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Physiology assignment

1.The kidney plays an important role in carbohydrate homeostasis, both in the post-absorptive period and in the postprandial period. The kidney produces glucose by neoglucogenesis in the cortex and uses glucose to meet the energy needs of the medulla. It also participates in the reabsorption of glucose filtered by the kidney in such a way that the final urine is devoid of glucose, as long as the glycemia does not exceed the threshold of 180 mg / dL. This reabsorption is ensured by sodium-glucose cotransporters (SGLT1 and SGLT2) expressed in the S1 and S3 segments of the proximal tubule. SGLT2 is the main cotransporter providing 90% of the glucose reabsorption. In type 2 diabetics, neoglucogenesis and renal use are increased by 30%. Surprisingly, the reabsorption of glucose is increased, which contributes to the worsening of hyperglycemia. This results from an increase in the renal glucose reabsorption threshold (220  mg / dL) and an overexpression of SGLT2 in response to hyperglycemia and the secretion of cytokines. Administration of SGLT2 inhibitors to patients with type 2 diabetes causes the renal glucose reabsorption threshold to decrease (80 mg / dL) and greatly reduces renal glucose reabsorption. SGLT2 inhibitors are therefore the only antidiabetic molecules capable of reducing excess renal glucose reabsorption in type 2 diabetics and therefore of contributing, by an original mechanism, to the reduction of glycemia.

2. Micturition is a process where urine is expelled from the body. Animals and humans have a specialised system of organs known as the excretory system to eliminate the waste products from the body. In other words**, the process of expelling urine from the body is called micturition.** It is brought about by reflex contraction of a special muscle called the detrusor muscle after voluntary relaxation of the sphincter muscle.

On average, a normal adult excretes 1 to 1.5 L of urine per day. Normal human urine is a light yellow fluid majorly consisting of 95 per cent water and 5 per cent solid wastes. It is slightly acidic with a pH close to 6.

Micturition process consists of two phases:

* Storage phase
* Voiding phase

### **Storage Phase**

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

### **Voiding Phase**

When the bladder is filled with urine, the nerves in it are triggered, which in turn stimulates 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](https://byjus.com/biology/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 involved is called the micturition reflex

3. The juxtaglomerular apparatus (also known as the juxtaglomerular complex) is a structure in the [kidney](https://en.m.wikipedia.org/wiki/Kidney) that regulates the function of each [nephron](https://en.m.wikipedia.org/wiki/Nephron" \o "Nephron), the functional units of the kidney. The juxtaglomerular apparatus is named because it is next to (juxta-[[1]](https://en.m.wikipedia.org/wiki/Juxtaglomerular_apparatus#cite_note-1)) the [glomerulus](https://en.m.wikipedia.org/wiki/Glomerulus_(kidney)" \o "Glomerulus (kidney)).

The juxtaglomerular apparatus consists of three types of cells:

1. the [macula densa](https://en.m.wikipedia.org/wiki/Macula_densa), a part of the distal convoluted tubule of the same nephron
2. [juxtaglomerular cells](https://en.m.wikipedia.org/wiki/Juxtaglomerular_cell), (also known as granular cells) which secrete [renin](https://en.m.wikipedia.org/wiki/Renin" \o "Renin)
3. [extraglomerular mesangial cells](https://en.m.wikipedia.org/wiki/Extraglomerular_mesangial_cells)

The juxtaglomerular apparatus is part of the kidney [nephron](https://en.m.wikipedia.org/wiki/Nephron" \o "Nephron), next to the [glomerulus](https://en.m.wikipedia.org/wiki/Glomerulus_(kidney)" \o "Glomerulus (kidney)). It is found between [afferent arteriole](https://en.m.wikipedia.org/wiki/Afferent_arteriole) and the [distal convoluted tubule](https://en.m.wikipedia.org/wiki/Distal_convoluted_tubule) of the same nephron. This location is critical to its function in regulating renal blood flow and [glomerular filtration rate](https://en.m.wikipedia.org/wiki/Glomerular_filtration_rate" \o "Glomerular filtration rate).

[Renin](https://en.m.wikipedia.org/wiki/Renin) is produced by [juxtaglomerular cells](https://en.m.wikipedia.org/wiki/Juxtaglomerular_cells" \o "Juxtaglomerular cells). These cells are similar to [epithelium](https://en.m.wikipedia.org/wiki/Epithelium) and are located in the tunica media of the afferent arterioles as they enter the glomeruli.[[2]](https://en.m.wikipedia.org/wiki/Juxtaglomerular_apparatus#cite_note-ganong-2) The juxtaglomerular cells secrete renin in response to:

* Stimulation of the [beta-1 adrenergic receptor](https://en.m.wikipedia.org/wiki/Beta-1_adrenergic_receptor)
* Decrease in renal perfusion pressure (detected directly by the granular cells)
* Decrease in NaCl concentration at the macula densa, often due to a decrease in [glomerular filtration rate](https://en.m.wikipedia.org/wiki/Glomerular_filtration_rate" \o "Glomerular filtration rate)

### Extraglomerular mesangial cells

[Extraglomerular mesangial cells](https://en.m.wikipedia.org/wiki/Extraglomerular_mesangial_cells) are located in the junction between the afferent and efferent arterioles. These cells have a contractile property similar to vascular smooth muscles and thus play a role in “regulating GFR” by altering the vessel diameter. [Renin](https://en.m.wikipedia.org/wiki/Renin" \o "Renin) is also found in these cells.

### Macula densa

At the point where the afferent arterioles enter the glomerulus and the efferent arteriole leaves it, the tubule of the [nephron](https://en.m.wikipedia.org/wiki/Nephron" \o "Nephron) touches the arterioles of the [glomerulus](https://en.m.wikipedia.org/wiki/Glomerulus" \o "Glomerulus) from which it rose. At this location, in the wall of the distal convoluted tubule, there is a modified region of tubular epithelium called the [macula densa](https://en.m.wikipedia.org/wiki/Macula_densa).

 Cells in the macula densa respond to changes in the [sodium chloride](https://en.m.wikipedia.org/wiki/Sodium_chloride) levels in the distal tubule of the nephron via the [tubuloglomerular feedback](https://en.m.wikipedia.org/wiki/Tubuloglomerular_feedback" \o "Tubuloglomerular feedback) (TGF) loop.

The macula densa's detection of elevated sodium chloride, which leads to an increase in GFR, is based on the concept of [purinergic signaling](https://en.m.wikipedia.org/wiki/Purinergic_signaling" \o "Purinergic signaling). An increase in the [salt](https://en.m.wikipedia.org/wiki/Sodium_chloride) concentration causes several [cell signals](https://en.m.wikipedia.org/wiki/Signal_transduction) to eventually cause the adjacent afferent arteriole to [constrict](https://en.m.wikipedia.org/wiki/Vasoconstriction). This decreases the amount of blood coming from the afferent arterioles to the glomerular capillaries, and therefore decreases the amount of fluid that goes from the glomerular capillaries into the Bowman's space (the [glomerular filtration rate (GFR)](https://en.m.wikipedia.org/wiki/Glomerular_filtration_rate" \o "Glomerular filtration rate)).

When there is a decrease in the sodium concentration, less sodium is reabsorbed in the macular densa cells. The cells increase the production of [nitric oxide](https://en.m.wikipedia.org/wiki/Nitric_oxide) and [Prostaglandins](https://en.m.wikipedia.org/wiki/Prostaglandins) to vasodilate the afferent arterioles and increase renin release.

1. 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 toblood 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 volumeSpecialized 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

1. The maintenance of calcium homeostasis is very important because calcium is the main component of bony skeleton and serves as the intracellular and extracellular messenger in numerous essential cellular events such as neuronal network, immune response, muscle contraction, and hormone secretion.

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.