**ASSIGNMENT**

Q1. Discuss the role of kidney in glucose homeostasis?

ANSWER

The kidneys play an important role in glucose homeostasis. It helps to maintain glucose homeostasis by at least two mechanisms:

* Under normal circumstances, the kidney filters and reabsorbs 100% of glucose, approximately 180 g (1 mole) of glucose, each day. The glucose transporters expressed in the renal proximal tubule ensure that less than 0.5 g/day (range 0.03-0.3 g/d) 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.
* It produces glucose by gluconeogenesis. The key enzymes of gluconeogenesis are phosphoenolpyruvate carboxykinase (PEPCK) and glucose 6-phosphatase (G6Pase). These are expressed in the renal proximal tubule only and not the renal medulla. The kidneys produce between 2.0-2.5umol of glucose/kg/min thereby contributing about 20-25% of circulating glucose.

Gluconeogenesis in the kidneys exceeds renal glucose consumption. It is important in the prevention of hypoglycemia, and its inappropriate increase in diabetic patients contributes to the development of hyperglycemia.

As plasma glucose concentration increases, there is concordant increase in the filtered load of glucose. As the rate of glucose entering the nephron rises above 260-350mg/1.73m2/min (14.5-19.5mmol/1.73m2/min), the excess glucose exceeds the reabsorptive capacity of proximal tubule and is excreted in the urine (i.e. glucosuria). In health individuals this equates to a blood glucose concentration of approximately 200mg/dL (11mmol/L), which is believed to be threshold for the appearance of glucosuria.

Q2. Discuss the process of micturition?

ANSWER

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](https://www.toppr.com/guides/biology/control-and-coordination/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.

There are two distinct stages or phases of Micturition:

### 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.

As mentioned earlier, 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.

Q3. Explain juxtaglomerular apparatus?

ANSWER

#### The juxtaglomerular apparatus is formed at the point of contact between distal convulated tubule and the afferent arteriole. Their close proximity to each other allows them to perform their function of blood pressure regulation. The juxtaglomerular apparatus of the kidney serves as a intrarenal baroreceptor. The juxtaglomerular apparatus consists of three cell types: the macula densa cells, the juxtaglomerular cells and the extraglomerular mesangial cells.

#### The Macula Densa

The macula densa cells of the distal convoluted tubule are smaller than the usual cuboidal cells of the tubule and packed rather closely together. They may be recognised by their close packing and dark staining nuclei. It is thought that the macula densa cells are sensory cells that respond to the sodium concentration in the fluid within the distal tubule and, perhaps, to the rate of fluid flow past them. An increase in sodium concentration in the tubular fluid leads to a reduction in the production of renin by extraglomerular mesangial cells and juxtaglomerular cells.

#### Juxtaglomerular Cells

The juxtaglomerular cells secrete renin, and as specialised smooth muscle cells surrounding the afferent arteriole also have the capacity to affect the perfusion of the glomerulus. Although they are activated by prostaglandins released from the macula densa cells, they can also release renin independently of the macula densa. Baroreceptors found in the arterioles trigger renin secretion if there is a fall in blood pressure in the arterioles. Activation of the sympathetic nervous system can also stimulate renin release through activation of beta-1 receptors. Renin is a protease enzyme that catalyses the conversion of angiotensinogen to angiotensin I. Angiotensin I is converted into the active vasoconstrictor angiotensin II by Angiotensin Converting Enzyme (ACE) found in the kidney and largely in the lung.

#### Extraglomerular Mesangial Cells

Extraglomerular mesangial cells, also known as lacis cells or Goormaghtigh cells, are located in the space between the afferent and efferent arterioles, and the glomerular capillaries. These pale staining, renin containing cells are located just outside the glomerulus, near the vascular pole. They are a type of smooth muscle cell, and although their function is yet to be fully clarified, they play a role in autoregulation of blood flow to the kidney and regulation of systemic blood pressure through the renin-angiotensin system.

Q4 Discuss the role of kidney in regulation of blood pressure?

ANSWER

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.

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 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:

* 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 get more filled, and the heart muscle gets more stretched.

The kidney influences blood pressure by:

* Causing the arteries and veins to constrict
* 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 (a peptide, or amino acid derivative) into angiotensin-1. Angiotensin-1 is thereafter converted to angiotensin-2 by an angiotensin-converting enzyme (ACE), found in the lungs. Angiotensin-2 causes blood vessels to contract -- the increased blood vessel constrictions elevate the blood pressure. 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.

Q5. Discuss the role of Kidney in Calcium homeostasis?

ANSWER

The kidney is critcally important in calcium homeostasis. Under normal blood calcium concentrations, almost all of 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 into urine.

About 50% of plasma calcium (ionized and complexed form; ultrafilterable fraction, excluding the protein bound form) is freely filtered through the renal glomerulus, and 99% of the filtered calcium is actually reabsorbed along renal tubules (Table 1). The excreted calcium in the final urine is about 200 mg per day in an adult person with an average diet. Several factors are involved in the regulation of calcium in renal tubules. PTH and activated vitamin D enhance calcium reabsorption in the thick ascending limb (TAL), distal convoluted tubule (DCT) and/or connecting tubule (CNT), and estrogen promotes calcium absorption in the DCT/CNT1, 2). Acidosis contributes to hypercalciuria by reducing calcium reabsorption in the proximal tubule (PT) and DCT, and alkalosis vice versa3). Diuretics like thiazide and furosemide also alter calcium absorption in the renal tubules; thiazide promotes calcium reabsorption and furosemide inhibits it4, 5). Plasma calcium itself also controls renal calcium absorption through altered PTH secretion as well as via binding to the calcium sensing receptor (CaSR) in the TAL. To facilitate Ca2+ reabsorption along renal tubules; (i) voltage difference between the lumen and blood compartment should be favorable for Ca2+ passage, i.e., a positive voltage in the lumen; (ii) concentration difference should be favorable for Ca2+ passage with a higher Ca2+ concentration in the lumen; (iii) an active transporter should exist if the voltage or concentration difference is not favorable for Ca2+ reabsorption. Each renal tubular segment has a different Ca2+ concentration difference or voltage environment for its unique mechanism for calcium reabsorption.