17/MHS01/101

**THE ROLE OF THE KIDNEY IN GLUCOSE HOMEOSTASIS**

Along with the liver, the kidney has an important role in ensuring the energy needs during fasting periods. This organ has a vital role in absorbing the entire quantity of the filtered glucose. Having a glomerular filtration rate of 180 liters per day, it filters approximately 180 grams of glucose per day, bringing its contribution in maintaining normal fasting plasma glucose (FPG) levels. The reabsorption of glucose is ensured by the sodium-glucose cotransporter (SGLT) 2, responsible for the reabsorption of 90% of glucose, and SGLT1, that reabsorbs the remaining glucose.

The plasma glucose concentration is determined by the amount of glucose synthesized, and the one removed from the circulation and metabolized. This concentration must be maintained within a relatively narrow range despite the wide daily fluctuations in glucose ingestion and glucose demands in various tissues. Other substrates such as free fatty acids (FFAs), glycerol, lactate and ketone bodies have greater daily fluctuations. This can be explained by the need of the body to protect himself against hyper- and hypoglycaemia. Hyperglycaemia is associated with both chronic effects (such as nephropathy, retinopathy, neuropathy and premature atherosclerosis) and also acute complications (including diabetic ketoacidosis and hyperosmolar hyperglycaemic state that are associated with higher morbidity and mortality). Hypoglycaemia is also harmful because it can cause neurological events (including coma, seizures), cardiac arrhythmias and death.

The regulation of endogenous production of glucose is determined by hormonal and neural factors. In the acute phase, glucoregulatory mechanisms involve insulin, glucagon and catecholamines and they can effect changes in plasma glucose levels in a matter of minutes. Insulin is able to suppress glucose release in both the kidney and liver by direct enzyme activation ⁄ deactivation and by reducing the availability of gluconeogenic substrates. Glucagon has no effect on the kidneys, but it stimulates glycogenolysis and gluconeogenesis in the liver. Catecholamines also have multiple acute actions. They can stimulate renal glucose release and glucagon secretion and inhibit insulin secretion.

The kidneys are involved in maintaining glucose homeostasis through three different mechanisms: gluconeogenesis; glucose uptake from the blood for its own energy requests and reabsorption into the general circulation of glucose from glomerular filtrate in order to preserve energy.

**PROCESS OF MICTURITION**

Micturition is a process where urine is expelled from the body. Animals and humans have a specialised system of organs known as the excretory system to eliminate the waste products from the body. In other words, the process of expelling urine from the body is called micturition. It is brought about by reflex contraction of a special muscle called the detrusor muscle after voluntary relaxation of the sphincter muscle.

The human excretory system consists of a pair of kidneys and ureters, a urinary bladder, and a urethra. The kidneys play a major role in the process of urine formation and its excretion. The urine formed is stored in the urinary bladder.

Micturition is also known as voiding phase of bladder control and lasts for a short time. As the bladder becomes full, the stretch receptors increase their firing rate. This increase the urge to urinate and causes micturition reflex. It sometimes even causes involuntary urination.

Micturition process consists of two phases:

Storage phase

Voiding phase

Storage Phase

The urinary bladder is a balloon-shaped, hollow, muscular, organ that acts as the storage organ for urine. The urinary bladder in a healthy urinary system can store up to 16 ounces of urine for 2 to 5 hours easily. The circular sphincter muscles prevent leakage of urine. They close tightly around the opening of the bladder into the tube (urethra) that allows the passage of urine outside the body.

Voiding Phase

When the bladder is filled with urine, the nerves in it are triggered, which in turn stimulates the need to urinate. The brain signals urinary bladder to contract. The receptors of the urinary bladder send a signal to the central nervous system, in response to which the nervous system sends a signal that incites the contraction of the urinary bladder. Through the urinary opening at the urethra, the urine is eliminated, and the process is called micturition. The neural mechanism involved is called the micturition reflex.

**THE JUXTAGLOMERULAR APPARATUS**

 The juxtaglomerular apparatus also known as the juxtaglomerular complex is a structure in the kidney that regulates the function of each nephron, the functional units of the kidney. The juxtaglomerular apparatus consists of three types of cells:

1. The macula densa, a part of the distal convoluted tubule of the same nephron.
2. Juxtaglomerular cells, also known as granular cells, which secrete renin.
3. Extraglomerular mesangial cells

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Extraglomerular mesangial cells:

Extraglomerular mesangial cells are located in the junction between the afferent and efferent arterioles. These cells have a contractile property similar to vascular smooth muscles and thus play a role in “regulating GFR” by altering the vessel diameter. Renin is also found in these cells.

Macula densa:

At the point where the afferent arterioles enter the glomerulus and the efferent arteriole leaves it, the tubule of the nephron touches the arterioles of the glomerulus from which it rose. At this location, in the wall of the distal convoluted tubule, there is a modified region of tubular epithelium called the macula densa. Cells in the macula densa respond to changes in the sodium chloride levels in the distal tubule of the nephron via the tubuloglomerular feedback (TGF) loop.

The macula densa's detection of elevated sodium chloride, which leads to an increase in GFR, is based on the concept of purinergic signaling. An increase in the salt concentration causes several cell signals to eventually cause the adjacent afferent arteriole to constrict. This decreases the amount of blood coming from the afferent arterioles to the glomerular capillaries, and therefore decreases the amount of fluid that goes from the glomerular capillaries into the Bowman's space (the glomerular filtration rate (GFR)).

When there is a decrease in the sodium concentration, less sodium is reabsorbed in the macular densa cells. The cells increase the production of nitric oxide and Prostaglandins to vasodilate the afferent arterioles and increase renin release.

Excess secretion of renin by the juxtaglomerular cells can lead to excess activity of the renin–angiotensin system, hypertension and an increase in blood volume. This is not responsive to the usual treatment for essential hypertension, namely medications and lifestyle modification.

One cause of this can be increased renin production due to narrowing of the renal artery, or a tumour of juxtaglomerular cells that produces renin. These will lead to secondary hyperaldosteronism, which will cause hypertension, high blood sodium, low blood potassium, and metabolic alkalosis.

**ROLE OF KIDNEY IN REGULATING BLOOD PRESSURE**

The kidneys help regulate blood pressure through Na+ and water retention and loss. The kidneys work with the adrenal cortex, lungs, and liver in the renin–angiotensin–aldosterone system to regulate blood pressure. They regulate osmolarity of the blood by regulating both solutes and water.

The blood pressure in your body depends upon the following conditions:

1. The force of contraction of the heart -- related to how much the heart muscle gets stretched by the incoming blood.
2. The degree to which the arteries and arterioles constrict -- increases the resistance to blood flow, thus requiring a higher blood pressure.
3. The circulating blood volume -- the higher the circulating blood volume, the more the heart muscle gets stretched by the incoming blood.

The kidney influences blood pressure by:

1. Causing the arteries and veins to constrict
2. Increasing the circulating blood volume

 Specialized cells are located in a portion of the distal tubule located near and in the wall of the afferent arteriole. The distal tubule cells (macula densa) sense the Na in the filtrate, and the arterial cells (juxtaglomerular cells) sense the blood pressure. When the blood pressure drops, the amount of filtered Na also drops. The juxtaglomerular cells sense the drop in blood pressure and the decrease in Na is relayed to them by the macula densa cells. The juxtaglomerular cells then release an enzyme called renin. Renin converts angiotensinogen (a peptide, or amino acid derivative) into angiotensin I. Angiotensin I is then converted to angiotensin II by an angiotensin-converting enzyme (ACE), which is found mainly in the lungs. Angiotensin II causes blood vessels to contract -- the increased blood vessel constrictions elevate the blood pressure.

**THE ROLE OF THE KIDNEY IN CALCIUM HOMEOSTASIS**

Vitamin D and parathyroid hormone (PTH) help regulate how much calcium is absorbed and how much calcium the kidneys eliminate. Healthy kidneys turn vitamin D into an active hormone (calcitriol), which helps increase calcium absorption from the intestines into the blood.