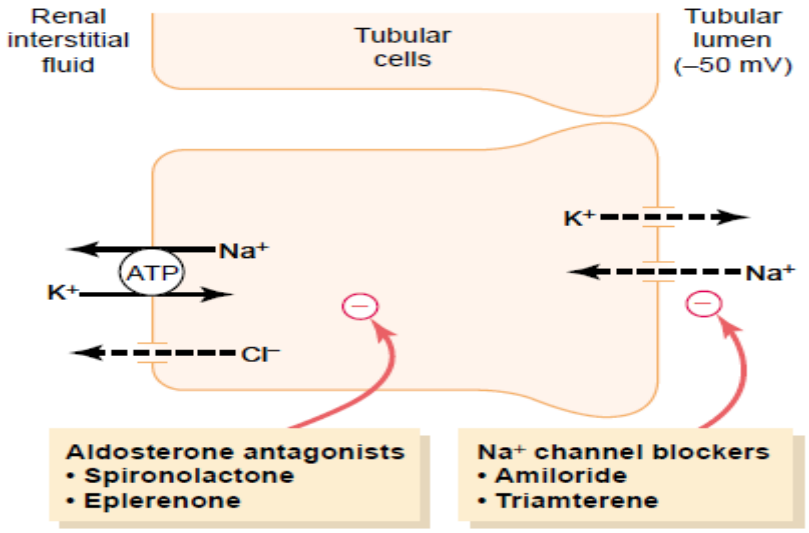


Figure (14): Na+ reabsorbtion at the late distal tubule and collecting ducts.

Reabsorption and secretion along different tubular segments

1-Proximal convoluted tubules (PCT):

I-Reabsorption of:

A- 67 % of filtered sodium, water.
K and Calcium
Most of HCO3-

And slightly less load of filtered chloride.

B-All filtered glucose and amino – acids in early PCT.

C-In first half of PCT ,Na+ is reabsorped by CO transport with glucose and amino -acids.
In second half Na+ is reabsorbed with CL ion because its concentration increases due to water Reabsorption.
The tubular fluid remains iso –osmolar along the PCT.

II-Secretion of.

a-Organic acids and bases which result from metabolism e.g bile salts and oxalates.
b-Secretes catecholamines and some drugs e.g pencillin.

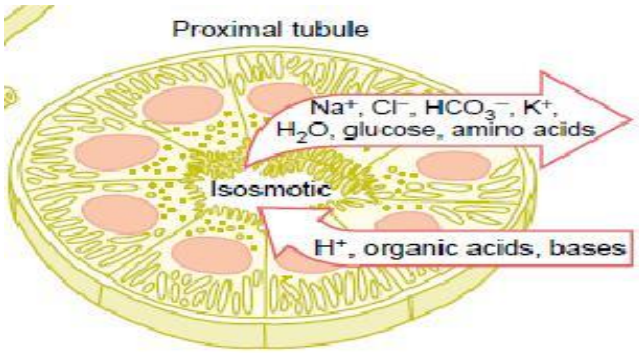


Figure (18): Transport characteristics of the proximal tubule.

2-The loop of Henle:
a-Thin descending segment.
Formed of simple epithelial lining.
Allow simple diffusion of H2O and solutes.
Highly permeable to H2O but moderetaly permeable to solutes.
10 % of filtered water is reabsorbed in this part so osmolarity is too much increased by the end of this segment.

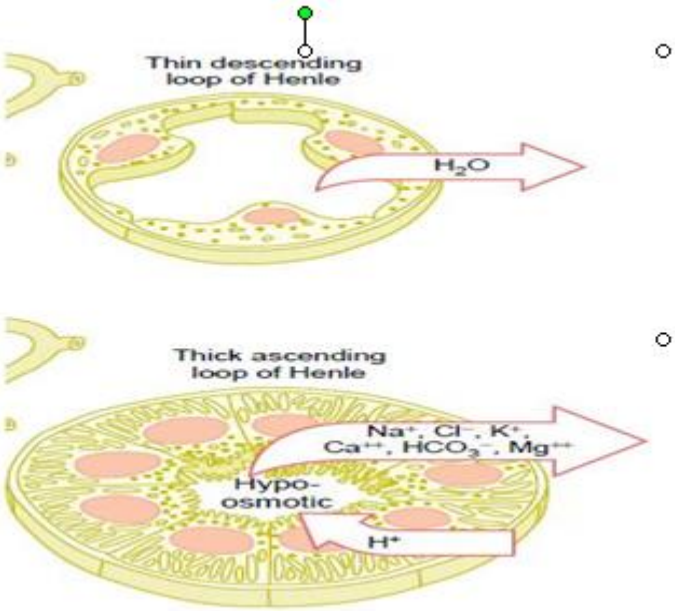
The descending limb of loops of Henle receive isotonic fluid from the proximal convoluted tubules.
Their walls are highly permeable to H2O and less permeable to NaCl so water diffuses freely from tubular lumen outwards by the high osmolarity of medullary interstatium.
Net result:
Tubular fluid become hypertonic and this hypertonicity increases gradually as it moves downward.
Maximal hypertonicity occurs at its bend reaching in humans to about 1200-1400 milliosmols.

b-Thin ascending segment.

Less absorptive capacity for solutes.
Na+ is absorbed passively after CL- Reabsorption.
It is impermeable to water.

c-Thick ascending segment.

It is thick epithelium with signs of activity.
Reabsorption of.
27 % of filtered Na+
20 % of filtered K+
27 % of filtered Ca+2
The luminal cell membrane contains Na+ - K+ - 2 CL transporter.
It is impereabile to water so osmolarity decreases due to Reabsorption of Na+ and K+ and Ca+2 to become hypotonic (having osmolarity of 100 – 200 milliosmoles) on reaching the distal convoluted tubules.



Figure(19): Transport characteristics of the thindescending loop of Henle (*top*) and the thick ascending segment of the loop of Henle (*bottom*).

3-The distal convoluted tubules:

It consists of.

a-The early diluting segment.

Has the same characters as thick ascending limb of loop of Henle.

b-Late distal tubule and cortical collecting tubule.

They have the same characters and contain two types of cells.

1-The principal cells.

Responsible for K+ secretion

2-The intercalated cells.

Secretes H+ and reabsorbs K+ in case of K+ depletion.

Characters of both segments.

1-Reabsorbes sodium and secretes K+ under influence of aldosterone hormone.

2-Secretes H+ via primary active transport by H+ pump ,that can transport H+ against gradients up to 1000 folds.

3-Water Reabsorption under the influence of ADH.

4-Impermeable to urea.

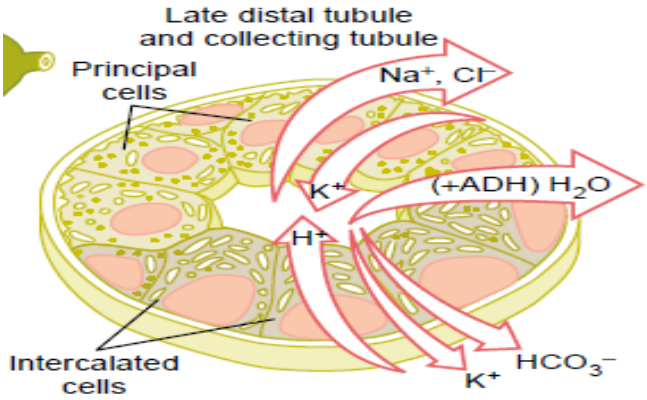


Figure (20): Transport characteristics of the late distal tubule and collecting tubule.

4-Medullary collecting duct.

It has the same characters as distal nephron except it is permeable to urea and ADH increases this permeability.

The transport via distal tubules differ from proximal tubule in the following.

A-Proximal tubules has a large capacity so reabsorb large quantities of salt and water, while distal tubules has a smaller capacity, it can reabsorb 9% of filtered sodium and 19 % of filtered water.

B-Na+ and H2O Reabsorption are closely coupled in proximal tubules because H2O permeability is high ,while in the distal tubules as H2O permeability is variable and low so Na+ and H2O Reabsorption may be uncoupled.

Keep in mind

Mechanisms of tubular Reabsorption:

1-Active transport , which may be primary or secondary.
2-Passive transport by diffusion.
3-Water transport by osmosis
4-endocytosis for protein molecules transport.

1-Active transport.

Requires energy because substances reabsorbed actively are transmitted through the tubular membrane against either:

-Concentration gradient (e.g glucose , amino acids)
-Electrical gradient.

The tubular cells especially those of the proximal convoluted tubules have a brush border rich in enzymes and carrier substances and their bases contain mitochondria which supply energy for active transport.

2-Passive transport.

Requires no energy and depend on 2 factors:

a-Concentration gradient

concentration difference between tubular fluid and the concentration in the interstitial fluid of the kidney.

b-Permeability of tubular cells to different substances.

Parameters of renal active transport

A-Renal tubular transport maximum (Tm)

The tubular transport maximum of (Tm) of a certain substance is the maximal amount of this substance (in mg) which can be transported (reabsorbed or secreted) by the tubular cells /minute.

The highest rate of Reabsorption is called maximum tubular Reabsorption capacity (Tm or Tr) examples of substances having Tm are glucose , phosphate , sulphates , many a.a , uric acid and albumin.

Tm of glucose (TmG):

It is the maximum amount of glucose (in mg) that can be reabsorped by renal tubules / minute.

It is used as a renal function test.
It was found that at normal blood glucose level ,all glucose filtered in the glomeruli is reabsorbed , as the blood glucose level is increased ,the amount of glucose filtered and reabsorbed are also increased up to a blood glucose of 180 mg % (**renal threshold for glucose**) as all filtered glucose is reabsorbed and no glucosuria occurs.

When blood glucose level exceeds 180 mg % ,the filtered and reabsorbed glucose are increased with the appearance of glucosuria, as reabsorbtive power of some tubules reach its maximal power at 180 mg % and any excess filtered glucose will be lost in urine .This explained by saturation of glucose carrier , so no more glucose can be reabsorbed.

The highest rate of secretion is called the maximum tubular secretory capacity (Tm or Ts) examples include pencillin , some diuretics , and para-amino –hippuric acid (PAHA)

The threshold concentration:
It is the plasma concentration at which a solute begins to appear in urine.
It is characteristic for each substance.

N.B
Uric acid is the only organic substance that can undergo both Reabsorption and secretion by the kidney, while K+ is the only inorganic cation that is both reabsorped and secreted by the kidney.

Some substances have no Tm e.g
The Reabsorption of Na+ along the nephron.
The secretion of K+ by the distal tubules.

B-Filtered load and excretion rate:

a-The filtered load.

Is the amount of a substance entering the tubule by filtration per unit time, it equals the product of GFR and the plasma concentration of the substance (P).

Filtered load = GFR X P mg / min.

b-The excretion rate.

Is the amount of a substance that appear in urine per unit time ,it equal to the product of urine volume in that time (V) and the concentration of the substance in urine (U)

Excretion rate = V X U mg / min.