MATRIC NO:17/MHS01/132

LEVEL:300L

Q1. Discuss the role of kidney in glucose homeostasis?

Q2. Discuss the process of micturition?

Q3. Explain juxtaglomerular apparatus?

Q4 Discuss the role of kidney in regulation of blood pressure?

Q5. Discuss the role of Kidney in Calcium homeostasis?

1. The kidney works to prevent pathologic consequences that could result from hyperglycemia and hypoglycemia via maintenance of glucose homeostasis. It plays an important role in regulating glucose homeostasis through the following processes:

- Utilization of glucose for its metabolic needs
- Gluconeogenesis, and
- Glucose reabsorption at the level of the proximal tubule

A. UTILIZATION OF GLUCOSE

The ability of the kidney to utilize glucose lies predominantly in the renal medulla. The cells in the renal medulla are obligate users of glucose because they possess significant glucose-phosphorylating and glycolytic enzyme activity which allows them to phosphorylate and accumulate glycogen.

B. **GLUCONEOGENESIS:** The cells in the renal cortex of the kidney possess gluconeogenic enzymes (glucose-6-phosphate) and can make and release glucose into the circulation. Theories, although not conclusively proven show that renal gluconeogenesis accounts for approximately 40% of all gluconeogenesis.

C. **GLUCOSE REABSORPTION**: The kidney also works to filter and reabsorb glucose for the maintenance of glucose homeostasis. Under normal conditions, the kidney would reabsorb as much glucose as possible via

glucose transporter proteins present in the cell membranes of the proximal tubules rendering the urine free of glucose. The kidneys have a threshold for the reabsorption of glucose, which is about 180-200mg/dl; once this threshold is reached and overcome by high amount of glucose (hyperglycemia), the capacity of the transporters is exceeded and glycosuria (glucose in the urine) occurs. Glycosuria can also occur at low plasma glucose levels in certain conditions like **HYPERFILTRATION** as seen in pregnancy rather than attributing the cause to hyperglycemia.

1. **PROCESS OF MICTURITION**

   Micturition, also known as Urination, is the process of expelling urine from the urinary bladder through the urethra to the outside of the body. It is brought about by a reflex contraction of a special muscle called the detrusor muscle after voluntary relaxation of the sphincter muscle. In physiological parlance, micturition involves the coordination of the central, autonomic and somatic nervous system. The brain centers that regulate urination include the pontine micturition center, periaqueductal gray and the cerebral cortex which cause both voluntary and involuntary control over micturition.

   The process of micturition consists of two phases:

   - Storage phase
   - Voiding phase

STORAGE PHASE: During this phase, the internal urethra sphincter is tense and the detrusor muscle is (bladder) relaxed by sympathetic stimulation. The relaxed bladder slowly fills with urine.

VOIDING PHASE: Here, the contracted bladder (detrusor muscle) forces the external urethral sphincter open and discharges urine through the urethra. During this phase, parasympathetic stimulation causes the internal urethra to relax. The external urethral sphincter is also relaxed, consciously though, and opened during micturition.

Micturition occurs through reflex called the **MICTURITION REFLEX**. It is elicited by stimulation of the stretch receptors located on the wall of the urinary bladder and the urethra. As the bladder fills with 300-400ml of urine, intravesical pressure is

increased. This pressure tends to stretch the wall of the bladder resulting in the stimulation of those stretch receptors and the generation of sensory impulses.

PATHWAY FOR THE MICTURITION REFLEX

The sensory impulses generated from the receptors reach the **sacral segments of the spinal cord** via the **sensory fibers** of the pelvis (parasympathetic) nerves. Motor impulses produced in the spinal cord travel through **motor fibers** of the pelvic nerve towards the bladder and internal sphincter. They cause contraction of the detrusor muscle and relaxation of the internal sphincter so as to allow the urine enter the urethra from the bladder. As the urine enters the **urethra**, stretch receptors also found there are stimulated and send sensory impulses to the spinal cord via the pelvic nerve fibres. The impulses from the spinal centers tend to **inhibit the pudendal nerve** (which normally keeps the external urethral sphincter contracted) resulting in its (external urethral sphincter) relaxation and the voiding of urine out of the body.

- This micturition process is facilitated by increased abdominal pressure due to the voluntary contraction of abdominal muscles.

CLINICAL PHYSIOLOGY

- **ATONIC BLADDER**: This occurs when the urinary bladder has a loss of tone in its detrusor muscle. It is caused by the destruction of sensory(pelvic) nerve fibres of urinary bladder. Due to this destruction, the bladder is filled without any stretch signals to the spinal cord. Hence, the detrusor muscle loses its tone and becomes flaccid due to the absence of the stretch signals.
- **NOCTURNAL MICTURITION**: This is the involuntary voiding of urine in the night. Also known as **ENEURESIS OR BEDWETTING**. **It occurs due to the involuntary control of urination that occurs due to incomplete myelination of motor nerve fibres of the bladder**. It is common and normal in infants and children below 3 years. Voluntary control is repossessed when there is complete myelination.

2. JUXTAGLOMERULAR APPARATUS

This is a specialized organ situated near the glomerulus of each nephron. It gives the kidney its autoregulatory property, in the sense that the kidney can control its blood pressure without interference from the central nervous system (CNS). It is made up of three different structures:

a. Macula densa
b. Juxtaglomerular cells; and
c. Extraglomerular mesangial cells.

A. **MACULA DENSA**: It is located between the afferent and efferent arterioles of the same nephron at the end portion of the thick ascending limb before it opens into the distal convoluted tubule. It is very close to the afferent arteriole.

FUNCTIONS

- It is responsible for the regulation of NaCl concentration.
- It also secretes thromboxane A2 when stimulated.
- Regulates renal blood flow and glomerular filtration rate.
- Role in tubuloglomerular feedback mechanism

B. **EXTRAGLOMERULAR MESANGIAL CELLS**: They are located in the triangular region bounded by the macula densa, afferent arteriole and efferent arteriole.

FUNCTIONS

- They secrete prostaglandins and cytokines (tumor necrosis factor, TNF, and interleukin 2)
- Control glomerular filtration

C. **JUXTAGLOMERULAR CELLS**: They are specialized smooth cells located in the wall of the afferent arteriole just before entry into the bowmans capsule. They are also called the GRANULAR CELLS, due to their possession of secretory granules in their cytoplasm.

FUNCTIONS

- Secretion of Renin, an important hormone in the regulation of blood pressure.

3. THE KIDNEY AND REGULATION OF BLOOD PRESSURE

The kidney plays a very important role in the regulation of blood pressure by means of the juxtaglomerular apparatus. The juxtaglomerular apparatus secrets a hormone known a RENIN, which work along with the ANGIOTENSINS, forming the renin-angiotensin system which makes the regulation of blood pressure by the kidney possible.

RENIN-ANGIOTENSIN SYSTEM

When a stimulant (fall in arterial blood pressure) causes the release of renin from the juxtaglomerular cells into the blood, it goes to the **liver** where it converts a proprotein (inactive), **ANGIOTENSINOGEN**, to **ANGIOTENSIN I**. Angiotensin I is inactive but becomes active when it is converted to **ANGIOTENSIN II** by the **ANGIOTENSIN CONVERTING ENZYME** in the **lungs**.

EFFECTS OF ANGIOTENSIN II

- It acts on the arterial blood pressure directly by constricting the blood vessels to increase total peripheral resistance, thereby increasing blood pressure.
- It acts on the arterial blood system indirectly by increasing the release of **NORADRENALINE** (a potent vasoconstrictor)
- It directly stlimulates the adrenal gland to release aldosterone, which acts on the renal tubules to increase retention of sodium. The sodium acts to increase blood pressure by increasing blood volume, venous return, cardiac output and blood supply.
- It directly stimulates thirst centres leading to increased blood volume and cardiac output.
- It directly stimulates the release of vasopressin or ADH which acts on the collecting duct to cause the reabsorption of water, thereby increasing blood volume, venous return and cardiac output.

4. KIDNEY AND CALCIUM HOMEOSTASIS

The kidney is critically important in calcium homeostasis. The kidney does this by activating 1,25-dihydroxycholecalciferol into vitamin D which is

responsible for the absorption of calcium from the intestine. The activation is carried out by the hormone, PARATHYROID HORMONE. It maximizes the tubular reabsorption of calcium within the kidney therefor minimizing the loss of calcium in the urine. Under normal blood calcium concentrations, almost all of the calcium that enters glomerular filtrate is reabsorbed from the tubular system back into blood, which preserves blood calcium levels. If tubular reabsorption of calcium decreases, calcium is lost by excretion into urine.