NAME: NWAOLISA CHIOMA SUCCESS

MATRIC NUMBER: 17/MHS01/207

COURSE CODE: 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

Answer 1

**Role of kidney in glucose homeostasis**

The kidneys are involved in maintaining glucose homeostasis through three different mechanisms: gluconeogenesis; glucose uptake from the blood for its own energy requests and reabsorption into the general circulation of glucose from glomerular filtrate in order to preserve energy.

Renal gluconeogenesis

From the point of view of glucose utilization, the kidney is considered as 2 separate organs; the renal medulla is characterized mainly by glucose utilization and the renal cortex is responsible for glucose release. The separation of these activities represents the consequence of differences in the distribution of numerous enzymes along the nephron. The cells in the renal medulla can use only glucose for their needs (like the brain) and they have enzymes capable of glucose-phosphorylation and glycolysis. They can therefore phosphorylate important amounts of glucose and accumulate glycogen but, because these cells do not have glucose-6-phosphatase or any other gluconeogenic enzymes, they are unable to release glucose into the bloodstream. Moreover, the cells in the renal cortex have gluconeogenic enzymes and they can produce and release glucose into the circulation. However these cells cannot synthesize glycogen because they have little phosphorylating capacity. After a 16-h overnight fast, approximately 10 µmol ⁄ (kg /min) of glucose is released into the circulation . Almost 50% of this is the result of glycogenolysis from the liver stocks and the other half is produced by liver and kidney gluconeogenesis. The renal cortex (like the liver) contains gluconeogenic enzymes and it can synthesize glucose-6-phosphate from precursors (lactate, glutamine, glycerol and alanine). Because it contains glucose-6-phosphatase, it is able to release glucose into the blood stream and the human liver and kidneys are the only organs that can perform gluconeogenesis. Therefore, after an overnight fast, the liver produces 75–80% of glucose released into the circulation and the remaining 20–25% is derived from the kidneys. Several studies have indicated that human kidneys and liver provide approximately the same amounts of glucose through gluconeogenesis in postabsorptive period. If the duration of fasting is increased, the glycogen stores are depleted and gluconeogenesis produces all the glucose released into circulation.

Glucose reabsorption

Apart from the important role in gluconeogenesis and the role of renal cortex in glucose uptake, the kidneys contribute to glucose homeostasis by filtering and reabsorbing glucose. In normal conditions, the kidneys can reabsorb as much glucose as possible, the result being a virtually glucose free urine. Approximately 180 grams of glucose are filtered by the glomeruli from plasma, daily but all of this quantity is reabsorbed through glucose transporters that are present in cell membranes located in the proximal tubules. These glucose transporters have a limited capacity of reabsorption. If this capacity is exceeded, glucose usually appears in the urine. The tubular maximum for glucose (TmG), the term used for the maximum capacity, can vary from 260 to 350 mg/min/1.73 m2 in healthy subjects. It corresponds to blood glucose levels of 180-200 mg/dL [24]. When the blood glucose is very high and the TmG is reached, the transporters cannot reabsorb all the glucose and glucosuria occurs . Nevertheless, there can be slight differences between the nephrons and the inaccurate nature of biological systems may potentially lead to the development of glucosuria when blood glucose is below TmG. Glucosuria may occur at lower plasma glucose levels in certain conditions of hyperfiltration (eg. pregnancy), but as a consequence of hyperfiltration and not of significant hyperglycemia. In a given day, the kidneys can produce, via gluconeogenesis, 15–55g glucose and it can metabolize 25–35g glucose. Regarding the glucose metabolic pathways, it is obvious that renal reabsorption represents the main mechanism by which the kidney is involved in glucose homeostasis. Therefore, the change in tubular glucose reabsorption may have a considerable impact on glucose homeostasis.

Answer 2

**Micturition** is the process by which the urinary bladder empties when it becomes filled. This involves two main steps: First, the bladder fills progressively until the tension in its walls rises above a threshold level; this elicits the second step, which is a nervous reflex called the micturition reflex that empties the bladder or, if this fails, at least 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 or brain stem.

. The main physiological events in the process of micturition are: Filling of urinary bladder and Emptying of urinary bladder.

FILLING OF URINARY BLADDER: Transport of urine into urinary bladder through ureters As urine collects in the renal pelvis, the pressure in the pelvis increases and initiates a peristaltic contraction beginning in the pelvis and spreading along the ureter to force urine towards the bladder.

EMPTYING OF THE BLADDER: Emptying of the bladder is basically a reflex action called the micturition reflex, which is controlled by supraspinal centres and is assisted by contraction of perineal and abdominal muscles. Therefore, emptying of the urinary bladder focuses on: Micturition reflex, Voluntary control of micturition and Role of perineal and abdominal muscles in micturition.

Micturition reflex

Micturition reflex is initiated by the stimulation of the stretch receptors located in the wall of urinary bladder Once micturition reflex is initiated, it is selfregenerative, i.e. initial contraction of the bladder wall Once micturition reflex is initiated, it is selfregenerative, i.e. initial contraction of the bladder wall further activates the receptors to increase the sensory impulses (afferents) from the bladder and urethra which cause further increase in the reflex contraction of detrusor muscle of the bladder. The cycle thus keeps on repeating itself again and again until the bladder has reached a strong degree of contraction. Once the micturition reflex becomes powerful enough, this causes another reflex which passes through pudendal nerves to external sphincter to cause its inhibition. If this inhibition is more potent than the voluntary constrictor signals from brain, then urination will not occur. If not so, urination will not occur unless the bladder fills still more and micturition reflex becomes more powerful.

Voluntary control

Voluntary control is gradually acquired as a learned ability of the toilet training. Once voluntary control is acquired, the supraspinal controlcentres exert final control of micturition by following means:

 The higher centres keep the micturition reflex partially inhibited all the time except when it is desired to micturate.

 When the convenient time to urinate present, the higher centres facilitate the sacral micturition centre (SMC) to initiate a micturition reflex and inhibit the external urinary sphincter so that urination can occur.

Role of perineal and abdominal muscles in micturition

Certain muscular movements, which aid the emptying of bladder, but are not the essential component of micturition process are:

\* At the onset of micturition, the levator ani and perineal muscles are relaxed, thereby shortening the post-urethra and decreasing the urethral resistance.

\* The diaphragm descends and

 \*The abdominal muscles contract, accelerating the flow of urine by raising intra-abdominal pressure which in turn secondarily increase the intravesical pressure thereby increasing the flow of urine.

Answer 3

**Juxtaglomerular apparatus**

Juxtaglomerular (JG) apparatus as the name indicates (juxtanear) refers to the collection of specialised cells located very near to the glomerulus. It forms the major component of renin–angiotensin–aldosterone system. The JG apparatus comprises three types of cells:

 Juxtaglomerular cells,

 Macula densa cells and

 Mesangial cells.

1. Juxtaglomerular cells. JG cells are specialised myoepithelial (modified vascular smooth muscle) cells located in the media of the afferent arteriole in the region of JG apparatus.

Characteristic features of JG cells are:

 They have well-developed Golgi apparatus and endoplasmic reticulum, abundant mitochondria and ribosomes.

 They synthesize, store and release an enzyme called renin. Renin is stored in the secretory granules of JG cells and, therefore, these are also called granular cells.

 They act as baroreceptors (tension receptors) and respond to changes in the transmural pressure gradient between the afferent arterioles and the interstitium.

 They are densely innervated by the sympathetic nerve fibres and release their renin content in response to the sympathetic discharge.

 As these cells act as vascular volume receptors, they monitor renal perfusion pressure and are stimulated by hypovolaemia or decreased renal perfusion pressure.

2. Macula densa cells. Macula densa cells refer to the specialised renal tubular epithelial cells of a short segment of the thick ascending limb of loop of Henle which passes between the afferent and efferent arterioles supplying its glomerulus of origin.

Characteristic features of macula densa cells are:

 They are not well adapted for reabsorption.

 They are not innervated.

 These cells are in direct contact with the mesangial cells and in close contact with the JG cells.

 They act as chemoreceptors and are stimulated by decreased NaCl concentration and thereby causing increased renin release.

3. Mesangial cells . Mesangial cells or lacis cells are the interstitial cells of the JG apparatus.

Characteristic features of these cells are:

 They are in contact with both the macula densa cells (on one side) and JG cells (on the other side).

 Functionally, these cells possibly relay the signals from macula densa to the granular cells after modulating the signals. In this way, a decreased intraluminal Na+ load, Cl– load, or both in the region of macula densa stimulates the JG cells to secrete renin.

 They also show granulation to secrete renin in conditions of extreme hyperactivity.

 They also secrete various substances and take up immune complexes.

Answer 4

**Role of kidney in blood pressure regulation**

The kidney plays a central role in the regulation of arterial blood pressure. The kidneys play a central role in the regulation of arterial blood pressure. A large body of experimental and physiological evidence indicates that renal control of extracellular volume and renal perfusion pressure are closely involved in maintaining the arterial circulation and blood pressure. Renal artery perfusion pressure directly regulates sodium excretion; a process known as pressure natriuresis, and influences the activity of various vasoactive systems such as the renin–angiotensin–aldosterone (RAS) system. Along with vessel morphology, blood viscosity is one of the key factors influencing resistance and hence blood pressure. A key modulator of blood viscosity is the renin-angiotensin system (RAS) or the renin-angiotensin-aldosterone system (RAAS), a hormone system that regulates blood pressure and water balance. The kidney influences blood pressure by:

• Causing the arteries and veins to constrict

• 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 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 thereafter 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. Angiotensin-2 also stimulates the secretion of the hormone aldosterone from the adrenal cortex . Aldosterone causes the tubules of the kidneys to increase the reabsorption of sodium and water into the blood. This increases the volume of fluid in the body, which also increases blood pressure.

How the kidneys increase circulating blood volume

Angiotensin-2 also stimulates the adrenal gland to secrete a hormone called aldosterone. Aldosterone stimulates more Na reabsorption in the distal tubule, and water gets reabsorbed along with the Na. The increased Na and water reabsorption from the distal tubule reduces urine output and increases the circulating blood volume. The increased blood volume helps stretch the heart muscle and causes it to generate more pressure with each beat, thereby increasing the blood pressure. The circulating blood volume is directly proportional to the stretch of the heart muscle.

The actions taken by the kidney to regulate blood pressure are especially important during traumatic injury, when they are necessary to maintain blood pressure and conserve the loss of fluids.

Answer 5

**Role of kidney in calcium homeostasis**

Calcium is both filtered and reabsorbed in the kidneys but not secreted. Only about 50 percent of the plasma calcium is ionized, with the remainder being bound to the plasma proteins or complexed with anions such as phosphate. Therefore, only about 50 percent of the plasma calcium can be filtered at the glomerulus. Normally, about 99 percent of the filtered calcium is reabsorbed by the tubules, with only about 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. 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, 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 the much higher concentration of calcium in the tubular lumen, compared with the epithelial cell cytoplasm, and because the cell interior has a negative 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. Vitamin D (Calcitrol) and calcitonin also stimulate calcium reabsorption in the thick ascending limb of Henle's loop and in the distal tubule, although these hormones are not as important quantitatively as PTH in reducing renal calcium excretion.