**Gwaivangmin Zumshok Dorcas**

**17/ MHS01/137**

**Medicine and Surgery**

**300level**

**Renal Physiology assignment (PHS 303)**

**Questions**

1. Discuss the role of kidney in glucose homeostasis.
2. Discuss the process of micturition.
3. Explain juxtaglomerular apparatus.
4. Discuss the role of kidney in regulation of blood pressure.
5. Discuss the role of kidney in calcium homeostasis.

**Answers**

1. The kidneys’ contributions to maintaining glucose homeostasis are significant and include such functions as release of glucose into the circulation via gluconeogenesis, uptake of glucose from the circulation to satisfy their energy needs, and 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 (lactate, glycerol, amino acids). With regard to renal reabsorption of glucose, the kidneys normally retrieve as much glucose as possible, rendering the urine virtually glucose free.

The kidneys are essentially designed to filter large quantities of plasma, reabsorb substances that the body must conserve, and secrete substances that must be eliminated. These basic functions are critical to regulation of fluid and electrolyte balance, body fluid osmolality, acid-based balance, excretion of metabolic waste and foreign chemicals, arterial pressure, hormone secretion, and, most relevant to this discussion, glucose balance. The kidneys help maintain glucose homeostasis by at least two mechanisms:

* Under normal circumstances, the kidney filters and reabsorbs 100% of glucose, approximately 180g of glucose each day. The glucose transporter in the renal proximal tubule ensures that less than 0.5g/day is excreted in the urine of healthy adults. More water than glucose is reabsorbed resulting in an increase in the glucose concentration in the urine along the tubule. Consequently the affinity of the transporters for glucose along the tubule increases to allow for complete reabsorption of glucose from the urine.
* It produces glucose by gluconeogenesis. The key enzymes of gluconeogenesis are phosphoenolpyruvate carboxykinase (PEPCK)and glucose 6-phosphate (G6Pase).These are expressed in the renal proximal tubule only and not the renal medulla. The kidneys produce between 2.0-2.5µmol of glucose/kg/min thereby contributing about 20-25% of circulating glucose

1. Micturition is the process by which the urinary bladder empties when it becomes filled. This process is also known as voiding. It involves two main steps; first, the bladder fills progressively until the tension in its wall rises progressively until the tension in its walls rises above a threshold level. This tension elicits the second step, which is a nervous reflex, called the micturition reflex that empties the bladder or if it fails, it causes a conscious desire to urinate. Although the micturition reflex is an autonomic spinal cord reflex, it can also be inhibited or facilitated by centers in the cerebral cortex of the brain stem.

Sensory signals from the bladder stretch receptors are conducted to the sacral segments of the cord through the pelvic nerves and then reflexively back again to the bladder through the parasympathetic nerve fibers by the same nerves.

When the bladder is partially filled, these micturition contractions usually relax spontaneously after a fraction of one minute, the detrusor muscle stops contracting, and pressure falls back to baseline. As the bladder continuous to fill, the micturition reflex becomes more frequent and causes greater contraction of the detrusor muscle.

Once a micturition reflex begins, it is self-regenerative. That is, initial contraction of the bladder activates the stretch receptors to cause a great increase in sensory impulses from the bladder and posterior urethra which causes a further increase in reflex contraction of the bladder; thus, the cycle is repeated again and again until the bladder has reached a strong degree of contraction. Then, after a few seconds to more than a minute, the self-regenerative reflex begins to fatigue and the regenerative cycle of micturition reflex ceases, permitting the bladder to relax.

Once a micturition reflex has occurred but has not succeeded in emptying the bladder, the nervous elements of this reflex usually remains in an inhibited state for a few minutes to an hour or more before another micturition reflex occurs. As the bladder becomes more and more filled, micturition reflexes occur more and more often and more and more powerfully.

Once the micturition reflex becomes powerful enough, it causes another reflex which passes through the pudendal nerves to the external sphincter to inhibit it. If this inhibition is more potent in the brain than the voluntary constrictor signals to the external sphincter, urination will occur. If nor, urination will not occur until the bladder still fills further and the micturition reflex becomes more powerful.

Voluntary urination is usually initiated the following ways: First, a person voluntarily contracts his or her abdominal muscles, which increase the pressure in the bladder and allows extra urine to enter the neck of the bladder and posterior urethra under pressure, thus stretching their wall. This action stimulates the stretch receptors, which excites the micturition reflex and simultaneously inhibits the external urethral sphincter. Ordinarily, all the urine will be emptied, with rarely more than 5 to 10 milliliters left in the bladder.

1. Juxtaglomerular apparatus is a specialized structure formed by the distal vascular pole of glomerulus. It is part of the kidney nephron, next to the glomerulus. It is found between the afferent and the distal convoluted tubule of the same nephron. Its location is critical to its function in regulating renal blood floe of the glomerular filtration rate. The juxtaglom- erular apparatus is made up of three types of cells:

* The macula densa, a part of the distal convoluted tubule of the same nephron. It is an area of closely packed specialized cells lining the wall of the distal tubule, at the point where the thick ascending limb of the Loop of Henle meets the distal convoluted tubule. The macula densa is a thickening where the distal tubule touches the glomerulus. The cells of the macula densa are sensitive to the concentration of sodium chloride in the distal convoluted tubule. A decrease in NaCl level initiates a signal to increase rennin release from the juxtaglomerular cells of the afferent and efferent arterioles, which are the major sites for rennin. They sense changes in sodium chloride level, and will trigger an autoregulatory response to increase or decrease reabsorption of ion and water to the blood in order to alter blood volume and return blood pressure to normal.
* The juxtaglomerular cell, also known as granular cells which secrete rennin. They are specialized smooth muscles cells mainly in the wall of the afferent arterioles that deliver blood to glomerulus. In synthesizing rennin, the play a role in renin-angiotensin system and thus in autoregulation of the kidney.
* The extraglomerular mesangial cells, also known as Lacis cells, Polkissen cells or Goormaghtigh cells are light-stained pericytes in the kidney found outside the glomerulus, near the vascular wall.

1. The kidney regulates arterial blood pressure by maintaining sodium homeostasis and through afferent sympathetic signals to the central nervous system. Renal artery perfusion pressure directly regulates sodium excretion and the renin-angiotensin-aldosterone system plays a role in maintaining the pressure-natriuresis relationship. Reduce nephron number contributes to the development of hypertension but not fully explain the increased risk of hypertension in the African American population. In patients with normal kidney function, disturbance of renal tubular sodium handling, which in some cases is associated with specific gene mutation, contribute to the development of essential hypertension. In cases of parenchymal renal disease, disturbed sodium homeostasis, reduced nephron mass, activation of the renin-angiotensin-aldosterone system and increase afferent renal sympathetic activity are responsible for the generation and maintenance of arterial hypertension. The blood pressure in the body depends upon:
2. The force by which the heart pumps out blood from the ventricles of the heart, and this is dependent on how much the heart muscle gets stretched by the inflowing blood into the ventricles.
3. The degree, to which the arteries and arterioles constrict, increases the resistance to blood flow, thus requiring a higher blood pressure.
4. The volume of blood circulating round the body; if the volume is high, the ventricles get more filled, and the heart muscle gets more stretched.

**The kidney influences blood pressure by:**

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

Specialized cells called macula densa are located in a portion of the distal tubule located near and in the wall of the afferent arteriole. These 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 sodium concentration is relayed to them by the macula densa cells. The juxtaglomerular cells then release an enzyme called renin. Renin converts angiotensinogeninto angiotensin-1 which is then converted to angiotensin-2 by an angiotensin-converting enzyme (ACE), found in the lungs. Angiotensin-2 causes blood vessels to contract. 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. Angiotensin-2 also stimulates the secretion of the hormone aldosterone from the adrenal cortex.

1. The maintenance of calcium homeostasis is very important because calcium is the main component of bony skeleton and serves as the intracellular and extracellular messenger in numerous essential cellular events such as neuronal network, immune response, muscle contraction and hormonal secretion. Total body calcium is about 1-2kg of 99% of total calcium exists in bone. About 50% of plasma calcium is freely filtered through the renal glomerulus, and 99% of the filtered calcium is actually reabsorbed along renal tubules. The excreted calcium in the final urine is about 200mg per day in an adult person with an average diet. Several factors are involved in the regulation of calcium in the renal tubules. Parathyroid hormone and activated vitamin D enhance calcium reabsorption in the thick ascending limb, distal convoluted tubule and/or connecting tubules and estrogen promotes calcium absorption in the distal convoluted tubule/connecting tubule. Acidosis contributes to hypercalciuria by reducing calcium reabsorption in the proximal tubule and distal convoluted tubule, and alkalosis vice versa. Diuretics like thiazide and furosemide also alter calcium reabsorption and flurosemide inhibits it. Plasma calcium itself also controls renal calcium absorption through altered parathyroid hormone secretion as well as via binding to the calcium sensing receptor in the thick ascending limb. To facilitate calcium ion reabsorption along renal tubules; voltage difference between the lumen and blood compartment should be favorable for calcium ion passage, concentration difference should be favorable for calcium ion passage with a higher calcium ion concentration in the lumen and an active transporter should exist if the voltage or concentration difference is not favorable for calcium ion reabsorption. Each renal tubular segment has a different calcium ion concentration difference or voltage environment for its unique mechanism for calcium reabsorption.