YU - Medicine Passion Academic Team

The Urogenital System

Sheet# 2 - Physiology

Lec. Title : Tubular Reabsorption & Secretion

Written By : Sawsan Radi
Rahma Marie

If you come by any mistake , please kindly report it to shaghafbatch@gmail.com

Tubular reabsorption and secretion

التفريغ شامل كلام الدكتورة والكتاب بإذن الله
دعواتكم، كل الحُبّ....

Reabsorption and secretion

- The amount of ultrafiltrate of plasma is more than10 fold the amount present in the entire ECF
- **Reabsorptive** mechanisms in the epithelial cells lining the renal tubule return these substances to the circulation and to the ECF
- **secretion** mechanisms in the epithelial cells remove certain substances from the peritubular capillary blood and add it to urine.

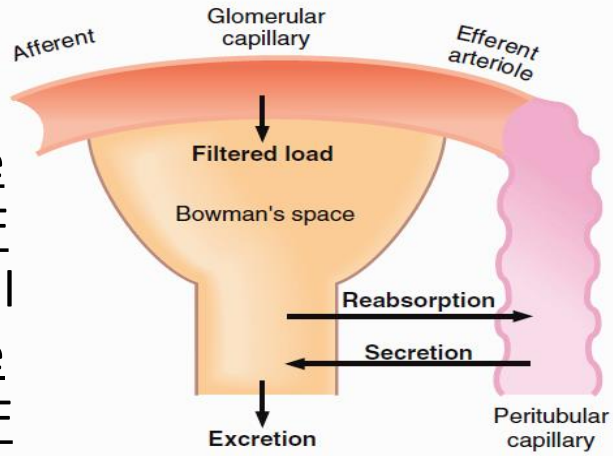


FIGURE 5.4 Processes of filtration, reabsorption, and secretion. The sum of the three processes is excretion.

- **Filtration.:** An interstitial-type fluid is filtered across the glomerular capillary into Bowman's space.
- The amount of a substance filtered into Bowman's space per unit time is called the **filtered load.**

Filtered load = GFR x [plasma] x % unbound in plasma

- The fluid in Bowman's space and in the lumen of the nephron is called tubular fluid or luminal fluid.

- **Reabsorption:** Water and many solutes (e.g., Na^+, Cl^-, HCO_3^-, glucose, amino acids…) are **reabsorbed from the glomerular** filtrate into the **peritubular capillary blood**.
  - The mechanisms for reabsorption **involve transporters** in the membranes of the renal epithelial cells

- **Secretion.** A few substances (e.g., organic acids, organic bases, K^+) are **secreted from peritubular capillary** blood into **tubular fluid.**
  - Thus in addition to filtration, secretion provides a mechanism for excreting substances in the urine. **involve transporters**.

- **Excretion.** Excretion, or **excretion rate**, refers to the amount of a substance excreted per unit time.
  - It is the **net result**, or sum, of the processes of filtration, reabsorption, and secretion.

Excretion rate = V x [urine]

- The excretion rate can be compared with the filtered load to determine whether a substance has been reabsorbed or secreted.

- If the ***filtered load is greater*** than the excretion rate, then **net reabsorption of the substance** has occurred.

- If the ***filtered load is less*** than the excretion rate, then **net secretion of the** substance has occurred.

Reabsorption rate = Filtered load – Excretion rate

Secretion rate = Excretion rate – Filtered load

Example:

A woman with untreated diabetes mellitus has a GFR of 120 mL/min, a plasma glucose concentration of 400 mg/dL, a urine glucose concentration of 2500 mg/dL, and a urine flow rate of 4 mL/min.

What is the reabsorption rate of glucose?

Solution:

$$\begin{aligned}
\text{Filtered load} &= \text{GFR} \times \text{Plasma [glucose]} \\
&= 120\ \text{mL/min} \times 400\ \text{mg/dL} \\
&= 480\ \text{mg/min} \\
\text{Excretion} &= \text{V} \times \text{Urine [glucose]} \\
&= 4\ \text{mL/min} \times 2500\ \text{mg/dL} \\
&= 100\ \text{mg/min} \\
\text{Reabsorption} &= 480\ \text{mg/min} - 100\ \text{mg/min} \\
&= 380\ \text{mg/min}
\end{aligned}$$

Reabsorption of glucose

Cellular mechanism for glucose reabsorption

- Glucose is filtered across glomerular capillaries and **reabsorbed** by the epithelial cells of the **proximal convoluted** tubule
- It is a two-step process; involving **Na+-glucose cotransport** across the **luminal membrane** and **facilitated glucose transport** across the **peritubular membrane**
- There are a **limited number of glucose transporters**, the mechanism is saturable; that is, it has a **transport maximum, or T_m.**

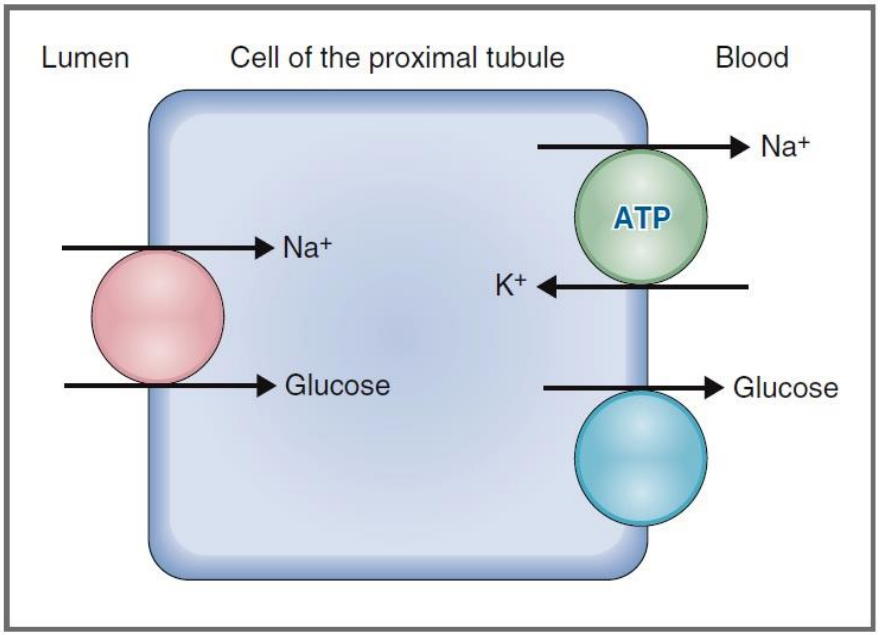


Fig. 6.14 Cellular mechanism of glucose reabsorption in the early proximal tubule. *ATP,* Adenosine triphosphate.

- From previous figure:

1. Glucose moves from tubular fluid into the cell on the **Na^+-glucose cotransporter** (called **SGLT**) in the **luminal** membrane.
   - **Two Na^+ ions and one glucose** bind to the cotransport protein.
   - In this step, **glucose** is transported **against** an electrochemical gradient; **the energy** for this uphill transport of glucose ***comes from the downhill movement of Na^+.***
   - **Na^+-K^+ ATPase** in the **peritubular** (basolateral) membrane **produces a Na^+ gradient** (ECF [Na^+] > ICF [Na^+])… in other words ***Na^+*** moves with its electrochemical gradient on SGLT.
   - Because ATP is used ***directly*** *to energize the Na^+-K^+ ATPase and* ***indirectly*** to maintain the Na^+ gradient, Na^+-glucose cotransport is called **secondary active transport.**

2. Glucose is transported from the cell into peritubular capillary blood by **facilitated diffusion.**

- In this step, glucose is moving **down** its electrochemical gradient and **no energy is required.** The proteins involved in facilitated diffusion of glucose are called **GLUT1 and GLUT2.**

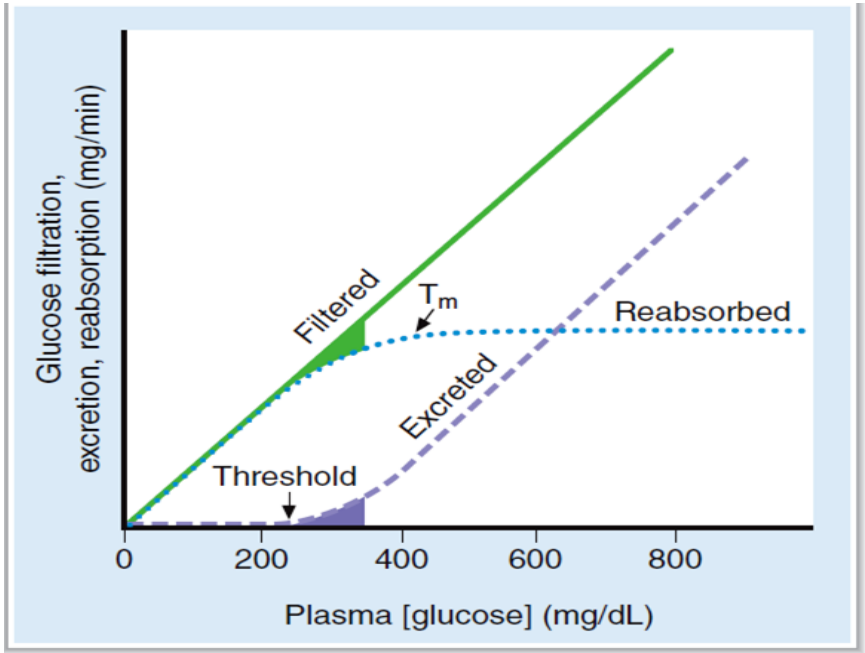
Glucose Titration Curve and Tm

- **glucose titration curve** depicts the relationship between plasma glucose concentration and glucose reabsorption
- obtained experimentally by infusing glucose and measuring its rate of reabsorption as the **plasma concentration is increased**.

- **Filtered load of glucose:** Glucose is freely filtered across glomerular capillaries, and the filtered load is the product of GFR and plasma glucose concentration.

$$\textbf{filtered load of glucose} = \textbf{GFR} \times [\textbf{P}]_{\textbf{glucose}}$$

-increases in direct proportion to the plasma glucose concentration



_ from previous curve:

- **Reabsorption:**

- At plasma glucose concentrations **less than 200 mg/dL**, **all** of the filtered glucose **can be reabsorbed** because *plenty of carriers are available*; in this range, the **line for reabsorption is the same as that for filtration**.
- At plasma glucose concentrations **greater than 350 mg/dL**, the *carriers are saturated*.
- in plasma concentration **above 350 mg/dL** do not result in increased rates of reabsorption. The **reabsorptive rate at which the carriers are saturated is the Tm.**

- **Excretion:**

- **less than 200 mg/dL, all** of the filtered glucose is **reabsorbed** and **excretion is zero.**
- **Threshold** (defined as the plasma concentration at which glucose **first** appears in the urine) is approximately **200-250 mg/dL.**
- **greater than 350 mg/dL,** reabsorption is saturated (Tm). Therefore, as the plasma concentration increases, the additional filtered glucose **cannot be reabsorbed** and is **excreted in the urine. (the excretion curve increases linearly)**

Splay

- Is the region of the glucose curves **between threshold and T_m.**
- Occurs between plasma glucose concentrations of approximately **250 and 350 mg/dL.**
- Represents the excretion of glucose in urine **before** saturation of reabsorption (T_m) is fully achieved.
- It is explained by:

- **heterogeneity of nephrons**:

T_m for the whole kidney reflects **the average T_m** of all nephrons, yet all nephrons **do not have exactly the same T_m.** Some nephrons will reach T_m at lower plasma concentration than others, and **glucose will be excreted** in the urine **before the average T_m is reached**.

- **relatively low affinity of the Na^+-glucose carriers:**

near T_m, if glucose **detaches** from its carrier, it will be **excreted** into the urine because there are few remaining binding sites where it may reattach.

- In uncontrolled **diabetes mellitus,** lack of insulin causes the plasma concentration of glucose to increase to abnormally high levels. In this condition, **the filtered load of glucose exceeds the reabsorptive capacity** (i.e., plasma glucose concentration is **above the Tm**), and **glucose is excreted in the urine**

- Doctor mentioned these drugs and this information from google:

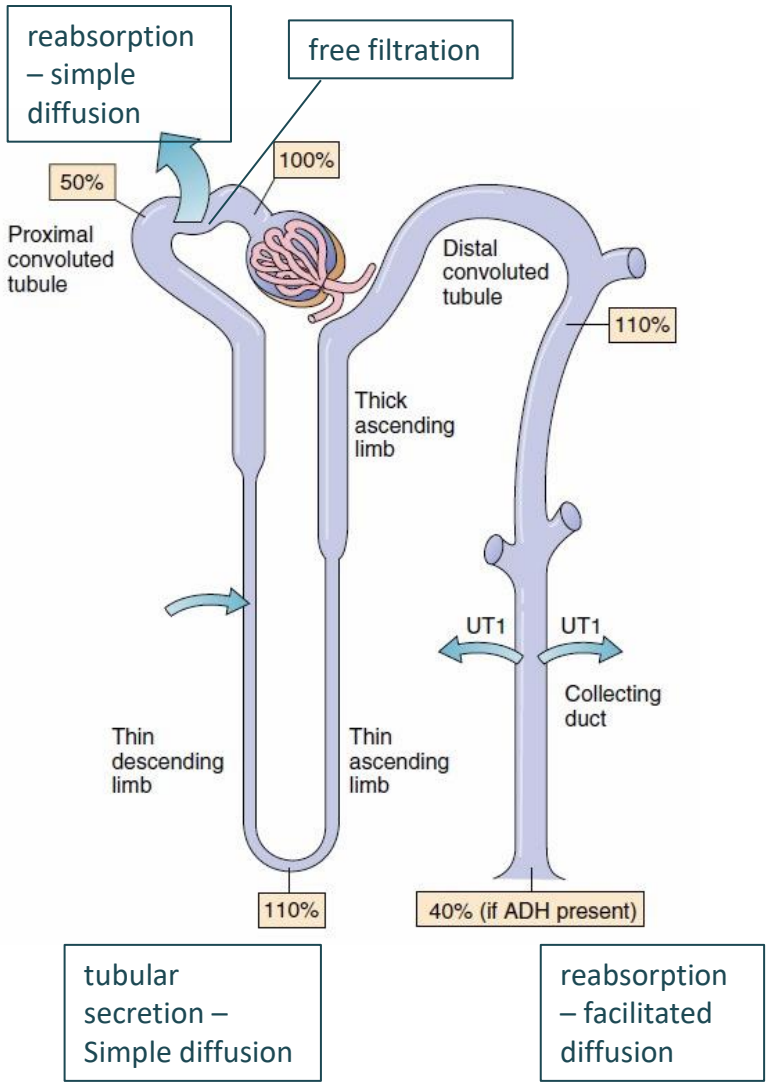
- **Gliflozin:** SGLT2 inhibitor, used with diet and exercise to **lower blood sugar in adults with type 2 diabetes.**

- **Resveratrol: plant anti-microbial/toxic ومعرفش هو ليه هِنا بس هي كانت حاطته بأول سلايد**

Urea—Example of Passive Reabsorption

- Urea is freely filtered across the glomerular capillaries, and the concentration in the initial filtrate is **identical** to that in blood
- Urea is reabsorbed (50% of it reabsorbed in **proximal tubule)** or secreted (in the **thin descending limb of Henle's loop)…** by diffusion (**simple diffusion and facilitated diffusion**)
- rate of reabsorption or secretion is **determined by the concentration difference** for urea between tubular fluid and blood and by the **permeability** of the epithelial cells to urea
- urea reabsorption generally follows the same pattern as water reabsorption, **water is reabsorbed** along the nephron, the urea concentration in tubular fluid **increases**, creating a **driving force for passive urea reabsorption**
- In the presence of ADH, **water is reabsorbed** in the late distal tubule and the cortical and outer medullary collecting ducts—consequently, in these segments, urea is "left behind" and the urea concentration of the tubular fluid becomes quite high.

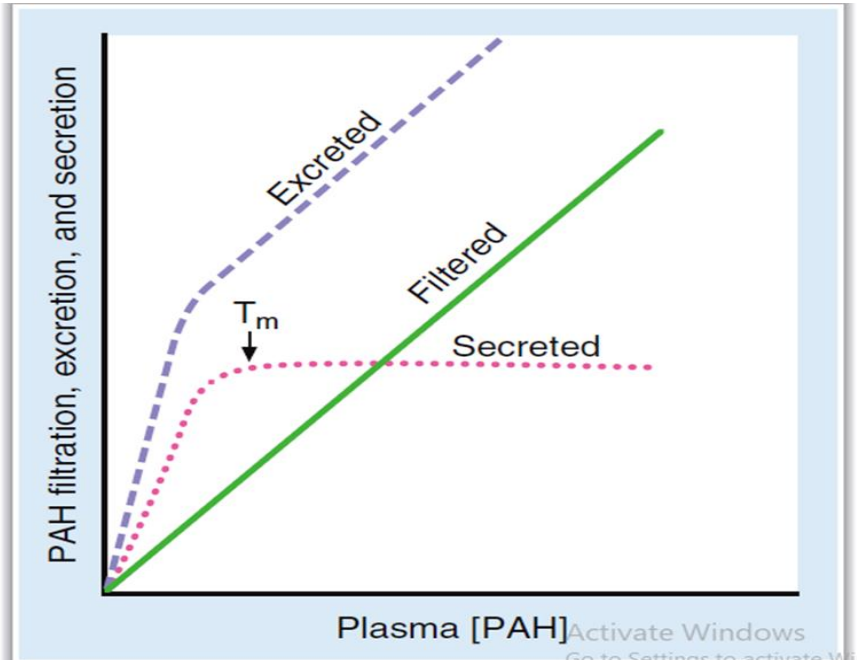
- In the **inner medullary collecting ducts,** there is a specific transporter for the facilitated diffusion of urea (urea transporter 1, **UT1**), which is up-regulated by ADH
- in the presence of ADH, urea is reabsorbed by UT1, moving down its concentration gradient from the lumen into the interstitial fluid of the inner medulla.
- 70% of the filtered urea is reabsorbed by UT1, leaving 40% of the filtered urea to be excreted in the urine



Para-aminohippuric acid (PAH) – a secreted substance

- PAH is an **organic acid** that is both **filtered** across **glomerular capillaries** and **secreted from peritubular capillary** blood into tubular fluid. Used to measure RPF.
- Ten percent of the PAH in blood is bound to plasma proteins, and **only the unbound portion is filterable** across glomerular capillaries.
- **Filtered load of PAH**
- The filtered load of PAH increases linearly as the *unbound* concentration of PAH increases

filtered load = GFR × unbound $[P]_X$



- **Secretion**:

- There are PAH carriers (and for other organic anions), also they're responsible for **secretion** of drugs such as **penicillin** and is **inhibited** by **probenecid.**
- At low concentrations, many carriers are available and secretion increases **linearly** as the plasma concentration increases.
- Once the carriers are saturated, **further increases** in plasma PAH concentration **do not cause further increases** in the secretion rate **(T_m).**

- **Excretion**:

- Excretion of PAH is **the sum of filtration** across the glomerular capillaries **plus secretion** from peritubular capillary blood.
- The curve for excretion is steepest at low plasma PAH concentrations (**lower than at Tm**). Once the Tm for secretion is exceeded and all of the carriers for secretion are saturated, the excretion curve flattens and becomes **parallel** to the curve for filtration.

- **RPF** is measured by the clearance of PAH at plasma concentrations of PAH that are **lower than at T_m.**
- There is no splay in PAH graph because it's a feature for glucose mainly.

Relative clearances of substances

- **Substances with the highest clearances**

  are those that are both filtered across the glomerular capillaries and secreted from the peritubular capillaries into urine (e.g., PAH).

- **Substances with the lowest clearances**

  are those that either are not filtered (e.g., protein) or are filtered and subsequently reabsorbed into peritubular capillary blood (e.g., Na^+, glucose, amino acids, $HCO3^-$, Cl^-).

Relative clearances of substances

- **Substances with clearances equal to GFR**
  - are **glomerular markers.**
  - are those that are freely filtered, but not reabsorbed or secreted (e.g., inulin).

- **Relative clearances**

  PAH > K^+ (high-K^+ diet) > inulin > urea > Na^+ > glucose, amino acids, and $HCO3^-$.

Nonionic diffusion

Weak acids

- have an HA form and an A^- **form.**
- The HA form, which is uncharged and lipid soluble, can "back-diffuse" from urine to blood.
- The A^- form, which is charged and not lipid soluble, cannot back-diffuse.
- At **acidic urine pH, the HA form predominates, there is more back-diffusion, and there is** decreased excretion of the weak acid.
- At **alkaline urine pH,** the A^- form predominates, there is less back-diffusion, and there is increased excretion of the weak acid. For example, the excretion of **salicylic acid** (a weak acid) can be increased by alkalinizing the urine.

Weak bases

- have a BH^+ form and a B form.
- The B form, which is uncharged and lipid soluble, can “back-diffuse” from urine to blood.
- The BH^+ form, which is charged and not lipid soluble, cannot back-diffuse.
- At **acidic urine pH, the BH^+ form predominates, there is less back-diffusion, and there** is increased excretion of the weak base. For example, the excretion of **morphine (a weak** base) can be increased by acidifying the urine.
- At **alkaline urine pH, the B form predominates, there is more back-diffusion, and there is** decreased excretion of the weak base.