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300l MBBS

Physiology Assignment

1. Discuss the role of kidney in glucose homeostasis

Along with the liver, the kidney has important role in ensuring the energy needs during fasting periods. Some of the important roles' incudes;

1. The organ has a vital role in absorbing the entire quantity of the filtered glucose.

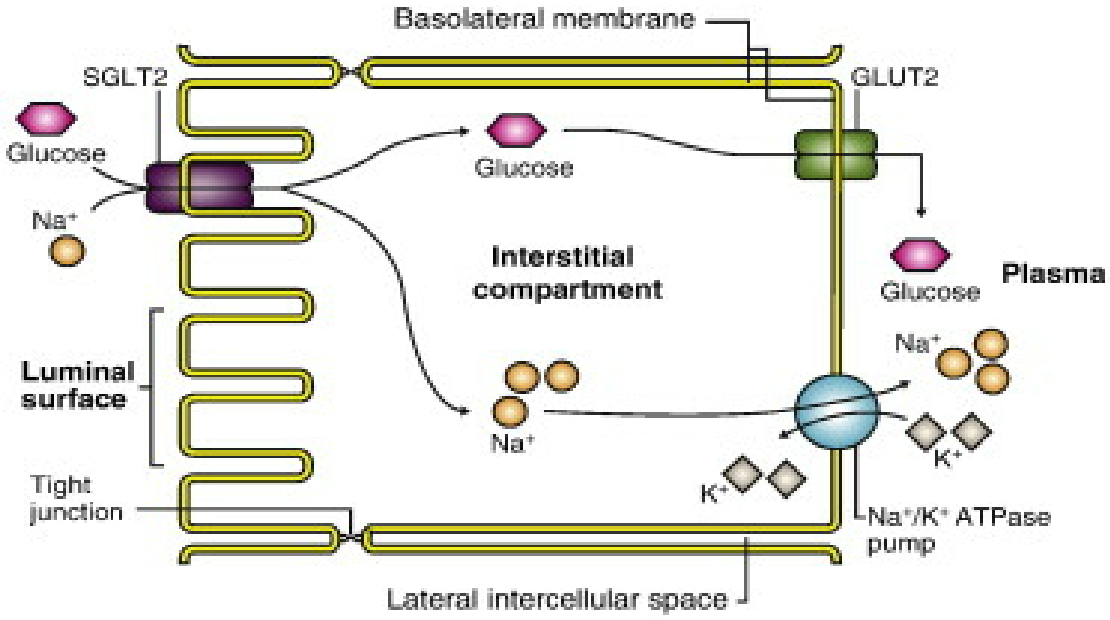
2. Having a glomerular filtration rate of 180 litres per day, it filters approximately 180 grams of glucose per day, bringing its contribution in maintaining normal fasting plasma glucose (FPG) levels.

3. The reabsorption of glucose is ensured by the sodium-glucose cotransporter (SGLT) 2, responsible for the reabsorption of 90% of glucose, and SGLT1 that reabsorbs the remaining glucose

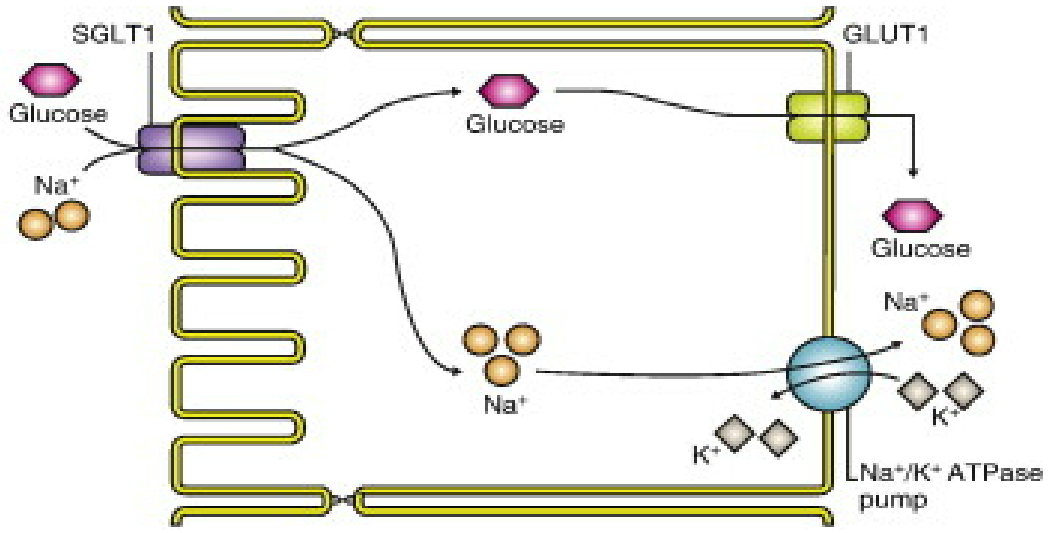
The plasma glucose concentration is determined by the amount of glucose synthesized, and the one removed fromthe circulation and metabolized. This concentration must be maintained within the relatively narrow range despite the wide daily fluctuations in glucose ingestion and glucose demands in various 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). Hyperglycaemia is also harmful because it can cause neurological events (including coma, seizures), cardiac arrhythmias and death.

Early portion of the proximal tubule



Distal proximal tubule



Diagramof kidney being involved in homeostasis.

The regulation of endogenous production of glucose is determined by hormonal and neural factors. In the acute phase, glucoregulatory mechanisms involve insulin, glucagon and catecholamine and they can affect 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 glycogenic substrates. Glucagon has no effect on the kidneys, but it stimulates glycogenolysis and gluconeogenesis in the liver. Catecholamine 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; renal gluconeogenesis, glycogenolysis, and glucose reabsorption.

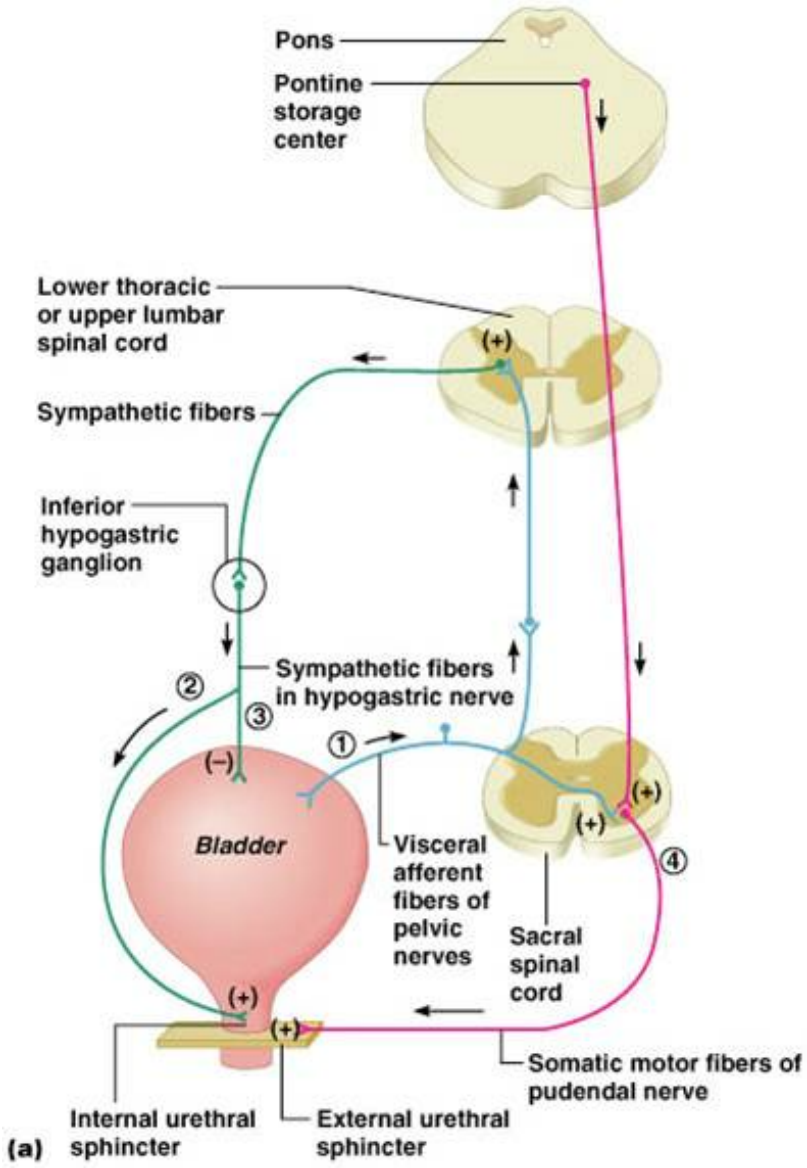
2. **Discuss the process of micturition**

Micturition is the process by which the urinary bladder empties when it becomes filled. Micturition or urination is the process of expelling urine from the bladder. This act is also known as VOIDING OF THE BLADDER. The excretory systemin 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 systemand the muscles of the bladder and urethra. The urinary bladder can store about 350-400ml of urine before it expels it out.

STAGES OF MICTURITION

The urinary bladder has two stages;

- Resting or filling stage: it is the phase of the bladder that the urine is transported fromthe kidneys via the ureters into the bladder. The ureters are thin muscular tubes that arise fromeach 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. The opening of the ureter into the urinary bladder is not guarded by any sphincter or muscles. Therefore, this oblique nature of opening prevents the urine fromre-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 urine.



Diagramillustrating process of Micturition

• 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. Both sphincters are in a contracted state during the filling stage.

PHYSIOLOGY OF MICTURITION

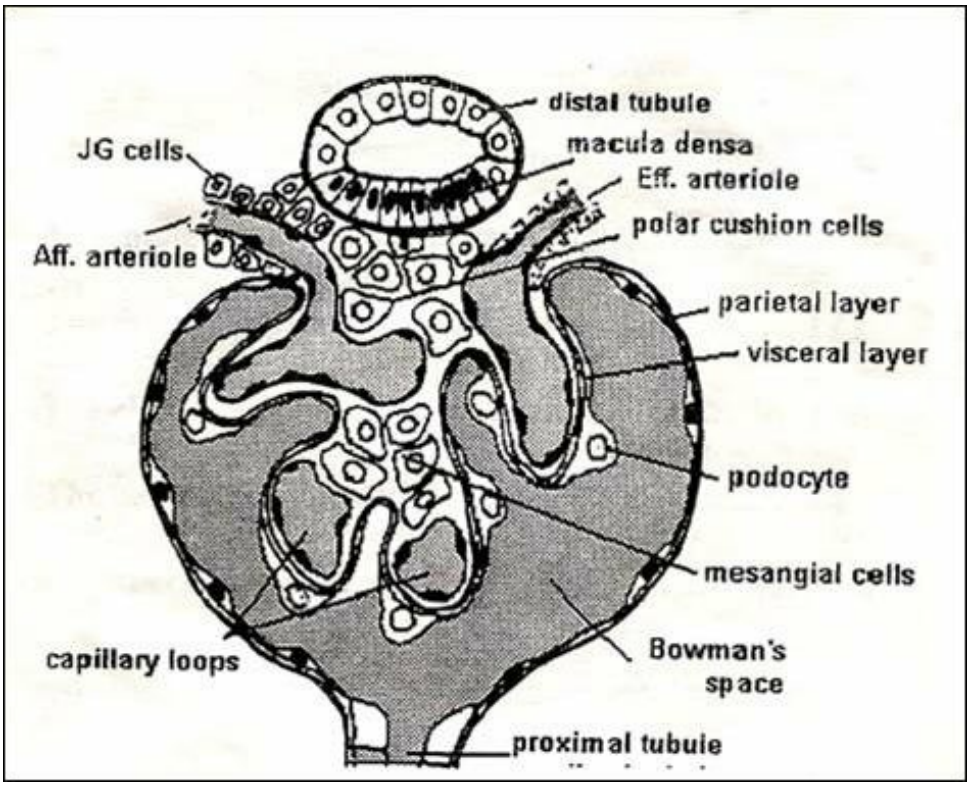
The process of micturition is governed by both the nervous and muscular systems. Within the nervous system, the process is governed by the autonomous nervous systemand the somatic system Once the urinary bladder reaches its maximumcapacity, the stretch receptors in the walls of the bladder send an impulse via the pelvic nerve to the brain via the spinal cord.

The micturition reflex is ultimately generated fromthe level of the spinal cord after it receives reflexes fromthe pontine region in the brain. Once the bladder and the urethra receive 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 on the bladder wall. This leads to complete emptying of the bladder.

Micturition is the process of emptying the bladder (urination). Micturition is under voluntary control, because the external sphincter of the bladder is skeletal muscle. However, the micturition reflex systemis under both sympathetic and parasympathetic control. While the bladder is filling, the sympathetic nerves relax the smooth muscle of the bladder wall, accommodating the urine, and contract the internal urethral sphincter smooth muscle. When the bladder becomes " full," mechanoreceptors signal a spinal reflex arc that stimulates parasympathetic contraction of the bladder (detrusor muscle) and relaxation of internal sphincters. The external urethral sphincter is skeletal muscle, and is voluntarily relaxed, allowing urination.

3. Explain juxtaglomerular apparatus

Juxtaglomerular (JG) apparatus as the name indicates (juxtanear) refers to the collection of specialised cells located very near to the glomerulus.



Diagramof Juxtaglomerular Apparatus

It forms the major component of renin– angiotensin– aldosterone system The JG apparatus comprises three types of cells

1. Juxtaglomerular cells
2. Macula densa cells
3. Mesangial cells.

1. Juxtaglomerular cells. JG cells are specialised myoepithelial (modified

vascular smooth muscle) cells located in the media of the afferent arteriole in the region of JG apparatus.

Characteristic features of JG cells are:

- They have well-developed Golgi apparatus and endoplasmic reticulum, abundant mitochondria and ribosomes.
- They synthesize, store and release an enzyme called renin. Renin is stored in the secretory granules of JG cells and, therefore, these are also called granular cell
- They act as baroreceptors (tension receptors) and respond to changes in the transmural pressure gradient between the afferent arterioles and the interstitium
- They are densely innervated by the sympathetic nerve fibres and release their renin content in response to the sympathetic discharge.
- As these cells act as vascular volume receptors, they monitor renal perfusion pressure and are stimulated by hypovolaemia or decreased renal perfusion pressure.

2. Macula densa cells. Macula densa cells refer to the specialised renal tubular epithelial cells of a short segment of the thick ascending limb of loop of Henle which passes between the afferent and efferent arterioles supplying its glomerulus of origin.

Characteristic features of macula densa cells are:

- They are not well adapted for reabsorption.
- They are not innervated.
- These cells are in direct contact with the mesangial cells and in close contact with the JG cells.

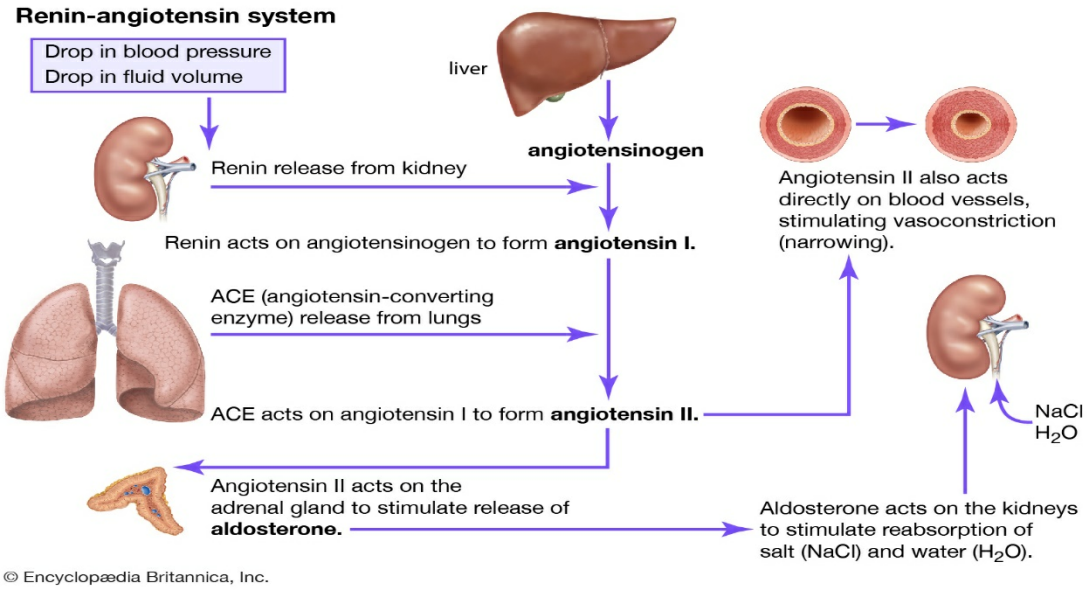
- They act as chemoreceptors and are stimulated by decreased NaCl concentration and thereby causing increased renin release.

3. Mesangial cells: Mesangial cells or lacis cells are the interstitial cells of the JG apparatus.

Characteristic features of these cells are:

- They are in contact with both the macula densa cells (on one side) and JG cells (on the other side).
- Functionally, these cells possibly relay the signals frommacula densa to the granular cells after modulating the signals. In this way, a decreased intraluminal Na^+ load, Cl^- load, or both in the region of macula densa stimulates the JG cells to secrete renin.
- They also show granulation to secrete renin in conditions of extreme hyperactivity.
- They also secrete various substances and take up immune complexes.

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



Diagramshowing the Renin-Angiotensin system

The kidneys play a central role in the regulation of arterial blood pressure. A large body of experimental and physiological evidence indicates that the 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 sodiumexcretion; a process known as pressure natriuretic, and influences the activity of various vasoactive systems such as the renin-angiotensin-aldosterone (RAS)system

The kidney influences blood pressure by:

1. Causing the arteries and veins to constrict
2. Increasing the circulating blood volume

Consistent and long – termcontrol of blood pressure is determined by the renin-angiotensin system When blood flows through the kidneys decrease the process of filtration decreases and less urine is formed. This decrease in urinary output preserves blood volume so that it does not decrease further, this is very important to maintain blood pressure during severe haemorrhage

or other types of dehydration. The kidneys are also involved in the renin angiotensin mechanism When blood pressure decreases, there will be a drop in renal blood flow or a decrease concentration of Na^+, this will stimulate volume receptors found in Juxtaglomerular apparatus of the kidney to secrete the renin. Renin initiates a series of reactions that result in the formation of angiotensin II. Angiotensin II causes vasoconstriction and stimulates secretion of aldosterone by adrenal cortex, both of which will increase blood pressure.

5. Discuss the role of the kidney in Calciumhomeostasis

The kidney is critically important in calciumhomeostasis.

The maintenance of calciumhomeostasis is very important because calciumis 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. Total body calciumin the adult human is about 1-2kg and 99% of total calciumexists in bone.

About 50% of plasma calciumis freely filtered through the renal glomerulus, and 99% of the filtered calciumis actually reabsorbed along renal tubules. The excreted calciumin the final urine is about 200mg per day in an adult person with an average diet. Several factors are involved in the regulation of calciumin renal tubules. PTH (parathyroid hormone) and activated vitamin D enhance calciumreabsorption in the thick ascending limb, distal convoluted tubule and/or connecting tubule, and estrogen promotes calciumabsorption in the distal convoluted tubule and connecting tubule.

Acidosis contributes to hypercalciuria by reducing calciumreabsorption in the proximal tubule and distal convoluted tubule, and alkalosis vice versa. Diuretics like thiazide and furosemide also alter calciumabsorption in the renal tubules; thiazide promotes calciumreabsorption and furosemide inhibits it. Plasma calciumitself controls renal calciumabsorption through altered PTH secretion as well as via binding to the calciumsensing receptor (CaSR) in the TAL.

Only about 50 percent of the plasma calciumis ionized, with the remainder being bound to the plasma proteins or completed with anions such as phosphate. Therefore, only about 50 percent of the plasma calciumcan be filtered at the glomerulus. Normally, about 99 percent of the filtered calcium is reabsorbed by the tubules, with only about 1 percent of the filtered calciumbeing excreted. About 65 percent of the filtered calciumis reabsorbed in the proximal tubule, 25 to 30 percent is reabsorbed in the loop of Henle, and 4 to 9 percent is reabsorbed in the distal and collecting tubules. This pattern of reabsorption is similar to that for sodium

As is true with the other ions, calciumexcretion is adjusted to meet the body's needs. With an increase in calciumintake, there is also increased renal calciumexcretion, although much of the increase of calciumintake is eliminated in the faeces. With calciumdepletion, calciumexcretion by the kidneys decreases as a result of enhanced tubular reabsorption.

PROXIMAL TUBULAR CALCIUMREABSORPTION

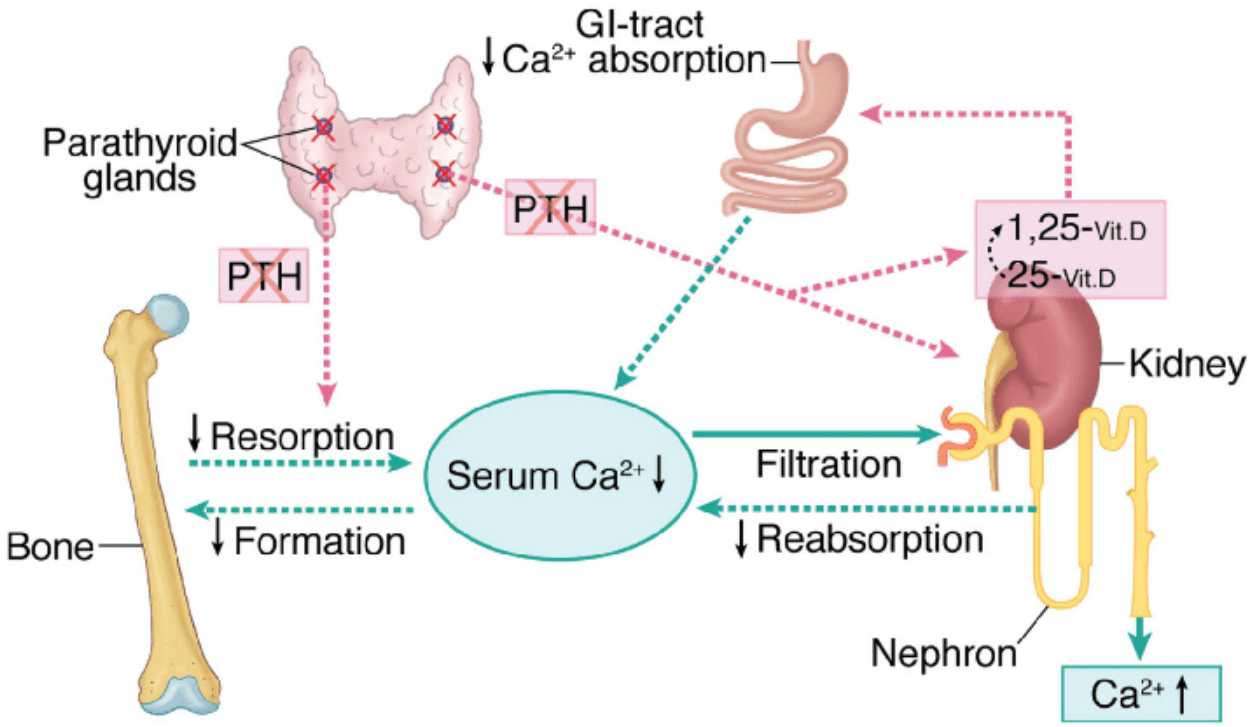
Most of the calciumreabsorption in the proximal tubule occurs through the paracellular pathway, dissolved in water and carried with the reabsorbed fluid as it flows between the cells. Only about 20%of proximal tubular calcium reabsorption occurs through the transcellular pathway in two steps:

1.Calciumdiffuses fromthe tubular lumen into the cell down an electrochemical gradient due to the much higher concentration of calciumin the tubular lumen, compared with the epithelial cell cytoplasm, and because the cell interior has a negative relative to the tubular lumen;

2. Calciumexits the cell across the basolateral membrane by a calcium-ATPase pump and by sodium-calciumcounter-transporter.

LOOP OF HENLE AND DISTAL TUBULE CALCIUMREABSORPTION

In the loop of Henle, calciumreabsorption is restricted to the thick ascending limb. Approximately 50% of calciumreabsorption in the thick ascending limb occurs through the paracellular route by passive diffusion due to the slight positive charge of the tubular lumen relative to the interstitial fluid. The remaining 50% of calciumreabsorption in the thick ascending limb occurs through the transcellular pathway, a process stimulated by parathyroid hormone (PTH)



Diagramof Kidney involved in Calciumhomeostasis.

In the distal tubule, calciumreabsorption occurs almost entirely by active transport through the cell membrane. The mechanismfor this active transport is similar to that in the proximal tubule and thick ascending limb and involves diffusion across the luminal membrane through calciumchannels and exit across the basolateral membrane by a calcium-ATPase pump, as well as a sodium-calciumcounter transport mechanism In this segment, as well as in the loops of Henle, PTH stimulates calciumreabsorption. Vitamin D (Calcitrol) and calcitonin also stimulate calciumreabsorption in the thick ascending limb of Henle's loop and in the distal tubule, although these hormones are not as important quantitatively as PTH in reducing renal calciumexcretion.

Under normal blood calciumconcentrations, almost all of the calciumthat

enters glomerular filtrate is reabsorbed fromthe tubular systemback into blood, which preserves blood calciumlevel. Vitamin D and parathyroid hormone (PTH) helps regulates how much calciumthe kidneys elimate.Healthy kidney turns vitamin D into an active hormone(Calcitrol), which helps increases calciumabsorption fromthe intestines into the blood.