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DEPARTMENT: MEDICINE AND SURGERY

COURSE: NEUROHISTOLOGY AND ANATOMY OF THE SPECIAL SENSES

**Assignment**

Q1. Discuss the role of kidney in glucose homeostasis?

Q2. Discuss the process of micturition?

Q3. Explain juxtaglomerular apparatus?

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

Q5. Discuss the role of Kidney in Calcium homeostasis?

Q1: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. Other substrates such as free fatty acids (FFAs), glycerol, lactate and ketone bodies have greater daily fluctuations. This can be explained by the need of the body to protect himself against hyper- and hypoglycaemia. Hyperglycaemia is associated with both chronic effects (such as nephropathy, retinopathy, neuropathy and premature atherosclerosis) and also acute complications (including diabetic ketoacidosis and hyperosmolar hyperglycaemic state that are associated with higher morbidity and mortality). Hypoglycaemia is also harmful because it can cause neurological events (including coma, seizures), cardiac arrhythmias and death.

The regulation of endogenous production of glucose is determined by hormonal and neural factors. In the acute phase, glucoregulatory mechanisms involve insulin, glucagon and catecholamines and they can effect changes in plasma glucose levels in a matter of minutes. Insulin is able to suppress glucose release in both the kidney and liver by direct enzyme activation ⁄ deactivation and by reducing the availability of gluconeogenic substrates. Glucagon has no effect on the kidneys, but it stimulates glycogenolysis and gluconeogenesis in the liver [[16](https://www.intechopen.com/books/treatment-of-type-2-diabetes/the-role-of-the-kidney-in-glucose-homeostasis#B16)]. Catecholamines also have multiple acute actions. They can stimulate renal glucose release and glucagon secretion and inhibit insulin secretion.

The kidneys are involved in maintaining glucose homeostasis through three different mechanisms: gluconeogenesis; glucose uptake from the blood for its own energy requests and reabsorption into the general circulation of glucose from glomerular filtrate in order to preserve energy.

3.1. Renal gluconeogenesis

From the point of view of glucose utilization, the kidney is considered as 2 separate organs; the renal medulla is characterized mainly by glucose utilization and the renal cortex is responsible for glucose release. The separation of these activities represents the consequence of differences in the distribution of numerous enzymes along the nephron. The cells in the renal medulla can use only glucose for their needs (like the brain) and they have enzymes capable of glucose-phosphorylation and glycolysis. They can therefore phosphorylate important amounts of glucose and accumulate glycogen but, because these cells do not have glucose-6-phosphatase or any other gluconeogenic enzymes, they are unable to release glucose into the bloodstream. Moreover, the cells in the renal cortex have gluconeogenic enzymes and they can produce and release glucose into the circulation. However these cells cannot synthesize glycogen because they have little phosphorylating capacity.

After a 16-h overnight fast, approximately 10 µmol ⁄ (kg /min) of glucose is released into the circulation. Almost 50% of this is the result of glycogenolysis from the liver stocks and the other half is produced by liver and kidney gluconeogenesis. The renal cortex (like the liver) contains gluconeogenic enzymes and it can synthesize glucose-6-phosphate from precursors (lactate, glutamine, glycerol and alanine). Because it contains glucose-6-phosphatase, it is able to release glucose into the blood stream [[18](https://www.intechopen.com/books/treatment-of-type-2-diabetes/the-role-of-the-kidney-in-glucose-homeostasis#B18)] and the human liver and kidneys are the only organs that can perform gluconeogenesis. Therefore, after an overnight fast, the liver produces 75–80% of glucose released into the circulation and the remaining 20–25% is derived from the kidneys [[4](https://www.intechopen.com/books/treatment-of-type-2-diabetes/the-role-of-the-kidney-in-glucose-homeostasis#B4)].

Several studies have indicated that human kidneys and liver provide approximately the same amounts of glucose through gluconeogenesis in postabsorptive period. If the duration of fasting is increased, the glycogen stores are depleted and gluconeogenesis produces all the glucose released into circulation.

An important aspect is that kidney and liver use different gluconeogenic precursors and several hormones have different effects on their release of glucose. Lactate represents the predominant gluconeogenic precursor in both organs, but regarding the aminoacids, the kidney prefers to use glutamine, whereas the liver preferentially uses alanine. Insulin can suppress glucose release in both organs with almost comparable efficacy, whereas glucagon stimulates hepatic glucose release only. Catecholamines normally have a direct effect only on renal glucose release [[22](https://www.intechopen.com/books/treatment-of-type-2-diabetes/the-role-of-the-kidney-in-glucose-homeostasis#B22)], but their effect on both hepatic and renal glucose release may be indirect by increasing the quantity of gluconeogenic substrates available and by suppressing insulin secretion. Other hormones, such as growth hormone, cortisol and thyroid hormones can stimulate hepatic glucose release over a great period of time. Their effects on the kidneys regarding glucose release in humans are not completely deciphered.

In the postprandial state the situation changes significantly. Postprandial glucose levels in the plasma are determined by insulin and glucagon levels. After glucose ingestion, plasma glucose levels reach the peak in 60–90 minutes and they return to post-absorptive levels in almost 3–4 h. The plasma insulin increases four times and the plasma glucagon levels decrease by 50% . Meyer et al. indicated that endogenous glucose release is reduced by almost 60% and hepatic glycogenolysis drops to zero in the 4- to 6-h period after meal ingestion [[23](https://www.intechopen.com/books/treatment-of-type-2-diabetes/the-role-of-the-kidney-in-glucose-homeostasis#B23)].This is happening because this period determines the refilling of hepatic glycogen stores and inhibition of endogenous glucose release is able to limit postprandial hyperglycaemia. There is also a reduction in hepatic gluconeogenesis by 82% and glucose molecules generated through hepatic gluconeogenesis are also directed into hepatic glycogen, not only released in the circulation.

Renal gluconeogenesis can increase by approximately twofold and it can represent ~60% of endogenous glucose production in the postprandial state. This mechanism is believed to facilitate the repletion of glycogen stocks in the liver.

A new concept of hepatorenal glucose reciprocity emerged from the differences observed in regulation and interchange between renal and hepatic glucose release. This concept refers to the facts that a pathological or physiological reduction in glucose release by kidney or liver determines a compensatory increase in glucose release of the other one (liver or kidney) in order to avoid hypoglycaemia. This situation occurs in the an hepatic phase during liver transplantation, prolonged fasting, meal ingestion, acidosis and insulin overdoses in diabetes mellitus.

3.2. Glycogenolysis

Glycogenolysis is the breakdown of glycogen to glucose-6-phosphate and a hydrolysis reaction (using glucose-6-phosphatase) in order to free glucose. The liver is the only organ that contains glucose-6-phosphatase. So, the cleavage of hepatic glycogen releases glucose, while the cleavage of glycogen from other sources can release only lactate. Lactate, that is generated via glycolysis, is often absorbed by other organs and helps regenerating glucose.

GLUCOSE ABSORBTION

Apart from the important role in gluconeogenesis and the role of renal cortex in glucose uptake, the kidneys contribute to glucose homeostasis by filtering and reabsorbing glucose.

Q2

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

Micturition process consists of two phases:

* Storage phase
* Voiding phase

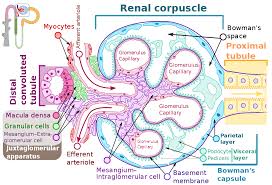
STORAGE PHASE

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 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.

Q3



JUXTAGLUMERULAR APPARATUS

The juxtaglomerular apparatus is a specialized structure formed by the distal convoluted tubule and the glomerular afferent arteriole. It is located near the vascular pole of the glomerulus and its main function is to regulate blood pressure and the filtration rate of the glomerulus. The macula densa is a collection of specialized epithelial cells in the distal convoluted tubule that detect sodium concentration of the fluid in the tubule. In response to elevated sodium, the macula densa cells trigger contraction of the afferent arteriole, reducing flow of blood to the glomerulus and the glomerular filtration rate. The juxtaglomerular cells, derived from smooth muscle cells, of the afferent arteriole secrete renin when blood pressure in the arteriole falls. Renin increases blood pressure via the renin-angiotensin-aldosterone system. Lacis cells, also called extraglomerular mesangial cells, are flat and elongated cells located near the macula densa. Their function remains unclear.

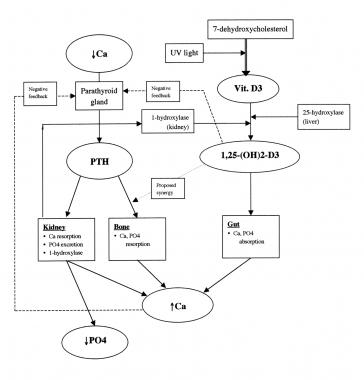
Q4

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.

Q5

Calcium homeostasis is a complex process involving the following 4 key components: serum calcium, serum phosphate, 1,25-dihydroxyvitamin D-3, and parathyroid hormone (PTH). More than 99% of the total body calcium is stored in bone in the form of phosphate and hydroxide salts, predominantly as hydroxyapatite. Normally, a very small portion of this calcium is available for exchange in the serum.

A schematic diagram of calcium homeostasis can be seen below.



### Parathyroid hormone (PTH)

Parathyroid hormone (PTH) is a polypeptide containing 84 amino acids that is secreted by the parathyroid glands after cleavage from preproparathyroid hormone (115 amino acids) to proparathyroid hormone (90 amino acids) to the mature hormone. The major target end organs for parathyroid hormone (PTH) action are the kidneys, skeletal system, and intestine.

The primary response to parathyroid hormone (PTH) by the kidney is to increase renal calcium resorption and phosphate excretion. In the kidney, parathyroid hormone (PTH) blocks reabsorption of phosphate in the proximal tubule while promoting calcium reabsorption in the ascending loop of Henle, distal tubule, and collecting tubule.

Parathyroid hormone (PTH) promotes absorption of calcium from the bone in 2 ways. The rapid phase brings about a rise in serum calcium within minutes and appears to occur at the level of the osteoblasts and osteocytes. Although it may seem counterintuitive that the cells that promote deposition of bone are involved in resorption, these cells form an interconnected network known as the osteocytic membrane overlying the bone matrix, but with a small layer of interposed fluid termed bone fluid. When parathyroid hormone (PTH) binds to receptors on these cells, the osteocytic membrane pumps calcium ions from the bone fluid into the extracellular fluid.

The slow phase of bone resorption occurs over several days and has 2 components. First, osteoclasts are activated to digest formed bone, and second, proliferation of osteoclasts occurs. Interestingly, mature osteoclasts lack parathyroid hormone (PTH) membrane receptors; activation and proliferation appear to be stimulated by cytokines released by activated osteoblasts and osteocytes or by differentiation of immature osteoclast precursors that possess parathyroid hormone (PTH) and vitamin D receptors.

The final important function of parathyroid hormone (PTH) is conversion of 25-hydroxyvitamin D to its most active metabolite, 1,25-dihydroxyvitamin D-3 [1,25-(OH)2 D3], by activation of the enzyme 1-hydroxylase in the proximal tubules of the kidney.

Feedback inhibition of parathyroid hormone (PTH) release occurs primarily by direct effect of calcium at the level of the parathyroid gland. Although not well elucidated, 1,25-(OH)2 D3 appears to exert a mild inhibitory effect on the parathyroid gland as well.

### Vitamin D

Vitamin D-3 (cholecalciferol) is formed in the skin when a cholesterol precursor, 7-dehydroxycholesterol, is exposed to ultraviolet light. Activation occurs when the substance undergoes 25-hydroxylation in the liver and 1-hydroxylation in the kidney.

The primary action of 1,25-(OH)2 D3 is to promote gut absorption of calcium by stimulating formation of calcium-binding protein within the intestinal epithelial cells. Vitamin D also promotes intestinal absorption of phosphate ion, although the exact mechanism is unclear. Negatively charged phosphate ion may passively flow through the intestinal cell because of flux of the positively charged calcium ion. In bone, vitamin D may play a synergistic role with parathyroid hormone (PTH) in stimulating osteoclast proliferation and bone resorption.

Compared to parathyroid hormone (PTH), vitamin D exerts a much slower regulatory effect on calcium balance.