**NAME: NWOYE CHINONYELUM OGOCHUKWU**

**ASSIGNMENT TITLE: RENAL PHYSIOLOGY FOR MBBS STUDENTS**

**RENAL PHYSIOLOGY BODY FLUID AND TEMPERATURE REGULATION.**

**COURSE CODE: PHS 303**

**MARIC NUMBER: 17/MHS01/212 DEPARTMENT: MBBS LEVEL: 300 LVL**

1. **DISCUSS THE ROLE OF KIDNEY IN GLUCOSE HOMEOSTASIS**

 The kidney 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 the energy needs and reabsorption of glucose at the level of 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-phospahate from precursors (e.g. lactate, glycerol, amino acid) with regard to renal reabsorption of glucose, the kidneys retrieve as much glucose possible, rendering the urine glucose free. The glomeruli filter from plasma approximately 180g of glucose of D-glucose per day, all of which is reabsorbed through glucose transporter proteins that are present in cell membrane within the proximal tubules. If the capacity of this transporter’s is exceeded, glucose appears in the urine. The process of renal glucose reabsorption is mediated by active (sodium coupled glucose co-transporters) and passive (glucose transporters) transporters. In hyperglycemia, the kidney may play exacerbating roles by reabsorbing excess glucose, ultimately contributing to chronic hyperglycemia which in turn contributes to chronic glycemic burden and the risk of microvascular consequences.

 However, the full significance of the kidney’s contribution to glucose homeostasis, under both psychologic and pathologic contributions has become well recognized, and it is thought to involve functions well beyond glucose function and release. Besides the liver, the kidney is the only organ capable of generating sufficient glucose (gluconeogenesis) to release into the circulation and it is also responsible for filtration and subsequent reabsorption or excretion of glucose. These findings have provided considerable insights into the myriad of pathophysiologic mechanisms involved in the development of hyperglycemia and type 2 diabetes Miletus.

 **MECHANISMS OF GLUCOSE HOMEOSTASIS IN THE KIDNEY**

Maintenance of glucose homeostasis is crucial in preventing pathological consequences that may result from hyperglycemia and hypoglycemia. Chronically, uncontrolled hyperglycemia leads to high risk of macrovascular a microvascular complication such as cardiovascular diseases, nephropathy, neuropathy and retinopathy. Hyperglycemia on the other hand, may lead to a myriad of central nervous system complications (e.g. confusion, behavioral changes, seizures, loss of consciousness and even death) since the brain is the body’s largest consumer of glucose in the fasting and in the postabsorptive state. Maintenance of glucose homeostasis involve several complimentary physiological processes including glucose absorption (in the gastrointestinal tract), glycogenolysis (in the liver), glucose reabsorption (in the kidney), gluconeogenesis (in the liver and kidneys), glucose excretion (in the kidney).

With respect to renal involvement in glucose homeostasis, the primary mechanism includes release of glucose into the circulation via gluconeogenesis, uptake of glucose from the circulation to satisfy the kidney’s energy need and reabsorption of glucose from at the levels of the proximal tubules.

1. **DISCUSS THE PROCESS OF MICTURITION**

Micturition is a process where urine is expelled from the body, animals and humans have a specialized system of organ known as the excretory system to eliminate the waste products from the body, “the process of expelling urine from the body is called micturition”. It is brought about by reflex contraction of a special muscle the detrusor muscle offers voluntary relaxation of the sphincter muscle. The human excretory system consists of pair of kidneys and ureters, a urinary bladder and a urethra. The kidney plays a major role in the process of urine formation and excretion. The urine formed is stored in the urinary bladder. Micturition is also known as voiding phase of bladder control and last for a short time. As the bladder becomes full, the stretch receptors increase their firing rate. This increases the urge to urinate and cause micturition reflex. It sometimes causes involuntary urination.

 **MICTURITION PROCESS**

Micturition process consists of two phases:

1. Storage phase
2. Voiding phase

**Storage phase:** the urinary bladder is a balloon shaped, hollow, muscular organ that acts a storage organ for urine. The urinary bladder in a healthy urinary system can store up to 16 ounces of urine for 2-5hrs easily. The circular sphincter muscles prevent leakage of urine. They close tightly around the opening of the bladder into the tube (urethra) that allows passage of urine outside the body.

**Voiding phase:** when the bladder is full with urine, the nerves in it are triggered which in turn stimulate the need to urinate. The brain signals urinary bladder to contract. The receptors of the urinary bladder send a signal to the central nervous system in response to which the nervous system sends a signal that incites the contraction of the urinary bladder. Through the urinary opening at the urethra, the urine is eliminated, and the process is called micturition. The neural mechanism involves is “micturition reflex”.

1. **EXPLAIN JUXTAGLOMERULAR APPARATUS**

The juxtaglomerular apparatus is a collective term referring to the cells near a structure called the glomerulus in the kidney. The juxtaglomerular are specialized cells that stimulate the secretion of adrenal hormone aldosterone and play a major role in renal autoregulation, the kidney self-governance. The juxtaglomerular is also important in salt excretion. The juxtaglomerular apparatus is located between the afferent arterioles and the returning distal convoluted tubules 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 major component of the juxtaglomerular are the following:

1. The juxtaglomerular cells of the afferent arterioles, 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 effectors arm of the renin angiotensin “aldosterone axis”.
2. The macula densa, a region of the distal convoluted tubules characterized by tubular epithelial cells which are more densely packed than in other region of the nephron (thereby leading to its characteristics appearance on light microscopy). The macula densa can be the “sensory arm” of the renin angiotensin-aldosterone as its these are the cells which sense decreased NACl delivery which determines downstream functions. They are also involved in the mechanism of tubule glomerular feedback.
3. Mesangial cells which form connections via actin and microtubules which allow for selective vasoconstriction/vasodilation of the renal afferent and efferent and arterioles with mesangial cell contraction.
4. **DISCUSS ROLE OF KIDNEY IN REGULATION OF BLOOD PRESSURE**

The kidney plays 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 activities of various vasoactive system such as the renin angiotensin-aldosterone (RAS) system. Along with vessel morphology, blood viscosity is one of the key factors influencing resistance and hence blood pressure. A key modulator of blood viscosity is the renin angiotensin-aldosterone system, a hormone system that regulates blood pressure and water balance.

The blood pressure in the system depends upon;

* 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.
* The degree to which the arteries and arterioles constrict- increases the resistance to blood flow, thus requiring a higher blood pressure.
* The volume of blood circulating round the body, if the volume is high, the ventricles gets more fluid 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 position of the distal tubules located near and in the walls of the afferent arterioles. These cells send sodium in the filtrate, while the arterial cells (juxtaglomerular cells) sense the blood pressure. When the blood pressure drops, the amount of filtered sodium also drops. The arterial cells sense the blood pressure and the decrease to NACl concentration is relayed to them by the macula densa cells. The juxtaglomerular cells then release an enzyme called renin. Renin converts angiotensinogen (a peptide or amino acid derivative) into angiotensin-1. Angiotensin-1 is thereafter converted to angiotensin-2 by angiotensin converting enzyme (ACE) found in the lungs. Angiotensin-2 causes blood vessels to contract. The increased blood constrictions elevate the blood pressure. When the volume of blood is low, arterial cells in the kidney secrete renin directly into the circulation. Plasma renin then carries out the conversion angiotensinogen released by the liver to angiotensin-1. Angiotensin-1 is subsequently converted to angiotensin-2 by the angiotensin converting enzyme found in the lungs. Angiotensin-2 a potent vasoactive peptide causes blood pressure. Angiotensin-2 also stimulate the secretion of the hormone aldosterone from the adrenal cortex. Aldosterone causes the tubules of the kidney to increase the reabsorption of sodium and water intro the blood. This increases the volume of liquid in the body which also increases blood pressure.
1. **DISCUSS THE ROLE OF KIDNEY IN CALCIUM HOMEOSTASIS**

The role of the kidney in calcium homeostasis has been reshaped from a classic view in which the kidney was regulated by system i.e. calciotropic hormones such as vitamin D3 or parathyroid hormone to an organ actively taking part in the regulation of calcium handling. With the identification of the intrinsic renal calcium sensory receptor feedback system, the regulation of paracellular calcium transport involving claudins and new paracrine regulators such as klotho, the kidney has emerged as a crucial modulator not only of calcinuria but also of calcium homeostasis. This fluxes of calcium between the small intestines (the place of calcium absorption), the bone (the main storage place for calcium), and the kidney (the main place of elimination of absorbed calcium) and highly controlled by numerous transport mechanisms hormones, and interconnected feedback loops. This is an absolute environment to prevent biomineralization in tissues. Indeed, the calcium is highly reactive ion which has high propensity to form micro crystals in fluids and tissues. In mammals the complex process of biomineralization takes place in a controlled manner in teeth and bones in which the matrix is calcified with hydroxyapatite, a calcium phosphate salt.

 In the kidney the only source of calcium reaching the tubules is ultra-filtered calcium containing salt filtered through the glomerulus. It represents approximately 50% of the total plasma calcium but it is impossible to be precisely measured in a clinical setting. This contributes to a major caveat when it comes to evaluating the fractional excretion of calcium. No secretion or breakdown of calcium contributes to the calcium delivered to the calcium delivered to the tubular system and to load to calcium filtered is the unique contributor of calcium reaching the proximal tubules (PT). Along the tubular system, complex transepithelial transport mechanism allow a highly regulated reabsorption of approximately 98% of filtrated calcium.

 Two main transepithelial transport pathways have been described along the tubules of kidneys; paracellular and transcellular. The paracellular pathways are dependent on transepithelial electrochemical gradients and can be regulated by specialized paracellular proteins the claudins. The transcellular part implies the presence of a tight epithelium and a three-step transport with apical entry, trans cytoplasmic transport and basolateral extrusion mechanisms. The driving force is mainly provided by basolateral Ca- or Na-K-ATPases.