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1 Discuss the role of kidney in glucose homeostasis?

The kidneys are involved in maintaining glucose homeostasis through 3 different mechanisms

A Gluconeogenesis.
B Glycogenolysis.
C Glucose Reabsorption.

A Gluconeogenesis:

From the point of view of glucose utilization, the kidney is considered as 2 separate organs; the renal medulla is characterized mainly by glucose utilization and the renal cortex is responsible for glucose release.

The cells in the renal medulla can use only glucose for their needs (like the brain) and they have enzymes capable of glucose-phosphorylation (phosphorylating important amounts of glucose and accumulate glycogen but because these cells lack glucose-6-phosphatase or any other gluconeogenic enzymes unlike the renal cortex, they are unable to release glucose into the blood stream) and glycolysis.

Almost 50% of approximately 10 μmol/(kg/min) of glucose released into the circulation after a 16-h overnight fast is the result of glycogenolysis from the liver and the other half is produced by liver and kidney gluconeogenesis.

The renal cortex (like the liver) contains gluconeogenic enzymes and it can synthesize glucose-6-phosphate from precursors (lactate, glutamine, glycerol and alanine). Due to this it is able to release glucose into the blood stream.

B Glycogenolysis

It is the breakdown of glycogen to glucose-6-phosphate and a hydrolysis reaction (using glucose-6-phosphatase) in order to free glucose. The liver is the only organ that contains glucose-6-phosphatase. So, the cleavage of hepatic glycogen releases glucose, while the cleavage of glycogen from other sources can release only lactate, Lactate, that

is generated via glycolysis, is often absorbed by other organs and helps in generating glucose.

c Glucose Reabsorption

Apart from the important role in gluconeogenesis and the role of the renal cortex in glucose uptake, the kidneys contribute to glucose homeostasis by filtering and reabsorbing glucose. In normal conditions, the kidneys can reabsorb as much glucose as possible, the result being a virtually glucose free urine. Approximately 180 grams of glucose are filtered by the glomeruli from plasma, daily, but all of this quantity is reabsorbed from / through glucose transporters that are present in cell membranes located in the proximal tubules. These glucose transporters have a limited capacity for reabsorption. If this capacity is exceeded, glucose usually appears in the urine.

2 Discuss the process of micturition?

Micturition also known as urination, is the ejection of urine from the urinary bladder through the urethra to the outside of the body. In healthy humans the process is under voluntary control. In infants and elderly individuals and those with neurological injury, urination may occur as an involuntary reflex.

Micturition process consists of two phases

Storage Phase

Voiding Phase

Storage Phase

The urinary bladder is a balloon shaped, hollow, muscular, organ that acts as the storage organ for urine. The urinary bladder in a healthy urinary system can store upto sixteen ounces of urine for 2 to 5 hours easily. The circular sphincter prevents leakage of urine. They close tightly round the opening of the bladder into the urethra.

Voiding Phase

This is controlled by a neural mechanism called the micturition reflex. It is a sacral and parasympathetic reflex which may be inhibited / facilitated by voluntary control from the higher centers in the CNS. The reflex originates from the stimulation of stretch receptor in the wall of the bladder when the urine volume reaches 200-400 mL. This causes impulses to flow from the parasympathetic afferents, through polysynaptic connections in the sacral cord and down the polysynaptic connections

Micturition then takes place as follows

The bladder changes shape from transversely oval to a more spherical configuration by active contraction of the detrusor. Thereafter the urogenital diaphram and the muscles of the pelvic floor relax, so that the base of the bladder descends. By contraction of the longitudinal fibres of the detrusor, presumably assisted by the trigonal muscle, the bladder neck and posterior urethra open as the latter shortens. Thereupon the external sphincter opens and thereby also the distal part of the urethra, not until then is the bladder neck completely open. During micturition the trigone rises towards the anterior bladder wall.

When the bladder has emptied, the urethral muscles express the last quantity of urine whereupon the external sphincter closes and detrusor relaxes.

3 Explain Juxtaglomerular Apparatus?

It is a specialized structure formed by the distal convoluted tubule and the glomerular afferent arteriole of the same nephron. It is responsible for regulating both intrarenal (tubuloglomerular feedback) and extrarenal (renin-angiotensin-aldosterone) mechanisms necessary to maintain both renal and entire body volume status.

The three main components of the apparatus are

A The Juxtaglomerular cells of the afferent arteriole

Synthesize and store renin, which is secreted in response to specific stimuli (eg low blood flow, decreased NaCl delivery). The juxtaglomerular cells could be considered the "effector arm" of the renin-angiotensin-aldosterone axis

B. The macula densa, a region of the distal convoluted tubule characterized by tubular epithelial cells which are more densely packed than in other regions of the nephron and thereby leading to its characteristic appearance on light microscopy. The macula densa can be considered the "sensory arm" of the renin angiotensin-aldosterone axis in that these are the cells which sense decreased NaCl delivery which determines downstream function. They are also involved in the feedback mechanism / mechanism of tubuloglomerular feedback.

C. Mesangial cells, which form connections via actin and microtubules which allow for selective vasoconstriction / vasodilation of the renal afferent and efferent arterioles with mesangial cell contraction

4. Assess the role of kidneys in regulation of blood pressure?

Renin-angiotensin Mechanism

The renin-angiotensin-mechanism operates to restore a low arterial blood-pressure to normal. The kidney has its own intrarenal baroreceptors in the juxtaglomerular cells (JGC) which detect a fall in BP by raising the volume of ECF and increasing peripheral resistance. When the BP in the afferent arteriole drops, the JGC secretes renin, an acid protease which forms angiotensin I from an α_2-globulin in plasma called angiotensinogen. The angiotensin I is converted by converting enzyme in the lungs to angiotensin II which raises the volume of ECF by 3 mechan-

nisms

a By stimulating the adrenal cortex to secrete aldosterone which promotes Na+ and water reabsorption

b By stimulating the posterior pituitary to secrete ADH which promotes water reabsorption)

c By inducing thirst (which promotes water intake)

The activities of the JGC are enhanced by the macula densa which senses fall in delivery or absorption of Na+ at the distal nephron and stimulates the JGC to release more renin.

The increase in ECF volume leads to an increase in cardiac output. Angiotensin II is also a powerful vasoconstrictor of peripheral vessels; the vasoconstriction increases peripheral resistance, which combined with the increase in cardiac output, hence increasing blood pressure

5 Discuss the role of kidney in calcium homeostasis?

The maintenance of calcium homeostasis is very important because calcium is the main component of bony skeleton and serves as the intracellular and extracellular messenger in numerous essential cellular events such as neuronal neuron immune response, muscle contraction, and hormone secretion

Total body calcium in the adult human is about 1-2kg and 99% of total calcium exist in bone. Even though only less than 1% of body calcium is in the extracellular space, maintaining its concentration within a narrow range of (8.5-10.5 mg/dL) is very important.

Kidney plays a role in this process by the fine regulation of calcium excretion. 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 Ca is reabsorbed by paracellular diffusion through paracellin-1

(claudin-16). The calcium sensing receptor (CaSR) in the basolateral membrane of the thick ascending limb senses the change in iCa^{2+} and inhibits calcium reabsorption independent to PTH and $1,25(OH)_2D_3$. The fine regulation of calcium excretion occurs in the distal convoluted and connecting tubules.