Name: Iroegbu Ugochi Miriam

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Department: Medicine and Surgery

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1. Discuss the role of kidney in glucose hemostasis

The human kidney is involved in the regulation of glucose homeostasis and in abnormalities found in diabetes mellitus via three different mechanisms: (i) release of glucose into the circulation via gluconeogenesis; (ii) uptake of glucose from the circulation to satisfy its energy needs; and (iii) reabsorption into the circulation of glucose from glomerular filtrate to conserve glucose carbon.Plasma glucose concentrations are determined by the relative rates of glucose entry into, and removal from, the circulation. Normally, despite wide daily fluctuations in the rate of delivery of glucose into the circulation (e.g. meal ingestion) and in the demands of tissues for glucose (e.g. during exercise), plasma levels are maintained within a relatively narrow range throughout the day. Maximal plasma concentrations following meal ingestion are usually < 9.0 mmol/l and minimal concentrations, after moderate fast or exercise, are usually > 3.0 mmol/l. This is in contrast to other substrates such as glycerol, lactate, free fatty acids (FFAs) and ketone bodies, for which daily fluctuation is much greater. Teleologically, this can be explained by the fact that, on the one hand, the body must defend itself from hyperglycaemia, which is associated with both chronic effects (including retinopathy, neuropathy, nephropathy and premature atherosclerosis) and acute effects (including diabetic ketoacidosis and hyperosmolar hyperglycaemic state, which have significant associated morbidity and mortality); on the other hand, the body must also defend itself against hypoglycaemia, which can cause cardiac arrhythmias, neurological dysfunction, coma, seizures and death .Brain function is particularly dependent on having adequate levels of plasma glucose because the brain is unable to either store or produce glucose and alternative sources of energy are either in short supply (e.g. ketone bodies) or are unable to pass the blood–brain barrier (e.g. FFAs) .The precise regulation of plasma glucose concentrations is mainly determined by hormonal and neural factors, which regulate endogenous production of glucose. Acute glucoregulatory mechanisms involve insulin, glucagon and catecholamines, which can effect changes in plasma glucose levels over a matter of minutes. Insulin suppresses glucose release in both the liver and kidney by direct enzyme activation/deactivation, as well as by reducing the availability of gluconeogenic substrates and actions on gluconeogenic activators. Glucagon has no effect on the kidney, but increases both gluconeogenesis and glycogenolysis in the liver.Catecholamines have multiple acute actions, including stimulation of renal glucose release, inhibition of insulin secretion, stimulation of glucagon secretion, and increases in gluconeogenic substrate supply, stimulation of lipolysis and reduced tissue glucose uptake.Growth hormone, thyroid hormone and cortisol influence glucose levels over a period of hours by altering the sensitivity of the liver, kidney, adipose tissue and muscle to insulin, glucagon and catecholamines, and by altering the activity of key enzymes, which effect glycogen stores and availability of gluconeogenic precursors (lactate, glycogen and amino acids) . In the post-absorptive state, glucose uptake by tissues is largely dependent on tissue needs and the mass-action effects of the ambient plasma glucose concentration and, to a lesser extent, on the permissive actions of insulin and counter-regulatory hormones (e.g. thyroid hormones, growth hormone, catecholamines and cortisol). In these circumstances, most uptake of glucose occurs in tissues that do not require insulin (e.g. brain, gastrointestinal tract, renal medulla). However, in the postprandial state, although insulin and other hormones exert greater influence on tissue uptake of glucose, changes in hepatic and renal glucose release into the circulation are still quite important

2.discuss the process of micturition

Micturition or urination is the process of expelling urine from the bladder. This act is also known as voiding of the bladder. The [excretory system](https://www.toppr.com/guides/biology/excretory-products/human-excretory-system/) in humans includes a pair of kidneys, two ureters, a urinary bladder and a urethra. The kidneys filter the urine and it is transported to the urinary bladder via the ureters where it is stored till its expulsion. The process of micturition is regulated by the nervous system and the [muscles](https://www.toppr.com/guides/biology/locomotion-and-movement/muscle/) of the bladder and urethra. The urinary bladder can store around 350-400ml of urine before it expels it out.

**Stages of Micturition**

The urinary bladder has two distinct stages or phases:

1. Resting or filling stage
2. Voiding stage

Resting or Filling Stage

It is in this phase of the bladder that the urine is transported from the kidneys via the ureters into the bladder. The ureters are thin muscular tubes that arise from each of the kidneys and extend downwards where they enter the bladder obliquely.

The oblique placement of the ureters in the bladder wall serves a very important [function](https://www.toppr.com/guides/maths/relations-and-functions/functions/). The opening of the ureter into the urinary bladder is not guarded by any sphincter or muscle. Therefore, this oblique [nature](https://www.toppr.com/guides/business-studies/business-services/nature-and-types-of-services/) of opening prevents the urine from re-entering the ureters. At the same time, the main muscle of the urinary bladder, the detrusor muscle, is relaxing allowing the bladder to distend and accommodate more urine.

Voiding Stage

During this stage, both the urinary bladder and the urethra come into play together. The detrusor muscle of the urinary bladder which was relaxing so far starts to contract once the bladder’s storage capacity is reached.

The urethra is controlled by two sets of muscles: The internal and external urethral sphincters. The internal sphincter is a smooth muscle whereas the external one is [skeletal](https://www.toppr.com/guides/biology/locomotion-and-movement/skeletal-system/). Both these sphincters are in a contracted state during the filling stage.  the process of [micturition](https://www.toppr.com/guides/biology/excretory-products/micturition/) is governed by both the nervous and muscular systems. Within the nervous system, the process is governed by the autonomous nervous system and the somatic system. Once the urinary bladder reaches its maximum capacity, the stretch receptors in the walls of the bladder send an impulse via the pelvic nerve to the brain via the spinal cord. The micturition reflex is ultimately generated from the level of the spinal cord after it receives reflexes from the pontine region in the brain. Once the bladder and the urethra receive the signals to empty the bladder, the two sphincters relax and the detrusor muscle causes the contractions of the bladder. Along with these muscles, the muscles of the abdomen also play a role by putting [pressure](https://www.toppr.com/guides/physics/force-and-pressure/introduction-to-pressure) on the bladder wall. This leads to complete emptying of the bladder.

**Physiology of Micturition**



3.Explain the juxtaglomerular apparatus? The juxtaglomerular apparatus lies between the glomerulus and the distal convoluted tubule of the same nephron. This location is critical to its function in regulating renal blood flow and thus the glomerular filtration rate (GFR). JGA is one component of an important feedback mechanism, the tubuloglomerular feedback mechanism. The following structures make up the JGA :

a.The **macula densa** of the thick ascending limb

b.The [extraglomerular mesangial cells](https://www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/extraglomerular-mesangial-cell%22%20%5Co%20%22Learn%20more%20about%20Extraglomerular%20Mesangial%20Cell%20from%20ScienceDirect%27s%20AI-generated%20Topic%20Pages)

The renin- and angiotensin II–producing **granular cells** of the afferent arteriole.The cells of the macula densa represent a morphologically distinct region of the thick ascending limb. This region passes through the angle formed by the afferent and efferent arterioles of the same nephron. The cells of the macula densa are in contact with the extraglomerular [mesangial cells](https://www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/mesangial-cell%22%20%5Co%20%22Learn%20more%20about%20Mesangial%20Cell%20from%20ScienceDirect%27s%20AI-generated%20Topic%20Pages) and the granular cells of the afferent arterioles. Granular cells of the afferent arterioles are derived from metanephric mesenchymal cells. They contain smooth muscle myofilaments and they manufacture, store, and release **renin**. Extraglomerular mesangial cells are a specialized group of distal tubular cells and lacis cells (Goormaghtigh cells, polar cushion, extraglomerular mesangial cells). Lacis cells form a pyramid situated between the afferent and efferent arterioles and with its base on the macula densa and apex continuous with the glomerular [mesangium](https://www.sciencedirect.com/topics/medicine-and-dentistry/mesangium%22%20%5Co%20%22Learn%20more%20about%20Mesangium%20from%20ScienceDirect%27s%20AI-generated%20Topic%20Pages). [Renin](https://www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/renin%22%20%5Co%20%22Learn%20more%20about%20Renin%20from%20ScienceDirect%27s%20AI-generated%20Topic%20Pages) is involved in the formation of **angiotensin II** and ultimately in the secretion of [aldosterone](https://www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/aldosterone%22%20%5Co%20%22Learn%20more%20about%20Aldosterone%20from%20ScienceDirect%27s%20AI-generated%20Topic%20Pages).The JGA is one component of the tubuloglomerular feedback mechanism that is involved in the [autoregulation](https://www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/autoregulation%22%20%5Co%20%22Learn%20more%20about%20Autoregulation%20from%20ScienceDirect%27s%20AI-generated%20Topic%20Pages) of [renal blood flow](https://www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/kidney-blood-flow) and the GFR.

4.Discuss the role of kidney in regulation of blood pressure?

The kidney regulates blood pressure through the Renin-angiotensin system.The renin-angiotensin system or RAS regulates blood pressure and fluid balance in the body. When blood volume or sodium levels in the body are low, or blood potassium is high, cells in the kidney release the enzyme, renin. Renin converts angiotensinogen, which is produced in the liver, to the hormone angiotensin I. An enzyme known as ACE or angiotensin-converting enzyme found in the lungs metabolizes angiotensin I into angiotensin II. Angiotensin II causes blood vessels to constrict and blood pressure to increase. Angiotensin II stimulates the release of the hormone aldosterone in the adrenal glands, which causes the renal tubules to retain sodium and water and excrete potassium. Together, angiotensin II and aldosterone work to raise blood volume, blood pressure and sodium levels in the blood to restore the balance of sodium, potassium, and fluids. If the renin-angiotensin system becomes overactive, consistently high blood pressure results.

5. discuss the role of kidney in calcium hemostasis?

The reabsorption of calcium in the proximal convoluted tubule parallels that of sodium and water. Proximal tubular calcium reabsorption is thought to occur mainly by passive diffusion and solvent drag. This is based on the observation that the ratio of calcium in the proximal tubule fluid to that in the glomerular filtrate is 1:1.2. The passive paracellular pathways account for approximately 80% of calcium reabsorption in this segment of the nephron. A small but significant component of active calcium transport is observed in the proximal tubules. The active transport of calcium proceeds in a two-step process, with calcium entry from the tubular fluid across the apical membrane and exit though the basolateral membrane. This active transport is generally considered to constitute 10%–15% of total proximal tubule calcium reabsorption and it is mainly regulated by parathyroid hormone (PTH) and calcitonin.

No reabsorption of calcium occurs within the thin segment of the loop of Henle. In the thick ascending limb of the loop of Henle, 20% of the filtered calcium is reabsorbed largely by the cortical thick ascending limb, through both transcellular and paracellular routes. In the thick ascending limb, the bulk of calcium reabsorption proceeds through the paracellular pathway and is proportional to the transtubular electrochemical driving force. The apical Na+-K+-2Cl− cotransporter NKCC2 and the renal outer medullary potassium K+ (ROMK) channel generate the “driving force” for paracellular cation transport. Whereas NaCl reabsorption through NKCC2 is electroneutral (NKCC2 translocates one Na+, one K+, and two Cl− ions from the lumen into the cell), apical potassium represents the rate-limiting step of this process and potassium ions back-diffuse into the lumen through the ROMK channels. Na+ and Cl− accumulated inside the cell are then transported into the bloodstream through basolateral Na+-K+-ATPase and Cl− channels, respectively. Overall, these processes yield a net cellular reabsorption of NaCl and the generation of a lumen-positive transepithelial potential difference, which drives nonselective calcium reabsorption through the paracellular route. Calcium transport in the thick ascending limb of the loop of Henle is also influenced by the calcium-sensing receptor (CaSR) , which is localized in the basolateral membrane. How CaSR controls the calcium reabsorption in the thick ascending limb is now better understood. Using microdissected, in vitro microperfused rat cortical thick ascending limb, Loupy et al. showed that an acute inhibition of the CaSR does not alter NaCl reabsorption or the transepithelial potential difference but increased the permeability to calcium of the paracellular pathway. The tight junction in the thick ascending limb expresses several claudins, including claudin-14, claudin-16, and claudin-19. A normal expression of claudin-16 and claudin-19 is required for a normal absorption of divalent cations in this tubular segment. Toka et al. reported that the disruption of CaSR decreases the abundance of the claudin-14 mRNA and increases that of the claudin-16 mRNA. A treatment by cinacalcet increases the abundance of claudin-14 mRNA, and in cell culture models overexpression of claudin-14, decreases the paracellular permeability to calcium . Calciotropic hormones, such as PTH and calcitonin, stimulate active cellular calcium absorption in the cortical thick ascending limb

In contrast with the proximal tubule and the thick ascending limb of the loop of Henle, the distal tubule reabsorbs calcium exclusively via the transcellular route. The distal convoluted tubule absorbs 5%–10% of the filtered calcium. Calcium absorption in this segment is active because it proceeds against a chemical and an electrical gradient. This active process can be divided into three steps. The first step requires calcium influx across the apical membrane. The transient receptor potential vanilloid 5 has been identified as the responsible protein in this process. The second step is the diffusion of calcium through the cytosol. During this process, calbindin-D28k binds intracellular calcium transported via transient receptor potential vanilloid 5 and shuttles it through the cytosol toward the basolateral membrane where calcium is extruded via sodium-calcium exchanger NCX1 and the plasma membrane calcium-ATPase PMCA1b, which is the final step in this process.