REABSORPTION AND SECRETION

Renal Block
Define tubular reabsorption, tubular secretion, transcellular and paracellular transport.

Identify and describe mechanisms of tubular transport & Describe tubular reabsorption of sodium and water.

Identify the tubular site and describe how Amino Acids, $\text{HCO}_3^-$, $\text{P}_4^-$ and Urea are reabsorbed.

Revise tubule-glomerular feedback and describe its physiological importance.

Identify and describe mechanism involved in Glucose reabsorption.

Study glucose titration curve in terms of renal threshold, tubular transport maximum, splay, excretion and filtration.

Identify the site and describe the influence of aldosterone on reabsorption of $\text{Na}^+$ in the late distal tubules.

Describe tubular secretion with PAH transport and $\text{K}^+$.

Identify and describe the characteristic of loop of Henle, distal convoluted tubule and collecting ducts for reabsorption and secretion.
**Mind Map**

**Reabsorption and Secretion**

- Regulation of tubular reabsorption
  - Hormonal mechanisms
    - Angiotensin II
    - Nerves
    - Sympathetic
  - Aldosterone

- Mechanisms of cellular transport in the nephron
  - Active transport
    - Primary active transport
      - Na-K pump
    - Secondary active transport
      - Na-K-2Cl co-transport
  - Passive transport
  - Osmosis (water)
  - Pinocytosis

- Glucose handling
  - Glucose reabsorption occurs in proximal tubule

- General characteristics of tubules
  - Proximal convoluted tubules
  - Loop of Henle
  - Distal convoluted tubules
  - Late distal tubule & Cortical Collecting ducts
  - Medullary Collecting ducts

- Facilitated diffusion
- Simple diffusion
As the glomerular filtrate enters the renal tubules, it flows sequentially through the successive parts of the tubule:
The proximal tubule → the loop of Henle → the distal tubule → the collecting tubule → finally, the collecting duct, before it is excreted as urine.

Along this course, some substances are selectively reabsorbed from the tubules back into the blood, whereas others are secreted from the blood into the tubular lumen.

The urine represents the sum of three basic renal processes: glomerular filtration, tubular reabsorption, and tubular secretion:

**Urinary excretion = Glomerular Filtration – Tubular reabsorption + Tubular secretion**
Mechanisms of cellular transport in the nephron are:

**Active transport**

“Active transport can move a solute against an electrochemical gradient and requires energy derived from metabolism.”

- **Primary active transport**
  - Transport that is coupled directly to an energy source such as ATP
  - Sodium-potassium pump
    - (found in basolateral membrane along renal tubules)
  - H+-pump

- **Secondary active transport**
  - Transport that is coupled indirectly to an energy source due to concentration gradient of ion
  - Sodium-potassium pump
  - Na-K-2Cl co-transport
  - glucose-sodium co-transport (SGLT)
  - amino acid-sodium co-transport
  - H+/Na counter-transport

**Passive Transport**

- **Simple diffusion** (without carrier protein)
  - Cl, HCO3-, urea, creatinine
- **Facilitated diffusion** (require carrier protein)
  - Glucose and amino acids at the basolateral border (GLUT)

**Osmosis**

- Water is always reabsorbed by a passive (nonactive) physical mechanism called osmosis, which means water diffusion from a region of low solute concentration (high water concentration) to one of high solute concentration (low water concentration).

**Pinocytosis\exocytosis**

(Additional reading)

The proximal tubule, reabsorb large molecules such as proteins by pinocytosis. In this process, the protein attaches to the brush border of the luminal membrane, then invaginates to the interior of the cell until it is completely pinched off and a vesicle is formed containing the protein. Once inside the cell the protein is digested into its constituent amino acids, which are reabsorbed through the basolateral membrane into the interstitial fluid. Because pinocytosis requires energy, it is considered a form of active transport.

**Co-transport**

1. Co-transport: movement of two molecules in the same direction but they opposite in concentration gradient
2. Counter-transport: movement of two molecules in opposite direction based on their concentration gradient
The ways of transport:

1- From lumen of tubules (Apical membrane”) to epithelial cells then from epithelial cells to interstitium (Basolateral membrane):
   A- Transcellular route: (through the cell membrane)
   B- Paracellular route: (between spaces of tight cell junction)

2- From interstitium (basolateral space) to the Peritubular capillaries: By ultrafiltration (bulk flow) that is mediated by: hydrostatic and colloid osmotic forces

(1) Apical membrane = brush border which is numerous to help in reabsorption
How is transportation take place from tubules to interstitium?

1. 
A. Sodium diffuses across the luminal membrane (also called the apical membrane) into the cell down an electrochemical gradient (with other substances such as glucose, amino acids etc.) established by the sodium-potassium ATPase pump on the basolateral side of the membrane.
B. Other molecules like water and Cl, Ca etc. by osmosis and diffusion

2. 
A. Sodium is transported across the basolateral membrane against an electrochemical gradient by the sodium-potassium ATPase pump
B. other substances will across the basolateral membrane by passive diffusion

3. Sodium, water, and other substances are reabsorbed from the interstitial fluid into the Peritubular capillaries by ultrafiltration (bulk flow \(^1\)), a passive process driven by the hydrostatic and colloid osmotic pressure gradients

\(^1\) Bulk flow = movement of water with other substances
While diffusion = movement of substances without water.
In Peritubular capillaries the high plasma oncotic pressure is due to fluid filtration in glomerulus.

- **increase GFR**: increase oncotic pressure & decrease hydrostatic pressure in efferent & Peritubular capillaries → increase bulk flow from lateral space to Peritubular capillaries → increase reabsorption.

- **decrease GFR**: decrease oncotic pressure & increase hydrostatic pressure → decrease bulk flow → fluid go back to lumen through tight junction → decrease reabsorption.
**General characteristic of tubules**

**Proximal convoluted tubule**

1. Proximal tubules is **coarse adjustment** (reabsorption a most of water and solutes)
2. Solute reabsorption in the proximal tubule is isosmotic (equal amount of solute and water are reabsorbed)
3. 100% of glucose and amino acids reabsorbed

**Loop of henle**

1. Responsible for producing a **concentrated urine** in the medulla.
2. When ADH (antidiuretic hormone) is present, **water** is reabsorbed and urine is concentrated.

**Descending limb**: (concentrate urine “1”)  
1. **Water** permeable and allow absorption of 25% of filtered H2O.  
2. It is **impermeable** to Na-CL.  
3. Fluid becomes **hyper-osmolar**

**Thin ascending limb**: (dilute urine “2”)  
1. **Impermeable** to H2O  
2. Permeable to NaCl (passive)  
3. By the end of ascending limb of loop, the tubular fluid becomes **hypo-osmolar**

**Thick ascending limb**: (dilute urine)  
1. **Impermeable** to H2O  
2. Na-K-2CL **co-transport** occur in this part. (active)  
3. The tubular fluid becomes **hypo-osmolar** to plasma in this part

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(1) **Concentrate urine** = remove water from fluid  
(2) **Dilute urine** = remove solutes from urine

* The main function of tubules is **concentrate urine** and that has done in **loop of henle of Juxtamedullary nephron**

* Sodium-potassium pump that found in **distal convoluted tubules** is under control of aldosterone
**Distal convoluted tubules**

1- Distal tubule is **fine adjustment** (reabsorption a fine amount of water and solutes by hormonal control based on body needs)

2- The first portion of DCT forms part of **Juxtaglomerular Apparatus**, that provides feedback control of GFR and RBF of the same nephron.

3- The next early portion has the same characteristics as **ascending limb of Henle** that is
   1-impermeable to water
   2-absorbs solutes.
   So it is called the **diluting segment** & the osmotic pressure of the fluid ~ 100 mOsm/L.

**Late distal convoluted tubules & cortical collecting ducts**

1- Composed of two types of cells:
   a. **Principal cells**: absorb Na+ & H2O and secrete K+
   b. **Intercalated cells**: absorb K+ & secrete H+
      • Secretion of K+ and reabsorption of Na+ controlled by aldosterone.

2- **water permeability under ADH control.** (works under body needs)

3- **Impermeable to Urea.**

**Medullary collecting ducts**

1- Under ADH control. (works under body needs)
2- **Highly permeable to urea.**
3- Final site for processing urea.
4- Secretes H+ helps to:
   a- maintain blood pH
   b- reabsorb HCO3 and generate new HCO3
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<thead>
<tr>
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<th><strong>Reabsorption</strong></th>
<th><strong>Secretion</strong></th>
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<tbody>
<tr>
<td><strong>Proximal convoluted tubules</strong></td>
<td>- Poorly reabsorbed of creatinine and urea</td>
<td>- H+</td>
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<tr>
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<td>- 60% - 75% of sodium and water</td>
<td>- Urea</td>
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<td></td>
<td>- 90% of HCO₃, K⁺, Ca and Cl⁻</td>
<td>- ammonia</td>
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<td>- 100% Glucose and amino acids</td>
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<tr>
<td><strong>Descending loop of henle</strong></td>
<td>-25% of water (H₂O)</td>
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<tr>
<td><strong>Thin ascending loop of henle</strong></td>
<td>- Sodium chloride (NaCl)</td>
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<tr>
<td><strong>Thick ascending loop of henle</strong></td>
<td>- Sodium</td>
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<td>- Potassium</td>
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<td>- Chloride</td>
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<td><strong>Distal convoluted tubules</strong></td>
<td>- Sodium in response to <strong>aldosterone</strong></td>
<td>- Potassium in response of <strong>aldosterone</strong></td>
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<td>- Water in response of <strong>ADH</strong></td>
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<td>- Calcium in response of <strong>parathyroid hormone</strong></td>
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<tr>
<td><strong>Late distal tubule &amp; Cortical Collecting ducts</strong></td>
<td>a. Principal cells: absorb Sodium Na⁺ &amp; H₂O</td>
<td>a. <strong>Principal cells</strong>: secret K⁺</td>
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<td>b. Intercalated cells: absorb Potassium K⁺ &amp; HCO₃</td>
<td>b. <strong>Intercalated cells</strong>: secret H⁺</td>
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<td>- H⁺</td>
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<td></td>
<td>- <strong>Highly permeable to urea</strong> (to maintain osmolarity of medulla)</td>
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### Site | Between | Functions
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**Primary Active Transport**
Sodium-potassium pump | All renal tubules | Basolateral membrane | Reabsorption of sodium and secrete potassium to maintain the intracellular and extracellular balance of Na and K

**Secondary Active Transport**
H+/Na counter-transport | Proximal convoluted tubules, Distal convoluted tubules and collecting ducts | Apical membrane | Reabsorption of sodium and secrete hydrogen ion and It is coupled with bicarbonate transport
HCO3/Na co-transport | Proximal convoluted tubules, Late distal convoluted tubules and collecting ducts | Basolateral membrane | Reabsorption of sodium and bicarbonate
Na-K-2Cl co-transport | Thick ascending limb of henle’s loop | Apical membrane | Reabsorption of sodium, potassium and two chloride to dilute water
Glucose-sodium co-transport (SGLT) | Proximal convoluted tubules | Apical membrane | Reabsorption of sodium and glucose
Amino acid-sodium co-transport | Proximal convoluted tubules | Apical membrane | Reabsorption of sodium and amino acid

**Simple diffusion**
Passive NaCl transport | Thin ascending limb of henle’s loop | Apical membrane | Reabsorption of NaCl to dilute fluid in tubules
Passive channels of K+, Cl, Ca etc. | All renal tubules | Apical membrane & Basolateral membrane | Reabsorption and secretion

**Facilitated diffusion**
Glucose transporter (GLUT) | Proximal convoluted tubules | Basolateral membrane | Reabsorption of glucose to interstitial fluid

**Osmosis**
Water | **All renal tubules except:** 1- thin and thick ascending limb and 2- early portion of distal convoluted tubules | Apical membrane & Basolateral membrane | Reabsorption of water
Glucose handling

**GLUCOSE REABSORPTION**

- Glucose enters the tubular cells by secondary active transport "co-transport", it uses SGLT "a specific transport protein which needs Na".
- Then it crosses the cell membrane into the interstitial spaces by facilitated transport "passive transport" which uses GLUT’s "do not need Na".
- Glucose reabsorption occurs in proximal tubule.

- Essentially all glucose is reabsorbed.
- The renal **threshold** for glucose = 180 mg/dl.
- The **tubular transport maximum** for glucose: Tmg = 375 mg/min in men and 300 mg/min in women.

**What is the difference between renal threshold and tubular transport maximum?**

- **Renal threshold**: it’s the rate that glucose begins to appear in the urine.
- **Transport maximum for glucose**: all nephrons have reached their maximal capacity to reabsorb glucose "maximum saturation of transporters".

**What cause the excretion of glucose in urine before reach to its maximum transport?**

- Not all nephrons have the same transport maximum for glucose, and some of the nephrons therefore begin to excrete glucose before others have reached their transport maximum.
• First of all, bicarbonate (HCO$_3^-$) attaches itself with hydrogen (H$^+$) then it becomes H$_2$CO$_3$ in the lumen

• Carbonic Anhydrase will break H$_2$CO$_3$ down to water (H$_2$O) + carbonic dioxide (CO$_2$) which diffuses into the proximal tubule

• Carbonic Anhydrase will convert the water (H$_2$O) + the carbon dioxide (CO$_2$) to HCO$_3^-$ + H$^+$

• Hydrogen will transport out and sodium (Na) will come in the proximal tubule

• Lastly, the HCO$_3^-$ will go into the blood
Relations among the filtered load of glucose, the rate of glucose reabsorption by the renal tubules, and the rate of glucose excretion in the urine
# Regulation of tubular reabsorption

There must be a balance between tubular reabsorption and glomerular filtration. This is controlled by local, nervous & hormonal mechanisms.

1. **Glomerulotubular balance**: prevents overloading of distal parts when GFR increases.

2. **Peritubular capillary reabsorption** is regulated by hydrostatic and colloidal pressures through the capillaries.

3. **Arterial blood pressure**: if increased it reduces tubular reabsorption. (increase in blood pressure will reduced GFR in response of myogenic mechanism and the decrease reabsorption)

4. **Nervous Sympathetic**:
   - Increases Na+ reabsorption.

5. **Tubuloglomerular feedback**: it will observe concentration of sodium chloride by macula dense in distal tubules and what will lead to:
   - 1- constriction and dilatation of afferent arteriole which affect on GFR
   - 2- release renin which increase reabsorbtion of sodium and play a role in production of angiotensin II

6. **Hormonal**:
   - **Angiotensin II**: release aldosterone
   - **ADH**: H2O reabsorption
   - **ANP**: Sodium excretion and diuresis
   - **Parathyroid hormone**: Increases Ca reabsorption & decreases phosphate reabsorption

(1) ADH: Antidiuretic hormone
(2) ANP: atrial nitric peptide
(3) Diuresis: increase urine output
Aldosterone

Function

- 1-increases Sodium reabsorption
- 2-stimulates Potassium secretion

When does it secreted?

- (1) Increased extracellular potassium concentration.
- (2) Increased angiotensin II levels, which typically occur in conditions associated with sodium and volume depletion or low blood pressure (so it will increase blood pressure)

Site of secretion

- Aldosterone, secreted by the zona glomerulosa cells of the adrenal cortex.

Mechanism of action

- by stimulating the sodium-potassium ATPase pump on the basolateral side of the cortical collecting tubule membrane.
- Aldosterone also increases the sodium permeability of the luminal side of the membrane.

Diseases associated with aldosterone

- Absence of aldosterone, as occurs with adrenal destruction or malfunction (Addison’s disease)
- Excess aldosterone, as occurs in patients with adrenal tumors (Conn’s syndrome) is associated with:
  1- sodium retention
  2- decreased plasma potassium concentration
**Summary**

- Absorption through apical membrane is done passively.
- Movement of Na through basal membrane is done Na/K ATPase.
- ↑ GFR → ↑ Absorption
- Sympathetic → ↑ Na absorption
- ADH → ↑ H2O absorption
- Aldosterone → ↑ Na absorption + K excretion
- ANP ↑ Na excretion

**Proximal tubules:**
1. has the greatest effect in all tubules.
2. the fluid inside it is isosmotic.

**Loop of Hele:**
- Descending: concentrate urine by reabsorption of water.
- Thin ascending: Absorbed Na Cl
- Thick ascending: Absorbed Na 2Cl K

**Distal tubules:**
1. Has muclad densa which is Na sensitive + excretes renin.
2. has principal cell: Na + H2o absorption & K secretion
3. has intercalated cell: absorbs K and secretes H+ (controls pH)
BLOODSTREAM

Renal arteriole

GLOMERULUS

Filtration

Water
Sugar
Salts
Urea/other wastes

Secrretion

Acids, potassium, & drugs

REABSORPTION

Water
Sugar
Salts

BOWMAN CAPSULE

RENAL TUBULE

Urea/wastes
Salts
Water
Acids & drugs

RENAL PELVIS

URETER

BLADDER

URETHRA

URINARY MEATUS

Urine leaves the body
Q1: One of these examples is control passively:
A/Transport maximum
B/Transcellular reabsorption
C/Paracellular reabsorption
D/co-transport

Q2: where is Sodium-potassium specific pumps?
A/Basement membrane
B/Basolateral membrane
C/Interstitial wall
D/Cytoplasmic membrane

Q3: Where can you found sodium-potassium pump? In between..
A/Tubular lumen & tubular cell.
B/interstitial fluid & tubular lumen.
C/interstitial fluid, tubular cell & tubular lumen.
D/interstitial fluid & tubular cell

Q4: When 3 Na / 2 K pumped in Basolateral membrane, the net result is:
A/High intracellular Na concentration
B/Low Extracellular Na concentration
C/↑ osmolarity in the basolateral space
D/↓ osmolarity in the basolateral space.

Q5: Most of filtered water is reabsorbed in:
A/Proximal convoluted tubule (PCT)
B/Distal convoluted tubule (DCT)
C/Ascending loop of henle
D/Descending loop of henle

Q6: Glucose reabsorption is the difference between:
A/the amount of glucose filtered and the amount secreted
B/the amount of glucose filtered and the amount excreted.
C/the amount of glucose reabsorbed and the amount excreted.
D/the amount of glucose reabsorbed and the amount secreted

Q7: When plasma glucose reach which called “glucose renal threshold” , How much is glucose level in vein that will lead to appear in urine ?
A/250mg/dl
B/375 mg/dl
C/180mg/dl
D/200mg/dl

Q8: How much is maximum absorptive capacity for glucose in men?
A/375mg/min
B/200mg/dl
C/250mg/min
D/300mg/min
Q9: Amino acid is reabsorbed in Basolateral membrane by:
A/ ATP
B/ Diffusion
C/ Co-transport with Na
D/ Na+/K+ ATPase

Q10: What is the main important mechanism for Na exchange on Bicarbonate reabsorption?
A/ Reabsorpetion of HCO₃
B/ Secreted H⁺
C/ Diffuses CO₂
D/ Filtered HCO₃

Q11: At the end of descending loop of henle the osmolarity will be:
A/ Decrease
B/ No change
C/ Minimal change
D/ Increase

Q12: Which site has a high permeability of water:
A/ Thick ascending loop of henle
B/ Thin ascending loop of henle
C/ Early portion of Distal convoluted tubule
D/ Thin descending loop of henle

Q13: Which of the following is an site of NaCl diffuses passively?
A/ Proximal convoluted tubule (PCT).
B/ thin ascending loop.
C/ Distal convoluted tubule (DCT).
D/ thick ascending limb.

Q14: The amount of water, solute reabsorption and secretion depends on:
A/ Age
B/ Weight
C/ body's needs
D/ secrete H⁺

Q15: During Reabsorption/secretion of H₂O in Late Distal Tubules and Collecting Tubules, the H₂O is more dependent on:
A/ Angiotensin II
B/ principal cells
C/ Aldosterone
D/ Anti-Diuretic hormone