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**18/mhs02/056**

**RENAL HANDLING OF GLUCOSE**

The kidney contributes to glucose homeostasis through processes of gluconeogenesis, glucose filtration, glucose reabsorption, and glucose consumption. Each of these processes can be altered in patients with type-2 diabetes (T2DM), providing potential targets for novel therapies. Recent studies have indicated that the kidney is responsible for up to 20% of all glucose production via gluconeogenesis. In patients with T2DM, overall glucose production increases by as much as 300%, with equal contributions from hepatic and renal sources. This increased production contributes not only to increased fasting glucose in T2DM patients but also to raised postprandial glucose because, in contrast to the liver, glucose ingestion increases renal gluconeogenesis. Under normal circumstances, up to 180 g/day of glucose is filtered by the renal glomerulus and virtually all of it is subsequently reabsorbed in the proximal convoluted tubule. This reabsorption is effected by two sodium-dependent glucose cotransporter (SGLT) proteins. SGLT2, situated in the S1 segment, is a low-affinity high-capacity transporter reabsorbing up to 90% of filtered glucose. SGLT1, situated in the S3 segment, is a high-affinity low-capacity transporter reabsorbing the remaining 10%. In patients with T2DM, renal reabsorptive capacity maladaptively increases from a normal level of 19.5 to 23.3 mmol/l/min. Once glucose has been reabsorbed into the tubular epithelial cells, it diffuses into the interstitium across specific facilitative glucose transporters (GLUTs). GLUT1 and GLUT2 are associated with SGLT1 and SGLT2, respectively.

Maintenance of glucose homeostasis is vital to preserve a constant source of glucose to the brain, an organ that uses glucose as its principal metabolic fuel. Despite wide variations in glucose influx and efflux, plasma glucose levels are kept within a narrow band in healthy individuals, a situation achieved by a well-coordinated system of hormones, neural pathways, and glucose transport proteins that regulate dietary glucose absorption, renal glucose loss, and endogenous glucose production in combination with glucose uptake and release by peripheral tissues.

The kidney performs a distinctive role in glucose homeostasis. Not only is it involved in glucose utilization, but it is also increasingly recognized as having a significant role in gluconeogenesis and uniquely contributes to plasma glucose regulation by controlling glucose reabsorption from renal tubules following glomerular filtration.

The focus of this review is to summarize these aspects of the kidney’s role in glucose homeostasis, with particular reference to those areas highlighted as potential targets in the management of diabetes.

**RENAL HANDLING OF ELECTROLYTES**

Well over half of the body's weight is made up of water. Doctors think about the body's water as being restricted to various spaces, called fluid compartments. The three main compartments are

Fluid within cells

Fluid in the space around cells

Blood

To function normally, the body must keep fluid levels from varying too much in these areas.

Some [minerals](/home/disorders-of-nutrition/minerals/overview-of-minerals)—especially the macrominerals (minerals the body needs in relatively large amounts)—are important as electrolytes. Electrolytes are minerals that carry an electric charge when they are dissolved in a liquid such as blood. The blood electrolytes—sodium, potassium, chloride, and bicarbonate—help regulate nerve and muscle function and maintain [acid-base balance](/home/hormonal-and-metabolic-disorders/acid-base-balance/overview-of-acid-base-balance) and [water balance](/home/hormonal-and-metabolic-disorders/water-balance/about-body-water).

Electrolytes, particularly [sodium](/home/hormonal-and-metabolic-disorders/electrolyte-balance/overview-of-sodium-s-role-in-the-body), help the body maintain normal fluid levels in the fluid compartments because the amount of fluid a compartment contains depends on the amount (concentration) of electrolytes in it. If the electrolyte concentration is high, fluid moves into that compartment (a process called osmosis). Likewise, if the electrolyte concentration is low, fluid moves out of that compartment. To adjust fluid levels, the body can actively move electrolytes in or out of cells. Thus, having electrolytes in the right concentrations (called electrolyte balance) is important in maintaining fluid balance among the compartments.

The kidneys help maintain electrolyte concentrations by filtering electrolytes and water from blood, returning some to the blood, and excreting any excess into the urine. Thus, the kidneys help maintain a balance between daily consumption and excretion of electrolytes and water.

If the balance of electrolytes is disturbed, disorders can develop. For example, an electrolyte imbalance can result from the following:

Becoming [dehydrated](/home/hormonal-and-metabolic-disorders/water-balance/dehydration) or over dehydrated

Taking certain drugs

Having certain heart, kidney, or liver disorders

Being given intravenous fluids or feedings in inappropriate amounts.