NAME: HALILU AMINA LAWAL

MATRIC NO: 17/MHS01/139

DEPARTMENT: MBBS

LEVEL: 300

COURSE: RENAL PHYSIOLOGY

ASSIGNMENT

Q1. Discuss the role of kidney in glucose homeostasis?

1. Along with the liver, the kidney has an important role in ensuring the energy needs during fasting periods. This organ has a vital role in absorbing the entire quantity of the filtered glucose. Having a glomerular filtration rate of 180 liters per day, it filters approximately 180 grams of glucose per day, bringing its contribution in maintaining normal fasting plasma glucose (FPG) levels. 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.

Despite the large amount of data regarding the implication of the kidneys in glucose homeostasis, this organ is often overlooked as a key player in glucose metabolism. But the awareness of the renal mechanisms of glucose control is likely to increase due to the development of new types of glucose-lowering drugs that target this metabolic pathway.

The first researchers in this field, Bergman and Drury brought the first clues about the involvement of the kidney in glucose homeostasis in 1938. They used the glucose clamp technique in order to maintain euglycemia in two groups of rabbits – one functionally hepatectomized and another one functionally hepatectomized and nephrectomized. In the group of hepatectomized and nephrectomized rabbits, the amount of glucose requested in order to maintain euglycemia was very high compared to the one required by the other group, These data led to the conclusion that the kidneys are an important source of plasma glucose

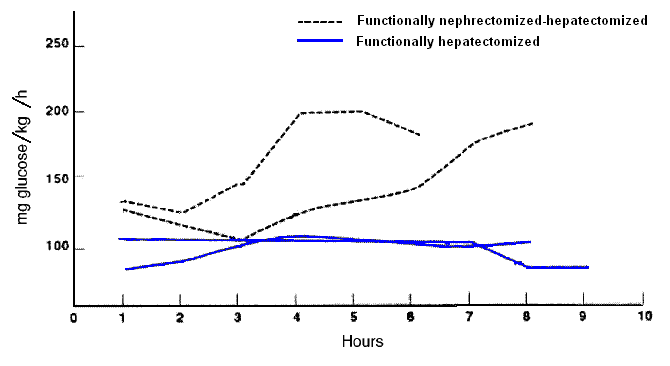


Figure 1.

Effect of nephrectomy on glucose needs for maintaining euglycemia in hepatectomized rabbits

A few years later, the study was reproduced by Reinecke in rats. He also determined the arteriorenal venous glucose concentrations in the hepatectomized rats. He found that the glucose levels in renal vein exceeded the arterial levels when the animals became hypoglycemic proving that, under these conditions, the kidneys can release glucose into the circulation.

In other experiments, Teng proved that the renal cortex of the animal models with diabetes released glucose at a very high rate, but treatment of these animals with insulin could reverse this effect. A few years later, in 1960, Landau was able to prove, having a similar model, that gluconeogenesis from pyruvate was increased by the diabetic kidney.

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 [4]. 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]. 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.

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.
* 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. The glomeruli filter from plasma approximately 180 grams of D-glucose per day, all of which is reabsorbed through glucose transporter proteins that are present in cell membranes within the proximal tubules. If the capacity of these transporters is exceeded, glucose appears in the urine.

The process of renal glucose reabsorption is mediated by active (sodium-coupled glucose cotransporters) and passive (glucose transporters) transporters. In hyperglycemia, the kidneys may play an exacerbating role by reabsorbing excess glucose, ultimately contributing to chronic hyperglycemia, which in turn contributes to chronic glycemic burden and the risk of microvascular consequences.

The kidneys are essentially designed to filter large quantities of plasma, reabsorb substances that the body must conserve, and secrete substances that must be eliminated. These basic functions are critical to regulation of fluid and electrolyte balance, body fluid osmolality, acid-based balance, excretion of metabolic waste and foreign chemicals, arterial pressure, hormone secretion, and, most relevant to this discussion, glucose balance. The 2 kidneys produce a total of approximately 120 mL/min of ultra filtrate, yet only 1 mL/min of urine is produced. The basic urine-forming unit of the kidney is the nephron, which serves to filter water and small solutes from plasma and reabsorb electrolytes, amino acids, glucose, and protein. The nephron, of which there are approximately 1 million in each kidney, consists of a filtering apparatus (the glomerulus) that is connected to a long tubular portion that reabsorbs and conditions the glomerular ultra filtrate. Fluid filtered from the glomerular capillaries flows into the tubular portion, which is made up of a proximal tubule, the Loop of Henle, and the distal tubule, all of which assist in reabsorbing essential substances and converting filtered fluid into urine.

Evaluation of renal function is an important part of care, and with that, creatinine clearance (CrCl) or glomerular filtration rate (GFR), most frequently estimated (eGFR), are considered most useful in determining the degree of renal insufficiency and the stage of chronic kidney disease in accordance with the National Kidney Foundation classification system. Since alterations in all renal functions (i.e., filtration, secretion, reabsorption, endocrine and metabolic function) have been associated primarily with GFR, this quantitative index may be used to measure any functional changes that result from kidney-related disease progression, therapeutic intervention, or toxic insult.

Mechanisms of Glucose Homeostasis

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 macrovascular and microvascular complications, such as cardiovascular disease, nephropathy, neuropathy, and retinopathy. Hypoglycemia, on the other hand, may lead to a myriad of central nervous system complications (e.g., confusion, behavioral changes, seizures, loss of consciousness, and even death), since the brain is the body’s largest consumer of glucose in the fasting or “postabsorptive” state. 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.

As alluded to previously, the kidneys are capable of synthesizing and secreting many important hormones (e.g., renin, prostaglandins, kinins, erythropoietin) and are involved in a wide variety of metabolic processes such as activation of vitamin D3, gluconeogenesis, and metabolism of numerous endogenous compounds (e.g., insulin, steroids). 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.

Glycogenolysis and Gluconeogenesis

s

Renal release of glucose into the circulation is the result of glycogenolysis and gluconeogenesis. Glycogenolysis involves the breakdown of glycogen to glucose-6-phosphate from precursors (e.g., lactate, glycerol, amino acids) and its subsequent hydrolysis (via glucose-6-phosphatase) to free glucose. Conversely, gluconeogenesis involves formation of glucose-6-phosphate from those same precursors and subsequent conversion to free glucose. Interestingly, the liver and skeletal muscles contain most of the body’s glycogen stores, but only the liver contains glucose-6-phosphatase. As such, the breakdown of hepatic glycogen leads to release of glucose, whereas the breakdown of muscle glycogen leads to release of lactate. Lactate (generated via glycolysis of glucose by blood cells, the renal medulla, and other tissues) may be absorbed by organs and reformed into glucose.2

With regard to glucose utilization, the kidney may be perceived as 2 separate organs, with glucose utilization occurring predominantly in the renal medulla and glucose release limited to the renal cortex. These activities are separated as a result of differences in the distribution of various enzymes along the nephron. To this point, cells in the renal medulla (which, like the brain, are obligate users of glucose) have significant glucose-phosphorylating and glycolytic enzyme activity, and can therefore phosphorylate and accumulate glycogen. However, since these cells lack glucose-6-phosphatase and other gluconeogenic enzymes, they cannot release free glucose into the circulation. On the other hand, renal cortex cells do possess gluconeogenic enzymes (including glucose-6-phosphatase), and therefore can make and release glucose into the circulation. But because these cells have little phosphorylating capacity, they cannot synthesize glycogen.

The magnitude of renal glucose release in humans is somewhat unclear, with inconclusive evidence regarding the contribution of the kidneys to total body gluconeogenesis. One analysis of 10 published studies concluded that the renal contribution to total body glucose release in the postabsorptive state is approximately 20%. Based on the assumption that gluconeogenesis accounts for approximately half of all circulatory glucose release during the fasting state, renal gluconeogenesis is projected, although not conclusively proven, to potentially be responsible for approximately 40% of all gluconeogenesis.2 Taking into consideration the potential contribution of renal gluconeogenesis, the kidneys appear to play a substantial role in overall glucose release in normal as well as pathophysiologic states (e.g., hepatic insufficiency, counterregulation of hypoglycemia). To this point, evidence suggests that in patients with T2DM, renal glucose release is increased in both the postprandial and postabsorptive states, implicating the kidneys’ contribution to the hyperglycemia that characterizes this condition. Insulin resistance (known to suppress renal/hepatic insulin release), increased free fatty acid (FFA) concentrations (FFAs stimulate gluconeogenesis), greater availability of gluconeogenic precursors, and increased glycogenolysis.3 Again, it is clear that there is a renal contribution to glucose output in the body, but the actual contribution in individual patients with T2DM is still controversial.

Glucose Reabsorption

In addition to their important role in gluconeogenesis, the kidneys contribute to glucose homeostasis by filtering and reabsorbing glucose. Under normal conditions, the kidneys retrieve as much glucose as possible, rendering the urine virtually glucose free. The glomeruli filter from plasma approximately 180 grams of D-glucose per day, all of which is reabsorbed through glucose transporter proteins that are present in cell membranes within the proximal tubules.4 If the capacity of these transporters is exceeded, glucose appears in the urine. This maximum capacity, known as the tubular maximum for glucose (TmG), ranges from 260 to 350 mg/min/1.73 m2 in healthy adults and children, and corresponds to a plasma glucose level of approximately 200 mg/dL.4 Once the TmG (the threshold) is reached and transporters are unable to reabsorb all the glucose (as in T2DM), glucosuria ocurrs.7,15 The correlation between the degree of hyperglycemia and degree of glucosuria becomes linear when blood glucose concentrations have increased beyond a threshold.4 It should be noted that slight differences between individual nephrons and the imprecise nature of biological systems may alter this linear concentration/reabsorption curve, as indicated by a splay from the theoretical as the TmG is approached.4 As such, glucosuria may potentially develop before the expected TmG is reached. Glucosuria may also occur at lower plasma glucose concentrations in certain conditions of hyperfiltration (e.g., pregnancy), but as a consequence of hyperfiltration rather than significant hyperglycemia.

Q2. Discuss the process of micturition.

Micturition is also called urination, which is a process by which urine is expelled from the bladder. This act is known as voiding of the bladder. The excretory systems in humans include 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, the muscles 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

In this stage, the urine is transported from the kidneys to the urinary bladder via the ureters. The ureters are thin muscular tubes that arise each of the kidneys and extend downwards where they enter the bladder obliquely. The opening of the ureter into the urinary bladder is not guarded by any sphincter or muscle, therefore the oblique nature of opening prevents the urine from re-entering the ureters. As the same time, the main muscle of the urinary bladder, the detrusor muscle, is relaxing allowing the bladder to distend and accommodate more urine.

Urine is continuously formed by nephrons and it flows into the urinary bladder drop by drop through ureters. When urine collects in the pelvis of ureter, the contraction sets up in the pelvis. This contraction is transmitted through the rest of the ureter in the form of peristaltic wave up to trigone of the urinary bladder. Peristaltic wave usually travels at a velocity of 3 cm/sec. It develops at a frequency of 1 to 5 per minute. The peristaltic wave moves the urine into the bladder. After leaving the kidney, the direction of the ureter is initially downward and outward. Then, it turns horizontally before entering the bladder. At the entrance of ureters into the urinary bladder, a valvular arrangement is present. When peristaltic wave pushes the urine towards the bladder, the valve opens towards the bladder. The position of the ureter and the valvular arrangement at the end of ureter prevent the backflow of urine when the detrusor muscle contracts.

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 starts to contract when 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 is a skeletal muscle. The emptying phase displays a coordinated relaxation of the inner and outer urethral sphincters, under sympathetic and somatic regulation respectively, with strong contractions of the detrusor muscle due to parasympathetic impulses. Micturition is thus characterized by:

* Relaxation of the striated sphincter (somatic innervation)
* Relaxation of the smooth muscle sphincter and opening of the bladder neck (sympathetic innervation)
* Detrusor contraction (parasympathetic innervation)

The distension of the urinary bladder wall causes wall tension to rise very slightly. However, when the bladder is almost full, at about 300-400ml, the inherent contractility of the detrusors causes reflex contractions to occur, which are less powerful than the voiding contraction. Afferent firing frequency increases with filling, but cortical control still overrides the micturition reflex until voluntary voiding is determined upon. During micturition, urinary flow is assisted by additional detrusor contractions and external sphincter relaxation which further lowers resistance to the passage of urine. The abdominal wall and pelvic floor musculature also participates by increasing the force on the bladder to help achieve complete emptying. The act of micturition is an autonomic reflex at the level of the spinal cord. This reflex also helps to complete micturition when the act is voluntarily initiated, or when it follows a period of inhibition by the brain, by relaxing the external sphincter.

Q3. Explain juxtaglomerular apparatus.

Juxtaglomerular apparatus is also known as the juxtaglomerular complex. These apparatus is a structure in the kidney that regulates the function of each nephron, the functional units of the kidney. The juxtaglomerular apparatus consists of three types of structures, namely;

1. The macula densa, a part of the distal convoluted tubule of the same nephron.
2. Juxtaglomerular cells (also known as granular cells) which secrete renin.
3. Extraglomerular mesengial cells.
4. MACULA DENSA: Macula densa is the end portion of thick ascending segment before it opens into distal convoluted tubule. It is situated between afferent and efferent arterioles of the same nephron but it is closer to afferent arteriole. Macula densa is formed by tightly packed cuboidal epithelial cells. Macula densa plays an important role in tubuloglomerular feedback mechanism. It also secretes thromboxane A2.
5. JUXTAGLOMERULAR CELLS: Juxtaglomerular cells are specialized smooth cells situated in the wall of the afferent arteriole just before it enters the Bowman’s capsule. These smooth muscle cells are mostly present in tunica media and tunica adventitia of the wall of the afferent arteriole. Juxtaglomerular cells are also called granular cells because of the presence of secretary granules in their cytoplasm. Juxtaglomerular cells form a thick cuff called polar cushion or polkissen around the afferent arteriole before it enters the Bowman’s capsule.
6. Extraglomerular Mesengial Cells: Extraglomerular mesengial cells are situated in the triangular region bound by afferent arteriole, efferent arteriole and macula densa. These cells are also called agranular cells, lacis cells or Goormaghtigh cells. These cells secrete prostaglandin and cytokines.

Besides extraglomerular mesengial cells, there is another type of mesengial cells situated in between glomerular capillaries called glomerular mesengial cells. Glomerular mesengial cells support the glomerular capillary loops by surrounding the capillaries in the form of a cellular network. These cells play a role in regulating the glomerular filtration by their contractile property. Glomerular mesengial cells are phagocytic in nature. These cells also secrete glomerular interstitial matrix, prostaglandins and cytokines.

FUNCTIONS OF JUXTAGLOMERULAR APPARATUS:

The main function of juxtaglomerular apparatus is the secretion of hormones. It also regulates the glomerular blood flow and glomerular filtration rate. The two hormones secreted by juxtaglomerular are:

1. Renin
2. Prostaglandin

RENIN: Renin is secreted by juxtaglomerular cells. Renin is a peptide with 340 amino acids. Along with angiotensins, renin forms renin-angiotensin system, which is a hormone system that plays a role in the maintenance of blood pressure. Secretion of renin is stimulated by four factors:

1. Fall in arterial blood pressure
2. Reduction in the ECF volume.
3. Increased sympathetic activity
4. Decreased load of sodium and chloride in macula densa.

RENIN-ANGIOTENSIN SYSTEM:

When renin is released into the blood, it acts on a specific plasma protein called angiotensinogen or renin sustrate. By the action of renin, the angiotensinogen is converted into a decapeptide called angiotensin I. Angiotensin I is converted into angiotensin II, which is an octapeptide by the activity of angiotensin-converting enzyme (ACE) secreted from the lungs. Most of the conversion of angiotensin I to II takes place in the lungs. Angiotensin has a short life of 1 to 2 minutes. Then it is rapidly degraded into a heptapeptide called angiotensin III by angiotensinases, which are present in RBCs and vascular beds in many tissues. Angiotensin III is converted into angiotensin IV, which is a hexapeptide.

ANGIOTENSIN I: is physiologically inactive, therefore it serves as precursors of angiotensin II.

ANGIOTENSIN II: is the most active form. It acts on:

On blood vessels:

* Increases arterial blood pressure by directly acting on the blood vessels and vasoconstriction.
* It also increases blood pressure indirectly by increasing the release of noradrenaline from post ganglionic sympathetic fibres.

On Adrenal Cortex: it stimulates zona glomerulosa of adrenal cortex to secrete aldosterone. Aldosterone acts on renal tubules and increases retention of sodium, which is responsible for elevation of blood pressure.

On Kidney: angiotensin II regulates glomerular filtration rate by two ways:

* It constricts the efferent arteriole, which causes decrease in filtration after initial increase.
* It contracts the glomerular mesengial cells leading to decrease in surface area of glomerular capillaries and filtration.

Angiotensin II also increases sodium reabsorption from renal tubules.

On Brain: Angiotensin II inhibits baroreceptor reflex and thereby indirectly increases the blood pressure. It increase water intake by stimulating thirst center. It also increases the secretion of corticotrophin-releasing hormone and anti diuretic hormone from hypothalamus.

ANGIOTENSIN III: Angiotensin III increases the blood pressure and stimulates aldosterone secretion from adrenal cortex. It has 100% adrenocortical stimulating activity and 40% vasopressor activity of angiotensin II.

ANGIOTENSIN IV: It also has adrenocortical-stimulating and vasopressor activities.

PROSTAGLANDIN: Extraglomerular mesengial cells secrete prostaglandin. It is also secreted by interstitial cells of medulla called type I medullary interstitial cells.

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

The kidney plays a central role in the regulation of arterial blood pressure. Evidences indicate the renal control of extracellular volume and renal perfusion pressure are closely involved in maintaining the arterial circulation and blood pressure. A key modulator of blood viscosity is the renin-angiotensin system or renin-angiotensin aldosterone system, a hormone system that regulates blood pressure and water balance. The blood pressure in the body depends on:

* 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 get stretched by the inflowing blood into the ventricles.
* The degree at which the arteries and arterioles constrict- increasing 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:

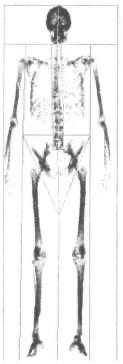
Causing the arteries and veins to constrict and by increasing the circulating blood volume. Specialized cells called macula densa sense the Na in the filtrate, while arterial cells (juxtaglomerular cells) sense the blood pressure. When the blood pressure drops, the amount of filtered Na also drops. The arterials cells sense the drop in the blood pressure and the decrease in Na concentration is relayed to them by the macula densa cells. The juxtaglomerular cells then secrete an enzyme called renin. These renin converts angiotensin-1. Angoitensin-1 is therefore converted to angiotensin-2 by ACE. Angiotensin-2 cause blood vessels to contract- the increased blood vessels constriction elevate the blood pressure. When the volume of blood is low, arterials cells in the kidney secrete renin directly into circulation. Plasma renin then carries out the conversion of angiotensinogen released by the liver to angiotensin-1. Angiotensin-1 is converted to angiotensin-2. Angiotensin-2, 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 renin-angiotensin aldosterone system is too active, blood pressure will be too high.

Q5. Discuss the role of kidney in calcium homeostasis.

Hypocalcemia refers to low blood calcium concentration. Clinical signs of this disorder reflect increased neuromuscular excitability and include muscle spasms, tetany and cardiac dysfunction.

Hypercalcemia indicates a concentration of blood calcium higher than normal. The normal concentration of calcium and phosphate in blood and extracellular fluid is near the saturation point; elevations can lead to diffuse precipitation of calcium phosphate in tissues, leading to widespread organ dysfunction and damage.

Preventing hypercalcemia and hypocalcemia is largely the result of robust endocrine control systems.



Body Distribution of Calcium and Phosphate

There are three major pools of calcium in the body:

* Intracellular calcium:

A large majority of calcium within cells is sequestered in mitochondria and endoplasmic reticulum. Intracellular free calcium concentrations fluctuate greatly, from roughly 100 nM to greater than 1 uM, due to release from cellular stores or influx from extracellular fluid. These fluctuations are integral to calcium's role in intracellular signaling, enzyme activation and muscle contractions.

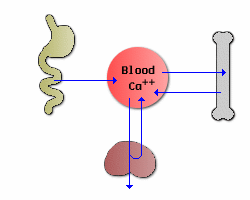
* Calcium in blood and extracellular fluid:

Roughly half of the calcium in blood is bound to proteins. The concentration of ionized calcium in this compartment is normally almost invariant at approximately 1 mM, or 10,000 times the basal concentration of free calcium within cells. Also, the concentration of phosphorus in blood is essentially identical to that of calcium.

* Bone calcium:

A vast majority of body calcium is in bone. Within bone, 99% of the calcium is tied up in the mineral phase, but the remaining 1% is in a pool that can rapidly exchange with extracellular calcium.

As with calcium, the majority of body phosphate (approximately 85%) is present in the mineral phase of bone. The remainder of body phosphate is present in a variety of inorganic and organic compounds distributed within both intracellular and extracellular compartments. Normal blood concentrations of phosphate are very similar to calcium.



Fluxes of Calcium and Phosphate

Maintaining constant concentrations of calcium in blood requires frequent adjustments, which can be described as fluxes of calcium between blood and other body compartments. Three organs participate in supplying calcium to blood and removing it from blood when necessary:

The small intestine is the site where dietary calcium is absorbed. Importantly, efficient absorption of calcium in the small intestine is dependent on expression of a calcium-binding protein in epithelial cells.

Bone serves as a vast reservoir of calcium. Stimulating net resorption of bone mineral releases calcium and phosphate into blood, and suppressing this effect allows calcium to be deposited in bone.

The kidney is critically 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.

Hormonal Control Systems

Maintaining normal blood calcium and phosphorus concentrations is managed through the concerted action of three hormones that control fluxes of calcium in and out of blood and extracellular fluid:

Parathyroid hormone serves to increase blood concentrations of calcium. Mechanistically, parathyroid hormone preserves blood calcium by several major effects:

Stimulates production of the biologically-active form of vitamin D within the kidney.

Facilitates mobilization of calcium and phosphate from bone. To prevent detrimental increases in phosphate, parathyroid hormone also has a potent effect on the kidney to eliminate phosphate (phosphaturic effect).

Maximizes tubular reabsorption of calcium within the kidney. This activity results in minimal losses of calcium in urine.

Vitamin D acts also to increase blood concentrations of calcium. It is generated through the activity of parathyroid hormone within the kidney. Far and away the most important effect of vitamin D is to facilitate absorption of calcium from the small intestine. In concert with parathyroid hormone, vitamin D also enhances fluxes of calcium out of bone.

Calcitonin is a hormone that functions to reduce blood calcium levels. It is secreted in response to hypercalcemia and has at least two effects:

Suppression of renal tubular reabsorption of calcium. In other words, calcitonin enhances excretion of calcium into urine.

Inhibition of bone resorption, which would minimize fluxes of calcium from bone into blood.

Although calcitonin has significant calcium-lowing effects in some species, it appears to have a minimal influence on blood calcium levels in humans.

A useful way of looking at how hormones affect tissues to preserve calcium homeostasis is to examine the effects of calcium deprivation and calcium loading. The following table summarizes body responses to conditions that would otherwise lead to serious imbalances in calcium and phosphate levels in blood.

