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PHYSIOLOGY ASSIGNMENT\

1. ROLE OF KIDNEY IN GLUCOSE HOMEOSTASIS

The kidneys contribute to glucose homeostasis through the process of gluconeogenesis, glucose filtration, and glucose consumption. Under normal conditions, the kidneys retrieve as much glucose as possible, rendering the urine glucose free. Under normal circumstances, up to 180g/day of glucose is filtered by renal glomerulus and virtually all of it is subsequently reabsorbed in the proximal covulated tubules.

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).

 The kidneys synthesize glucose from amino acids and other precursors during prolonged fasting, a process referred to as gluconeogenesis. The kidneys’ capacity to add glucose to the blood during prolonged periods of fasting rivals that of the liver. With chronic kidney disease or acute failure of the kidneys, these homeostatic functions are disrupted, and severe abnormalities of body ﬂuid volumes and composition rapidly occur. With complete renal failure, enough potassium, acids, ﬂuid, and other substances accumulate in the body to cause death within a few days, unless clinical interventions such as hemodialysis are initiated to restore, at least partially, the body ﬂuid and electrolyte balances.

1. 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 the tension in its walls rises above a threshold level; this elicits the second step,which is a nervous reﬂex called the micturition reﬂexthat 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.

Micturition Reﬂex

Referring again to Figure 26–7,one can see that as the bladder ﬁlls, many superimposed micturition contractions begin to appear, as shown by the dashed spikes. They are the result of a stretch reﬂex initiated by sensory stretch receptors in the bladder wall,especially by the receptors in the posterior urethra when this area begins to ﬁll with urine at the higher bladder pressures. Sensory signals from the bladder stretch receptors are conducted to the sacral segments of the cord through the pelvic nerves and then reﬂexively back again to the bladder through the parasympathetic nerve ﬁbers by way of these same nerves. When the bladder is only partially ﬁlled, these micturition contractions usually relax spontaneously after a fraction of a minute, the detrusor muscles stop contracting,and pressure falls back to the baseline.As the bladder continues to ﬁll, the micturition reﬂexes become more frequent and cause greater contractions of the detrusor muscle. Once a micturition reﬂex begins, it is “self-regenerative.” That is, initial contraction of the bladder activates the stretch receptors to cause a greater increase in sensory impulses to the bladder and posterior urethra, which causes a further increase in reﬂex contraction of the bladder;thus,the cycle is repeated again and again until the bladder has reached a strong degree of contraction. Then, after a few seconds to more than a minute,the self-regenerative reﬂex begins to fatigue and the regenerative cycle of the micturition reﬂex ceases, permitting the bladder to relax

Thus,the micturition reﬂex is a single complete cycle of (1) progressive and rapid increase of pressure,(2) a period of sustained pressure, and (3) return of the pressure to the basal tone of the bladder.Once a micturition reﬂex has occurred but has not succeeded in emptying the bladder, the nervous elements of this reﬂex usually remain in an inhibited state for a few minutes to 1 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 will occur. If not, urination will not occur until the bladder ﬁlls still further and the micturition reﬂex becomes more powerful.

Facilitation or Inhibition of Micturition by the Brain

The micturition reﬂex is a completely autonomic spinal cord reﬂex,but it can be inhibited or facilitated by centers in the brain. These centers include (1) strong facilitative and inhibitory centers in the brain stem, located mainly in the pons, and (2) several centre’s located in the cerebral cortex that are mainly inhibitory but can become excitatory. The micturition reﬂex is the basic cause of micturition, but the higher centers normally exert ﬁnal control of micturition as follows: 1. The higher centers keep the micturition reﬂex partially inhibited, except when micturition is desired. 2. The higher centers can prevent micturition, even if the micturition reﬂex occurs, by continual tonic contraction of the external bladder sphincter until a convenient time presents itself. 3. When it is time to urinate, the cortical centers can facilitate the sacral micturition centers to help initiate a micturition reﬂex and at the same time inhibit the external urinary sphincter so that urination can occur. Voluntary urination is usually initiated in the following way: First, a person voluntarily contracts his or her abdominal muscles, which increases the pressure in the bladder and allows extra urine to enter the bladder neck and posterior urethra under pressure, thus stretching their walls. This stimulates the stretch receptors, which excites the micturition reﬂex and simultaneously inhibits the external urethral sphincter. Ordinarily, all the urine will be emptied, with rarely more than 5 to 10 millilitres left in the bladder.

1. JUXTAGLOMERULAR APPARATUS

DEFINITION: Juxtaglomerular apparatus is a specialized organ situated near the glomerulus of each nephron (juxta = near).

 STRUCTURE OF JUXTAGLOMERULAR APPARATUS

 Juxtaglomerular apparatus is formed by three different structures :

1. Macula densa

2. Extraglomerular mesangial cells

3. Juxtaglomerular cells.

1. MACULA DENSA: Macula densa is the end portion of thick ascending segment before it opens into distal convoluted tubule. It is situated between afferent and efferent arterioles of the same nephron. It is very close to afferent arteriole. Macula densa is formed by tightly packed cuboidal epithelial cells.

2. EXTRAGLOMERULAR MESANGIAL CELLS: Extraglomerular mesangial cells are situated in the triangular region bound by afferent arteriole, efferent arteriole and macula densa. These cells are also called agranular cells, lacis cells or Goormaghtigh cells.

Glomerular Mesangial Cells Besides extraglomerular mesangial cells there is another type of mesangial cells situated in between glomerular capillaries called glomerular mesangial or intraglomerular mesangial cells. Glomerular mesangial cells support the glomerular capillary loops by surrounding the capillaries in the form of a cellular network. These cells play an important role in regulating the glomerular filtration by their contractile property.

Glomerular mesangial cells are phagocytic in nature. These cells also secrete glomerular interstitial matrix, prostaglandins and cytokines.

3.JUXTAGLOMERULAR CELLS Juxtaglomerular cells are specialized smooth muscle cells situated in the wall of afferent arteriole just before it enters the Bowman capsule. These smooth muscle cells are mostly present in tunica media and tunica adventitia of the wall of the afferent arteriole. Juxtaglomerular cells are also called granular cells because of the presence of secretary granules in their cytoplasm.

Polar Cushion or Polkissen Juxtaglomerular cells form a thick cuff called polar cushion or polkissen around the afferent arteriole before it enters the Bowman capsule.

 FUNCTIONS OF JUXTAGLOMERULAR APPARATUS

 Primary function of juxtaglomerular apparatus is the secretion of hormones. It also regulates the glomerular blood flow and glomerular filtration rate.

 Juxtaglomerular apparatus secretes two hormones: 1. Renin 2. Prostaglandin

1. ROLE OF KIDNEY IN REGULATION OF BLOOD PRESSURE

Regulation of Arterial Pressure. the kidneys play a dominant role in long-term regulation of arterial pressure by excreting variable amounts of sodium and water. The kidneys also contribute to short-term arterial pressure regulation by secreting vasoactive factors or substances, such as renin, that lead to the formation of vasoactive products (e.g., angiotensin II).

Renal–Body Fluid System for Arterial Pressure

 Control The renal–body ﬂuid system for arterial pressure control is a simple one: When the body contains too much extracellular ﬂuid, the blood volume and arterial pressure rise. The rising pressure in turn has a direct effect to cause the kidneys to excrete the excess extracellular ﬂuid, thus returning the pressure back toward normal.

RENIN-ANGIOTENSIN MECHANISM

Consistent and long term control of blood pressure is determined by renin-angiotensin system. When blood flow through the kidney decreases the process of filtration is decreased and less urine is formed. This decrease in urinary output preserves blood volume so that it does not decrease further, this is very important to maintain blood pressure during severe haemorrhage or any type of dehydration. The kidneys are also involved in the renin-angiotensin mechanism. When blood pressure decreases, there will be a drop in renal blood flow or decreased consentration of Na, this will stimulate volume receptors found in juxtaglomerular apparatus of the kidneys to secrete the enzyme renin. Renin stimulates a series of reactions, that result in the formation of angiotensin II. Angiotensin II causes vasoconstriction and stimulates secretion of aldosterone by the adrenal cortex, both of which will increase blood pressure.

1. ROLE OF KIDNEY IN CALCIUM HOMEOSTASIS

Kidneys play a role in the regulation of blood calcium level by activating 1,25dihydroxycholecalciferol into vitamin D.

1,25-dihydroxycholecalciferol – Calcitriol: Calcitriol is a steroid hormone synthesized in kidney. It is the activated form of vitamin D. Its main action is to increase the blood calcium level by increasing the calcium absorption from the small intestine.

The kidney is critically important in calcium homeostasis. Under normal blood calcium concentrations, almost all 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.

Plasma calcium concentration is maintained within a narrow range (8.5-10.5 mg/dL) by the coordinated action of parathyroid hormone (PTH), 1,25(OH)2D3, calcitonin, and ionized calcium (iCa2+) itself. The kidney plays a key 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 calcium 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 iCa2+ and inhibits calcium reabsorption independent to PTH and 1,25(OH)2D3. The fine regulation of calcium excretion occurs in the distal convoluted tubules and connecting tubules despite the fact that only 10-15% of filtered calcium is reabsorbed there. Transient receptor potential vanilloid 5 (TRPV5) and 6 (TRPV6) in the apical membrane act as the main portal of entry, calbindin-D28K delivers Ca2+ in the cytoplasm, and then Na2+/Ca2+ exchanger (NCX1) and plasma membrane Ca2+-ATPase in the basolateral membrane serve as an exit. In the cortical collecting duct, TRPV6 is expressed, but the role might be negligible. In addition to PTH and 1,25(OH)2D3, acid-base disturbance, diuretics, and estrogen affect on these calcium channels. Recently, klotho and fibroblast growth factor 23 (FGF23) are suggested as new players in the calcium metabolism. Klotho is exclusively expressed in the kidney and co-localized with TRPV5, NCX1, and calbindin-D28K. Klotho increases calcium reabsorption through trafficking of TRPV5 to the plasma membrane, and also converts FGF receptor to the specific FGF23 receptor. FGF23: klotho complex bound to FGF receptor inhibits 1α-hydroxylase of vitamin D, and contributes to calcium reabsorption and phosphate excretion in the kidney.