**Name**: Ayenor E. Christabel

**Matric no**: 17/mhs01/076

**Physiology assignment**

**1.) Discuss the role of kidney in glucose homeostasis?**

The role of the kidney in glucose homeostasis is by filtering and reabsorbing glucose. Under normal conditions, the kidneys retrieve as much glucose as possible, rendering the urine virtually glucose free. Renal release of glucose into the circulation is the result of glycogenolysis and gluconeogenesis, respectively. This involves breaking down and formation of glucose-6-phosphate from precursors (eg, lactate, glycerol, amino acids). With regard to renal reabsorption of glucose, the kidneys normally retrieve most glucose from the urine. 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. If the capacity of these transporters is exceeded, glucose appears in the urine. 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, which in turn contributes to chronic glycemic burden and the risk of microvascular consequences. The full significance of the kidneys’ contribution to glucose homeostasis, under both physiologic and pathologic conditions, has become well recognized, and is thought to involve functions well beyond glucose uptake and release. Besides the liver, the kidney is the only organ capable of generating sufficient glucose (gluconeogenesis) to release into the circulation, and it is also responsible for filtration and subsequent reabsorption or excretion of glucose.  
  
Maintenance of glucose homeostasis is crucial in preventing pathological consequences that may result from 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).  
The kidneys are capable of synthesizing and secreting many important hormones (eg, renin, prostaglandins, kinins, erythropoietin) and are involved in a wide variety of metabolic processes such as activation of vitamin D3, gluconeogenesis, and metabolism of numerous endogenous compounds (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.  
  
***Glycogenolysis and Gluconeogenesis***  
  
Renal release of glucose into the circulation is the result of glycogenolysis and gluconeogenesis. Glycogenolysis involves the breakdown of glycogen to glucose-6-phosphate from precursors (eg, lactate, glycerol, amino acids) and its subsequent hydrolysis (via glucose-6-phosphatase) to free glucose. Conversely, gluconeogenesis involves formation of glucose-6-phosphate from those same precursors and subsequent conversion to free glucose. The liver and skeletal muscles contain most of the body’s glycogen stores, but only the liver contains glucose-6-phosphatase. As such, the breakdown of hepatic glycogen leads to release of glucose, whereas the breakdown of muscle glycogen leads to release of lactate. Lactate (generated via glycolysis of glucose by blood cells, the renal medulla, and other tissues) may be absorbed by organs and reformed into glucose.2  
  
With regard to glucose utilization, the kidney may be 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 a result 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-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.  
  
***Glucose Reabsorption***  
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.If the capacity of these transporters is exceeded, glucose appears in the urine. This maximum capacity, known as the tubular maximum for glucose (TmG), ranges from 260 to 350 mg/min/1.73 m2 in healthy adults and children, and corresponds to a plasma glucose level of approximately 200 mg/dL.Once the TmG (the threshold) is reached and transporters are unable to reabsorb all the glucose (as in T2DM), glucosuria ocurrs.

***Renal Glucose Transporters***

The transport of glucose into and across cells is dependent on specialized carrier proteins: the facilitated glucose transporters (GLUTs) and the sodium-coupled glucose cotransporters (SGLTs). These transporters control glucose transport and reabsorption in several tissue types, including the proximal renal tubule, small intestine, blood-brain barrier, and peripheral tissues. GLUTs are involved in the passive transport of glucose across cell membranes, facilitating its downhill movement as it equilibrates across a membrane. SGLTs, on the other hand, mediate active transport of glucose against a concentration gradient by means of cotransport with sodium. Mutations of the gene encoding this protein result in Fanconi-Bickel syndrome, a rare autosomal recessive glycogen storage disease that encompasses a multitude of complications (glucose and galactose intolerance, postprandial hyperglycemia, fasting hypoglycemia, tubular nephropathy, hepatomegaly, renomegaly, rickets, and stunted growth). Because GLUT2 is involved in the tubular reabsorption of glucose, glucosuria is a feature of the nephropathy.

**2.) Discuss the process of micturition?**

In micturition, the stretch receptors detect the filling of the bladder and transmit afferent signals to spinal cord. The signals then return to the bladder from the S2 and S3 spinal segments via parasympathetic fibers in the pelvic nerve, the efferent signals then excites the detrusor muscle and also relax the internal urethral sphincter. The Urine will be involuntary voided if not inhibited by brain. For voluntary control, the micturition center in the pons receive signals from stretch receptors when it is the right time to urinate pons returns signals to spinal interneurons that excite the detrusor muscle and relax the internal urethral sphincter. If it Is not the right time to urinate, signals from pons excite spinal interneurons that keep the external urethral sphincter contracted, then the urine is retained in bladder. When its time to urinate, the signals from pons cease and external urethral sphincter relaxes, then the Urine is voided.

**3.) Explain juxtaglomerular apparatus?**

The juxtaglomerular apparatus is a specialized structure in the kidney formed by the distal convoluted tubule and the glomerular afferent arteriole that regulates the function of each nephron, the functional units of the kidney. 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 juxtaglomerular apparatus consists of three types of cells;

**a.) The Macula densa**, this is a part of the distal convoluted tubule of the same nephron. Cells in the macula densa respond to changes in the sodium chloride levels in the distal tubule of the nephron via the tubuloglomerular feedback loop. When the macula densa detects elevated sodium chloride, it leads to an increase in Glomerular filtration rate (GFR). The increase in the salt concentration causes several cell signals to eventually cause the adjacent afferent arteriole to constrict, which 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.

**b.) Juxtaglomerular cells**, which secrete renin and these cells are similar to epithelium and are located in the tunica media of the afferent arterioles as the enter the glomeruli. The renin is secreted in response to stimulation of beta-1 adrenergic receptoe, decreases in renal perfusion pressure, decrease in NaCl concentration at the macula densa, often due to a decrease on glomerular filtration rate.

**c.) Extraglomerular mesangial cells** These 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 can be found here.

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

The kidneys play a central role in the regulation of arterial blood pressure. The kidney influences blood pressure by causing the arteries and veins to constrict, Increasing the circulating blood volume. The Macula densa cells, sense the Na in the filtrate, while the arterial cells (juxtaglomerular cells) sense the blood pressure. When the blood pressure drops, the amount of filtered Na also drops. The arterial cells sense the drop in blood pressure, and the decrease in Na concentration 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-1. Angiotensin-1 is then converted to angiotensin-2 by an angiotensin-converting enzyme (ACE), found in the lungs. Angiotensin-2 causes blood vessels to contract -- the increased blood vessel constrictions elevate the blood pressure. When the volume of blood is low, arterial cells in the kidneys secrete renin directly into circulation. Plasma renin then carries out the conversion of angiotensinogen released by the liver to angiotensin-1. Angiotensin-1 is subsequently converted to angiotensin-2 by the enzyme angiotensin converting enzyme found in the lungs. Angiotensin-2m a potent vasoactive peptide causes blood vessels to constrict, resulting in increased blood pressure.

**5.) Discuss the role of Kidney in Calcium homeostasis?**

Calcium homeostasis is the mechanism by which the body maintains adequate calcium levels. Derangements of this mechanism lead to hypercalcemia or hypocalcemia, both of which can have important consequences for health. Vitamin D is converted to calcidiol in the liver. Part of the calcidiol is converted by the kidneys to calcitriol, the biologically active form of vitamin D. It circulates as a hormone in the blood, regulating the concentration of calcium and phosphate in the bloodstream and promoting the healthy growth and remodeling of bone. Reabsorption of calcium occurs in the kidney.