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**RENAL PHYSIOLOGY**

**PHS303**

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1. ROLE OF KIDNEY IN GLUCOSE HOMEOSTASIS.

The functions of the kidney in glucose homeostasis includes;

1. Release of glucose into the circulation via gluconeogenesis.

2. Uptake of glucose from the circulation to satisfy their energy needs.

3. Reabsorption of glucose at the level of the proximal tubule.

Renal release of glucose into the circulation is the result of glycogenolysis and gluconeogenesis, respectively involving the breaking down and formation of glucose-6-phosphate from precursors. The kidneys retrieve as much glucose as possible, making the urine glucose free. The glomeruli filter from plasma approximately 180 grams of D-glucose per day, which is reabsorbed through glucose transporter proteins that are present in cell membranes within the proximal tubules. The process of renal glucose reabsorption is mediated by active (sodium-coupled glucose cotransporters) and passive (glucose transporters) transporters. In hyperglycemia, the kidneys may play an exacerbating role by reabsorbing excess glucose, ultimately contributing to chronic hyperglycemia.

Mechanisms of Glucose Homeostasis in the Kidneys.

Maintenance of glucose homeostasis is important in preventing hyperglycemia or hypoglycemia. Chronically uncontrolled hyperglycemia leads to a higher risk of macrovascular and microvascular complications, such as cardiovascular disease, nephropathy, neuropathy, and retinopathy. Hypoglycemia, on the other hand, may lead to a myriad of central nervous system complications eg, confusion, behavioral changes, seizures, loss of consciousness, and even death, since the brain is the body’s largest consumer of glucose in the fasting or “postabsorptive” state. Maintenance of glucose homeostasis involves several complementary physiologic processes, including glucose absorption (in the gastrointestinal tract), glycogenolysis (in the liver), glucose reabsorption (in the kidneys), gluconeogenesis (in the liver and kidneys), and glucose excretion (in the kidneys).

Glucose utilization occurs predominantly in the renal medulla and glucose release is limited to the renal cortex. These activities are separated as a result of differences in the distribution of various enzymes along the nephron. Cells in the renal medulla have significant glucose-phosphorylating and glycolytic enzyme activity, and can therefore phosphorylate and accumulate glycogen. However, since these cells lack glucose-6-phosphatase and other gluconeogenic enzymes, they cannot release free glucose into the circulation. On the other hand, renal cortex cells do possess gluconeogenic enzymes (including glucose-6-phosphatase), and therefore can make and release glucose into the circulation. But because these cells have little phosphorylating capacity, they cannot synthesize glycogen.

2. PROCESS OF MICTURITION.

Micturition or urination is the process of expelling urine from the bladder. This act is also known as voiding of the bladder. The excretory system in humans includes a pair of kidneys, two ureters, a urinary bladder and a urethra. The kidneys filter the urine and it is transported to the urinary bladder via the ureters where it is stored till its expulsion. The process of micturition is regulated by the nervous system and the muscles of the bladder and urethra. The urinary bladder can store around 350-400ml of urine before it expels it out.

Stages of Micturition.

The urinary bladder has two distinct stages or phases:

1. Resting or filling stage.

2. Voiding stage.

Resting or Filling Stage.

It is in this phase of the bladder that the urine is transported from the kidneys via the ureters into the bladder. The ureters are thin muscular tubes that arise from each of the kidneys and extend downwards where they enter the bladder obliquely.

The oblique placement of the ureters in the bladder wall serves a very important function. The opening of the ureter into the urinary bladder is not guarded by any sphincter or muscle. Therefore, this oblique nature of opening prevents the urine from re-entering the ureters. At the same time, the main muscle of the urinary bladder, the detrusor muscle, is relaxing allowing the bladder to distend and accommodate more urine.

Voiding Stage.

During this stage, both the urinary bladder and the urethra come into play together. The detrusor muscle of the urinary bladder which was relaxing so far starts to contract once the bladder’s storage capacity is reached.

The urethra is controlled by two sets of muscles: The internal and external urethral sphincters. The internal sphincter is a smooth muscle whereas the external one is skeletal. Both these sphincters are in a contracted state during the filling stage.

Physiology of Micturition.

The process of micturition is governed by both the nervous and muscular systems. Within the nervous system, the process is governed by the autonomous nervous system and the somatic system. Once the urinary bladder reaches its maximum capacity, the stretch receptors in the walls of the bladder send an impulse via the pelvic nerve to the brain via the spinal cord.

The micturition reflex is ultimately generated from the level of the spinal cord after it receives reflexes from the pontine region in the brain. Once the bladder and the urethra receive the signals to empty the bladder, the two sphincters relax and the detrusor muscle causes the contractions of the bladder.

Along with these muscles, the muscles of the abdomen also play a role by putting pressure on the bladder wall. This leads to complete emptying of the bladder.

3. JUXTAGLOMERULAR APPARATUS.

The juxtaglomerular apparatus is a specialized structure formed by the distal convoluted tubule and the glomerular afferent arteriole. It is located near the vascular pole of the glomerulus and its main function is to regulate blood pressure and the filtration rate of the glomerulus. The macula densa is a collection of specialized epithelial cells in the distal convoluted tubule that detect sodium concentration of the fluid in the tubule. In response to elevated sodium, the macula densa cells trigger contraction of the afferent arteriole, reducing flow of blood to the glomerulus and the glomerular filtration rate. The juxtaglomerular cells, derived from smooth muscle cells, of the afferent arteriole secrete renin when blood pressure in the arteriole falls. Renin increases blood pressure via the renin-angiotensin-aldosterone system. Lacis cells, also called extraglomerular mesangial cells, are flat and elongated cells located near the macula densa. Their function remains unknown

4. ROLE OF THE KIDNEY IN BLOOD REGULATION.

Arterial blood pressure is not regulated by a single pressure controlling mechanism but by several interrelated mechanism.

The kidney plays a dominant role in long-term regulation of arterial pressure. It is found that urine volume increases as the arterial blood pressure rises. This is the phenomenon of pressure-diuresis. Arterial blood pressure can be kept constant by the action of pressure-diuresis when accumulation of excess extracellular fluid in the body occurs. When this happens the kidney excretes a larger amount of urine volume. Under the conditions of the excess accumulation of extracellular fluid in the body, high level of the arterial blood pressure can be observed as the renal function is abnormal.

Another mechanism is the Renin-Angiotensin System. The juxtaglomerular cells sense the blood pressure. When blood pressure drops, the amount of filtered Na drops. When this is sensed the juxtaglomerular cells release an enzyme RENIN. The renin converts Angiotensinogen into Angiotensin-1. Angiotensin-1 is then converted into Angiotensin-2 by Angiotensin-Converting-Enzyme found in the lungs. Angiotensin-2 causes the blood vessels to contract thereby increasing blood pressure. Angiotensin-2 also acts on the adrenal gland to stimulate release of aldosterone. Aldosterone acts on the kidneys to stimulate the reabsorption salt and water. This also increases blood pressure.

5. ROLE OF THE KIDNEY IN CALCIUM HOMEOSTASIS.

The calcium in the body is filtered, reabsorbed,excreted and not secreted in the kidney. Only 60% of plasma calcium is reabsorbed by the kidney. 1% of the plasma calcium is excreted. Out of the 60%; 65% is reabsorbed in the proximal tubules, 25-30% is reabsorbed in the loop of Henle and 4-9% is reabsorbed in the distal tubule and collecting tubules. An increase in calcium intake will increase the renal calcium excretion. Excretion of calcium in excess will decrease as a result of enhanced tubular excretion.

In the proximal the reabsorption takes place through the paracellular pathway; dissolved in water and carried with the reabsorped fluid between cells. Only 20% out of the 65% of calcium is rrabsorped through the transcellular pathway in 2 steps:

**.** Calcium diffuses from the tubular lumen into the cell down an electrochemical gradient due to much higher concentration of calcium in the lumen and there is a negative charge in the cell interior compared to the tubular lumen.

**.** Calcium exits the cell across the basolateral membrane by a calcium ATPase pump and by sodium-calcium counter transporter.

In the loop of Henle, it is restricted to the thick ascending limb. Out of the 25-30%, 50% occurs through the paracellular route by passive diffusion due to slight positive charge in the tubular lumen relative to the interstitial fluid. The other 50% occurs through the transcellular pathway; stimulated by the para-thyroid hormone.

In the distal tubule, calcium reabsorption occurs by active transport through the cell membrane. It involves diffusion across the luminal membrane through calcium channels and exit across the basolateral membrane by a calcium-ATPase pump. Para-thyroid hormone stimulates this mechanism.