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**17/MHS01/032**

**300L MBBS**

**RENAL PHYSIOLOGY ASSIGNMENT: PHS303**

**QUESTION ONE: DISCUSS THE ROLE OF KIDNEY IN GLUCOSE HOMEOSTASIS.**

The kidney maintains glucose homeostasis by releasing glucose into circulation via gluconeogenesis, uptake of glucose from the circulation to satisfy the energy needs and reabsorption of glucose at the level of proximal tubule. Renal release of glucose into circulation is as a result of glycogenolysis and gluconeogenesis respectively, which involves the breaking down and formation of glucose-6-phosphate from precursors like lactate, amino acids, glycerol etc.

With regard to renal absorption of glucose, the kidneys normally retrieve as much glucose as possible rendering the urine virtually glucose free. The glomeruli filter from plasma about 180 grams of glucose per day all of which is reabsorbed through glucose transporter proteins that are present in all cell membranes within the proximal tubules. If the capacity of these transporters is exceeded, glucose appears in urine.

The process of renal glucose absorption is mediated by active(sodium-coupled glucose cotransporters) and passive(glucose transporters) transporters.

In hyperglycemia(High blood sugar levels), the Kidneys may play a negative role by reabsorbing excess glucose hereby contributing to chronic hyperglycemia which in turn contributes to chronic glycemic burden and the risk of microvascular consequences.

**QUESTION TWO: DISCUSS THE PROCESSES OF MICTURITION.**

Micturition is a process by which urine is voided from the urinary bladder. It is a reflex process. However, in grown up children and adults, it can be controlled voluntarily to some extent. The functional anatomy and nerve supply of urinary bladder are essential for the process of micturition.

**FUNCTIONAL ANATOMY OF URINARY BLADDER AND URETHRA.**

**Urinary Bladder.**

Urinary bladder is a triangular hollow organ located in lower abdomen. It consists of a body and neck. Wall of the bladder is formed by smooth muscle. It consists of three ill-defined layers of muscle fibers called detrusor muscle that is, the inner longitudinal layer, middle circular layer and outer longitudinal layer. Inner surface of urinary bladder is lined by mucus membrane. In empty bladder, the mucosa falls into many folds called **rugae**.

At the posterior surface of the bladder wall, there is a triangular area called trigone. At the upper angles of this trigone, two ureters enter the bladder. Lower part of the bladder is narrow and forms the neck. It opens into urethra via internal urethral sphincter.

**Urethra.**

Male urethra has both urinary function and reproductive function. It carries urine and semen. Female urethra has only urinary function and it carries only urine. So, male urethra is structurally different from female urethra.

1. **Male Urethra**

Male urethra is about 20 cm long. After origin from bladder it traverses the prostate gland, which lies below the bladder and then runs through the penis.

The urethra has mucus glands called **glands of Littre.**

Male urethra is divided into three parts:

1. Prostatic urethra

2. Membranous urethra

3. Spongy urethra.

**Prostatic urethra.**

Prostatic urethra is 3 cm long and it runs through prostate gland. Sperms from vas deferens and the fluid from seminal vesicles are also emptied into prostatic urethra via ejaculatory ducts

Part of the urethra after taking origin from neck of bladder before entering the prostate gland is known as **preprostatic urethra.** Its length is about 0.5 to 1.5 cm. This part of urethra is considered as part of prostatic urethra.

**Membranous urethra**

Membranous urethra is about 1 to 2 cm long. It runs from base of the prostate gland through urogenital diaphragm up to the bulb of urethra.

**Spongy urethra.**

Spongy urethra is also known as cavernous urethra and its length is about 15 cm. Spongy urethra is surrounded by corpus spongiosum of penis. It is divided into a proximal bulbar urethra and a distal penil urethra. Penile urethra is narrow with a length of about 6 cm. It ends with external urethral meatus or orifice, which is located at the end of penis.

The bilateral bulbourethral glands open into spongy urethra. Bulbourethral glands are also called **Cowper glands.**

1. **Female Urethra**

Female urethra is narrower and shorter than male urethra. It is about 3.5 to 4 cm long. After origin from bladder it traverses through urogenital diaphragm and runs along anterior wall of vagina. Then it terminates at external orifice of urethra, which is located between clitoris and vaginal opening.

**Urethral Sphincters.**

There are two urethral sphincters in urinary tract:

1. Internal urethral sphincter.

2. External urethral sphincter.

**Internal Urethral sphincter.**

This sphincter is situated between neck of the bladder and upper end of urethra. It is made up of smooth muscle fibers and formed by thickening of detrusor muscle. It is innervated by autonomic nerve fibers. This sphincter closes the urethra when bladder is emptied.

**External Urethral sphincter.**

External sphincter is located in the urogenital diaphragm. This sphincter is made up of circular skeletal muscle fibers, which are innervated by somatic nerve fibers.

**NERVE SUPPLY TO URINARY BLADDER AND SPHINCTERS.**

Urinary bladder and the internal sphincter are supplied by sympathetic and parasympathetic divisions of auto­ nomic nervous system where as, the external sphincter is supplied by the somatic nerve fibers.

The stimulation of sympathetic (hypogastric) nerve causes relaxation of detrusor muscle and constriction of the internal sphincter. It results in filling of urinary bladder and so, the sympathetic nerve is called **nerve of filling.**

The stimulation of parasympathetic (pelvic) nerve causes contraction of detrusor muscle and relaxation of the internal sphincter leading to emptying of urinary bladder. So, parasympathetic nerve is called the **nerve of emptying or nerve of micturition.**

Pelvic nerve has also the sensory fibers, which carry impulses from stretch receptors present on the wall of the urinary bladder and urethra to the central nervous system.

External sphincter is innervated by the somatic nerve called pudendal nerve. Pudendal nerve maintains the tonic contraction of the skeletal muscle fibers of the external sphincter and keeps the external sphincter constricted always. During micturition, this nerve is inhibited. It causes relaxation of external sphincter leading to voiding of urine. Thus, the pudendal nerve is responsible for voluntary control of micturition.

**MICTURITION PHASE.**

1. **Filling/storage phase.**

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 (intravesical pressure). It is due to the adaptation of detrusor muscle. This can be explained by **cystometrogram**. This is the technique used to study the relationship between intravesical pressure and volume of urine in the bladder. Cystometrogram is the graphical registration (recording) of pressure changes in urinary bladder in relation to volume of urine collected in it.

1. **Voiding phase.**

When the bladder is filled with urine, the nerves in it are triggered which in turn stimulates the need to urinate. The brain signals the urinary bladder to contract, the receptors of the urinary bladder send a signal to the central nervous system in response to which the nervous system sends a signal that incites the contraction of the urinary bladder. Urine is eliminated through the urinalysis opening at the urethra. This process is called micturition and the neural mechanism involved is called the micturition reflex.

**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.

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.

**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:** 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 cerebral cortex also facilitate micturition.

**QUESTION THREE: EXPLAIN THE JUXTAGLOMERULAR APPARATUS.**

Juxtaglomerular apparatus is a specialized organ situated near the glomerulus of each nephron. It is formed by 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 mesengial 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. 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. Juxtaglomerular cells form a thick cuff called polar cushion or polkissen around the afferent arteriole before it enters the Bowman capsule.

**Function of juxtaglomerular apparatus.**

1. **Secretion of hormones.**

Juxtaglomerular apparatus secretes two hormones:

1. Renin.

2. Prostaglandin.

**Renin.**

Juxtaglomerular cells secrete 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

**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. **Secretion of other substance.**

1. Extraglomerular mesangial cells of juxtaglomerular apparatus secrete cytokines like interleukin-2 and tumor necrosis factor.

2. Macula densa secretes thromboxane A2.

1. **Regulation of glomerular blood flow and glomerular filtration rate.**

Macula densa of juxtaglomerular apparatus plays an important role in the feedback mechanism called **tubuloglomerular feedback mechanism**, which regulates the renal blood flow and glomerular filtration rate.

**QUESTION FOUR: DISCUSS THE ROLE OF KIDNEY IN REGULATION OF BLOOD PRESSURE.**

Kidneys play an important role in the long­term regulation of arterial blood pressure. When blood pressure alters slowly in several days/months/years, the nervous mechanism adapts to the altered pressure and looses the sensitivity for the changes. It cannot regulate the pressure any more. In such conditions, the renal mechanism operates efficiently to regulate the blood pressure. Therefore, it is called long­term regulation.

Kidneys regulate arterial blood pressure by two ways:

1. By regulation of ECF( extra cellular fluid) volume.
2. Through renin­angiotensin mechanism.

**Regulation of extracellular fluid 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.

**Renin-Angiotensin mechanism.**

Actions of Angiotensin II

When blood pressure and ECF volume decrease, renin secretion from kidneys is increased. It converts angiotensinogen into angiotensin I. This is converted into angiotensin II by ACE (angiotensin­converting enzyme).

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.

Actions of Angiotensin III and Angiotensin IV

Like angiotensin II, the angiotensins III and IV also increase the blood pressure and stimulate adrenal cortex to secrete aldosterone.

**QUESTION FIVE: DISCUSS THE ROLE OF KIDNEY IN CALCIUM HOMEOSTASIS.**

The kidney maintains calcium level with the use of 1,25-dihydroxycholecalciferol(Calcitriol) hormone. Calcitriol is a steroid hormone synthesized in kidney. It is the activated form of vitamin D. Its main action is to increase the blood calcium level by increasing the calcium absorption from the small intestine