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**MATRIC NO.: 17/MHS01/138**

**COURSE: RENAL PHYSIOLOGY, BODY FLUID AND TEMPERATURE REGULATION.**

1) **DISCUSS THE ROLE OF KIDNEY IN GLUCOSE HOMEOSTASIS**

Glucose is synthesized and reabsorbed by the kidney.

- **Gluconeogenesis:** the kidney synthesizes glucose from amino acids and other precursors during prolonged fasting. The kidney plays this role during starvation and it is known as gluconeogenesis.
- **Glucose reabsorption:** the kidney engages in the reabsorption of glucose. It is completely reabsorbed in the proximal convoluted tubule and is transported by the secondary transport mechanism (sodium co-transport). The carrier protein used in moving the glucose across the epithelium is the sodium-dependent glucose co-transporter (SGLT2). It is transported into the medullary interstitium via glucose transporter 2 (GLUT 2). In the first half of the proximal tubule, sodium is reabsorbed by co-transport along with glucose, amino acids and other solutes. However, in the second half of the proximal tubule, $Na^+$ is reabsorbed mainly with chloride ions due to its high concentration in that part of the tubule.

  Glucose and other organic solutes are much more avidly reabsorbed than water thus its concentration decrease markedly along the length of the tubule.

2) **DISCUSS THE PROCESS OF MICTURITION**

Micturition is the process by which urine is voided from the urinary bladder.

Micturition reflex is the reflex by which micturition occurs. The reflex is elicited by the stimulation of stretch receptors situated in the wall of the urinary bladder and urethra. When about 300 to 400ml of urine is collected in the bladder, intravesical pressure increases. The pressure stretches the wall of the bladder resulting in the stimulation of stretch receptors and generation of sensory impulses.

Sensory impulses from the receptors reach the sacral segments of the spinal cord via the sensory fibers of pelvic (parasympathetic) nerve. Motor or efferent impulses travel to motor fibers of the pelvic nerve towards the bladder and internal sphincter. Motor impulses cause contraction of the detrusor muscle and relaxation of the internal sphincter so that urine enters the urethra from the bladder.

Once urine enters the urethra, the stretch receptors in the urethra are stimulated and send afferent impulses to the spinal cord via the pelvic nerve fibers. The impulses generated from the spinal centers inhibit pudendal nerve so the external sphincter relaxes and micturition occurs.

Once micturition reflex begins, it is self-generative. The cycle continues repeatedly until the force of contraction of the bladder reaches the maximum and urine is voided out completely. The flow of urine during micturition is facilitated by increase in abdominal pressure due to the voluntary contraction of abdominal muscles.

Spinal centers for micturition are located in the lumbar and sacral segments, however these centers are regulated by higher centers which are either inhibitory or facilitatory:

- Inhibitory centers for micturition: centers in mid brain and cerebral cortex by suppressing spinal micturition centers
- Facilitatory centers: centers in the pons and some centers in the cerebral cortex facilitate micturition.

**3) EXPLAIN JUXTAGLOMERULAR APPARATUS**

The juxtaglomerular apparatus is a specialized organ located near the glomerulus of each nephrons. It is an organ because it is made up of types of cells which are:

i. Juxtaglomerular cells
ii. Macula densa
iii. Extramesangial cells

i. **Juxtaglomerular cells:** these are specialized smooth muscle cells that are located mainly in the walls of the afferent arteriole just before it enters the bowman's capsule and some

in the walls of the efferent arterioles. It is located in the tunica media and tunica adventitia of the arteriole and forms a cuff called 'polar cushion' or 'polkissen' around the afferent arteriole before it enters the bowman's capsule. The juxtaglomerular cells secrete renin which maintains blood pressure (increases blood pressure).

ii. **Macula densa:** this is located at the end portion of the thick ascending limb before it opens into the distal convoluted tubule. It is situated between the afferent arteriole and the efferent arteriole. It is made up of tightly packed cuboidal cells. It secretes thromboxane $A_2$ and plays a role in the tubuloglomerular feedback.

iii. **Extra-mesangial cells:** are located outside the glomerulus, in the triangular region between the efferent and afferent arteriole, and macula densa. They are known as agranular cells, lacis cells pr goormaghtigh/ cells. These cells secrete prostaglandin and cytokines.

**Function of juxtaglomerular apparatus**

i. Primary function: secretion of hormones rennin, prostaglandin and other substances

- Renin: secreted by juxtaglomerular cells under the stimulation by decrease in blood pressure, decreased extracellular fluid volume, increase in sympathetic activity and decreased load of sodium and chloride in macula densa. It plays a role in the renin-angiotensin system.
- Prostaglandins: it is secreted by extramesangial cells and type I medullary interstitial cells. It decreases blood pressure via vasodilation.
- Secretion of cytokines: like interlukin-2 and tumor necrosis factor by extra mesangial cells.

- Secretion of thromboxane $A_2$: by macula densa cells

ii. Regulation of blood flow and glomerular filtration rate: via the regulation carried out by the tubuloglomerular feedback which is a function of the macula densa.

**4) DISCUSS THE ROLE OF KIDNEY IN REGULATION OF BLOOD PRESSURE**

The kidney plays a role in the regulation of blood pressure via a long-term regulation mechanism. This mechanism involves two ways:

**I. Regulation of ECF volume:**

When blood pressure increases, kidneys excrete large amount of salt and water, particularly sodium. The kidney does this by pressure diuresis and pressure natriuresis. Due to these, there is decrease in ECF and blood volume thus restoring blood pressure back to normal.

When blood pressure decreases, the reabsorption of water from the renal tubules is increased. This will in turn increase ECF volume, blood volume and cardiac output resulting in the restoration of blood pressure.

**II. Renin-Angiotensin system:**

Renin is released from the juxtaglomerular cells of the juxtaglomerular apparatus which in turn acts on the plasma protein angiotensinogen. Angiotensinogen is converted to angiotensin I, it is in turn converted to angiotensin II via angiotensin converting enzyme (ACE). Angiotensin II is the most potent and it has a short half life of 1 to 2 minutes. It is rapidly degraded by angiotensinases which is found in RBC's and vascular beds. Angiotensin III is then converted to angiotensin IV.

- **Angiotensin II** which is the most potent increases blood pressure by:
  - Constriction of arterioles: in the body so that the peripheral resistance increases and blood pressure rises. It also causes constriction of afferent arterioles of the kidney which in turn reduces glomerular filtration rate, retains water and sodium and in turn increases ECF volume.

- It stimulates the adrenal cortex: to secrete aldosterone which facilitates sodium retention which is followed by water reabsorption and in turn increases ECF volume, blood volume and in turn increases blood pressure.
- It increases blood pressure indirectly by increasing the release of nor-adrenaline from post Ganglionic sympathetic fibers, which acts as a vasoconstrictor.

- **Angiotensin III:** increases aldosterone secretion and causes vasoconstriction
- **Angiotensin IV:** has an adrenocortical-stimulating and vasopressor activity.

**5) DISCUSS THE ROLE OF KIDNEY IN CALCIUM HOMEOSTASIS**

The kidney plays a role in calcium homeostasis vi its absorption and excretion:

- **Reabsorption:** the kidney aids the absorption of calcium from the intestine by converting vitamin $D_3$ (25-hydrocholecalciferol) into active (1, 25-dihydrocholecalciferol) via alpha-1-hydroxylase enzyme in the proximal convoluted tubule under the action of parathyroid hormone. Vitamin D's active form 1, 25-dihydrocholecalciferol (Calcitriol) is necessary for the absorption of calcium from the intestine. The reabsorption is regulated by:
    a) <u>Parathyroid hormone:</u> renal tubular reabsorption of calcium is increased in the thick ascending limb of the loop of henle and distal tubules with increase in PTH thus reducing calcium excretion.
    b) In the proximal tubule, calcium reabsorption is independent of parathyroid hormone but depends on/parallels sodium and water reabsorption.
    c) <u>Plasma phosphate:</u> increased plasma phosphate increases parathyroid hormone and in turn increases calcium reabsorption and decreases calcium excretion

d) Metabolic alkalosis stimulates calcium reabsorption and metabolic acidosis stimulates calcium excretion.

- **Excretion:** for calcium excretion by the kidneys, calcium is filtered and reabsorbed but not secreted. About 60% of plasma calcium is ionized, 40% is bound to plasma proteins and about 10% is complexed with anions such as phosphate. The 60% that is ionized can be filtered at the glomerulus. Out of the filtrate, about 65% is reabsorbed in the proximal tubule, 25-30% is reabsorbed in the loop of henle and 4-9% is absorbed in the distal and collecting tubules. Parathyroid hormone (PTH) stimulates calcium reabsorption in the distal convoluted tubule, collecting tubule as well as the loop of henle. While at the proximal convoluted tubule, most of the calcium is dissolved in water and reabsorbed through the paracellular pathway while 20% is by the transcellular pathway. Only 1% of the filtrate is excreted.