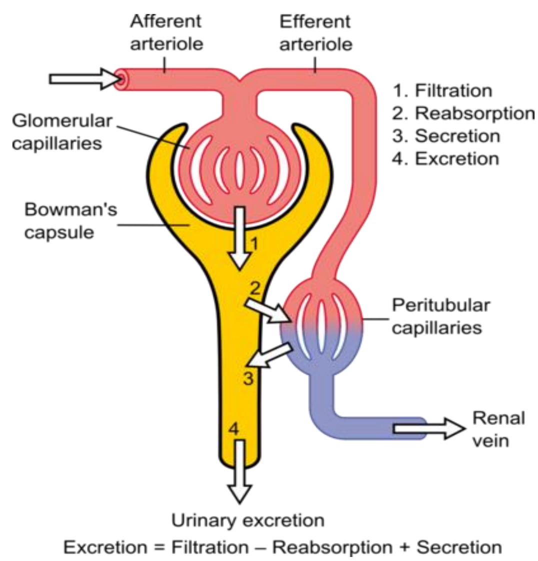
PHYSIOLOGY

- Sheet no. 4
- Writer :
- Corrector :
- Doctor :

Quick recap:

- In the previous 3 lectures, we talked about 3 basic mechanisms of urine formation, all of which occur in the functional unit of the kidney (the nephron, a microstructure presents in the kidney)
- The afferent arteriole from where the blood comes into the nephron contains smooth muscle cells, while the glomerulus consists only of a single layer of endothelial cells. This different structure is due to the difference in function since the filtration process occurs across the wall of the glomerulus and the endothelial cells of the glomerulus have fenestrations making the filtration process more effective
- Filtered fluid will enter the Bowman's capsule (the capsular space) and then it will travel into a tubular system starting from the proximal convoluted tubule, to the loop of Henle, the Distal convoluted tubule, the connecting tubule, and lastly the collecting duct
- The filtered fluid will empty through the renal papilla into the major and minor calyces and then into the renal pelvis to reach the ureters
- **In this lecture, we will discuss the second and third processes of urine formation (Reabsorption & Secretion)**



- ✓ The first process of urine formation (filtration) is a passive and non-selective process that filtrates substances based on their sizes, and charges, while **reabsorption** is a highly selective process. So, **the reabsorption rate** will be different for each substance
- ✓ The valuable substances that are important for our body such as **glucose and amino acids** will have a **high** reabsorption rate while the waste substance such as **urea, creatinine, and ammonia** will have a **poor** reabsorption rate to be excreted.
- ✓ **The secretion** process (the third process of urine formation) is an active process through which waste substances are removed from the circulation (peritubular capillaries) into the filtered fluid in the tubular system and finally to the urine at a higher rate than the filtration rate
- ✓ Whatever is left in the tubules after the end of those three processes will be eliminated through a process called the **urinary excretion**
- ✓ **Excretion = Filtration – Reabsorption + Secretion**
- ✓ From 180 L filtered daily, less than 1% is excreted (1-2 L/day)

Reabsorption of Water and Solutes

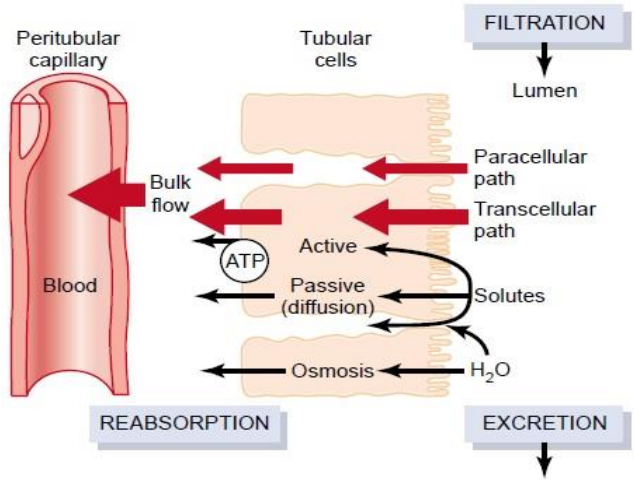
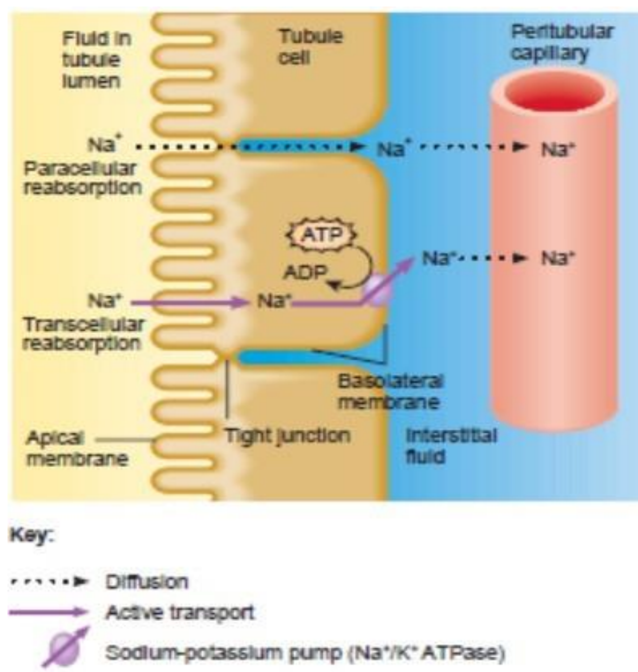


Figure 27–1

Reabsorption of filtered water and solutes from the tubular lumen across the tubular epithelial cells, through the renal interstitium, and back into the blood. Solutes are transported through the cells (transcellular route) by passive diffusion or active transport, or between the cells (paracellular route) by diffusion. Water is transported through the cells and between the tubular cells by osmosis. Transport of water and solutes from the interstitial fluid into the peritubular capillaries occurs by ultrafiltration (bulk flow).

- ✓ Starting from the proximal convoluted tubules and along the rest of the tubular system, the wall is made of a single layer of epithelial cells. The substances should pass through the epithelial cells either **across** their plasma membranes or in **between** to be reabsorbed into the peritubular capillaries
- ✓ There are **3** main paths for the reabsorption process:
  1. **Paracellular path** (through the tight junctions, the intercellular space, the interstitial fluid, and across the capillary wall into the lumen), in that path, water pull whatever solutes dissolved in it.
  2. **Transcellular path** (across the plasma membrane), the mechanism by which substances cross the plasma membrane of the endothelial cells depends on their nature (ions pass through specific channels, water passes through aquaporins, glucose needs transporters…etc). From the figure, we can notice that solutes can pass either through active (against gradient) or passive (toward gradient) processes (such as NaCl)

- ✓ Water transport through **the osmosis process** (passive process) from the hypotonic area to the hypertonic area
- ✓ Na+ can transport through both roots (para- and trans-cellular) using certain channels. The main player in sodium reabsorption is **the NA+/K+ ATPase channel** (sodium outside – potassium inside), it keeps Na+ intracellularly very low that favors sodium reabsorption down its gradient (from the tubular fluid into the intracellular lumen and then into the interstitial fluid). Paracellular reabsorption also depends on the gradient
- ✓ The basal membrane is near the capillary and the apical membrane



faces the tubular lumen. The apical membrane of the proximal convoluted tubule has microvilli called the **Burch border** to increase the surface area of reabsorption

- ✓ The Na+/K+ ATPase is presented also on the lateral membrane (in addition to the basal membrane)>>> **Basolateral ATPase**
- ✓ **Na+/K+ ATPase** creates an electrochemical gradient that drives the transport of NA+.

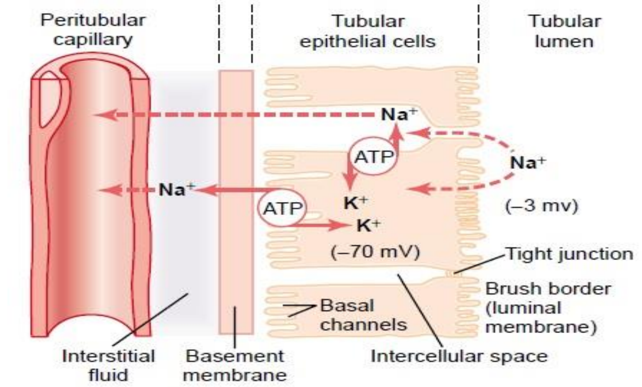
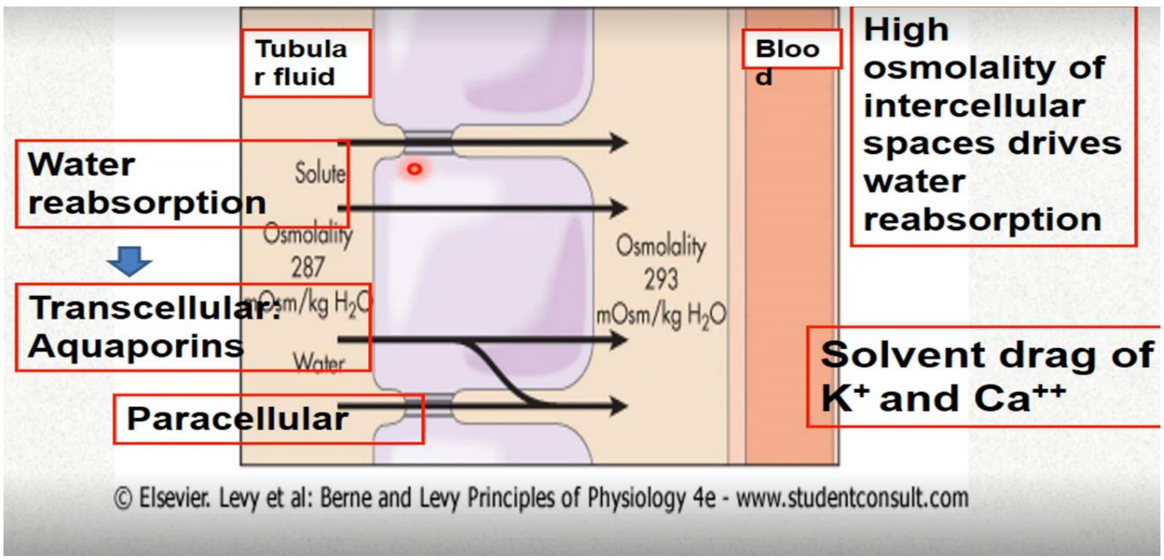


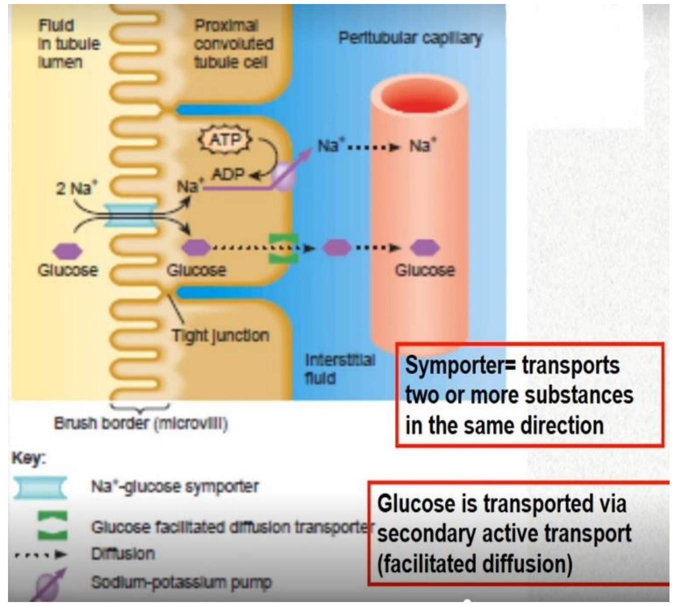
Figure 27–2

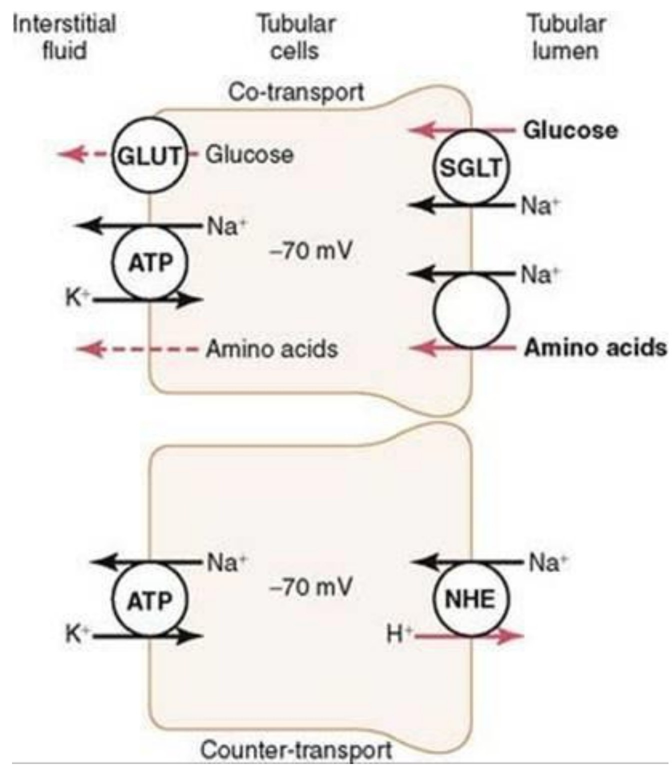
Basic mechanism for active transport of sodium through the tubular epithelial cell. The sodium-potassium pump transports sodium from the interior of the cell across the basolateral membrane, creating a low intracellular sodium concentration and a negative intracellular electrical potential. The low intracellular sodium concentration and the negative electrical potential cause sodium ions to diffuse from the tubular lumen into the cell through the brush border.



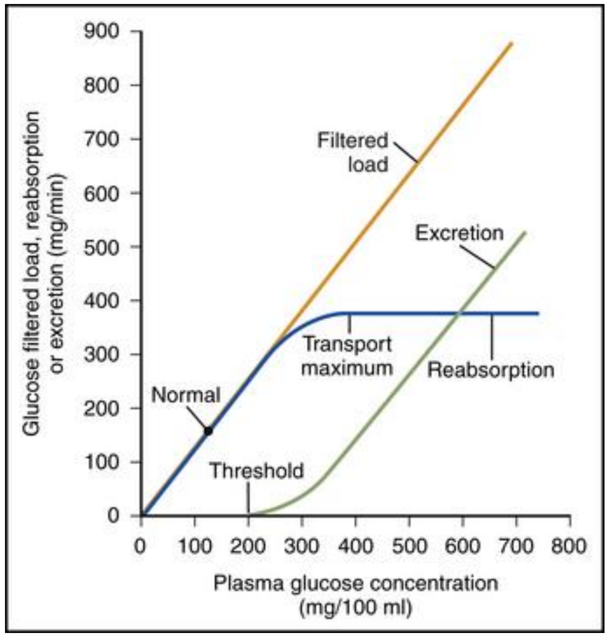
- ➢ In the proximal convoluted tubule, there is an extensive transport of Na+ which cause a change in the osmolality (the osmolality in the tubular fluid will be less than the osmolality in the interstitial fluid and this will make water move toward the blood capillaries. This change in the osmolality is caused by the activity of the Na+/k+ ATPase)
- ➢ In the paracellular path**, the solvent drag of K+ and Ca+** happens which means that water itself has ions dissolved within which contributes to the reabsorption of many ions particularly K+ and Ca+ ions

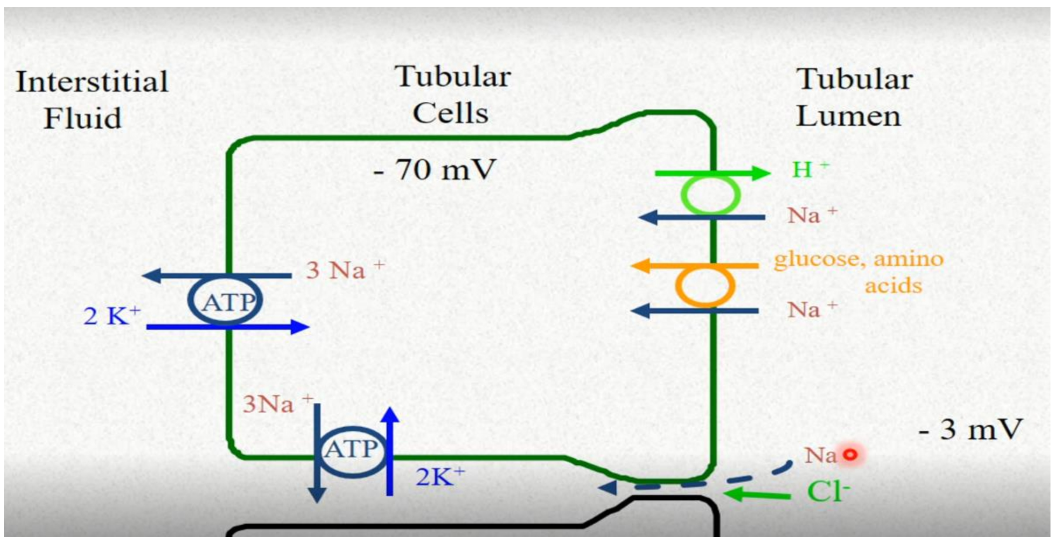
- ✓ Glucose and amino acids should be **completely** reabsorbed. Absorption of these substances occurs through the proximal convoluted tubules
- ✓ Reabsorption of amino acids and glucose occurs through **co-transportation** (using **symporters**), also **called secondary active transport** (secondary because we benefit from the gradient created by the NA+/K+ ATPase -that uses the ATP- to allow sodium to pass from the tubular fluid into the inside of the cell and simultaneously transporting glucose with the sodium ions through the symporter against its gradient). Then the glucose is transported from the high gradient area (inside the cell) into the low gradient one (outside the epithelial cell) through the **facilitated diffusion using a certain carrier.** **(The same mechanism applies to the amino acids but with different specific transporters)**
- ✓ It’s abnormal to see glucose or amino acids in urine
- ✓ In the figure below we can see symporters and **counter-transporters** (it’s also secondary active transport but the direction of transportation of the substances is the opposite for example; sodium ions will be transported into the inside, hydrogen ions into the outside). Na+/H+ counter-transporter benefits the sodium ions gradient to **excrete** the hydrogen ions into the urine to eliminate acids.





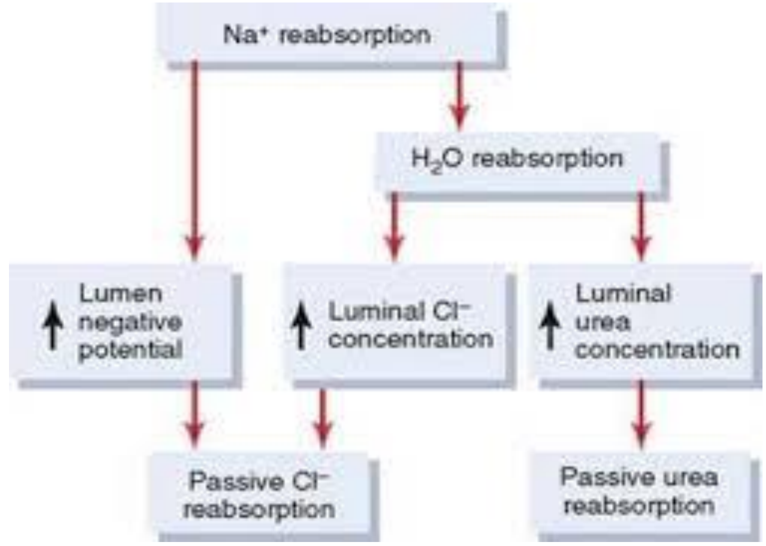
- ✓ we mentioned earlier that glucose and amino acids should be reabsorbed completely from the tubular fluid but is that unlimited? (Meaning that is it reabsorbed completely regardless of the amount of glucose in the filtered fluid, or there is a certain limit for the amount of glucose that can be reabsorbed?)
- ✓ Substances that are transported through transporters or carriers are limited by the **number of transporters available**.
- ✓ **Transport maximum** is the maximum transporting capacity of the SGLT (sodium-glucose cotransporter) transportation system where the transporters are saturated and cannot increase the reabsorption rate, excessive glucose is not reabsorbed and consequently passes into urine.





Reabsorption of water and solutes id couples to Na+ reabsorption

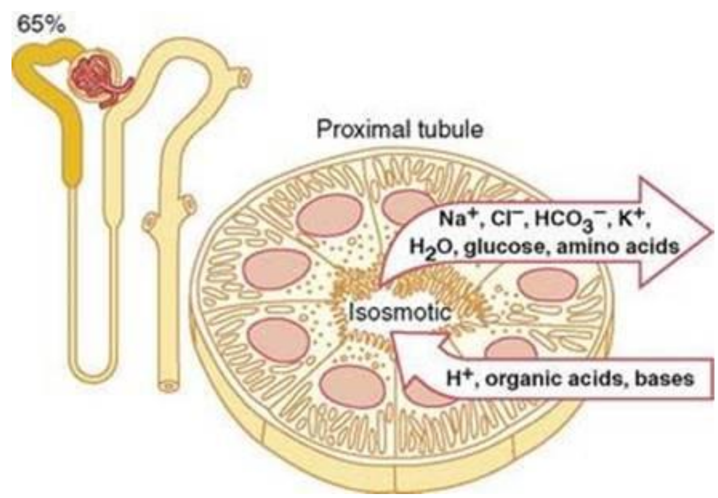
- We discussed before the mechanism of water reabsorption and its relation to sodium reabsorption.
- Sodium and water reabsorption will increase the negative potential in the tubular lumen which will drive the reabsorption of the negatively charged chloride ions down its gradient (passive Cl- reabsorption)
- As urea is hydrophilic in nature, reabsorption of water will make urea to be passively reabsorbed



Mechanisms by which water, chloride, and urea reabsorption are coupled with sodium reabsorption

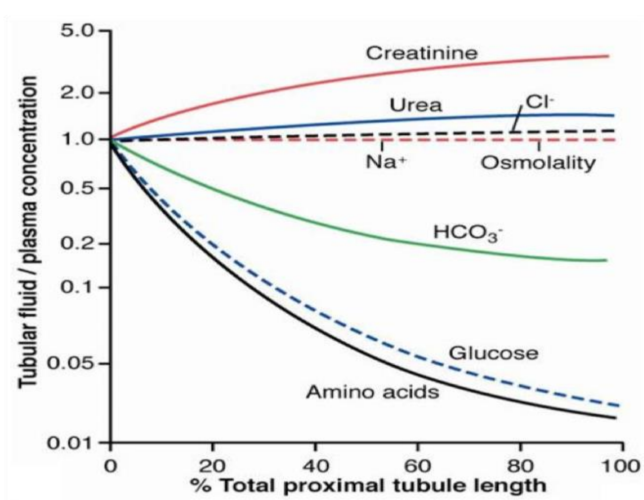
Proximal tubules

- The proximal tubules reabsorb about 67% of the filtered water, Na+, Cl-, K+, HCO-3
- The proximal tubules reabsorb almost all glucose and amino acids filtered by the glomeruli
- The key transporter element is the Na, k – ATPase in the basolateral membrane



Change in concentration in the proximal tubule

- on the x-axis, we have % Total tubular length (0 means the beginning of the proximal convoluted tubule, 100% is the end of it)
- on the Y-axis, there is the ratio between the tubular fluid concentration of certain substances/ the plasma concentration



- We can notice that creatinine and urea have poor reabsorption and the ratio is >1 meaning that their concentrations in the tubular fluid are higher than their concentrations in the plasma
- For sodium and chloride ions the ratio is around 1. So, their concentrations are almost the same in the tubular fluid and in the plasma
- Glucose and amino acids have the least ratio, their concentrations in the tubular fluid are lower than that in the plasma (near the end f the proximal convoluted it’s almost 0)
- That ratio depends on both water reabsorption and the substance reabsorption itself (as we proceed in the proximal convoluted tubule water reabsorption increases. If the substance reabsorption also increases as we proceed then we will approach 0)

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الله يعطيكم العافية و يبارك أوقاتكم