

RENAL SYSTEM 2
TRANSPORT PROPERTIES OF NEPHRON SEGMENTS

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Learning Objectives

1. Identify the region of the renal tubule in which reabsorption and secretion occur.
2. Describe the cellular mechanisms for transport of Na+, glucose, amino acids, and water by the major tubular segments.
3. Contrast transcellular and paracellular pathways for movement solutes and water across the renal tubular epithelium. Define solvent drag.
4. Explain clearance and how it can measure glomerular filtration rate (GFR).
5. Contrast the handling of inulin, glucose, urea, and penicillin by the kidney.

Formation of urine involves 3 basic processes: filtration, reabsorption and secretion. The kidney filters the entire plasma volume 60 times per day. If the amino acids, glucose, and ions in the filtrate were not reabsorbed, they would be depleted within 24 minutes of filtration! The processes of reabsorption and secretion enable the cells lining the renal tubules (epithelium) to modulate both the volume and content of urine. In doing so, the renal tubules control the volume, osmolality, composition, and pH of the ECF and ICF compartments.

The renal tubule epithelium is polarized with distinct luminal and basal surfaces. Specific transporter proteins are inserted into these distinct cell membranes which mediate reabsorption and secretion of solutes and water. Defects in their location and/or expression along the renal tubule underlie many kidney diseases.

REABSORPTION OF SOLUTES & WATER

The **primary site for reabsorption is the proximal convoluted tubule (PCT)**. In the initial 2/3 of the PCT, 100% of filtered glucose and amino acids, and 80% of filtered bicarbonate (HCO3-) are reabsorbed. In addition, 65% of filtered Na+ is reabsorbed.

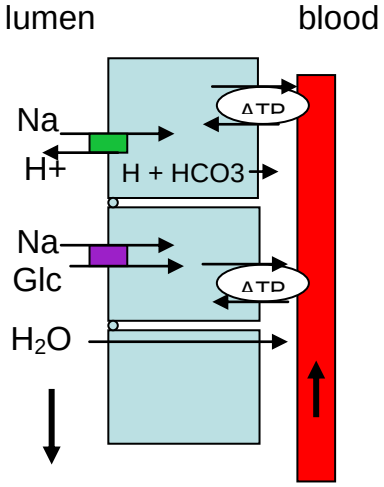

Figure 1. Resorption of solutes and organic substances (glucose) by secondary active transport. The sodium gradient is maintained by the Na-K ATPase located at the basal surface of the epithelial cells.

Reabsorption of these solutes occurs as secondary active transport using co-transporters located on the luminal surface of the epithelial cells coupled to the extrusion of Na+ at the basal surface by the Na+-K+ ATPase (Fig 1).

At saturation, all of the transporters are occupied and a **maximal rate of transport (Tm)** for that substance is reached (Fig 2). This is called the **renal threshold** for that substance. Below saturation, the rate of transport is proportional to the concentration of the substrate.

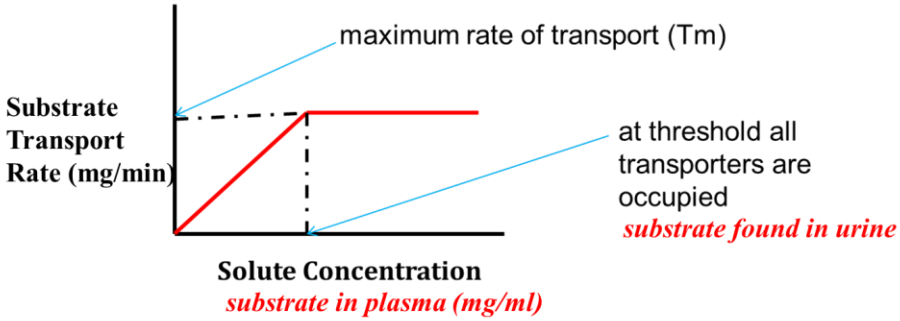

Figure 2. Saturation of solute transport.

As Na+ moves across the epithelium in the PCT, water follows by osmosis (Fig 1). Consequently the tubule filtrate remains isosmotic to the ICF and ECF. Note that the movement of water occurs in both a **transcellular** (across cells) and **paracellular** manner (between the cells). As water leaves the tubule, then solutes such as K+ increase in concentration. This establishes a diffusion gradient for K+. Potassium ions exit the tubule in a paracellular manner to enter the blood. This is known as **solvent drag**.

Solutes such as Cl- and urea are not reabsorbed efficiently in the first 2/3 of the PCT. As water exits the tubule, these solutes become more concentrated. In the last 1/3 of the PCT, Cl- and urea move across the epithelium by facilitated diffusion. Water follows by osmosis.

What happens if some of the filtered solutes are not reabsorbed in the PCT? Under these conditions, more water would be lost from the body because the later regions of the renal tubule do not contain transporters for these solutes. For example, in diabetes *mellitus*, the glucose transporters of the PCT are saturated, the excess filtered glucose remains within the renal tubule and is excreted in the urine. Because glucose is osmotically active, its presence in the renal tubules opposes the movement of water in the collecting duct (CD). As a result, water is lost from the body and must be replenished by drinking.

Where does the reabsorbed solutes and water go? They enter the interstitial fluid (ISF) and then enter the capillaries that are aligned with the tubules (Fig 1). The reabsorbed solutes and water pass from the capillaries to the venous circulation, exit the kidney via the renal vein, and return to the heart.

Reabsorption of Na+ occurs in most parts of the renal tubule and collecting duct. The exception is the descending thin loop of Henle which is impermeable to Na+. About 65% of the filtered Na+ is reabsorbed in the PCT. Another 25% is reabsorbed in the thick ascending loop of Henle. Reabsorption of the remaining Na+ occurs in the principal cells of the distal convoluted tubule (DCT) and collecting duct (CD).

SECRETION

Secretion of organic molecules such as vitamins

Secretion increases the excretion of a filtered molecule and enables removal of molecules that are not filtered by the glomerulus. Secretion of organic compounds by the PCT plays a key role in limiting the body's exposure to toxic compounds and metabolic wastes. These molecules move across the epithelial cells from the blood into the renal tubules by secondary active transport. Penicillin, vitamins, epinephrine, and norepinephrine are important organic molecules secreted by the kidneys.

Secretion of K+ and reabsorption of Na+

The last segment of the distal convoluted tubule (DCT) and the collecting duct (CD) contain principal cells. The principal cells reabsorb Na+ and water and secrete K+ into the urine.
Both Na+ reabsorption and K+ secretion by principal cells depend on the activity of the Na+-K+ ATPase (Fig 3).

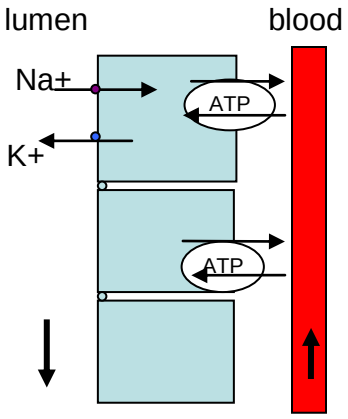

Figure 3. Transport pathways in principal cell of CD. Na+ and K+ channels are located on the luminal surface. Na+-K+ ATPase is located on the basal surface.

Recall that the Na-K ATPase moves 3 Na+ ions for 2 K+ ions. As Na+ is reabsorbed, a charge potential is established across these epithelial cells such that the luminal surface membrane is more negative than the basal surface facing the blood. This charge gradient is used to move Cl- in a paracellular manner from filtrate to blood and to increase the secretion of K+ into the filtrate.

In addition to the charge gradient, the reabsorption of Na+ across the principal cells establishes a chemical gradient. As Na+ exits via the Na-K ATPase, K+ enters the cells. This raises the intracellular content of K+ in the principal cells. Consequently, the diffusion gradient favors the exit of K+ ions at the luminal cell surface. K+ exits the CD cells to enter the filtrate via the K+ channel.

Note that two conditions favor the secretion of K+:

1. increased delivery of Na+ to the CD principal cells.
2. increased fluid flow in the CD which "removes" K+ from the luminal surface of the CD principal cells thereby maintaining a steep diffusion gradient for K+ exit.

Aldosterone regulates the secretion of K+ and reabsorption of Na+ in the CD. It acts to increase the number of Na+-K+ ATPases, Na+ Channels and K+ channels in the principal cells (Fig 3).

EXCRETION

Urine output is the end result of all processes in the kidney. The excretion rate of a substance in the urine is called **CLEARANCE** (C)**.** Clearance for solute Y is calculated as:

$$C = \frac{\text{(urine volume/time ml/min) X [urine concentration of Y (mg/ml)]}}{\text{[plasma concentration of Y (mg/ml)]}}$$

Because only the filtration and excretion of a substance can be measured, the net handling of substance Y by the kidney is determined by comparing the clearance of Y to that of inulin, a large sugar (polysaccharide), that is freely filtered and neither secreted nor reabsorbed (Table 1).

The **clearance of inulin equals GFR**. Inulin can be used to measure the function of the kidney (GFR) in a human by taking only a blood sample and a timed urine sample. In actual practice, inulin is not used for routine clinical applications because it must be administered by continuous intravenous infusion. Instead creatinine, a breakdown product of muscle protein, is used to estimate clearance and GFR. Creatinine is used because it is constantly produced by the body, is not reabsorbed, and is secreted only to a small extent.

TABLE 1. Renal handling of solute (Y)

Clearance rate	**Consequence**
Clearance of Y < inulin clearance	net reabsorption of Y
Clearance of Y = inulin clearance	neither reabsorption nor secretion
Clearance of Y > inulin clearance	net secretion of Y

Freely filtered solutes differ in whether they are reabsorbed and /or secreted. For example, glucose is 100 % reabsorbed and is not found in the urine of individuals with normal kidney function. In contrast, urea is freely filtered and reabsorbed partially. Urea has a clearance rate that is less than inulin but urea is found in urine.

KEY CONCEPTS

1. Formation of urine involves 3 basic processes: filtration, reabsorption and secretion.
2. The kidney modulates both the volume and content of urine, as well as controls the volume, osmolality, composition, and pH of the ECF and ICF compartments.
3. Reabsorption of solutes occurs predominantly within the PCT. Some reabsorption of Na+, K+ and Cl- also occurs in the TAL. Aldosterone regulates reabsorption of Na+ in the DCT and CD.
4. Water moves by osmosis within the PCT to maintain isosmotic conditions. Water can move across this epithelium in transcellular manner via aquaporin channels and in a paracellular manner.
5. Potassium reabsorption in the PCT is by solvent drag.
6. Secretion of toxins and organic waste products occurs in the PCT by secondary active transport.
7. Secretion of K+ occurs in the CD in response either to increased delivery of Na+ or increased fluid flow. Secretion of K+ can be increased by aldosterone.
8. Clearance is the excretion rate of a substance. It equals GFR when the substance is freely filtered and not reabsorbed or secreted by the renal tubule. Handling of a substance can be determined using either inulin, an exogenous standard or creatinine, an endogenous standard.

QUESTIONS

1. If the clearance rate of drug Y is equal to that of inulin, then there was a
    A. net reabsorption of drug Y
    B. net secretion of drug Y
    C. neither reabsorption nor secretion of drug Y
    D. no filtration of drug Y

2. Which of the following will produce the greatest increase in K+ secretion?
    A. decrease in urinary flow from the collecting duct
    B. increase in Na+ concentration in the lumen of the collecting duct
    C. increase in mean arterial pressure (MAP) to 105 mmHg

ANSWERS

1. C

2. B.