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

The kidneys’ contributions to maintaining glucose homeostasis are significant and include such functions as release of glucose into the circulation via gluconeogenesis, uptake of glucose from the circulation to satisfy their energy needs, and reabsorption of glucose at the level of the proximal tubule. Renal release of glucose into the circulation is the result of glycogenolysis and gluconeogenesis, respectively involving the breaking down and formation of glucose-6-phosphate from precursors (lactate, glycerol, amino acids). With regard to renal reabsorption of glucose, the kidneys normally retrieve as much glucose as possible, rendering the urine virtually glucose free.

The kidneys are essentially designed to filter large quantities of plasma, reabsorb substances that the body must conserve, and secrete substances that must be eliminated. These basic functions are critical to regulation of fluid and electrolyte balance, body fluid osmolality, acid-based balance, excretion of metabolic waste and foreign chemicals, arterial pressure, hormone secretion, and, most relevant to this discussion, glucose balance. The kidneys help maintain glucose homeostasis by at least two mechanisms:

1. Under normal circumstances, the kidney filters and reabsorbs 100% of glucose, approximately 180g of glucose each day. The glucose transporters in the renal proximal tubule ensures that less than 0.5g/day is excreted in the urine of healthy adults. More water than glucose is reabsorbed resulting in an increase in the glucose concentration in the urine along the tubule. Consequently the affinity of the transporters for glucose along the tubule increases to allow for complete reabsorption of glucose from the urine.
2. It produces glucose by gluconeogenesis. The key enzymes of gluconeogenesis are **phosphoenolpyruvate carboxykinase (PEPCK)** and **glucose 6-phosphate (G6Pase).** These are expressed in the renal proximal tubule only and not the renal medulla. The kidneys produce between 2.0-2.5µmol of glucose/kg/min thereby contributing about 20-25% of circulating glucose

**2: Discuss the process of micturition**

Micturition is the process by which the urinary bladder empties when it becomes filled.This involves two main steps: First, the bladder fills progressively until thetension in its walls rises above a threshold level; this elicits the second step, which is a nervous reflex called the micturition reflex that empties the bladder or, if this fails, at least causes a conscious desire to urinate.

Although the micturition reflex is an autonomic spinal cord reflex, it can also be inhibited or facilitated by centers in the cerebral cortex or brain stem.

**3: Explain the juxtaglomerular apparatus.**

The juxtaglomerular apparatus (JGA) is located between the afferent arteriole and the returning distal convoluted tubule of the same nephron. It is responsible for regulating both intrarenal (tubule-glomerular feedback) and extrarenal (renin-angiotensin-aldosterone) mechanisms necessary to maintain both renal and entire body volume status. The three components of the JGA are the following:

1. **The juxtaglomerular cells of the afferent arteriole**: They synthesize and store renin, which is secreted in response to specific stimuli (e.g., low blood flow, decreased NaCl delivery). The juxtaglomerular cells could be considered the “effector arm” of the renin-angiotensin-aldosterone axis.
2. **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 Na Cl delivery which determines downstream function. They are also involved in the mechanism of tubule-glomerular feedback.
3. **Mesangial cells**: form connections via actin and microtubules which allow for selective vasoconstriction/vasodilation of the renal afferent and efferent arterioles with mesangial cell contraction.

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

Based on the capacity for the kidney to excrete sodium, this blood pressure-altering mechanism should have sufficient advantage to limit intravascular volume and consequently lower blood pressure in response to a range of stimuli from elevated heart rate to increase peripheral vascular resistance.

**The kidneys and their influence on blood pressure**

The kidneys play a central role in the regulation of arterial blood pressure. A large body of experimental and physiological evidence indicates that renal control of extracellular volume and renal perfusion pressure are closely involved in maintaining the arterial circulation and blood pressure. Renal artery perfusion pressure directly regulates sodium excretion; a process known as pressure natriuresis, and influences the activity of various vasoactive systems such as the renin–angiotensin–aldosterone (RAS) system. Blood viscosity is one of the key factors influencing resistance and hence blood pressure. A key modulator of blood viscosity is the renin-angiotensin system (RAS) or the renin-angiotensin-aldosterone system (RAAS), a hormone system that regulates blood pressure and water balance. The blood pressure in the body depends upon:

1. The force by which the heart pumps out blood from the ventricles of the heart, and this is dependent on how much the heart muscle gets stretched by the inflowing blood into the ventricles.
2. The degree to which the arteries and arterioles constrict, increases the resistance to blood flow, thus requiring a higher blood pressure.
3. The volume of blood circulating round the body; if the volume is high, the ventricles get more filled, and the heart muscle gets more stretched.

**The kidney influences blood pressure by:**

1. Causing the arteries and veins to constrict
2. Increasing the circulating blood volume

Specialized cells called macula densa are located in a portion of the distal tubule located near and in the wall of the afferent arteriole. These cells sense the Na in the filtrate, while the arterial cells (juxtaglomerular cells) sense the blood pressure. When the blood pressure drops, the amount of filtered Na also drops. The arterial cells sense the drop in blood pressure, and the decrease in Na concentration is relayed to them by the macula densa cells. The juxtaglomerular cells then release an enzyme called **renin**. Renin converts angiotensinogen into angiotensin-1 which is then converted to angiotensin-2 by an angiotensin-converting enzyme (ACE), found in the lungs. Angiotensin-2 causes blood vessels to contract. When the volume of blood is low, arterial cells in the kidneys secrete renin directly into circulation. Plasma renin then carries out the conversion of angiotensinogen released by the liver to angiotensin-1. Angiotensin-1 is subsequently converted to angiotensin-2 by the enzyme angiotensin converting enzyme found in the lungs. Angiotensin-2m a potent vasoactive peptide causes blood vessels to constrict, resulting in increased blood pressure. Angiotensin-2 also stimulates the secretion of the hormone aldosterone from the adrenal cortex.

Aldosterone causes the tubules of the kidneys to increase the reabsorption of sodium and water into the blood. This increases the volume of fluid in the body, which also increases blood pressure. If the renin-angiotensin-aldosterone system is too active, blood pressure will be too high. Many drugs interrupt different steps in this system to lower blood pressure. These drugs are one of the main ways to control high blood pressure (hypertension), heart failure, kidney failure, and harmful effects of diabetes. It is believed that angiotensin-1 may have some minor activity, but angiotensin-2 is the major bioactive product. Angiotensin-2 has a variety of effects on the body: throughout the body, it is a potent vasoconstrictor of arterioles.

**How the kidneys increase circulating blood volume**

Angiotensin-2 also stimulates the adrenal gland to secrete a hormone called aldosterone. Aldosterone stimulates more Na reabsorption in the distal tubule, and water gets reabsorbed along with the Na. The increased Na and water reabsorption from the distal tubule reduces urine output and increases the circulating blood volume. The increased blood volume helps stretch the heart muscle and causes it to generate more pressure with each beat, thereby increasing the blood pressure.

The actions taken by the kidney to regulate blood pressure are especially important during traumatic injury, when they are necessary to maintain blood pressure and conserve the loss of fluids.

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

Kidneys play a role in the regulation of blood calcium level by activating 1,25-dihydroxycholecalciferol into vitamin D. Vitamin D is necessary for the absorption of calcium from intestine. The role of the kidney in calcium homeostasis is heavily influenced by parathormone (PTH). Parathormone is secreted by parathyroid gland is essential for the maintenance of blood calcium level within a very narrow critical level. PTH increases the reabsorption of calcium from the renal tubules along with magnesium ions and hydrogen ions. It increases calcium reabsorption mainly from distal convoluted tubule and proximal part of collecting duct. PTH also increases the formation of 1,25- dihydroxycholecalciferol (activated form of vitamin D) from 25-hydroxycholecalciferol in kidneys.

**ACTIONS OF 1,25-DIHYDROXYCHOLECALCIFEROL**:

1. It increases the absorption of calcium from the intestine, by increasing the formation of calcium binding proteins in the intestinal epithelial cells. These proteins act as carrier proteins for facilitated diffusion, by which the calcium ions are transported. The proteins remain in the cells for several weeks after 1,25-dihydroxycholecalciferol has been removed from the body, thus causing a prolonged effect on calcium absorption

2. It increases the synthesis of calcium-induced ATPase in the intestinal epithelium

3. It increases the synthesis of alkaline phophatase in the intestinal epithelium

4. It increases the absorption of phosphate from intestine along with calcium.