Renal Glucose Reabsorption: Glucose in the Urine & Disease Correlation

See online here

The kidney is a key player in glucose hemostasis by two mechanisms. It filters and reabsorbs glucose from the urine and it releases the sugar during times of fasting through gluconeogenesis. Here you will read everything about it.

Glucose in the Urine

Recall that **kidney function** can be broken down into four steps:

1. **Filtration**
2. **Reabsorption**
3. **Secretion**
4. **Excretion**

About 180 liters of plasma is filtered through the kidney per day. This equates to the glomerular filtration rate. During the filtration process large quantities of water, electrolytes, and other small molecules pass from the circulatory vasculature (renal arterioles) and into the lumen of the glomerulus (**Bowman's capsule**). As this filtrate passes through the nephron a great deal of water and other material is reabsorbed. This functions to concentrate the nitrogenous waste and maintain homeostasis.

Material is also actively secreted depending on conditions in the body such as pH and

potassium concentrations. The final concentrated urine passes through the ureters, into the bladder, and is excreted. **D-glucose** is **filtered** and **almost completely reabsorbed** under normal conditions.

Glucose is a polar molecule and dissolves in water and blood plasma. It easily passes through the glomerular basement membrane. It is almost completely **reabsorbed from the tubules by active transport molecules** found in the proximal convoluted tubule **(PCT)** called sodium-coupled glucose cotransporters **(SGLT)**.

Recall that a cotransporter moves two molecules: one with its electrochemical gradient and one against its electrochemical gradient. In this case, sodium is moving down its gradient into the cell while glucose is also moving into the cell but against its electrochemical gradient. These transporters are found on the luminal side of the epithelial cells that line the PCT.

Intracellular sodium concentration is maintained low by an ATP-dependent sodium/potassium pump that actively transports potassium into the cell and sodium out of the cell and into the bloodstream. These pumps are found on the basolateral side of the PCT cells.

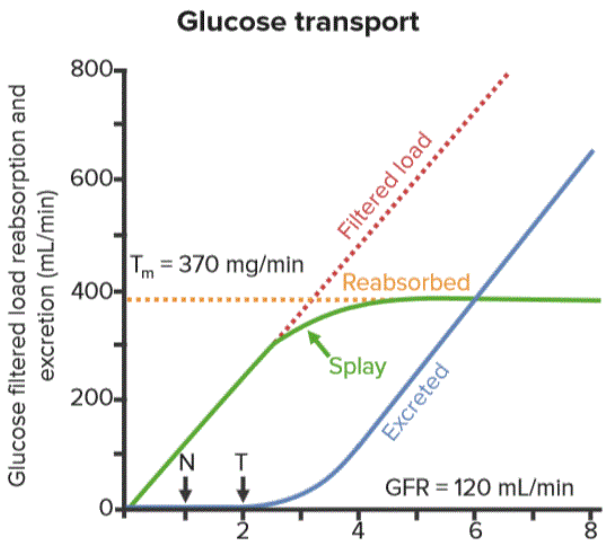
There are two types of SGLT:

SGLT2 is found in the first part of PCT (S1 and S2) and are low-affinity, high capacity transport proteins and are responsible for 90 % of reabsorption.

SGLT1 are high-affinity, low capacity transport proteins, responsible for 10 % of glucose reabsorption and are found in the distal part of the PCT where glucose concentrations are much lower. Recall that affinity is a term that characterizes the interaction between a ligand and its receptor. A high-affinity system requires only a lower concentration to fill all binding sites while a low-affinity system requires a higher concentration. Therefore, SGLT1 (high-affinity transporters) are active even with a low concentration of filtrate glucose.

Once inside the cell, the glucose is then passively transported into the bloodstream through the glucose transporter (GLUT)2 found on the basolateral border of the epithelial cells that line the PCT.

Transporter	Location on cell	Character of the transporter	Location in nephron
SGLT1	Luminal	High affinity, low concentration cotransporter	S1, S2 of PCT
SGLT2	Luminal	Low affinity, high concentration cotransporter	S3 of PCT
GLUT2	Basolateral	Bidirectional transporter	S1, S2, S3 of PCT
ATP-Na/K Pump	Basolateral	Active transport	S1, S2, S3 of PCT



"Glucose transport" Image created by Lecturio

SGLT1 and SLGT2 will absorb filtrate glucose until all of their receptor sites are full. This is called the transport maximum for glucose (TmG). It corresponds to **a plasma glucose level of about 200mg/dL**. At this point extra glucose will pass into the bladder and will be excreted (glycosuria). Each nephron may reach TmG at different times due to a non-uniform distribution of transporters; therefore, glycosuria may be detected before the tubular maximum is reached. This is called **splay**.

Disease Correlation

SGLT2 inhibitors are a relatively new type of medication to treat diabetes type 2. The **gliflozin** family of medication prevent glucose reabsorption in the PCT, allowing the excretion of more glucose and lowering plasma glucose levels. **Dapagliflozin** is the oldest member of this class of drugs. Side effects include increased risk for ketoacidosis, urinary tract infection, hypoglycemia, and candida infection.

Glucose Homeostasis in the Kidney

The kidney can be considered two organs when considering glucose homeostasis. The renal medulla consumes a great deal of glucose. It has the enzymes to store glucose as glycogen and the glycolytic enzymes necessary to use those stores. The renal cortex has the glycos-6-phosphatase, an enzyme that is necessary to release glucose into the bloodstream. **The renal cortex works with the liver to regulate glucose hemostasis.** The cortex does not have the correct enzymes to store and use glycogen.

Review Questions

The answers are below the references.

1. How is sodium concentration maintained at a low concentration in the tubular epithelial cells that line the proximal convoluted tubule?

A. Basolateral ATP dependent sodium/potassium pump
B. Luminal NKCC transporter
C. Paracellular diffusion
D. Luminal SGLT2

E. Basolateral SGLT1

2. Tissue that required a great deal of glucose to function (such as the brain) would need which characteristics in a glucose transporter?

A. Low-affinity, high capacity
B. High-affinity, low capacity
C. High-affinity, high capacity
D. Low-affinity, low capacity

References

DeFronzo R, Davidson J, Del Prato S. (2012). The role of the kidneys in glucose homeostasis: a new path towards normalizing glycaemia. Diabetes Obes Metab, 14(1):5-14.

Gerich J. (2010). Role of the kidney in normal glucose homeostasis and in the hyperglycaemia of diabetes mellitus: therapeutic implications. Diabet Med, 27(2):136-42.

Triplitt C. (2012). Understanding the kidneys' role in blood glucose regulation. Am J Manag Care, 18(1 Suppl):S11-6.

Correct answers: 1A, 2C

Notes