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1. Discuss the role of kidney in glucose homeostasis.

Maintaining of glucose homeostasis is crucial in preventing pathological consequences that may result from hypoglycemia or hyperglycemia leads to a higher risk of macrovascular and microvascular complications such as cardiovascular disease, neuropathy and retinopathy. Hypoglycemia, on the other hand, may lead to a myriad of central nervous system complications (eg, confusions, behavioral changes, seizures, loss of consciousness and even death), since the brain is the body’s largest consumer of the 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). The kidneys are capable of synthesizing and secreting many important hormones(eg, renin,prostaglandis,kinins,erythropoietin) and are involved in wide variety of metabolic processes such as activation of vitamin D3, gluconeogenesis and metabolism of numerous endogenous co pounds( eg, insulin,steroids). With respect to renal involvement in glucose homeostasis, the primary mechanisms include release of glucose into the circulation via gluconeogenesis, uptake of glucose from the circulation to satisfy the kidneys’ energy needs, and reabsorption of glucose at the level of the proximal tubule. With regard to glucose utilization, the kidney maybe perceived as 2 separate organs, with glucose utilization occurring predominantly in the renal medulla and glucose release limited to the renal cortex. These activities are separated as aresult of differences in the distribution of various enzymes along the nephron. To this point, cells in the renal medulla (which, like the brain, are obligate users of glucose) have significant glucose-phosphorylating and glycolytic enzyme activity, and can therefore phosphorylate and accumulate glycogen. However, since these cells lack glucose-6-phosphate 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.

In addition to their important role in gluconeogenesis, the kidneys contribute to glucose homeostasis by filtering and reabsorbing glucose. Under normal conditions, the kidneys retrieve as much glucose as possible, rendering the urine virtually glucose free. The glomeruli filter from plasma approximately 180 grams of glucose per day, all of which is reabsorbed through glucose transporter proteins that are present in cell membranes within the proximal tubules.

2.)Discuss the 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 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.

The urinary bladder has two distinct stages or phases:

1. Resting or Filling Stage

It is in the 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.

1. 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.

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.

3.)Explain juxtaglomerular apparatus

The juxtaglomerular apparatus also known as juxtaglomerular complex is a structure in the kidney that regulates the function of each nephron, the functional units of the kidney. The juxtaglomerular apparatus is named because it is next ( juxta) the glomerulus.

The juxtaglomerular apparus consists of three types of cells;

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

Renin is produced by juxtaglomerular cells.These cells are similar to epithelium and are located in the tunica media of the afferent arterioles as they enter the glomeruli. The juxtaglomerular cells secrete renin in response to:

* Stimulation of the beta-1-adregenic receptor
* Decrerase in renal perfusion pressure( detected directly by the granular cells)
* Decrease in NaCl concentration at the macula densa, often due to a decrease in glomerular filteration rate.

Exraglomerular mesangial cells

They 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 convulated tubule, there is a modified region of tubular epithelium called the macula densa. Cells in the macula densa respond to changes in the the sodium chloride levels in the distal tubule of the nephron via the tubuloglomerular feedback loop

The macula densa’s detection of evaluated 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 filteration rate). When there is a decrease in the sodium concentration, less sodium is reabsorbs in the macular densa cells. The cells increase the production of nitric oxide and prostaglandins to vasodilate the afferent arterioles and increase renin release.

4.)Discuss the role of kidney in regulation of blood pressure

The renin-angiotensin system or RAS regulates blood pressure and fluid balancer in the body. When blood volume or sodium levels in the body are low, or potassium is high, cells in the kidney release the enzyme, renin. Renin converts angiotensinogen, which is produced in the liver, to the hormone angiotensin I. An enzyme known as ACE or angiotensin-converting enzyme found in the lungs metabolizes angiotensin I into angiotensin II. Angiotensin II causes blood vessels to constrict and blood pressure to increase. Angiotensin II stimulates the release of the hormone aldosterone in the adrenal glands, which causes the renal tubules to retain sodium and water and excrete potassium. Together,angiotensin II and aldosterone works to raise blood volume, blood pressure and sodium levels in the blood to restore the balance of sodium, potassium and fluids. If the renin-angiotensin system becomes overactive, consistently high blood pressure results.

5.)Discuss the role of kidney in calcium homeostasis.

Calcium is both filtered and reabsorbed in the kidneys but not secreted. Therefore, the rate of renal calcium excretion is calculated as

Renal calcium excretion= Calcium filtered-Calcium reabsorbed

Only about 60 percent of the plasma calcium is ionized, with 40 percent being bound to the plasma proteins and 10 percent complexed with anions such as phosphate. Therefore, only about 60 percent of the plasma calcium can be filtered at the glomerulus. Normally, about 99 percent of the filtered at the glomerulus. Normally, about 99 percent of the filtered calcium is reabsorbed by the tubules with only 1 percent of the filtered calcium being excreted. About 65 percent of the filtered calcium is reabsorbed in the proximal tubule, 25 to 30 percent is reabsorbed in the loop of Henle, and 4 to 9 percent is reabsorbed in the distal and collecting tubules. This pattern of reabsorption is similar to that for sodium. As is true with the other ions, calcium excretion is adjusted to meet the body’s needs. With an increase in calcium intake, there is also increased renal calcium excretion, although much of the increase of calcium intake is eliminated in the feces. With calcium depletion, calcium excretion by the kidneys decreases as a result of enhanced tubular reabsorption.

Proximal Tubular Calcium Reabsorption. Most of the calcium reabsorption in the proximal tubule occurs through the paracellular pathway; it is dissolved in water and carried with the reabsorbed fluid as it flows between the cells. Only about 20% of proximal tubular calcium reabsorption occurs through the transcellular pathway in two steps (1) Calcium diffuses from the tubular lumen into the cell down an electrochemical gradient due to much higher concentration of calcium in the tubular lumen, compared with the epithelial cell cytoplasm and because the cell interior has a negative charge relative to the tubular lumen, compared with the epithelial cell cytoplasm and because the cell interior has a negative charge relative to the tubular lumen.(2) Calcium exits the cell across the basolateral membrane by a calcium-ATPase pump and by sodium-calcium counter-transporter.

Loop Of Henle and Distal Tubule Calcium Reabsorption. In the loop of Henle, calcium reabsorption is restricted to the thick ascending limb. Approximately 50% of calcium reabsorption in the thick ascending limb occurs through the paracellular route by passive diffusion due to the slight positive charge of the tubular lumen relative to the interstitial fluid. The remaining 50% of calcium reabsorption in the thick ascending limb occurs through the transcellular pathway, a process that is stimulated by PTH. In the distal tubule, calcium reabsorption occurs almost entirely by active transport through the cell membrane. The mechanism for this active transport is similar to that in the proximal tubule and thick ascending limb and involves diffusion across the luminal membrane through calcium channels and exit across the basolateral membrane by a calcium-ATPase pump, as well as a sodium-calcium counter-transport mechanism. In this segment, as well as in the loops of Henle, PTH stimulates calcium reabsorption.