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

**PHS 303 ASSIGNMENT**

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

The kidneys’ contributions to maintaining glucose homeostasis are significant and include such functions as; release of glucose into circulation via gluconeogenesis, uptake of glucose from circulation to satisfy their energy needs and reabsorption of glucose at the level of the proximal tubule.

When blood glucose rises to relatively high levels, the kidney also exerts a regulatory effect. Glucose is continuously filtered by the glomeruli but is normally reabsorbed completely in renal tubules. The capacity of the tubular system to reabsorb glucose is limited.

If the blood glucose level is raised above 180 mg/100 ml, complete tubular reabsorption of glucose does not occur and the extra amount appears in the urine causing glycosuria.

180 mg/100 ml is the limiting level of glucose in the blood, above which tubular reabsorption does not occur which is known as renal threshold value for glucose.

Thus, by excreting extra amount of sugar in the urine during hyperglycemic state and reabsorbing sugar during the hypoglycemic state, the kidney helps in regulating the level of glucose in blood.

1. Discuss the process of micturition.

Micturition is the process by which urine is voided from the bladder when it becomes filled. This is a reflex process. However, it can be voluntarily controlled to some extent in grown children and adults. Micturition involves two stages, first, the bladder fills progressively until the tension in its walls rises above threshold level, this elicits the second step which is a nervous reflex called 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

1. **FILLING PROCESS**: Urine is continuously formed by nephrons and it flows into urinary bladder drop by drop through ureters. When urine collects in the pelvis of ureter, the contraction sets up in pelvis. This contraction is transmitted through rest of the ureter in the form of peristaltic wave up to trigone of the urinary bladder. Peristaltic wave usually travels at a velocity of 3 cm/second. It develops at a frequency of 1 to 5 per minute. The peristaltic wave moves the urine into the bladder. After leaving the kidney, the direction of the ureter is initially downward and outward. Then, it turns horizontally before entering the bladder. At the entrance of ureters into urinary bladder, a valvular arrangement is present. When peristaltic wave pushes the urine towards bladder, this valve opens towards the bladder. The position of ureter and the valvular arrangement at the end of ureter prevent the back flow of urine from bladder into the ureter when the detrusor muscle contracts. Thus, urine is collected in bladder drop by drop. A reasonable volume of urine can be stored in urinary bladder without any discomfort and without much increase in pressure inside the bladder.
2. **MICTURITION REFLEX**: Micturition reflex is the reflex by which micturition occurs. This reflex is elicited by the stimulation of stretch receptors situated on the wall of urinary bladder and urethra. When about 300 to 400 mL of urine is collected in the bladder, intravesical pressure increases. This stretches the wall of bladder resulting in stimulation of stretch receptors and generation of sensory impulses.

Pathway for Micturition reflex: Sensory (afferent) impulses from the receptors reach the sacral segments of spinal cord via the sensory fibers of pelvic (parasympathetic) nerve. Motor (efferent) impulses produced in spinal cord, travel through motor fibers of pelvic nerve towards bladder and internal sphincter. Motor impulses cause contraction of detrusor muscle and relaxation of internal sphincter so that, urine enters the urethra from the bladder (Fig. 57.5). Once urine enters urethra, the stretch receptors in the urethra are stimulated and send afferent impulses to spinal cord via pelvic nerve fibers. Now the impulses generated from spinal centers inhibit pudendal nerve. So, the external sphincter relaxes and micturition occurs. Once a micturition reflex begins, it is self-regenerative, i.e. the initial contraction of bladder further activates the receptors to cause still further increase in sensory impulses from the bladder and urethra. These impulses, in turn cause further increase in reflex contraction of bladder. The cycle continues repeatedly until the force of contraction of bladder reaches the maximum and the urine is voided out completely. During micturition, the flow of urine is facilitated by the increase in the abdominal pressure due to the voluntary contraction of abdominal muscles.

1. Explain Juxtaglomerular Apparatus.

Juxtaglomerular apparatus is a specialized organ situated near the glomerulus of each nephron (juxta = near). The juxtaglomerular apparatus is formed by three different structures: macula densa, extraglomerular mesangial cells and juxtaglomerular cells.

1. **MACULA DENSA**: Macula densa is the end portion of thick ascending segment before it opens into distal convoluted tubule. It is situated between afferent and efferent arterioles of the same nephron. It is very close to afferent arteriole. Macula densa is formed by tightly packed cuboidal epithelial cells.
2. **EXTRAGLOMERULAR MESANGIAL CELLS**: Extraglomerular mesangial cells are situated in the triangular region bound by afferent arteriole, efferent arteriole and macula densa. These cells are also called agranular cells, lacis cells or Goormaghtigh cells.
3. **JUXTAGLOMERULAR CELLS**: Juxtaglomerular cells are specialized smooth muscle cells situated in the wall of afferent arteriole just before it enters the Bowman capsule. These smooth muscle cells are mostly present in tunica media and tunica adventitia of the wall of the afferent arteriole. Juxtaglomerular cells are also called granular cells because of the presence of secretary granules in their cytoplasm.

**FUNCTIONS OF JUXTAGLOMERULAR APPARATUS**: Primary function of juxtaglomerular apparatus is the secretion of hormones. It also regulates the glomerular blood flow and glomerular filtration rate. The hormones secreted by juxtaglomerular apparatus are renin and prostaglandin.

**RENIN**: Renin is a peptide with 340 amino acids. Along with angiotensins, renin forms the renin-angiotensin system, which is a hormone system that plays an important role in the maintenance of blood pressure.

**RENIN**-**ANGIOTENSIN SYSTEM**: When renin is released into the blood, it acts on a specific plasma protein called angiotensinogen or renin substrate. It is the α2 -globulin. By the activity of renin, the angiotensinogen is converted into a decapeptide called angiotensin I. Angiotensin I is converted into angiotensin II, which is an octapeptide by the activity of angiotensin-converting enzyme (ACE) secreted from lungs. Most of the conversion of angiotensin I into angiotensin II takes place in lungs. Angiotensin II has a short half-life of about 1 to 2 minutes. Then it is rapidly degraded into a heptapeptide called angiotensin III by angiotensinases, which are present in RBCs and vascular beds in many tissues. Angiotensin III is converted into angiotensin IV, which is a hexapeptide.

**PROSTAGLANDIN**: Extraglomerular mesangial cells of juxtaglomerular apparatus secrete prostaglandin. Prostaglandin is also secreted by interstitial cells of medulla called type I medullary interstitial cells.

1. Explain the role of kidney in regulation of blood pressure.

Kidneys play an important role in the long-term regulation of arterial blood pressure by two ways:

i. By regulating the volume of extracellular fluid (ECF)

 ii. Through renin-angiotensin mechanism.

1. **By regulating the ECF volume**: When the blood pressure increases, kidneys excrete large amounts of water and salt, particularly sodium, by means of pressure diuresis and pressure natriuresis. Pressure diuresis is the excretion of large quantity of water in urine because of increased blood pressure. Even a slight increase in blood pressure doubles the water excretion. Pressure natriuresis is the excretion of large quantity of sodium in urine.

Because of diuresis and natriuresis, there is a decrease in ECF volume and blood volume, which in turn brings the arterial blood pressure back to normal level.

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

1. **Through renin**-**angiotensin mechanism**: When renin is released into the blood, it acts on a specific plasma protein called angiotensinogen or renin substrate. It is the α2 -globulin. By the activity of renin, the angiotensinogen is converted into a decapeptide called angiotensin I. Angiotensin I is converted into angiotensin II, which is an octapeptide by the activity of angiotensin-converting enzyme (ACE) secreted from lungs. Most of the conversion of angiotensin I into angiotensin II takes place in lungs. Angiotensin II has a short half-life of about 1 to 2 minutes. Then it is rapidly degraded into a heptapeptide called angiotensin III by angiotensinases, which are present in RBCs and vascular beds in many tissues. Angiotensin III is converted into angiotensin IV, which is a hexapeptide. Angiotensin II is the most active form.

Actions of Angiotensin II: Angiotensin II acts in two ways to restore the blood pressure:

1. It causes constriction of arterioles in the body so that the peripheral resistance is increased and blood pressure rises. In addition, angiotensin II causes constriction of afferent arterioles in kidneys, so that glomerular filtration reduces. This results in retention of water and salts, increases ECF volume to normal level. This in turn increases the blood pressure to normal level.
2. Simultaneously, angiotensin II stimulates the adrenal cortex to secrete aldosterone. This hormone increases reabsorption of sodium from renal tubules. Sodium reabsorption is followed by water reabsorption, resulting in increased ECF volume and blood volume. It increases the blood pressure to normal level.

Angiotensin III also increases the blood pressure and stimulates aldosterone secretion from adrenal cortex. It has 100% adrenocortical stimulating activity and 40% vasopressor activity of angiotensin II. Angiotensin IV also has adrenocortical and vasopressor activities.

1. Discuss the role of kidney in calcium homeostasis.

Kidneys play a role in the regulation of blood calcium level by activating 1,25-dihydroxycholecalciferol into vitamin D. Vitamin D is necessary for the absorption of calcium from intestine. The role of the kidney in calcium homeostasis is heavily influenced by parathormone (PTH). Parathormone is secreted by parathyroid gland is essential for the maintenance of blood calcium level within a very narrow critical level. PTH increases the reabsorption of calcium from the renal tubules along with magnesium ions and hydrogen ions. It increases calcium reabsorption mainly from distal convoluted tubule and proximal part of collecting duct. PTH also increases the formation of 1,25- dihydroxycholecalciferol (activated form of vitamin D) from 25-hydroxycholecalciferol in kidneys.

**ACTIONS OF 1,25-DIHYDROXYCHOLECALCIFEROL**:

1. It increases the absorption of calcium from the intestine, by increasing the formation of calcium binding proteins in the intestinal epithelial cells. These proteins act as carrier proteins for facilitated diffusion, by which the calcium ions are transported. The proteins remain in the cells for several weeks after 1,25-dihydroxycholecalciferol has been removed from the body, thus causing a prolonged effect on calcium absorption

 2. It increases the synthesis of calcium-induced ATPase in the intestinal epithelium

 3. It increases the synthesis of alkaline phophatase in the intestinal epithelium

4. It increases the absorption of phosphate from intestine along with calcium.