**17/MHS01/204**

1. ***Discuss the role of the kidney in glucose homeostasis.***

The kidneys’ 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 their energy needs, and reabsorption of glucose at the level of the proximal tubule.

The plasma glucose concentration is determined by the amount of glucose synthesized, and the one removed from the circulation and metabolized. This concentration must be maintained within a relatively narrow range despite the wide daily fluctuations in glucose ingestion and glucose demands in various tissues

Renal release of glucose into the circulation is the result of glycogenolysis and gluconeogenesis, respectively involving the breaking down and formation of glucose-6-phosphate from precursors (e.g., lactate, glycerol, amino acids). With regard to renal reabsorption of glucose, the kidneys normally retrieve as much glucose as possible, rendering the urine virtually glucose free. If the capacity of these transporters is exceeded, glucose appears in the urine.

However, the full significance of the kidneys’ contribution to glucose homeostasis, under both physiologic and pathologic conditions, has become well recognized, and is thought to involve functions well beyond glucose uptake 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.

The maintenance of glucose homeostasis is crucial in preventing pathological consequences that may result from hyperglycemia or hypoglycemia. Chronically uncontrolled hyperglycemia leads to a higher risk of macro vascular and micro vascular complications, such as cardiovascular disease, nephropathy, neuropathy, and retinopathy. Maintenance of glucose homeostasis involves several complementary physiologic processes, including glucose absorption (in the gastrointestinal tract), glycogenolysis (in the liver), glucose reabsorption (in the kidneys), gluconeogenesis (in the liver and kidneys), and glucose excretion (in the kidneys).

With respect to renal involvement in glucose homeostasis, the primary mechanisms include release of glucose into the circulation via gluconeogenesis, uptake of glucose from the circulation to satisfy the kidneys’ energy needs, and reabsorption of glucose at the level of the proximal tubule.

1. ***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. It is brought about by reflex contraction of a special muscle called the detrusor muscle after voluntary relaxation of the sphincter muscle. 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.

**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.

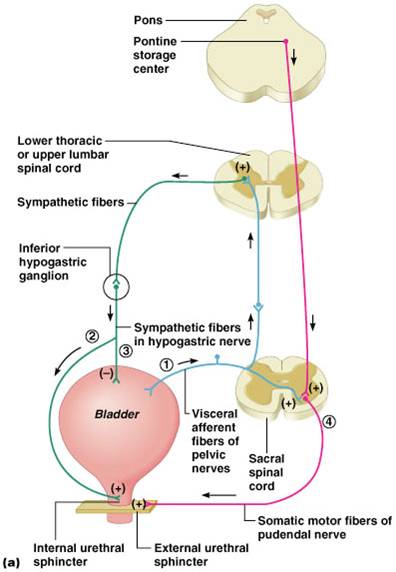
The oblique placement of the ureters in the bladder wall serves a very important [function](https://www.toppr.com/guides/maths/relations-and-functions/functions/). The opening of the ureter into the urinary bladder is not guarded by any sphincter or muscle. Therefore, this oblique [nature](https://www.toppr.com/guides/business-studies/business-services/nature-and-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.

**Physiology of Micturition**



*(Image Source: austincommunitycollege.com)*

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.

Problems Associated With Micturition

There are several factors which affect the process of micturition. Some of these can be due to physical trauma or disease; others are psychological in nature. Following are a few disorders that affect micturition:

* **Detrusor Instability –**This is a condition where the detrusor muscle contracts without any apparent reason. This muscle is responsible for contracting the bladder and help with the micturition process. As a result, detrusor instability results in urinary incontinence.
* **Urinary Retention –** This condition is characterized by the inability to empty the bladder completely. The onset may be gradual or sudden. The causes can range from a blockage in the urethra, nerve problems and weak bladder muscles.
* **Spinal Cord Trauma –**Injuries to the spinal cord, specifically the tenth thoracic vertebra (T10) can cause the bladder to be overactive or cause urinary incontinence.

Management of Micturition Disorders

* The nerve pathway to the urinary tract should be intact.
* The bladder capacity should be normal.
* Normal muscle tone should be observed in the sphincters, detrusors, and pelvic floor muscles.
* There should be no obstruction to the urine flow in any region of the urinary tract.
* The environmental and psychological factors that inhibit micturition should be absent.
* The coordinated activity of sympathetic, parasympathetic, and somatic nerves help in normal micturition.

1. ***Explain juxtaglomerular apparatus***

The **juxtaglomerular apparatus** (also known as the **juxtaglomerular complex**) is a structure in the [kidney](https://en.wikipedia.org/wiki/Kidney) that regulates the function of each [nephron](https://en.wikipedia.org/wiki/Nephron), the functional units of the kidney. The juxtaglomerular apparatus is named because it is next to (juxta) the [glomerulus](https://en.wikipedia.org/wiki/Glomerulus_(kidney)).

The juxtaglomerular apparatus consists of three types of cells:

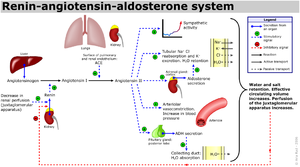
1. the [macula densa](https://en.wikipedia.org/wiki/Macula_densa), a part of the distal convoluted tubule of the same nephron
2. [juxtaglomerular cells](https://en.wikipedia.org/wiki/Juxtaglomerular_cell), (also known as granular cells) which secrete [renin](https://en.wikipedia.org/wiki/Renin)
3. [extraglomerular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

**Structure**

The juxtaglomerular apparatus is part of the kidney [nephron](https://en.wikipedia.org/wiki/Nephron), next to the [glomerulus](https://en.wikipedia.org/wiki/Glomerulus_(kidney)). It is found between [afferent arteriole](https://en.wikipedia.org/wiki/Afferent_arteriole) and the [distal convoluted tubule](https://en.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.wikipedia.org/wiki/Glomerular_filtration_rate).

Functions

**Juxtaglomerular cells**

[](https://en.wikipedia.org/wiki/File:Renin-angiotensin-aldosterone_system.png)

The [renin–angiotensin system](https://en.wikipedia.org/wiki/Renin%E2%80%93angiotensin_system); It is activated when juxtaglomerular cells are poorly perfused.

[Renin](https://en.wikipedia.org/wiki/Renin) is produced by [juxtaglomerular cells](https://en.wikipedia.org/wiki/Juxtaglomerular_cells). These cells are similar to [epithelium](https://en.wikipedia.org/wiki/Epithelium) and are located in the tunica media of the afferent arterioles as they enter the glomeruli. The juxtaglomerular cells secrete renin in response to:

* Stimulation of the [beta-1 adrenergic receptor](https://en.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.wikipedia.org/wiki/Glomerular_filtration_rate)

**Extraglomerular mesangial cells**

[Extraglomerular mesangial cells](https://en.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.wikipedia.org/wiki/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.wikipedia.org/wiki/Nephron) touches the arterioles of the [glomerulus](https://en.wikipedia.org/wiki/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 densaCells in the macula densa respond to changes in the [sodium chloride](https://en.wikipedia.org/wiki/Sodium_chloride) levels in the distal tubule of the nephron via the [tubuloglomerular feedback](https://en.wikipedia.org/wiki/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.wikipedia.org/wiki/Purinergic_signaling). An increase in the [salt](https://en.wikipedia.org/wiki/Sodium_chloride) concentration causes several [cell signals](https://en.wikipedia.org/wiki/Signal_transduction) to eventually cause the adjacent afferent arteriole to [constrict](https://en.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.wikipedia.org/wiki/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.wikipedia.org/wiki/Nitric_oxide) and [Prostaglandins](https://en.wikipedia.org/wiki/Prostaglandins) to vasodilate the afferent arterioles and increase renin release..

**Clinical significance**

Excess secretion of renin by the [juxtaglomerular cells](https://en.wikipedia.org/wiki/Juxtaglomerular_cells) can lead to excess activity of the renin–angiotensin system, [hypertension](https://en.wikipedia.org/wiki/Hypertension) and an increase in [blood volume](https://en.wikipedia.org/wiki/Blood_volume). This is not responsive to the usual treatment for [essential hypertension](https://en.wikipedia.org/wiki/Essential_hypertension), namely medications and lifestyle modification.

One cause of this can be increased renin production due to [narrowing of the renal artery](https://en.wikipedia.org/wiki/Renal_artery_stenosis), or a tumor of juxtaglomerular cells that produces renin. These will lead to [secondary hyperaldosteronism](https://en.wikipedia.org/wiki/Secondary_hyperaldosteronism), which will cause hypertension, [high blood sodium](https://en.wikipedia.org/wiki/Hypernatremia), [low blood potassium](https://en.wikipedia.org/wiki/Hypokalemia), and metabolic alkalosis.

1. ***Discuss the role of kidney in regulating 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 activity of various vasoactive systems such as the renin-angiotensin-aldosterone system. As a result, many researchers argue that identifying any marked rise in blood pressure requires resetting of the relationship between arterial blood pressure and urinary sodium excretion, which can occur by an array of systemic or local mechanisms. Almost all of the monogenic forms of hypertension affect sites in the kidney associated with sodium handling and transport. Experimental models of spontaneous hypertension, such as the Dahl salt-sensitive rat, have been used to study the effects of kidney transplantation on blood pressure. Results from studies of kidney transplantation indicate that pressure sensitivity to sodium intake 'follows' the kidney, meaning that the recipient of a 'salt-resistant kidney' acquires sodium resistance, and that the recipient of a 'salt-sensitive kidney' acquires pressure sensitivity. The examples above and discussed in this Review demonstrate that it should come as no surprise that most disorders that affect the kidney or the renal vasculature commonly lead to secondary forms of hypertension.

1. ***Discuss the role of kidney in calcium homeostasis***

The kidney, intestine, and bone are the main target organs of these regulators, and the kidney plays a key role in the fine regulation of calcium excretion. 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 has been known as the central organ for calcium homeostasis through fine regulation of renal calcium excretion. Calcium homeostasis is under the direct control of the [parathyroid](https://www.sciencedirect.com/topics/medicine-and-dentistry/parathyroid) gland, [PTH](https://www.sciencedirect.com/topics/medicine-and-dentistry/parathyroid-hormone), [calcitonin](https://www.sciencedirect.com/topics/medicine-and-dentistry/calcitonin), and [calcitriol](https://www.sciencedirect.com/topics/medicine-and-dentistry/calcitriol), which is a [vitamin D](https://www.sciencedirect.com/topics/medicine-and-dentistry/vitamin-d) metabolite. The ionized form is the physiologically active form. [*Hypercalcemia*](https://www.sciencedirect.com/topics/medicine-and-dentistry/hypercalcaemia) is defined as an ionized Ca+ concentration greater than 2.7 mEq/L or a total [serum Ca](https://www.sciencedirect.com/topics/nursing-and-health-professions/calcium-blood-level)+ concentration greater than 10.5 mg/dl.