# PHYSIOLOGY TEAM 432

## LECTURE : 5

## Tubular Reabsorption

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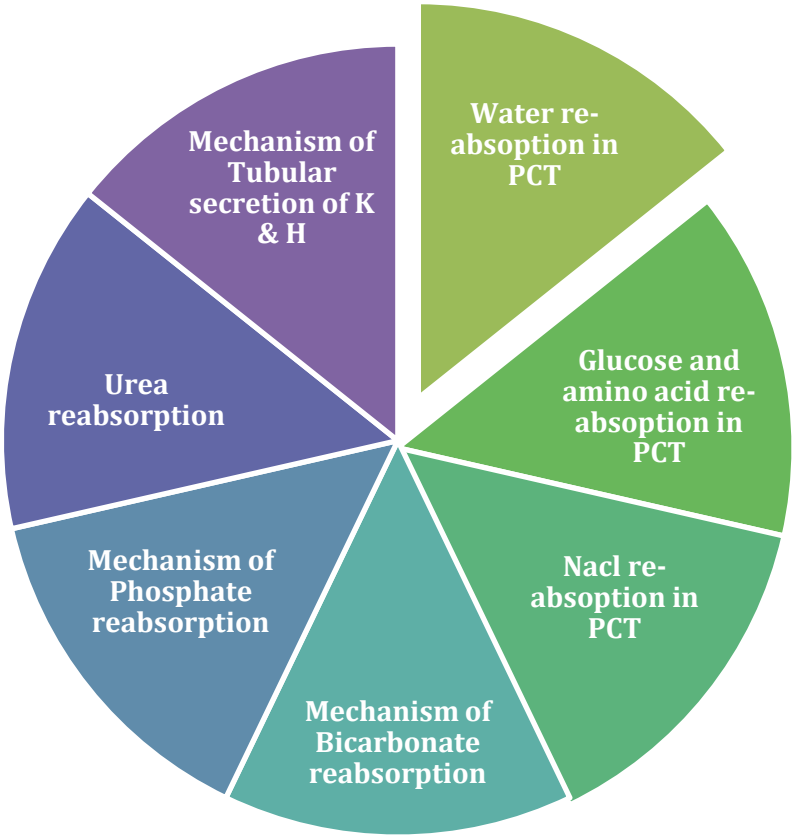
# OBJECTIVES

Absorption part in lecture 6 was brought to this lecture

**At the end of this lecture student should be able to describe:**

- Mechanism of urine formation
- Renal tubular transport
- Nacl re-absoption in PCT
- Water re-absoption in PCT
- Glucose and amino acid re-absoption in PCT
- Mechanism of Bicarbonate reabsorption
- Mechanism of Phosphate reabsorption
- Urea reabsorption
- Mechanism of Tubular secretion of K & H

# MIND MAP

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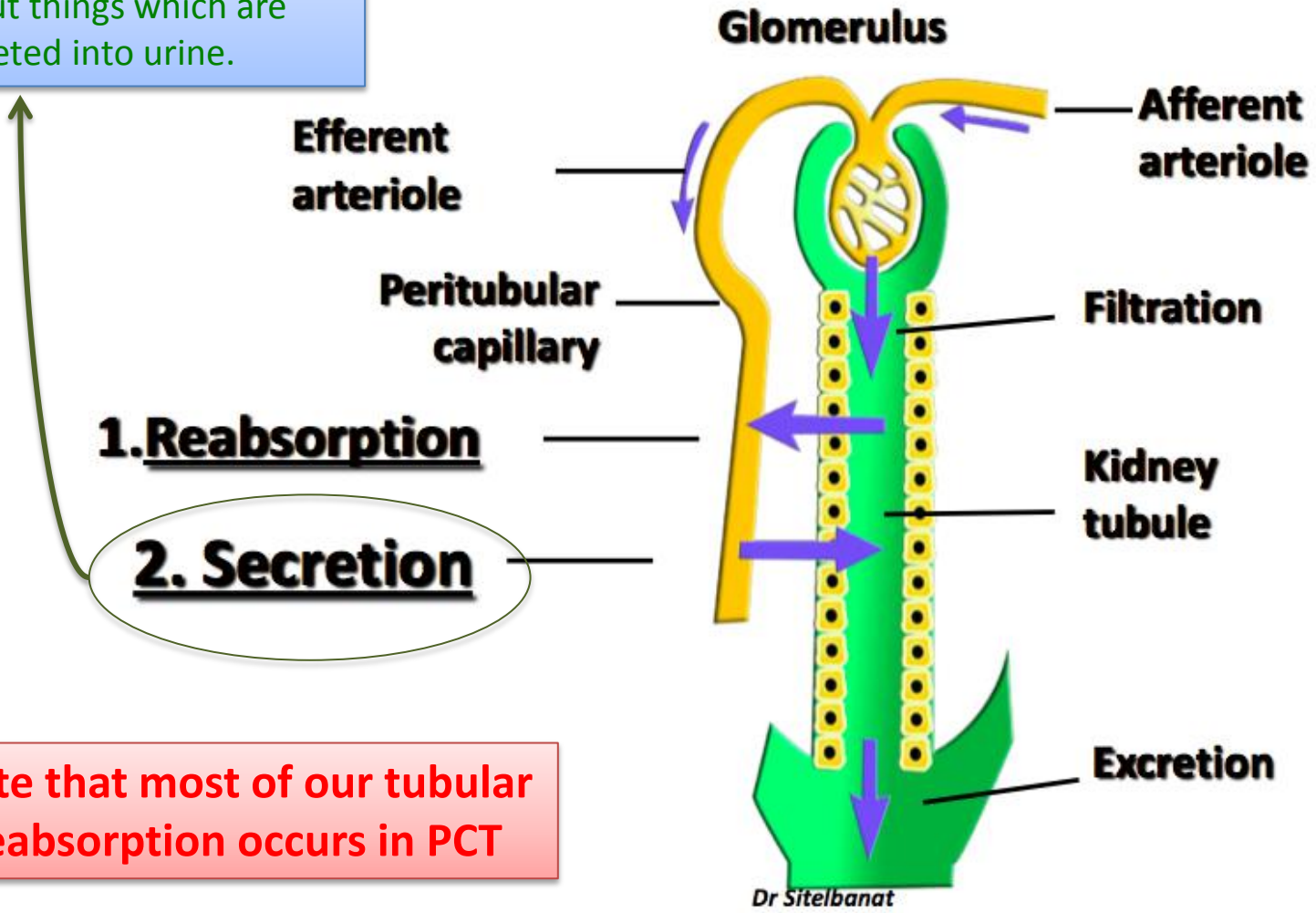
- This is not excretion, this is different.
- Excretion is when we talk about things which are excreted into urine.

# Tubular Function




**Note that most of our tubular reabsorption occurs in PCT**

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# Filtration, Reabsorption and excretion rate

Absorbed/filtered%

| | Filtered | Absorb. | Excreted | A/F % |
|---|---|---|---|---|
| Glucose (g/d) | 180 | 180 | 0 | 100 |
| HCO3 (meq/d) | 4320 | 4318 | 2 | 99.98 * |
| Na (meq/d) | 25560 | 25410 | 150 | 99.4 |
| Cl (meq/d) | 19440 | 19260 | 180 | 99.1 |
| K (meq/d) | 756 | 664 | 92 | 87.7 |
| Urea (g/d) | 46.8 | 23.4 | 23.4 | 50 |
| creatinine (meq/d) | 1.8 | 0 | 1.8 | 0 |

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*Meaning that 0.02 of HCO3 is being excreted (as a percentage).

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# Calculation of tubular reabsorption or secretion from renal clearances

## Reabsorption or secretion =

Quantity Filtrated – Quantity excreted

- Quantity Filtrated = Px x GFR
- Quantity Excreted = Ux x V

Amount filtered > amount excreted = substance is reabsorption
Amount filtered < amount excreted = substance is secreted

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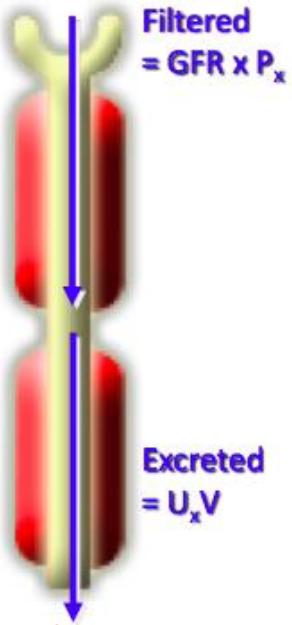
# Calculation of renal transport (Tx)

Transport = reabsorption

$$T_x = GFR \times P_x - U_xV$$



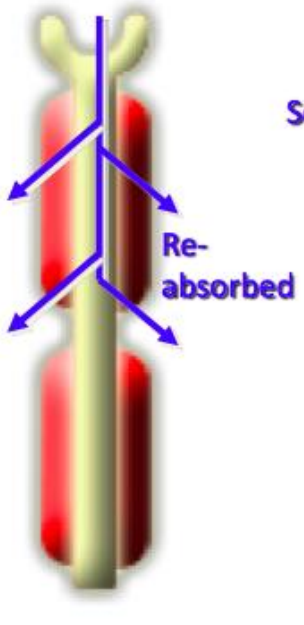

Filtrate = urine

$T_x = 0$

$GFR \times P_x = U_xV$

e.g. Inulin

Freely filtered not reabsorbed nor secreted



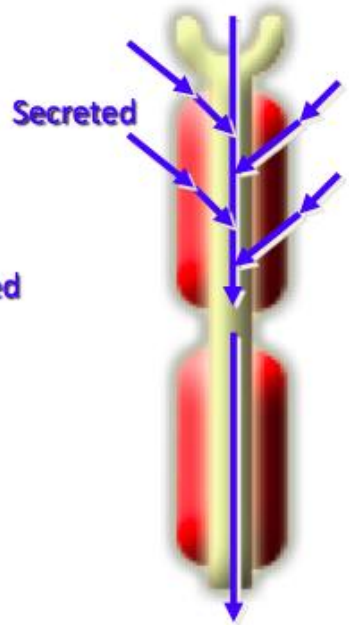

Filtrate > urine

$T_x$ = positive

$GFR \times P_x > U_xV$

e.g. glucose

Freely filtered and completely reabsorbed.




Filtrate < urine

$T_x$ = negative

$GFR \times P_x < U_xV$

e.g. PAH

Freely filtered, not reabsorbed but secreted.

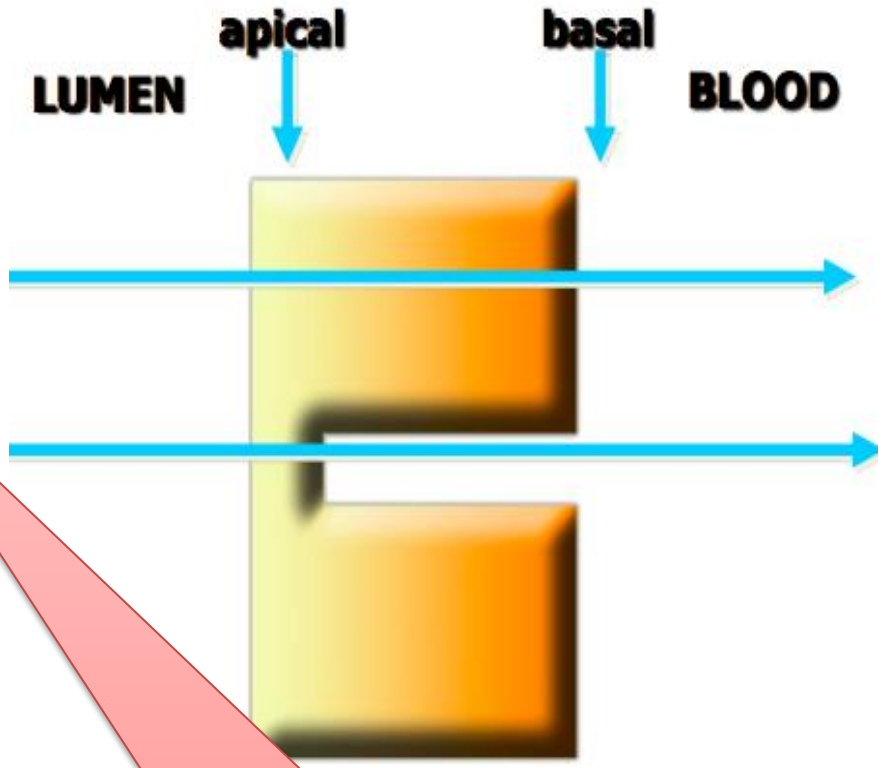
✓ Transcellular: Across renal cell

- Primary active transport
- Secondary active transport; depends on other active process.
- Passive: ion channel

✓ Paracellular: Through tight* junction

- Passive diffusion ;

* not actually very tight ; as it will allow diffusion of some substance ( wastes and electrolytes).




Transcellular more difficult because molecules have to cross two membrane; the lamina membrane and the basal membrane.

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# Types of transport processes

Male

- **Diffusion:**

Random movement of substance either through the membrane directly (simple diffusion) or in Combination with carrier protein (facilitated diffusion) down an electrochemical gradient.

- **Active Transport :** from low concentration to high concentration:

*1- Primary active transport :* energy is supplied directly from ATP (e.g Na-K ATPase)

*2-Secondary active transport :* energy is supplied indirectly from ATP, can be:

A- cotransport : Transported substances move in the same direction across the membrane, e.g.

- o Na glucose Co transport.
- o Na – amino acid Co transport.

B- counter transport: Transported substances move in opposite directions across the membrane (e.g Na –H+ exchange ).

- **Pinocytosis:** Uptake by cells of particles too large to diffuse through the cell membrane (e.g reabsorption of filtered proteins in PCT)

- **Solvent drag:** Solvent such as water moving across an epithelium by osmosis can drag dissolved solutes with it.

# Secondary active transport Characteristics

Male

- "Uphill" transport of one substance linked to "downhill" transport of another substance
- Carrier must be occupied by both substances, mobile in membrane
- Saturable (has a $V_{max}$)
- Specificity and affinity of carrier for substance transported
- "Uphill" transport occurs without direct input of metabolic

# Proximal convoluted tubule

These structures are making it the best site for reabsorption.

- **High capacity for reabsorption**

✓ Special tubular epithelial cell
✓ Metabolically active (lot of mitochondria)
✓ Brush border (surface area)
✓ Tight junction is not so tight
✓ Contain a lot of carrier protein

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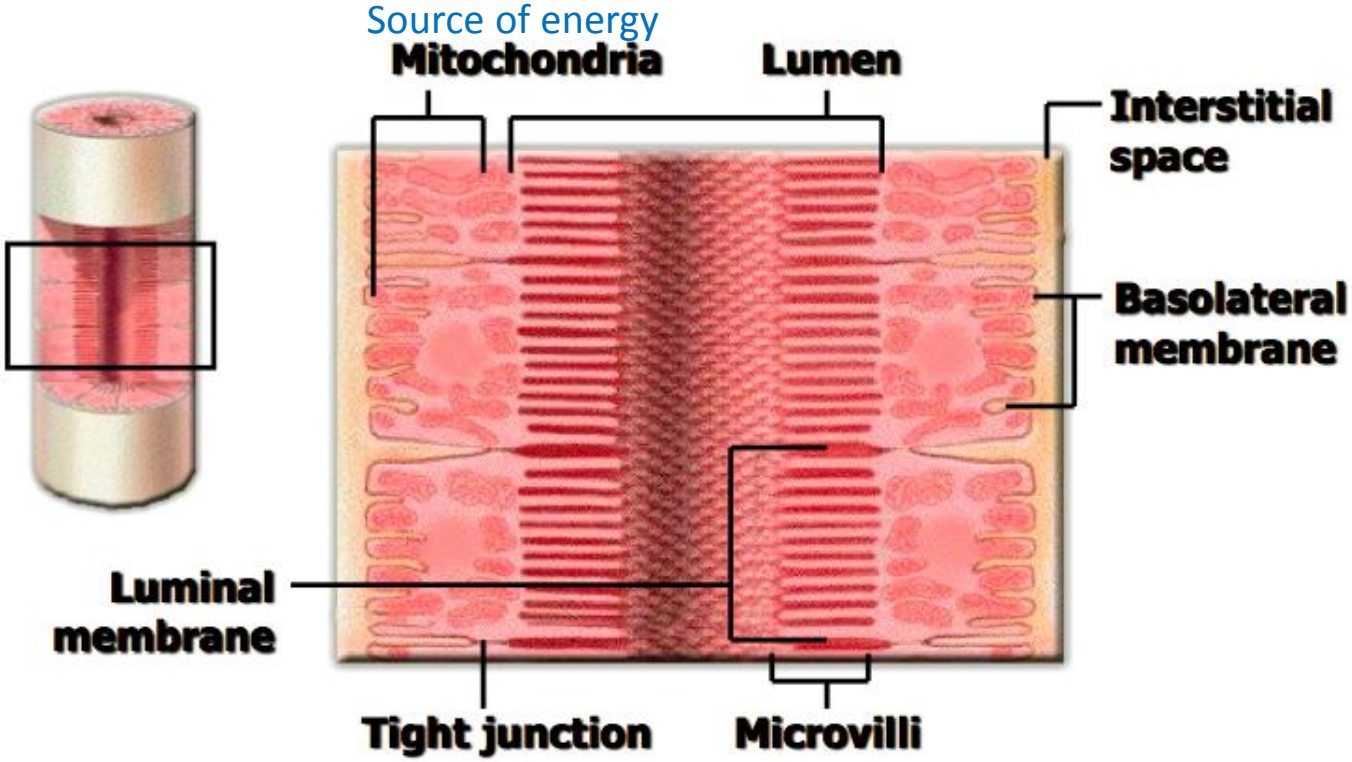
# Cells of the Proximal Convoluted Tubule (PCT)

**Simple cuboidal cells with brush border Highly permeable to water and many solutes.**

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# SUBSTANCES ABSORBED IN PCT

## Tubular absorption:

- Sodium
- Chloride
- Glucose
- Water
- Amino acid
- Bicarbonate
- Phosphate
- Urea
- K

End product of metabolism, 50% of the filtrate will be reabsorbed back to blood to ↑ osmotic pressure in kidney

## Secretion:

- PAH
- H+
- K

**K** : has a character to be reabsorbed or secreted as I need .
*The Dr. said this twice*
(Very important)

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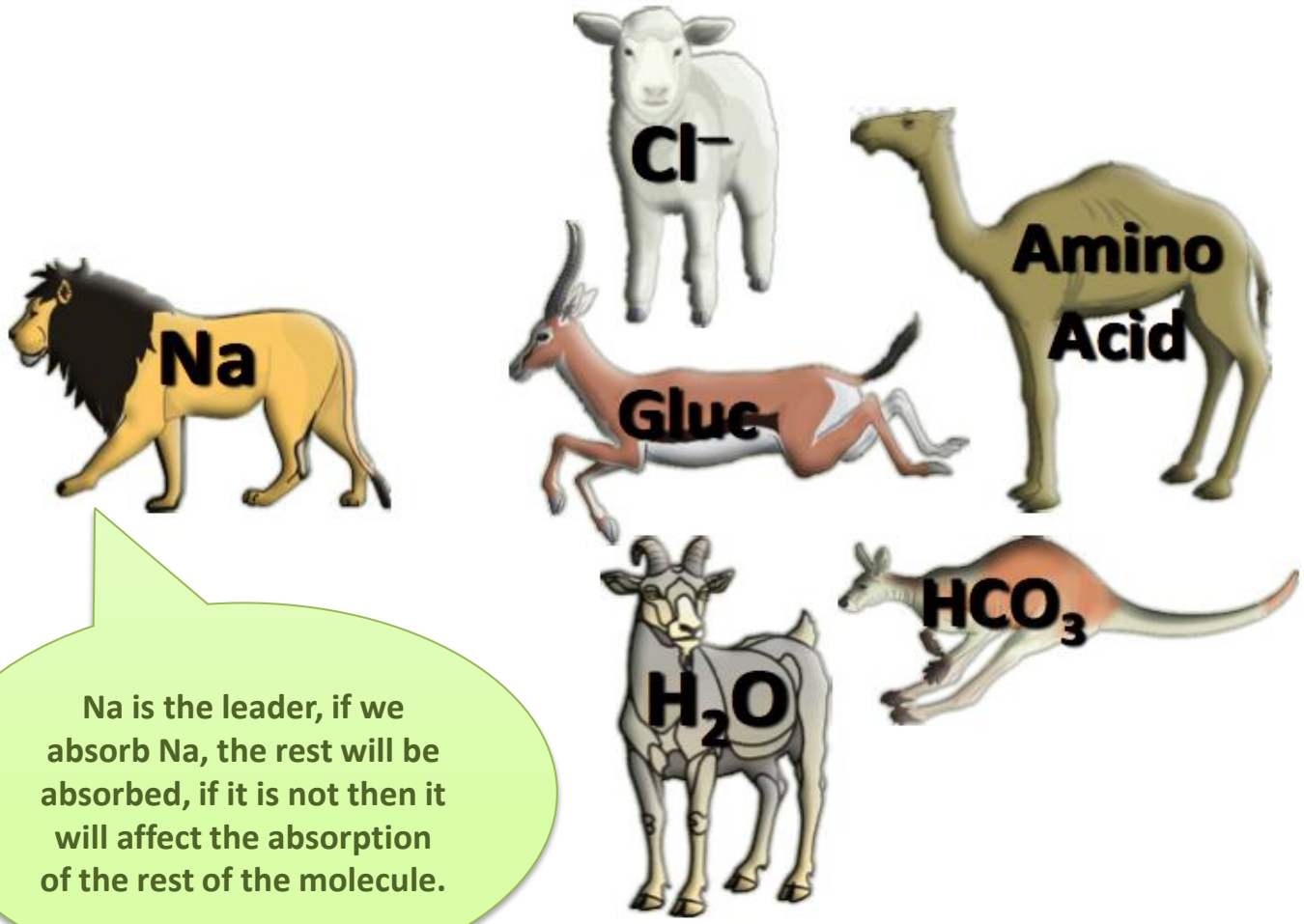


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# Sodium reabsorption in PCT

- 65-70% of filtered sodium is reabsorbed in PCT
- Followed by water & chloride (passively)
  - Iso-osomotic (Isotonic) absorption : equal quantity of solute & water.
  - Important for the absorption of:
    - Glucose
    - Amino acids
    - phosphates

If I'm going to absorb 70% of salt then 70% of water will be absorbed.

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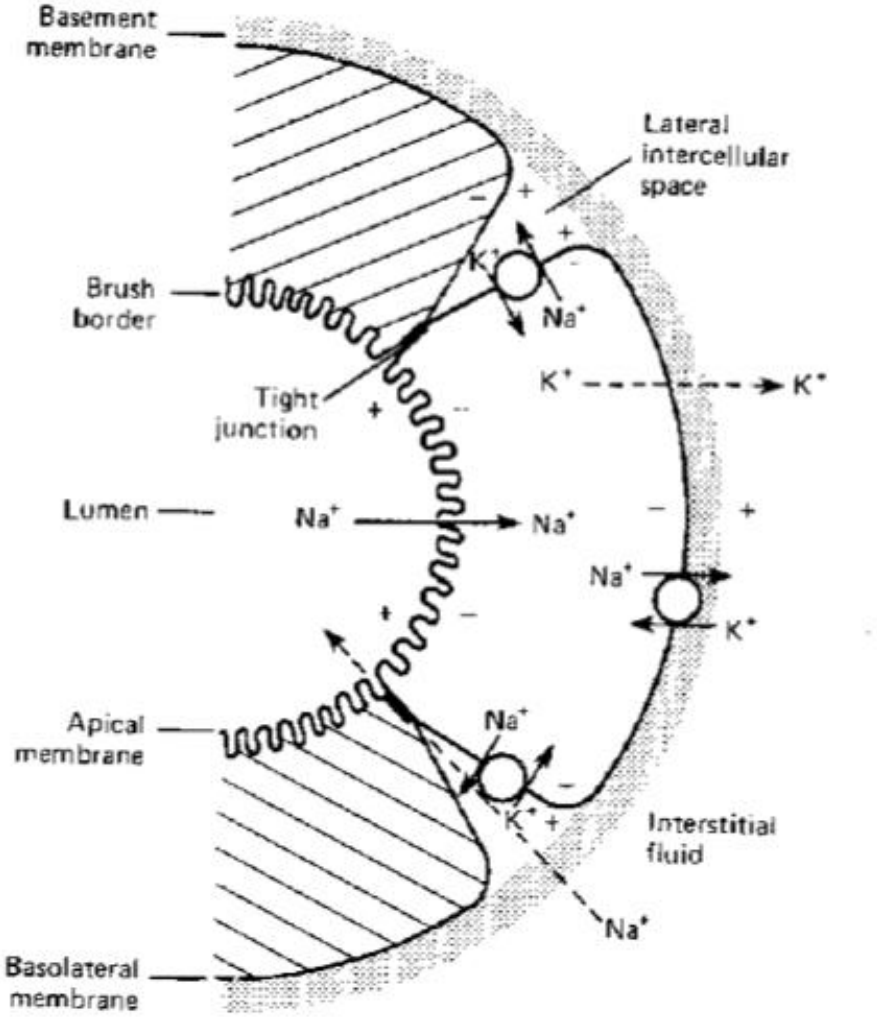
# PASSAGE OF SODIUM ABSORPTION

Na starts from lumen, goes and crosses the luminal membrane.
Now Na is inside the cell,
It leaves it through basolateral membrane to peritubular space to the blood.

Lumen
↓
Luminal membrane
↓
Cell
↓
Basolateral membrane
↓
peritubular space
↓
Blood

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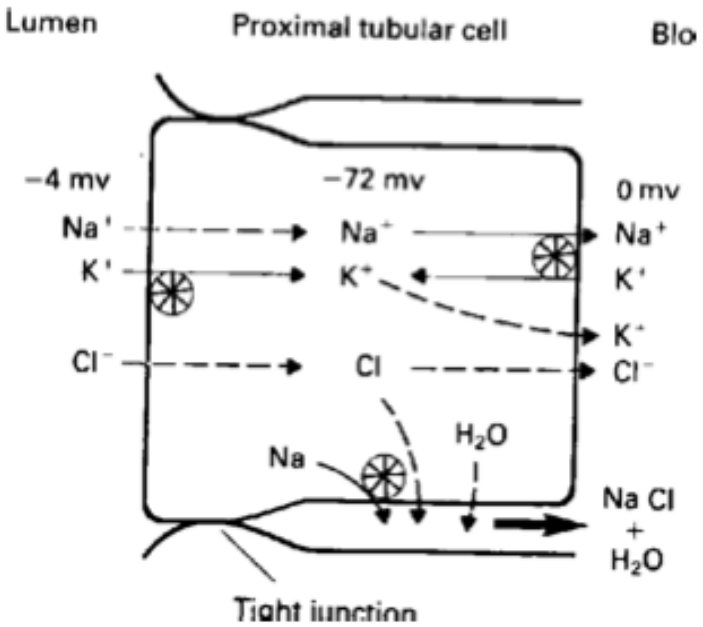
# MECHANISM OF SODIUM REABSORPTION

- ✓ **Basolateral membrane of renal tubules.**
- Na+/K+ ATPase (Active Pump)
  - i. 3Na/2K *
  - ii. K leak out of the cell

**Results in :**

- Low intracellular Na Concentration, ↑ K.
- High peritubular osmolality




*Na : outside the cells. K : inside the cells.

Active process, exist in all cells but excessively in kidneys.

Continues pumping of Na will create a negative pressure inside the cell ⇨ Na will absorbed passively from lumen to the cell.

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# MECHANISM OF SODIUM REABSORPTION

✓ **Na enter the cell passively following:**

- **Electrical difference (inside the cell -70mv, lumen -4mv)** therefore, positive molecule like Na will move toward the more negative site ( inside the cells).
- **Na concentration differences (140 mEq/L(in the lumen) to 12mEq/L(inside the cells))**

✓ **Na enter the cell across the luminal membrane through:**

- **Co-transport with glucose, amino acids**
- **Na in exchange H (counter transport)** =(Na in , H out)
- **Na channel**

**If I block the active Na/K pump → no absorption →effect glucose and Amino acid absorption.**

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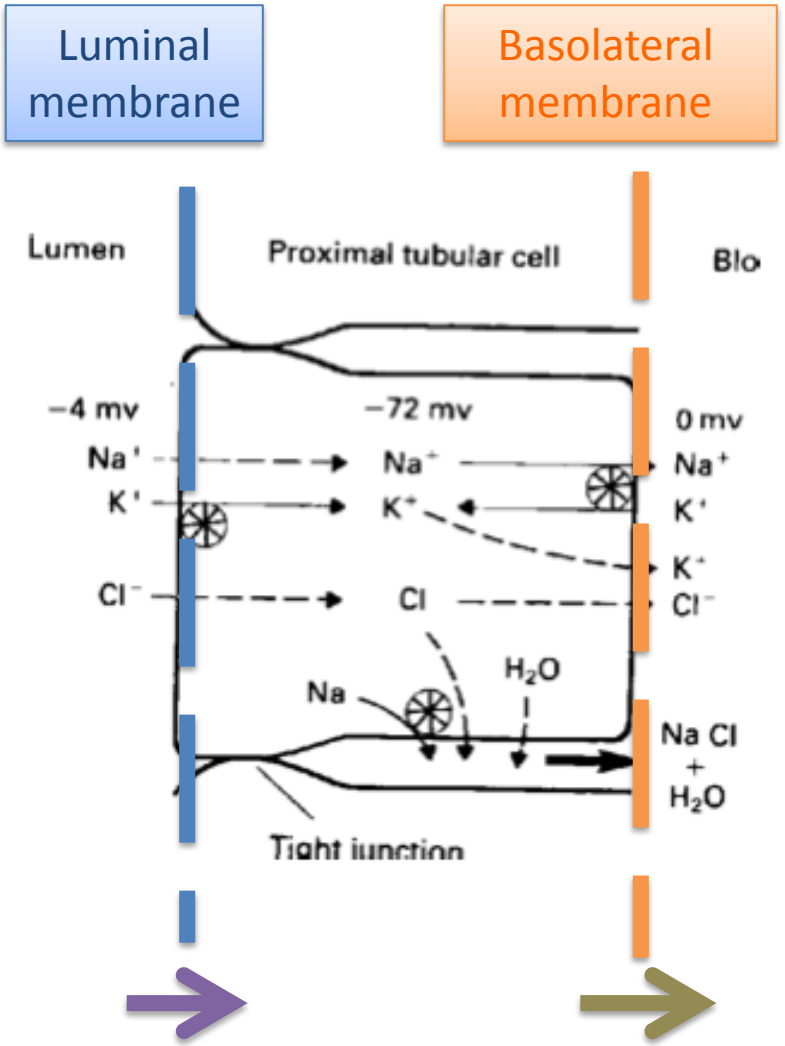
**summery** : in basolateral* membrane we have active pump continuously pumping 3 Na out and 2 K in , this will create negative pressure of Na inside ( low voltage) , and con. is low ( low con.) and due to that ⇨ Na will be absorbed passively from the lumen* into the cells.

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# CHLORIDE REABSORPTION

- ✓ Cl reabsorbed down concentration gradient following the positively charge Na.
- ✓ Cl usually follows Na.

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# WATER REABSORPTION

- **60-70% of filtered water is reabsorbed in PCT**
  - Active pump of Na from renal cell to peritubular space* results in increase of the osmolality of peritubular space.
  - Drag water by osmosis
- **Filterate remains iso-osmotic (~equal quantity of water & solute are absorbed)**

* Has two effects :
- lower con. of Na inside the cells
- Increase con. (negativity) in peritubular space.

Therefore, the increased osmolality in peritubular space will allow the reabsorption of water.

**Remember we are still @the level of PCT, because the rest of the nephron will be different.**

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# GLOMERULO-TUBULAR BALANCE

Note that this is **NOT** (tubuloglomerular), which is the tubuloglomerular feedback we took in lecture 3, this is something different.

- Feed back mechanism to keep a fixed percentage of reabsorbed glomerular filtrate.

- The higher the filtration in the glomerulus →the higher oncotic pressure in efferent & peritubular capillaries → ↑ reabsorption in PCT

- **And vice versa**
- **(All for keeping the amount of reabsorption in PCT constant ; constant filtration )**

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# GLUCOSE REABSORPTION

- ✓ **In healthy adult, all filtered glucose is reabsorbed and no glucose will appear in urine.**
- ✓ **If plasma glucose ($P_G$) reach 200 mg/dl, glucose appear in the urine – this level is the "Renal threshold"**

200mg/dl in arterial, 180 mg/dl in venous

- If some one has Plasma glucose of 230mg/dl then I should be expecting to see glucose in the urine.

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# GLUCOSE REABSORPTION

- ✓ The amount of reabsorped glucose at very high filtered glucose, remains constant, this is called tubular transport maximum for glucose ($Tm_G$)= 375 mg/min (female 300mg/min)

anything more than that, will appear in urine.

- ✓ At this maximum transport, all the glucose **carriers are saturated** and no more glucose can be transported.

**Note that the (TmG) is different than the renal threshold, because when we talk about the threshold we are talking about blood but here we are talking about urine.**

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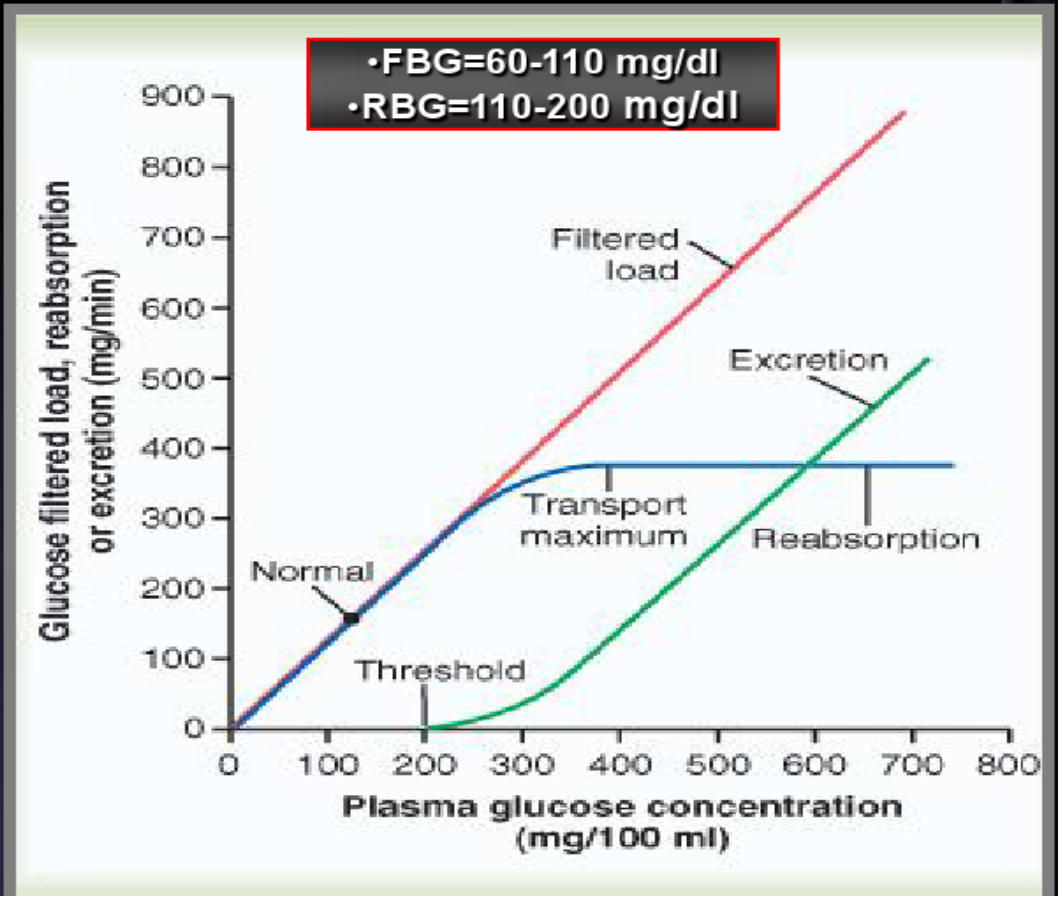
# GLUCOSE REABSORPTION

**Tmax**
375 mg/min

**Filtered Load**
125 mg/min
(GFRxPlasmaGlu)

**Renal Threshold**
200mg/dl



# MECHANISM OF GLUCOSE REABSORPTION

- **Secondary active transport**
- **Luminal membrane**
  - Cotransport with Na
- **Basolatera lmembrane**
  - GLUT 1 & 2

why secondary? because it depends on the primary active Na transport.

they are 7 transporters, but only 1-2 are present in kidneys.

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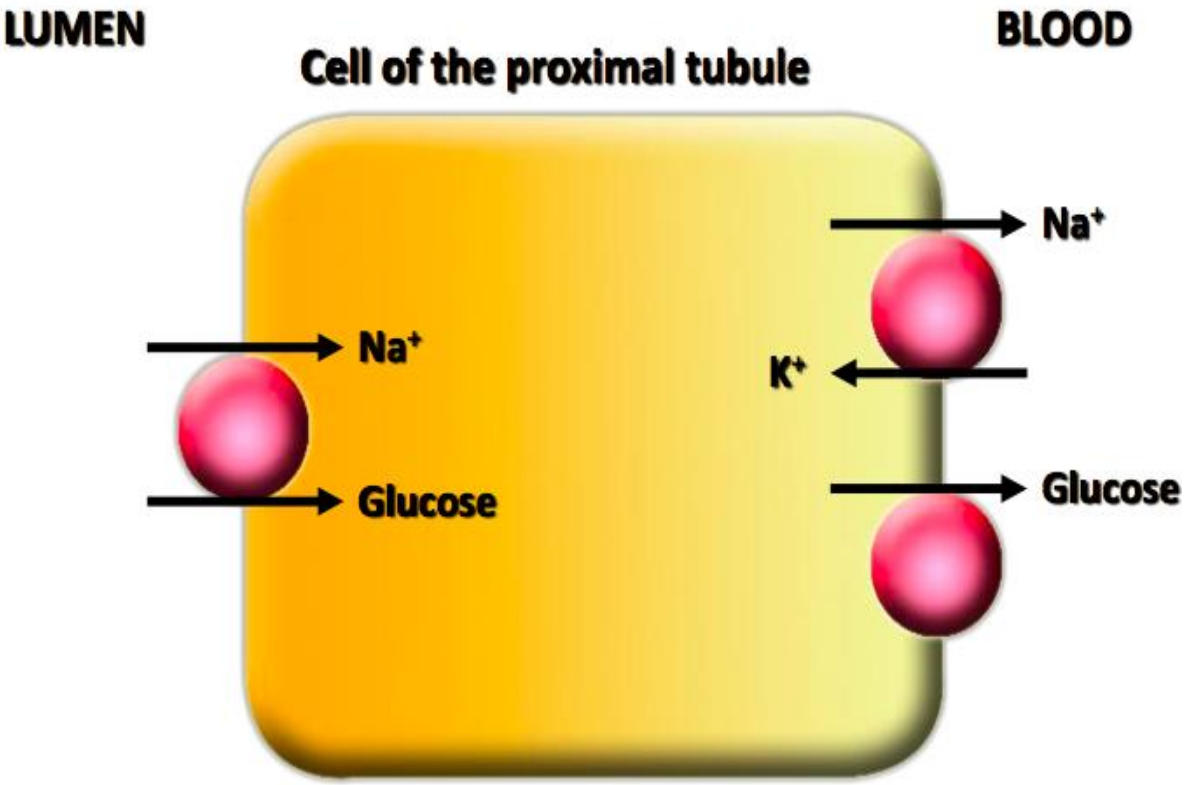
**Glucose enters the cell with Na, and leaves from the other side to blood through glucose transporters 1 and 2**




**Cellular Mechanism for Glucose Reabsorption**

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# AMINO ACID RESORPTION

- All filtered AAs are reabsorbed in PCT
- Luminal membrane
  - ❑ Cotransport with Na
- Basolateral membrane
  - ❑ diffusion

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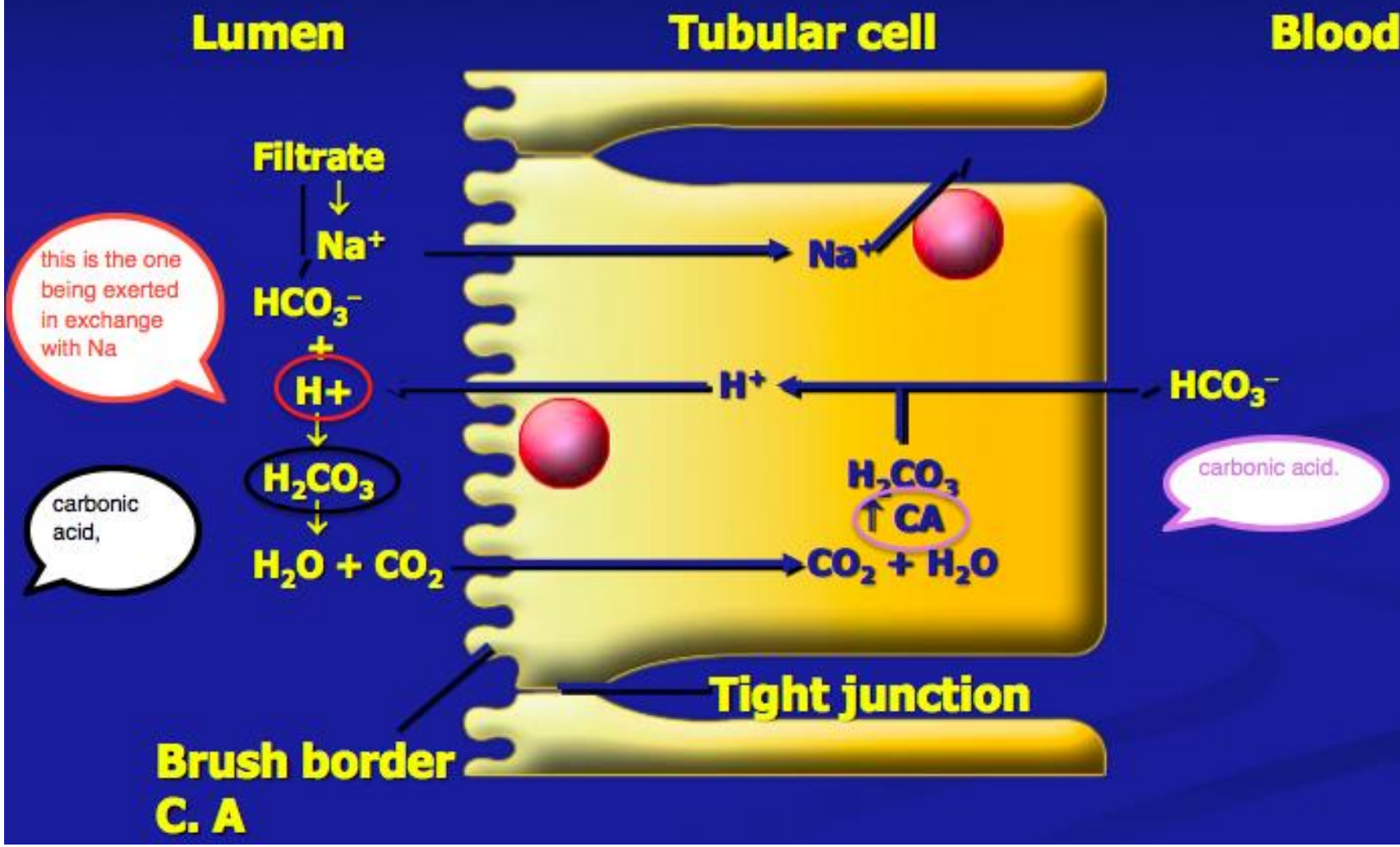
# Bicarbonate reabsorption *cont.*



# BICARBONATE REABSORPTION

- It is filtered in the form of sodium bicarbonate (after dissociation, Na is reabsorbed but HCO3 stays in lumen).
- 90% of filtered bicarbonate is reabsorbed in PCT after some steps:
  - Filtered $H^+ + HCO_3^- \xrightarrow[\text{Carbonic anhydrase}]{} H_2CO_3$
  - $H_2CO_3 \xrightarrow{\text{carbonic anhydrase}} CO_2 + H_2O$ in the presence of carbonic anhydrase enzyme*
  - $CO_2$ (gas) diffuses easily into the cell + $H_2O \xrightarrow[\text{Carbonic anhydrase}]{} H_2CO_3$
  - $H_2CO_3 \rightarrow HCO_3^- + H^+$
  - $HCO_3^-$ is reabsorbed by simple diffusion
  - $H^+$ is secreted in exchange for $Na^+$

- **Note that Bicarbonate is big, we have to break it down first then reabsorb it.**
  ***abundant in brush border + renal cells**
- Bicarbonate which is being absorbed is newly formed inside the cells for each filtered one.

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# PHOSPHATE REABSORPTION

- Bones, teeth & skeleton = 80%
- Intracellular P =20%
- Plasma P= 1mmol/L freely filtered
- 1/3 of filtered P is excreted in urine
- 2/3 Reabsorbed co-transported with Na
- Rate of absorption is under the control of PTH & VD = vitamin D + Parathyroid hormone.

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# UREA REABSORPTION

- Plasma urea concentration =15-40mg /100ml *
- End product of protein metabolism
- 40-50% of filtered urea reabsorbed
- Reabsorbed by Passive diffusion following Na and water
- 50-60% excreted

* In renal failure, it is higher than 40.

❑ What is the mechanism that makes urea high in renal failure?

- GFR is low, less urea is being filtrate.
- More urea is absorbed into the blood, because of slow rate of filtrate.

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# UREA REABSORPTION

- If GFR ↓ (due to renal disease; low renal blood flow) → ↑ urea concentration in plasma due:
  - Reduction in urea filtration
  - more urea reabsorbed to blood due to slow flow rate of filtrate

- Normally we filtrate more and absorb less.
- If we filtrate less and absorb more → High urea in blood

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# CALCULATION OF NA REABSORPTION EXAMPLE

- Plasma Na concentration = 140 mEq/L
- GFR (inulin clearance) = 125 ml/min
- Urine flow rate = 1 ml/min
- Urine concentration of Na= 70 mEq/L

Calculate the amount of Na transported?

**Similar Q was already covered in lecture 3**

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# Information that may be helpful

- Secondary active transport, is also known as coupled transport or co-transport
- Oncotic pressure or colloid osmotic pressure, is a form of osmotic pressure exerted by proteins in a blood vessel's plasma

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# SUMMARY

## Qs Asked by Dr. Sitelbanat :

***If I want to calculate the amount of substance which is being reabsorbed or secreted, what would I do?**

Follow this, Reabsorption or secretion =Quantity Filtrated – Quantity excreted

***If i blocked the active pump of Na/K, what will happen ?**

No Na will be absorbed

***Does this affect the Glucose and Amino acid?**

yes, as we said before if we blocked the active transport of Na, the rest of the molecule will be affected.

***How Na cross the luminal membrane?**

Passively either co-transported with glucose, amino acids or via (counter transport) or via Na channel

***But, how Na cross the basolateral membrane?**

Active transport (Na/K)

***How Na is being reabsorbed in the kidney ?**

Secondary active (in general).

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# SUMMARY

From 431

- Absorption: From filtrate to blood, Secretion: From blood to filtrate.
- 65-70% of filtered sodium is reabsorbed in PCT ,Iso-osomotic absorption (equal quantity of solute & water)
- Sodium Na is the leading substance
- Types of transport:
  1) Transcellular: Across renal cell
  2) Paracellular: Through tight junction
- Renal transport : Tx = GFR x Px - UxV = the amount that is transported of molecule
- (TmG)= The amount of reabsorbed glucose at very high filtered glucose= 375 mg/min (female 300mg/min)
- Reabsorption or secretion = Quantity Filtrated – Quantity excreted
  = ( Px x GFR ) - ( Ux x V )
- All filtered AAs are reabsorbed in PCT

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# SUMMARY

From 431

- Vegetarian pass alkaline urine
- Sodium, potassium depends on your diet intake
- Does the loop of henle contain glucose, portion, or amino acid normally? no
- Simple diffusion: without carrier
- Facilitated diffusion: with carrier
- Primary active transport: use energy directly by ATP
- Secondary active transport : energy is indirectly by co and counter transport
- glucose and amino acid transported from cell to interstitium by facilitated diffusion

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# Questions

**6.** The reabsorption of filtered $HCO_3^-$

**(A)** results in reabsorption of less than 50% of the filtered load when the plasma concentration of $HCO_3^-$ is 24 mEq/L

**(B)** acidifies tubular fluid to a pH of 4.4

**(C)** is directly linked to excretion of $H^+$ as $NH_4^+$

**(D)** is inhibited by decreases in arterial $P_{CO_2}$

**(E)** can proceed normally in the presence of a renal carbonic anhydrase inhibitor

**10.** At plasma concentrations of glucose higher than occur at transport maximum ($T_m$), the

**(A)** clearance of glucose is zero

**(B)** excretion rate of glucose equals the filtration rate of glucose

**(C)** reabsorption rate of glucose equals the filtration rate of glucose

**(D)** excretion rate of glucose increases with increasing plasma glucose concentrations

**(E)** renal vein glucose concentration equals the renal artery glucose concentration

**13.** Which of the following would produce an increase in the reabsorption of isosmotic fluid in the proximal tubule?

**(A)** Increased filtration fraction

**(B)** Extracellular fluid (ECF) volume expansion

**(C)** Decreased peritubular capillary protein concentration

**(D)** Increased peritubular capillary hydrostatic pressure

**(E)** Oxygen deprivation

6. **The answer is D** [IX C 1 a–b]. Decreases in arterial $P_{CO_2}$ cause a decrease in the reabsorption of filtered $HCO_3^-$ by diminishing the supply of $H^+$ in the cell for secretion into the lumen. Reabsorption of filtered $HCO_3^-$ is nearly 100% of the filtered load and requires carbonic anhydrase in the brush border to convert filtered $HCO_3^-$ to $CO_2$ to proceed normally. This process causes little acidification of the urine and is not linked to net excretion of $H^+$ as titratable acid or $NH_4^+$.

10. **The answer is D** [III B; Figure 5-5]. At concentrations greater than at the transport maximum ($T_m$) for glucose, the carriers are saturated so that the reabsorption rate no longer matches the filtration rate. The difference is excreted in the urine. As the plasma glucose concentration increases, the excretion of glucose increases. When it is greater than the $T_m$, the renal vein glucose concentration will be less than the renal artery concentration because some glucose is being excreted in urine and therefore is not returned to the blood. The clearance of glucose is zero at concentrations lower than at $T_m$ (or lower than threshold) when all of the filtered glucose is reabsorbed, but is greater than zero at concentrations greater than $T_m$.

13. **The answer is A** [II C 3; IV C 1 d (2)]. Increasing filtration fraction means that a larger portion of the renal plasma flow (RPF) is filtered across the glomerular capillaries. This increased flow causes an increase in the protein concentration and oncotic pressure of the blood leaving the glomerular capillaries. This blood becomes the peritubular capillary blood supply. The increased oncotic pressure in the peritubular capillary blood is a driving force *favoring reabsorption* in the proximal tubule. Extracellular fluid (ECF) volume expansion, decreased peritubular capillary protein concentration, and increased peritubular capillary hydrostatic pressure all inhibit proximal reabsorption. Oxygen deprivation would also inhibit reabsorption by stopping the $Na^+$–$K^+$ pump in the basolateral membranes.

# THE END

**If there are any problems or suggestions**
**Feel free to contact:**


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# THANK YOU

**Actions speak louder than Words**