ONYEMA FAVOUR CHINAZAM

17/MHS01/266

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RENAL PHYSIOLOGY

1 Discuss the role of kidney in glucose homeostasis?

Role of kidney in Glucose homeostasis

Homeostasis is the maintenance of a steady internal environment of the human body by coordinated physiological mechanisms in response to changes in the external environment. The term glucose homeostasis involves physiological mechanisms that maintain standard plasma glucose level. Normal blood glucose level while fasting is between 70 to 130 mg/dL. This concentration must be maintained despite the wide daily fluctuations in glucose ingestion and glucose demands in various tissues.

Glucose homeostasis is maintained by hormonal and neural factors. The hormones responsible for this are: insulin, glucagon and catecholamines. While glucagon has no effect on the kidneys, insulin suppresses glucose release in ~~liver~~ kidney and catecholamines stimulate renal glucose release and glucagon secretion as well as inhibits insulin secretion.

The kidneys maintain glucose homeostasis in three mechanisms; Gluconeogenesis, glucose uptake from blood and reabsorption of glucose from glomerular filtrate. Renal gluconeogenesis is carried out by the renal cortex which have cells that contain gluconeogenic enzymes. ~~that~~ These enzymes produce and release glucose into circulation. The kidney uses precursors such as lactate, glutamine and glycerol. Lactate is the largest source of precursor. It is important to note that the kidney only undergoes gluconeogenesis during prolonged fasting period. During this period there is reduction in blood plasma glucose causing the renal cortex to be stimulated due to release of Catecholamines. The catecholamines stimulated by decrease in blood glucose stimulates glucagon secretion and inhibits insulin secretion as well as stimulating renal cortex to carry out gluconeogenesis. Gluconeogenesis then leads to

glucose release into the blood thereby increasing blood glucose back to normal

Glucose uptake is another mechanism of maintaining blood glucose homeostasis by the kidney. This glucose uptake from blood is performed by the renal medulla which utilizes the glucose for its own energy requests. The renal medulla have enzymes capable of glucose-phosphorylation and glycolysis. During fed state, there is an increase in blood glucose activating insulin secretion. Insulin increases glucose uptake in cells including the renal medulla. This leads to decrease in blood glucose back to normal

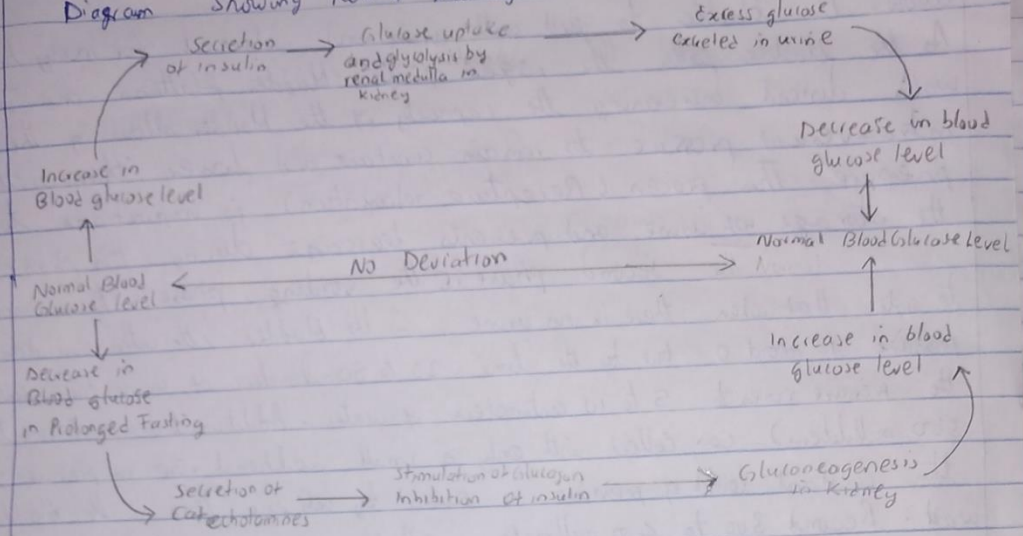
The third mechanism for glucose homeostasis is Reabsorption of glucose from glomerular filtrate into circulation. The function of the glomerulus is also to reabsorb needed minerals and glucose into the blood stream even as it filters it. The glomeruli filters about 180g of glucose daily but all of this quantity is reabsorbed through glucose transporters present in cell membranes in proximal tubules. This reabsorption has a threshold called Renal threshold. The renal threshold is 180mg/dl and after which no other glucose can be reabsorbed leading to glucose present in urine (Glucosuria). This is a process by which the kidney get rid of excess glucose in blood thereby returning blood plasma glucose level to normal.

Applied Physiology

1. Diabetes Mellitus: All the mechanism of glucose homeostasis by kidney are modified in patients with diabetes mellitus. Both renal glucose uptake and glucose production are increased in the post prandial and post-absorptive states in diabetic patients. Glucosuria occurs at different plasma glucose levels due to increased glucose reabsorption in diabetes mellitus patients. Glucosuria occurs only at very high plasma glucose levels here. There is also acidosis which increase renal gluconeogenesis.

Diagram showing homeostasis cycle.

Diagram Showing Role of Kidney in Homeostasis



2 Discuss the process of micturition

Micturition

Micturition is a process by which the urinary bladder empties when it becomes filled. It is an excretion process involving the expelling of urine from bladder or voiding of the bladder. It is mediated by activation of the sacral parasympathetic efferent pathway to the bladder and urethra. Micturition has two phases; The storage phase and the voiding phase. It is important to note that micturition occurs involuntarily in infants and children until the age of 3 to 5 years after which it is regulated voluntarily.

The storage phase is also called the Continence phase. It is the stage where urine is stored in the bladder. During this phase, impulses are sent from Cerebral Cortex to pons to the sympathetic nuclei in spinal cord to the sympathetic hypogastric nerve ($T_{10}-L_2$) which relaxes the detrusor muscle in the bladder wall and contracts the internal Urethra Sphincter of the bladder. Impulses from pudendal nerve contract the External Urethra sphincter. This coordinated relaxation of detrusor muscle and contraction of the External and Internal Urethra Sphincters

allow the bladder to fill with urine and store it for many hours. As the bladder fills the rugae of the bladder flatten and the walls distend increasing the capacity of the bladder allowing the intra-vesical pressure to remain constant and lower than urethral pressure. This process (Receptive relaxation) is important to the storage of urine and prevents leakage during this phase.

The second phase is the voiding phase. It is important to note that when there is no urine in the bladder, the intravesicular pressure is about 0 but by the time 30 to 50 millimeters of urine have collected the pressure rises to 5 to 10 centimeters of water. Additional urine (200 to 300 milliliters) can collect with only a small additional rise in pressure; this constant level of pressure is caused by intrinsic tone of the bladder wall. Beyond 300 to 400 millimeters, collection of more urine in the bladder causes the pressure to rise rapidly. Periodic acute increases in pressure last from a few seconds to more than a minute and are caused by the micturition reflex. For voiding phase to occur the micturition reflex must complete its cycle.

Micturition reflex is a single complete cycle of progressive and rapid increase of pressure, a period of sustained pressure, and return of the pressure to the basal tone of the bladder. As the bladder fills micturition contractions appears due to stretch reflex initiated by sensory stretch receptors in the bladder wall (especially by the receptors in the posterior urethra due to higher bladder pressures) The sensory signals from sensory stretch receptors are transmitted through pelvic nerves to sacral segments of spinal cord and reflexively back to bladder through parasympathetic nerve fibres. When bladder is partially filled, the micturition contractions usually relax spontaneously after a fraction of a minute, the detrusor muscle stop contracting and pressure reduces back to the baseline. As the bladder continues to fill, the micturition contractions become more frequent and cause greater contractions of the detrusor muscle, thus micturition reflex is initiated. Micturition reflex is self-regenerative and once it has occurred but not succeeded in emptying the bladder, the nervous elements of this reflex remain in an inhibited state for a few minutes to an hour

or more before another micturition reflex occurs. As the bladder becomes more and more filled, micturition reflexes occur more and more often and more and more powerfully. Once the micturition reflex becomes powerful enough it causes another reflex which passes through the pudendal nerves to the external sphincter to inhibit it. If this inhibition is more potent in the brain than the voluntary constrictor signals to the external sphincter, Urination (void phase) occurs. If not, the urination will not occur until the bladder fills still further and the micturition reflex becomes more powerful.

Voluntary urination (voiding phase) is initiated when a person voluntarily contracts his or her abdominal muscles increasing the pressure of the bladder allowing extra urine to enter the bladder neck and posterior urethra under pressure thus stretching their walls. This action stimulates the stretch receptors which excites the micturition reflex and inhibits the external urethral sphincter. After micturition reflex, all of the urine will be emptied with rarely more than 5 to 10ml left in the bladder.

Abnormalities

1. Atonic Bladder and Incontinence: It may be caused by destruction of sensory nerve fibres. Micturition reflex contraction cannot occur, there is loss of bladder control. Instead of emptying periodically, the bladder fills to capacity and overflows a few drops at a time through the urethra (This is called overflow incontinence).

3 Explain Juxtaglomerular apparatus?

Juxtaglomerular apparatus is a structure in the kidney that regulates the function of each nephron. It is a part of the kidney nephron next to the glomerulus (hence the name) and found between the afferent arteriole and the distal convoluted tubule of the same nephron. This location is critical to its function in regulating renal blood flow and glomerular filtrate rate.

The juxtaglomerular apparatus consists of three types

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of cells; macula densa, juxtaglomerular cells and the extraglomerular mesangial cells.

i The macula densa: This is a part of the distal convoluted tubule of the same nephron. It is a modified region of tubular, Cuboidal epithelium located in the wall of the distal convulated tubule at the point where the afferent arteriole enters the glomerulus and the efferent arteriole leaves it. Cells in the macula densa respond to changes in sodium chloride levels in the distal tubule of the nephron via tubuloglomerular feedback loop (TGF loop). The function of the macula densa is to regulate the levels of NaCl in blood plasma. When there is an increase in salt concentration, it causes vasoconstriction of the adjacent afferent arteriole to constrict. This decreases the amount of blood going to the glomerular capillaries hence decreasing amount of fluid that goes from glomerular capillaries into the Bowman's space. The Glomerular Filtration Rate (GFR) decreases. This causes elevated filtration at the glomerulus or reduced reabsorption of Na and water by proximal Convulated Tubule. There is also diffusion of Na into macula densa cells. When there is a decrease in sodium concentration less sodium is reabsorbed in macular dense cells, the cells increase the production of nitric oxide and prostaglandins to vasodilate the afferent arterioles and increase renin release. Macula dense is close to Bowman's Capsule

II Juxtaglomerular cells: These are cells similar to epithelium and are located in the tunica media of the afferent arterioles as they enter the glomerulus. They are located between the afferent arterioles just before ~~and efferent~~ It enters glomerulus ~~arterioles~~. They secrete renin in response to stimulation of the beta-1 adrenergic receptor, decrease in NaCl Concentration at macula densa, decrease in glomerular filtrate Rate and decrease in renal perfusion pressure. They are also known as granular cells

III Extraglomerular mesangial cells: They are also called Lacis cells and are located in the space between the afferent and efferent arterioles in the bowman's space. They have contractile properties similar to vascular smooth muscles and play a role in regulating glomerular Filtration Rate by altering the vessel diameter. Renin is found in them and they secrete prostaglandins.

4 Discuss the role of kidney in regulation of Blood Pressure

Role of Kidney in Regulation of Blood Pressure

Once there is a decrease in the blood pressure, impulses are sent to the macula densa due to the decrease in the renal perfusion. The macula densa in the Juxtaglomerular Apparatus stimulates the juxtaglomerular cells to release Renin. The renin ~~Converts~~ acts on the pro-protein Angiotensinogen ~~dan~~ the liver and Converts it to Angiotensin I in the liver. The Angiotensin-Converting -enzyme in the lungs Converts Angiotenten I to the activated form Angiotensin II which is a potent vasoconstructor causing vasoconstriction in blood vessels leading to increase in blood Pressure. Angiotensin II also acts on adrenal cortex to secrete aldosterone which cause reabsorption of Na^+ and Cl^- leading to an increase in water retention as well as excretion of K^+ hence increasing blood volume which increases blood pressure. Angiotensin II stimulates secretion of Anti-Diuretic Hormone by acting on the pituitary gland causing water reabsorption from collecting duct. It also stimulates thirst leading to water intake leading to increased blood volume and stimulates sympathetic discharge directly to also increase blood pressure.

5. Dicuss the role of kidney in Calcium homeostasis

Role of Kidney in Calcium Homeostasis

Homeostasis is the maintenance of steady internal environment of the human body by coordinated physiological mechanisms in response to changes in the external environment. Calcium homeostasis involves the physiological mechanisms that maintain standard calcium level.

The kidney is critically 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 preserves blood calcium levels. If tubular reabsorption of calcium decreases calcium is lost by excretion into urine. The normal rate of dietary calcium intake is about 1000 mg/day with about 900mg/day of calcium excreted in feces. Total amount of calcium in the human

body is about 1000 to 1200g with about 99% of body Calcium residing in the skeleton while the remaining 1% resides in extracellular and intracellular spaces.

Calcium homeostasis is regulated by three major hormones or factors; Parathyroid hormone, Calcitonin and Vitamin D.

i Parathyroid hormone: It is stimulated by decrease in calcium concentration and it stimulates production of 1,25-dihydroxy cholecalciferol (biologically active form of Vitamin D) within the kidneys as well as causing kidney to eliminate phosphate (phosphaturia effect). It maximizes tubular reabsorption of calcium within the kidney decreasing loss of calcium in urine and increasing blood calcium.

ii Calcitonin: It is secreted in response to hypercalcemia and aids or causes suppression of renal tubular reabsorption of calcium causing excretion of calcium into urine. It ~~also inhibits~~ thereby decreases blood calcium levels.

iii Vitamin D: It generated through the activity of parathyroid hormone within the kidney. The kidney produces the active form of Vitamin D (1,25-dihydroxy (cholecalciferol) which facilitates absorption of calcium from the small intestine and enhances release of calcium out of the bone increasing blood calcium levels.