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**COURSE TITLE: RENAL PHYSIOLOGY**

**ANSWER TO QUESTION 1 (THE ROLE OF KIDNEY IN GLUCOSE HOMEOSTASIS)**

The kidney’s 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 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-phospahte from precursors (e.g. lactate, glycerol, amino acids). The kidney’s capacity to add glucose to the blood during prolonged periods of fasting rivals that of the liver. 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 180g of 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 co-transporters) and passive (glucose transporters) transporters.

With chronic kidney disease or acute failure of the kidneys, these homeostatic functions are disrupted and severe abnormalities of the body fluid volumes and composition rapidly occurs. With complete renal failure, enough potassium, acids, fluids and other substances accumulate in the body to cause death within a few days, unless clinical interventions such as hemodialysis are initiated to restore, at least partially, the body fluid and electrolyte balances.

**ANSWER TO QUESTION 2 (THE PROCESS OF MICTURITION)**

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.

**PROCESS OF FILLING**

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 the 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 3cm/sec. 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. This, 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 (intravesical pressure). It is due to the adaptation of detrusor muscle. This can be explained by cystometrogram (the graphical recording of pressure changes in urinary bladder in relation to volume of urine collected in it.)

**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 400ml of urine is collected in bladder, intravesical pressures 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 fiibers 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 causes contraction of detrusor muscle and relaxation of internal sphincter so that. Urine enters the urethra from the bladder. once urine enters urethra, th stretch receptors in the urethra are stimulated and send afferent impulses to spinal cord via pelvic nerve fibers. The impulses generated from soinal 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 increase in sensory impulses from the bladder and urethra. Theses 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 bladde reaches the maximum and 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.

***Higher Centers for Micturition***

Spinal centers for micturition are present in sacral and lumbar segments. But, these spinal centers are regulated by higher centers. The higher centers, which control micturition, are of two types, inhibitory centers and facilitatory centers. Inhibitory centers for micturition are of two types, inhibitory centers and facilitatory centers.

Inhibitory centers for micturition: centers in midbrain and cerebral cortex inhibit the micturition by suppressing spinal micturition centers.

Facilitatory centers for micturition: centers in pons facilitate micturition via spinal centers. Some centers in the cerebral cortex also facilitate micturition.

**ANSWER TO QUESTION 3 (JUXTAGLOMERULAR APPARATUS)**

Juxtaglomerular apparatus is a specialized organ situated near the glomerulus of each nephron (juxta=near).

Juxtaglomerular apparatus is formed by three different structures:

1. Macula densa

2. Extraglomerular mesangial cells

3. Juxtaglomerular cells.

 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.

 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.

Glomerular Mesangial Cells

Besides extraglomerular mesangial cells there is another type of mesangial cells situated in between glomerular capillaries called glomerular mesangial or intraglomerular mesangial cells. Glomerular mesangial cells support the glomerular capillary loops by surrounding the capillaries in the form of a cellular network. These cells play an important role in regulating the glomerular filtration by their contractile property.

Glomerular mesangial cells are phagocytic in nature. These cells also secrete glomerular interstitial matrix, prostaglandins and cytokines.

 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

* Secretion of hormones (e.g. renin, prostaglandin)

Juxtaglomerular cells secrete renin while Extraglomerular mesangial cells secrete prostaglandin.

* Secretion of other substances (e.g. Extraglomerular mesangial cells secrete cytokines while macula densa secretes thromboxane A2 ).
* The macula densa regulates glomerular blood flow and glomerular filtration rate.

**ANSWER TO QUESTION 4 (THE ROLE OF KIDNEY IN REGULATING BLOOD PRESSURE)**

The kidney plays a dominant role in long term regulation of arterial pressure by excreting variable amounts of sodium and water.

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 (vasoactive factor). Renin converts angiotensinogen, which is produced in the liver, to the hormone angiotensin I (vasoactive product). 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.

**ANSWER TO QUESTION 5 (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.

More than 95% of filtered calcium is reabsorbed along the renal tubules. In the proximal tubules, 60% of filtered calcium is reabsorbed by passive mechanisms. In the thick ascending limb, 15% of calcium is reabsorbed by paracellular diffusion through paracellin-1 (claudin-16). The fine regulation of calcium excretion occurs in the distal convoluted tubules and connecting tubules despite the fact that only 10-15% of filtered calcium is reabsorbed there.