

**NAME: UYANWANNE DANIEL AMARACHI**

**MATRIC. NO: 17/MHS01/318**

**DEPARTMENT: MEDICINE AND SURGERY**

**LEVEL: 300L**

**COURSE CODE: PHS 303**

**COURSE TITLE: RENAL PHYSIOLOGY, BODY FLUID &  
TEMPERATURE REGULATION**

**Question 1: Discuss the 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 (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:

- a. Under normal circumstances, the kidney filters and reabsorbs 100% of glucose, approximately 180g of glucose each day. The glucose transporters 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.
- b. 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 2.0-2.5 $\mu$ mol of glucose/kg/min thereby contributing about 20-25% of circulating glucose

## **Question 2: Discuss the process of micturition**

Micturition is the process of expelling urine from the bladder. This act is also known as voiding of the bladder. We depend on micturition (urination) to eliminate organic waste products, which are produced as a result of cell metabolism in the body

### **Formation of urine**

Each kidney weighs about 150g and has a marked indentation medially (**the hilus**) where the renal artery and renal nerves enter and the renal vein and ureter leave. Between them, the kidneys make approximately 30ml or more of urine every hour. Normal urine production depends on normal blood flow to the kidneys. The nephron is the functional unit of the kidney. Nephrons permit the passage of some substances out of the body but restrict the passage of others, for example, blood cells and large proteins.

### **Filtration**

As blood flows through the glomerulus, much of the fluid and waste products in the blood are forced out through the walls of the capillaries, filtered, and then flow into the Bowman's capsule. This glomerular filtrate (about 125ml per minute) consists of water, glucose, waste salts such as sodium and potassium, and urea. Urea is the most abundant waste product excreted by the kidneys and is formed from ammonia, a highly toxic substance. Ammonia is formed in the liver from the breakdown of amino acids.

### **Absorption**

Much of the glomerular filtrate, including most of the water, is reabsorbed into the capillaries surrounding the proximal and distal convoluted tubules, the loop of Henle and the collecting tubules. All of the glucose will be reabsorbed unless blood glucose levels are high [more than 8.9 millimoles per litre (mmol/l) or 160 milligrams per decilitre (mg/dl)] in which case some glucose will be excreted in the urine. Sodium is also reabsorbed but the amount varies, depending on how much the body requires to maintain a constant concentration of sodium ions in the blood.

### **Secretion**

This is the final stage of urine formation, and occurs at the distal and collecting tubules. Substances either diffuse or are actively transported out of the capillaries and into the collecting tubules to be excreted in the urine. Hydrogen ions, potassium ions, ammonia and some drugs are all secreted at this stage and the kidneys play an important role in maintaining the acid-base balance within the body.

### **Final composition of urine**

The final composition of urine is the result of filtration, absorption and secretion by the nephrons. The kidneys produce, on average, one and a half litres of urine each day - this is mostly composed of water,

is straw coloured and has a specific gravity of 1.005 to 1.030. **Urea, uric acid, creatinine, sodium chloride** and **potassium ions** are all normal constituents of urine while **blood, ketones** and **glucose** are not, and their presence may indicate the presence of a disease.

Urine passes from the kidneys to the bladder through the ureters where it is stored until it is eliminated via the urethra. Urine is moved along the ureters to the bladder by peristaltic contraction and gravity. The ureters are muscular tubes about 30cm long. They are firmly attached to the posterior abdominal wall and are retroperitoneal; they do not enter the peritoneal cavity.

**NOTE: The ureteral openings into the bladder are flattened (slit-shaped) rather than round. This is due to the oblique angle at which the ureters enter the bladder, which helps to prevent the back-flow of urine into the ureters when the bladder contracts.**

### **Storage of urine**

The bladder is a hollow, muscular sac which sits in the pelvis. The bladder stores urine and can contain approximately one litre when full. During micturition, strong muscles in the bladder walls (the detrusor muscles) compress the bladder, pushing its contents into the urethra.

### **Control of bladder emptying**

The opening, described as the neck of the bladder, between the bladder and the urethra, is closed by two rings of muscle - the internal and external sphincters. The internal sphincter contains smooth muscle fibres and the normal muscle tone of these fibres keeps it contracted; **it is therefore not under voluntary control**. The external sphincter is formed of a circular band of skeletal muscle which is supplied by the pudendal nerve and is under voluntary control. These fibres remain contracted, as a result of central nervous system stimulation, except during micturition when they relax.

When the volume of urine in the bladder reaches about 250ml, stretch receptors in the bladder walls are stimulated and excite sensory parasympathetic fibres which relay information to the sacral area of the spine. This information is integrated in the spine and relayed to two different sets of neurons. Parasympathetic motor neurons are excited and act to contract the detrusor muscles in the bladder so that bladder pressure increases and the internal sphincter opens. At the same time, somatic motor neurons supplying the external sphincter via the pudendal nerve are inhibited, allowing the external sphincter to open and urine to flow out, assisted by gravity.

### **Question 3: Explain the juxtaglomerular apparatus.**

The juxtaglomerular apparatus (JGA) is located between the afferent arteriole and the returning distal convoluted tubule of the same nephron. It is responsible for regulating both intrarenal (tubule-glomerular feedback) and extrarenal (renin-angiotensin-aldosterone) mechanisms necessary to maintain both renal and entire body volume status. The three components of the JGA are the following:

1. **The juxtaglomerular cells of the afferent arteriole:** They 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.

2. **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 Na Cl delivery which determines downstream function. They are also involved in the mechanism of tubule-glomerular feedback.
3. **Mesangial cells:** form connections via actin and microtubules which allow for selective vasoconstriction/vasodilation of the renal afferent and efferent arterioles with mesangial cell contraction.

#### **Question 4: Discuss the role of kidney in regulation of blood pressure.**

Based on the capacity for the kidney to excrete sodium, this blood pressure-altering mechanism should have sufficient advantage to limit intravascular volume and consequently lower blood pressure in response to a range of stimuli from elevated heart rate to increase peripheral vascular resistance.

#### **The kidneys and their influence on 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. 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 blood pressure in the body depends upon:

- i. 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.
- ii. The degree to which the arteries and arterioles constrict, increases the resistance to blood flow, thus requiring a higher blood pressure.
- iii. 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:**

- i. Causing the arteries and veins to constrict
- ii. 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 into 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.

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. If the renin-angiotensin-aldosterone system is too active, blood pressure will be too high. Many drugs interrupt different steps in this system to lower blood pressure. These drugs are one of the main ways to control high blood pressure (hypertension), heart failure, kidney failure, and harmful effects of diabetes. It is believed that angiotensin-1 may have some minor activity, but angiotensin-2 is the major bioactive product. Angiotensin-2 has a variety of effects on the body: throughout the body, it is a potent vasoconstrictor of arterioles.

### **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 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.

### **Question 5: Discuss the role of the kidney in calcium homeostasis.**

Calcium is both filtered and reabsorbed in the kidney but not secreted. As is true with the other ions, 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; it is 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 charge 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 (calcitriol) 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