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

The human kidney is involved in glucose homeostasis through the following mechanisms:

 (i) Release of glucose into the circulation via gluconeogenesis; (ii) Uptake of glucose from the circulation to satisfy its energy needs (iii) Reabsorption into the circulation of glucose from glomerular filtrate to conserve glucose carbon.

 Gluconeogenesis is the synthesis of glucose from noncarbohydrate sources such as glucogenic amino acid, lactate, glycerol etc. During prolonged starvation, the kidney produces glucose through gluconeogenesis but during normal fasting the liver is the main organ that produces glucose.

In the post-absorptive setting after an overnight fast, the kidneys utilize approximately 10% of all glucose utilized by the body. After meal ingestion their glucose utilization increases in an absolute sense. In terms of whole-body glucose economy, normally approximately 45% of ingested glucose is thought to be converted to glycogen in the liver, 30% is taken up by skeletal muscle and later converted to glycogen, 15% is taken up by the brain, 5% is taken up by the adipose tissue and 10% is taken up by the kidneys.

In addition to releasing glucose into the circulation by synthesizing new glucose molecules via gluconeogenesis and its utilization of glucose, the kidney can also influence glucose homeostasis by returning glucose to the circulation via the reabsorption of glucose from glomerular filtrate. Glucose is completely reabsorbed in the proximal convoluted tubule. It is transported by secondary active transport (sodium cotransport) mechanism. Glucose and sodium bind to a common carrier protein in the luminal membrane of tubular epithelium and enter the cell. The carrier protein is called sodium-dependant glucose cotransporter 2(SGLT2). From tubular cell glucose is transported into medullary interstitium by another carrier protein called glucose transporter 2(GLUT2).

**2. Discuss the process of Micturition.**

Micturition is the process by which the urinary bladder empties when it becomes filled. This process involves two main steps which are: -filling of the bladder progressively until the tension in its walls rises above threshold level. - micturition reflex which empties the bladder.

 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 which is enhanced by parasympathetic stimulation and inhibited by sympathetic stimulation up to trigone of the urinary bladder. Peristaltic waveusually 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, each peristaltic wave along the ureter increases the pressure within the ureter so that the region passing through the bladder wall opens and allows urine to flow into the bladder.

 Micturition reflex is the reflex by which micturition occurs. This reflex is initiated 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 receptorsin 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.

**3. Explain juxtaglomerular apparatus.**

Juxtaglomerular (JG) apparatus refers to the collection of specialised cells located very near to the glomerulus. It forms the major component of renin–angiotensin–aldosterone system. The primary function of the juxtaglomerular apparatus is the secretion of hormones. It also regulates the glomerular blood flow and glomerular filtration rate. The JG apparatus comprises of three types of cells which include;

\_ Juxtaglomerular cells,

\_ Macula densa cells and

\_ Mesangial cells.

 Juxtaglomerular cells:

These cells are specialized *myoepithelial* (modified vascular smooth muscle) cells located in themedia of the *afferent arteriole* in the region of JG apparatus.

**Characteristic featuresof JG cells are:**

-They have well-developed Golgi apparatus and endoplasmic reticulum, abundant mitochondria and ribosomes.

-They synthesize, store and release an enzyme called *renin.* Renin is stored in the secretory granules of JG cells and, therefore, these are also called *granular cells.*

-They act as *baroreceptors* (tension receptors) and respond to changes in the transmural pressure gradient between the afferent arterioles and the interstitium.

- They are densely innervated by the *sympathetic nerve* fibres and release their renin content in response to the sympathetic discharge.

- As these cells act as vascular volume receptors, they monitor renal perfusion pressure and are stimulated by hypovolaemia or decreased renal perfusion pressure.

 **Macula densa cells** Macula densa cells refer to the specialized renal tubular epithelial cells of a short segment of the thick ascending limb of loop of Henle which passes between the afferent and efferent arterioles supplying its glomerulus of origin. The macula densa is formed by thightly packed cuboidal cells.

***Characteristic features*** of macula densa cells are:

-They are not well adapted for reabsorption.

-They are not innervated.

-These cells are in direct contact with the mesangial cells and in close contact with the JG cells.

-They act as *chemoreceptors* and are stimulated by decreased NaCl concentration and thereby causing increased renin release.

**Mesangial cells** Mesangial cells or *lacis* cells are the interstitial cells of the JG apparatus.

***Characteristic features*** of these cells are:

-They are in contact with both the macula densa cells (on one side) and JG cells (on the other side).

-Functionally, these cells possibly relay the signals from macula densa to the granular cells after modulating the signals. In this way, a decreased intraluminal Na+ load, Cl – load, or both in the region of macula densa stimulates the JG cells to secrete rennin.

- They also show granulation to secrete renin in conditions of extreme hyperactivity.

- They also secrete various substances and take up immune complexes.

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

Kidneys play an important role in regulation of blood pressure by two ways namely; -by regulating the volume of Extracellular Fluid (ECF) -through rennin-angiotensin mechanism

By regulating the volume of ECF: this way of regulating blood pressure by the kidney acts slowly but powerfully. If blood volume increases and vascular capacitance is not altered, arterial pressure will also increase. The rising pressure, in turn causes the kidney to excrete the excess volume, thus returning the pressure back to normal.

 When blood pressure increases kidneys excrete large amount of water and salt particularly sodium by means of pressure dieresis (excretion of large amount of water in urine because of increased pressure) and pressure natriuresis (excretion of large quantity of sodium in urine). Due to dieresis 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 the renal tuble is increased. This in turn increases the ECF volume and cardiac output, resulting in restoration of blood pressure.

Through rennin-angiotensin mechanism: rennin is a protein enzyme released by kidneys when arterial pressure falls too low, in turn it raises the arterial pressure in several ways. If there’s a decrease in blood pressure , impulses are generated and the juxtaglomerular apparatus is stimulated to secrete renin. Renin acts on angiotensinogen to convert it to angiotensin I. Angiotensin I have mild vasoconstrictor properties but not enough to cause significant changes in circulatory function. After few minutes, angiotensin I is converted to angiotensin II by the enzyme angiotensin-converting enzyme.

 Angiotensin II acts in two wayss to restore the blood pressure;

i. It causes constriction of arterioles in the body so that the peripheral resistance is increased and blood pressure rises. Also mild constriction of veins promotes increased venous return of blood to the heart , thereby helping the heat pump blood against the increasing pressure. 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.

ii. 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.

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**5. Discuss the role of kidney in calcium homeostasis.**

The **kidney** is very important in calcium homeostasis. Under normal blood calcium concentrations, almost all of the calcium that enters glomerular filtrate is reabsorbed from the tubular system back into blood, which maintains blood calcium levels. If tubular reabsorption of calcium decreases, calcium is lost by excretion into urine.

In humans who have a GFR of 170 liters per 24 hours, roughly 10 g of calcium is filtered per day. The amount of calcium excreted in the urine usually ranges from 100 to 200 mg per 24 hours; hence, 98%–99% of the filtered load of calcium is reabsorbed by the renal tubules. Approximately 60%–70% of the filtered calcium is reabsorbed in the proximal convoluted tubule, 20% in the loop of Henle, 10% by the distal convoluted tubule, and 5% by the collecting duct. The terminal nephron, although responsible for the reabsorption of only 5%–10% of the filtered calcium load, is the major site for regulation of calcium excretion. The reabsorption of calcium in the proximal convoluted tubule parallels that of sodium and water. Proximal tubular calcium reabsorption is thought to occur mainly by passive transport. The passive paracellular pathways account for approximately 80% of calcium reabsorption in this segment of the nephron. A small but significant component of active calcium transport is observed in the proximal tubules. The active transport of calcium proceeds in a two-step process, with calcium entry from the tubular fluid across the apical membrane and exit though the basolateral membrane. This active transport is generally considered to constitute 10%–15% of total proximal tubule calcium reabsorption and it is mainly regulated by parathyroid hormone (PTH) and calcitonin.