NAME: OKOLO AWELE CHRISTABEL

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DEPARTMENT: MEDICINE & SURGERY

COURSE CODE: PHS 303(RENAL PHYSIOLOGY)

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

2.) Discuss the process of micturition.

3.) Explain the juxtaglomerular apparatus.

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

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

Answers

1.) Role of kidney in glucose homeostasis

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 (eg, 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 glomeruli filter from plasma approximately 180 grams of ***D-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 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.

Glycogenolysis

Glycogenolysis is the breakdown of glycogen to glucose-6-phosphate and a hydrolysis reaction (using glucose-6-phosphatase) in order to free glucose. The liver is the only organ that contains glucose-6-phosphatase. So, the cleavage of hepatic glycogen releases glucose, while the cleavage of glycogen from other sources can release only lactate. Lactate, that is generated via glycolysis, is often absorbed by other organs and helps regenerating glucose

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

2.) 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 before it expels it out.

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.

Physiology of Micturition

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.

3.) The 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 three components of the juxtaglomerular apparatus are:

- The ***juxtaglomerular cells*** of the afferent arteriole , synthesize and store renin, which is secreted in response to specific stimuli (e.g., low blood flow, decreased NaCl delivery). The juxtaglomerular cells could be considered the "effector arm" of the renin-angiotensin-aldosterone axis.
- The ***macula densa,*** a region of the distal convoluted tubule characterized by tubular epithelial cells which are more densely-packed than in other regions of the nephron(and thereby leading to its characteristic appearance on light microscopy). The macula densa can be considered the "sensory arm" of the renin-angiotensin-aldosterone axis in that these are the cells which sense decreased NaCl delivery which determines downstream function. They're also involved in the mechanism of tubuloglomerular feedback.
- ***Mesangial cells,*** which form connections via actin and microtubules which allow for selective vasoconstriction/vasodilation of the renal afferent and efferent arterioles with mesangial cell constraction.

4.) 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.

The renin-angiotensin system regulates blood pressure and fluid balance in the body. When blood volume or sodium levels in the body are low, or blood 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 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 work 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.) Role of kidney in calcium homeostasis

The kidney is critically 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. Vitamin D and parathyroid hormone help regulate how much calcium is absorbed and how much calcium the kidneys eliminate. Healthy kidneys turn vitamin D into an active hormone(calcitriol), which helps increase calcium absorption from the intestines into the blood.

The principal function of vitamin D in calcium homeostasis is to increase calcium absorption from the intestine. Calcium is absorbed by both an active transcellular pathway, which is energy dependent, and by a passive paracellular pathway through tight junctions, 1,25Dihydroxyvitamin D3 (1,25(OH)2D3) the hormonally active form of vitamin D, through its genomic actions, is the major stimulator of active intestinal calcium absorption which involves calcium influx, translocation of calcium through the interior of the enterocyte and basolateral extrusion of calcium by the intestinal plasma membrane pump.

The kidney excretes calcium by: nearly 98% of filtered calcium (i.e., glomerular filtrate) is reabsorbed by either passive or active processes occurin at four sites in the kidney, each contributing to maintaining neutral calcium balance. 70% of the filtered calcium is reabsorbed passively in the proximal tubule. Active calcium transport is regulated by the calcium sensing receptor located in the ascending loop of Henle, where, in response to high calcium levels in the extracellular fluid, active reabsorption in the loop is blocked through actions of the calcium sensing receptor. In contrast, when the filtered calcium load is low, the calcium sensing receptor is activated, and a greater fraction of the filtered calcium is reabsorbed.