**ASSIGNMENT**

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**QUESTION 1:** DISCUSS THE ROLE OF KIDNEY IN GLUCOSE HOMEOSTASIS.

 It is only in recent years that the attention was drawn on the important role of the kidney in glucose homeostasis. Nevertheless, along with the liver, the kidney has an important role in ensuring the energy needs during fasting periods. Kidney plays an important role in glucose homeostasis, both in the post-absorptive and postprandial period. Kidney produces glucose by gluconeogenesis in the renal cortex and uses glucose for covering energy needs of the medulla. Kidney participates also to the reabsorption of filtered glucose in order the terminal urine was devoided of glucose, as long as blood glucose did not exceed 180mg/dL. Reabsorption of glucose is mediated by sodium-glucose cotransporters (SGLT1 and SGLT2) expressed in S1 and S3 segments of proximal tubule. SGLT2 is the main sodium-glucose cotransporter responsible for 90% of glucose reabsorption. In type 2 diabetics, renal gluconeogenesis and glucose utilisation are increased by 30%. Surprisingly, renal glucose reabsorption is increased, participating to worsening of hyperglycemia. This results from the increase in the renal threshhold of glucose reabsorption (220mg/dL) and from an overexpression of SGLT2 in response to hyperglycemia and of cytokine secretion. The administration of SGLT2 inhibitors to type 2 diabetic patients induced a decreased in the renal threshhold of glucose reabsorption (80mg/dL) and strongly reduced kidney glucose reabsorption. The inhibitors of SGLT2 are the only antidiabetic molecules able to correct the excessive renal glucose reabsorption in type 2 diabetics and thus to contribute, by an original mechanism, to the lowering of blood glucose level.

**QUESTION 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 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.

**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.

 As mentioned earlier, 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.

**QUESTION 3:** EXPLAIN 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 unclear.

**QUESTION 4:** DISCUSS THE ROLE OF KIDNEY IN REGULATION OF BLOOD PRESSURE.

 The kidneys ensure that the make-up and volume of the fluids in the body is correct. They help control the chemical balance of the blood and regulate the body's level of sodium, potassium and calcium. The kidneys remove waste products and excess water from the body and so help to regulate blood pressure. They activate [vitamin D](https://www.yourhormones.info/hormones/vitamin-d/), which helps to maintain strong bones, and produce [erythropoietin](https://www.yourhormones.info/hormones/erythropoietin/), a hormone that is vital for the production of red blood cells.

Each kidney contains 1.0–1.5 million small tubes called nephrons. The kidneys filter blood through a network of small blood vessels called the glomerulus. This produces a solution that then flows through the nephrons. As this fluid passes through the nephron, substances that the body wants to retain (such as sodium, potassium, proteins and most of the water) are re-absorbed back into the blood. The substances that need to be removed from the body, such as waste products including the remains of drugs and alcohol, are retained in the fluid and removed from the body in the form of urine. The kidneys filter around 200 litres of blood a day and produce between one to two litres of urine.

**QUESTION 5:** DISCUSS THE ROLE OF KIDNEY IN CALCIUM HOMEOSTASIS

 The **kidney** is critcally important in calcium homeostasis. Under normal blood calcium concentrations, almost all of the calcium that enters glomerular filtrate is reabsorbed from the tubular system back into blood, which preserves blood calcium levels. If tubular reabsorption of calcium decreases, calcium is lost by excretion into urine.

 More than 95% of filtered calcium is reabsorbed along the renal tubules. In the proximal tubules, 60% of filtered calcium is reabsorbed by passive mechanisms. In the thick ascending limb, 15% of calcium is reabsorbed by paracellular diffusion through paracellin-1 (claudin-16). The calcium sensing receptor (CaSR) in the basolateral membrane of the thick ascending limb senses the change in iCa2+ and inhibits calcium reabsorption independent to PTH and 1,25(OH)2D3. The fine regulation of calcium excretion occurs in the distal convoluted tubules and connecting tubules despite the fact that only 10-15% of filtered calcium is reabsorbed there. Transient receptor potential vanilloid 5 (TRPV5) and 6 (TRPV6) in the apical membrane act as the main portal of entry, calbindin-D28K delivers Ca2+ in the cytoplasm, and then Na2+/Ca2+ exchanger (NCX1) and plasma membrane Ca2+-ATPase in the basolateral membrane serve as an exit. In the cortical collecting duct, TRPV6 is expressed, but the role might be negligible. In addition to PTH and 1,25(OH)2D3, acid-base disturbance, diuretics, and estrogen affect on these calcium channels. Recently, klotho and fibroblast growth factor 23 (FGF23) are suggested as new players in the calcium metabolism. Klotho is exclusively expressed in the kidney and co-localized with TRPV5, NCX1, and calbindin-D28K. Klotho increases calcium reabsorption through trafficking of TRPV5 to the plasma membrane, and also converts FGF receptor to the specific FGF23 receptor. FGF23:klotho complex bound to FGF receptor inhibits 1α-hydroxylase of vitamin D, and contributes to calcium reabsorption and phosphate excretion in the kidney.