UNIT 7 PHYSIOLOGY OF RENAL SYSTEM

Structure

7.1 INTRODUCTION

In the last unit we learnt about the gastrointestinal tract. Now in this unit, we will deal with the physiology of the renal system including an in-depth study and understanding of the key organs of the excretory system.

The body excretes substances which are unwanted and harmful to the body through urine, faeces, sweat etc. The excretory system consists of organs like kidneys, ureters, urinary bladder and urethra.

Kidneys are *a pair of bean-shaped organs in the dorsal region of the vertebrate abdominal cavity*, important to the health of an individual. Their function is to form urine and to pass urine to the ureters and bladder for excretion. In doing this function, several regulatory functions are carried out such as maintenance of water and electrolyte balance, regulation of acid-base concentration and filtration and disposal of metabolic waste materials (which are then excreted as urine). The discussion on kidneys, in this unit, will include mechanism of formation of urine and the regulation of volume of body fluids. It will also focus on structure, functions (both normal and abnormal) and certain medical aspects related to the abnormal functioning, such as dialysis and renal transplant.

Besides kidneys other excretory organs i.e. ureters, urinary bladder and urethra also have a specific role in storing and passage of urine outside the body. What are the functions of these organs? A detailed discussion is presented in this unit.

Objectives

After studying this unit, you will be able to:

- illustrate the structure and describe the functions of the various organs of the urinary system,

- discuss the mechanism of urine formation,
- explain the non-excretory functions of the kidneys, and
- describe the medical aspects related to the abnormal or non-functioning of the kidneys, such as dialysis and renal transplant.

7.2 ORGANS OF THE URINARY SYSTEM

Look at Figure 7.1. It illustrates the organs of the urinary system. As is evident, the organs of the urinary system consist of 2 kidneys, 2 ureters, 1 urinary bladder and a urethra, through which the urine is discharged from the urinary bladder to the exterior.

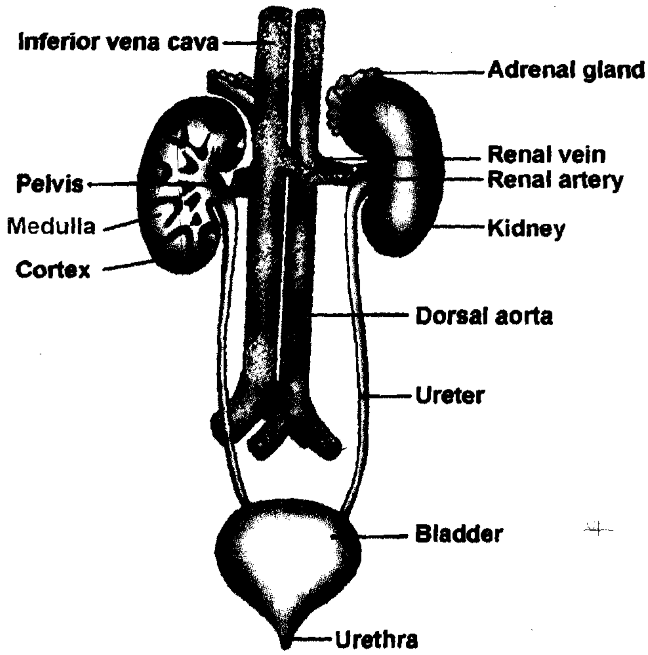

Figure 7.1: Organs of the urinary system

As you will read, you will learn that the kidneys form urine, the ureters thereby convey the urine from the kidneys to the urinary bladder, where the urine is temporarily stored. Finally, from the urethra the urine is discharged to the exterior. The complex function performed by each of these organs along with the structure is discussed in the subsequent sections. We shall start our study of the urinary system by getting to know the structure and functions of the kidney.

7.3 KIDNEY: STRUCTURE AND FUNCTIONS

Looking at Figure 7.1, you would have got a clear idea as to where the kidneys are situated. Yes, the kidneys are located in the posterior part of the abdomen, one on each side of the vertebral column. Vertebral column, as you may already know, is *a column formed of a series of bones, called vertebrae forming the axis of the skeleton and protecting the spinal cord.* The kidneys are described as the bean-shaped organs surrounded by the renal fat. Let us study about the structure of kidneys in detail.

7.3.1 Gross and Microscopic Structure of Kidney and Nephron

Our bean shaped kidneys are enclosed in capsule. If we were to cut a kidney in half, as shown in Figure 7.2, the internal structures of the kidney would be exposed. Underlying the capsule you will find the external part of the kidney known as *cortex.* The inner part is known as *medulla*. Medial to the medulla is a fissure, which is known as the *hilum* of the kidney. *Hilum*, in general, is that part of a kidney where the blood vessels and nerves enter. At the hilum, the renal artery and renal nerves enter the kidney and the renal vein leaves the kidney as can be seen in Figure 7.2.

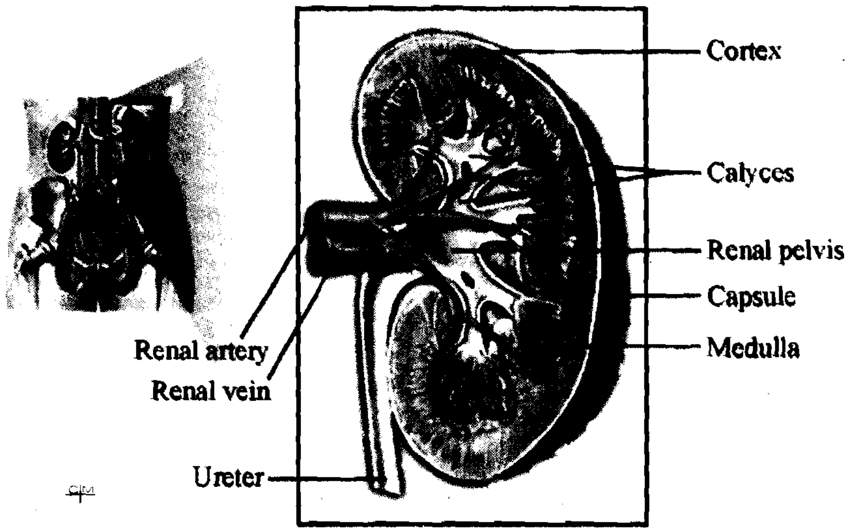

Figure 7.2: Parts of the kidney

To further understand how our kidneys work (to eliminate the waste materials), let us have a look at the microscopic structure of the kidneys. Here, we shall focus on the basic unit of kidney i.e. the nephron which is responsible for the kidney's functioning.

Look at the microscopic structure of kidneys in Figure 7.2. If you look closely at the cortex and medulla, many tiny tubular structures can be seen, that stretch across both regions perpendicular to the surface of the kidneys. In each kidney, there are one million of these structures, called *nephrons*. The nephron is described as *the functional unit of kidney*. It is a long thin tube, as can be seen in the Figure 7.3, packed between the cortex and medulla of the kidney. It is closed at one end and the other end opens at the collecting tubule and is surrounded by the capillaries i.e., tiny blood vessels that distribute oxygen-rich blood to the various parts of the body.

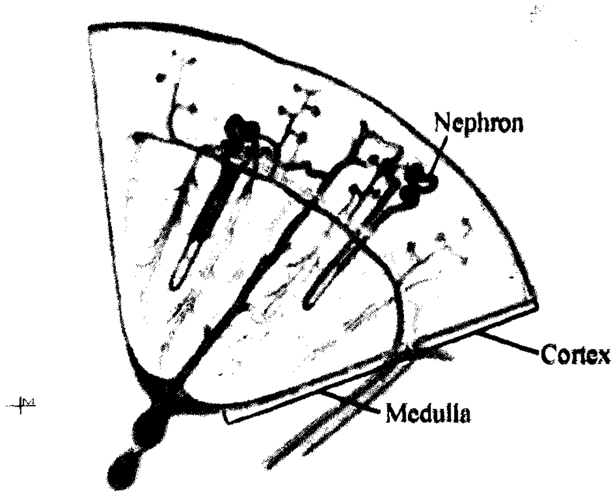

Figure 7.3: Nephron the functional unit of the kidney

So we have seen that the basic structural and functional unit of the kidney is the nephron. Each kidney has about 1 million nephrons. What constitutes the nephron? Each nephron consists of a renal corpuscle and a renal tubule as illustrated in Figure 7.4. The renal corpuscle is composed of a glomerulus (a network of fine capillaries), associated with a surrounding, cup-shaped section of renal tubule called the *glomerular (or Bowman's) capsule*. The renal tubule is divided into three morphologically and functionally distinct regions, as illustrated in the Figure 7.4 which are:

1) the proximal convoluted tubule (PCT),
2) the loop of Henle (with its thin descending limb, thin ascending limb and thick ascending limb), and
3) the distal convoluted tubule (DCT).

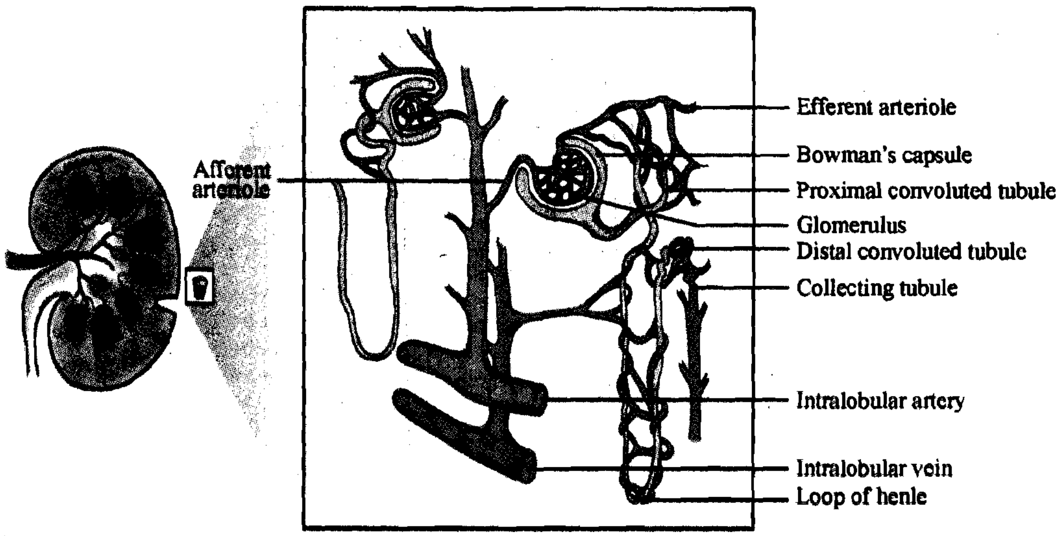

Figure 7.4: Basic structure of a nephron

Let us get to know a bit more about these structures of a nephron.

- *Glomerulus:* It is the main filter of the nephron and lies within the Bowman's capsule. It resembles a twisted mass of tiny tubes as can be seen in Figure 7.4, through which the blood passes. Being semi-permeable, it allows the passage of water and the soluble wastes. The glomerular capsule forms a cup-like structure and is a thin double membrane enclosing the glomerulus. The main function of glomerulus is to filter the waste products from the blood and thus, initiate urine formation.

- *Bowman's capsule:* It contains the primary filtering device of the nephron, that is, glomerulus. It is a double-walled, cup-shaped structure around the glomerulus of each nephron of the vertebrate kidney. It serves as a filter to remove organic wastes, excess inorganic salts and water. It is located in the cortex.

- *Proximal Convoluted Tubule or proximal tubule (PCT):* The proximal tubule is the most proximal part of the renal tubule which lies in the cortex. Once the glomerular filtrate passes through the opening in the Bowman's capsule, it goes through the PCT from where it passes through the Loop of Henle and the distal tubule (DCT), about which we shall learn next.

- *Loop of Henle:* The Loop of Henle is a long U-shaped part of the renal tubule, extending through the medulla from the end of the PCT to the beginning of the DCT. It begins with a descending limb having a thick-walled segment called the *proximal straight tubule*, followed by a thin-walled segment called the *thin* or *attenuated tubule*; this is followed by the ascending limb, which sometimes includes the distal end of the attenuated tubule and always ends with a long thick-walled segment called the *distal straight tubule.* The loops vary in the lengths of their segments according to their locations in the kidney. It is also called as *ansa nephroni* and is responsible for carrying urine out of the nephron.

- *Distal Convoluted Tubule or Distal Tubule (DCT):* A distal, rolled-together or coiled part of the ascending limb of the renal tubule. It lies in the cortex. The urine from here passes into the collecting duct.

- *Collecting Duct/Tubules:* A long straight portion after the distal tubule is the open end of the nephron. It extends from the cortex down through the medulla. These are responsible for collecting urine from DCT of the nephron and passing it to the renal pelvis. These are also of two types, proximal straight tubule and distal straight tubule.

Now that we have an understanding of the anatomy of the kidney and the nephron, let's have a look at how these parts allow the kidneys to do its jobs. But first let us check what we have learnt so far.

Check Your Progress Exercise 1

1) List the various parts of the urinary system.

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2) What is the functional unit of the kidney? List the major parts of the functional unit, giving their roles, wherever possible.

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7.3.2 Functions of the Kidney

The functions of the kidneys, as you already know, are to form urine and to pass urine for excretion, maintain water and electrolyte balance. The bean-shaped kidneys, each about the size of a child's fist, performs several functions essential to health, the most important of which is to filter blood and produce urine. Without the kidneys, waste products and other toxins would soon build up in the blood to fatal levels. The kidneys also regulate blood pressure and the level of vital salts in the blood, as well as, secrete the hormone that controls the production of red blood cells. Hence, the physiological functions of the kidneys are many. These are enumerated herewith. The kidneys function to:

- *keep the concentrations of various ions and other important substances constant.* A number of chemicals are important to the blood chemistry, such as potassium, sodium, phosphorous, calcium, magnesium and chloride. The healthy kidneys ensure the right amounts of these in the blood.

- *keep the volume of water in the body constant* by removing excess fluid from the body. The kidneys regulate the volume of extra-cellular fluid by eliminating or retaining water. The re-absorption of water in the tubules is controlled by pituitary and hypothalamic actions. The pituitary is an endocrine gland found in the body about which we will learn later in Unit 11. The posterior pituitary produces anti-diuretic hormone (ADH), which increases the amount of water reabsorbed, the adrenal cortex (another endocrine gland) produces the hormone aldosterone, which influences the re-absorption of sodium and water.

- *regulate the osmolarity of extra-cellular fluid* by regulating the amount of sodium chloride and water excreted.

- *remove the wastes from the body.* Many metabolic waste products such as urea, uric acid, ammonia and creatinine need to be filtered, are removed from the body, by the kidneys.

- *keep the acid/base concentration of the blood constant and regulate the blood pressure.* Renin, an enzyme– like substance of the kidney, helps in coverting angiotensinogen to angiotensin which is responsible for producing vascular constriction, thereby increasing the blood pressure. It also stimulates the secretion of aldosterone from the adrenal glands and causes sodium and water to be retained, increasing blood volume and blood pressure.

- *stimulate the making of red blood cells.* Erythropoietin is a hormone responsible for maintaining the right amount of RBC count in the body by stimulating the bone marrow to make more RBCs.

- *maintain the body's calcium levels.* Along with parathormone and calcitriol, kidney helps the body to absorb calcium.

Now we shall study in detail about a few major functions of the kidney, which we enumerated above and which makes it an important part of the excretory system. Let us get to know about the process of urine formation first, which as you know by now, is the main function of the kidney.

7.3.3 How the Kidney Works

In the section above we learnt about the urine formation, water balance, maintenance of electrolyte and pH balance functions of the kidneys. Let us have a look at the urine formation function of the kidneys, first.

A) *Formation of Urine*

The kidneys form urine in three phases: simple filtration, selective re-absorption and secretion. Let us begin with the process of filtration.

1) *Simple filtration:* The process of filtration takes place in the nephron where approximately 10% of the blood which the kidney receives gets filtered under pressure through the walls of the glomerular capillaries and Bowman's capsule. The filtrate is composed of water, ions (e.g., sodium, potassium and chloride), glucose and small proteins. The rate of filtration is approximately 125 ml/minute or 180 L each day. Also, the amount of any substance that gets filtered is the product of the concentration of that substance in the blood and the rate of filtration. So, higher the concentration, greater the filtration rate, the more substance gets filtered.

   A filter separates large and small particles by retaining the larger particles and allowing the smaller particles to pass through. The semi-permeable wall of the glomerulus acts as a filter. It allows the blood constituents having a molecular weight less than 68,000 (such as water, food substances like glucose and amino acids, inorganic salts, waste products like urea, uric acid and creatinine etc.) to pass through. It retains the larger molecules (red blood cells, white blood cells, platelets and plasma proteins etc.). These high molecular weight substances are unable to pass through the semi-permeable membrane of the glomerulus.

The volume of filtrate produced per minute is termed as the *glomerular filtration rate.* Let us get to know more about the GFR.

Glomerular Filtration Rate (GFR): The kidneys receive a large amount of blood flow. The kidney blood flow is approximately 1200 ml per minute. One-tenth of this is filtered as the blood flows through the glomeruli i.e., about 120 ml. Filtration takes place through the semi-permeable walls of the glomerular capillaries, which are almost impermeable to proteins and large molecules. The filtrate is thus virtually free of proteins and has no cellular elements. The glomerular filtrate is formed by squeezing the fluid through the glomerular capillary bed. The driving hydrostatic pressure (the pressure exerted by a liquid as a result of its potential energy) is controlled by the afferent and efferent arterioles (the muscular walled vessels leading to and from each glomerulus as shown in Figure 7.4), and is provided by the arterial pressure, that is, the pressure of the circulating blood on the arteries. The glomerular filtration rate decreases with age and disease.

In order to keep the renal blood flow and GFR relatively constant, the hydrostatic pressure in the glomerulus has to be kept fairly constant. When there is a change in the arterial blood pressure, there is a constriction or dilatation of the afferent and efferent arterioles. This process is called as *autoregulation* and can be more precisely defined as *the tendency of the blood flow to organ to remain constant inspite of the pressure changes in the artery that delivers blood to that organ.*

Various factors influence GFR. These include:

1) *Renal blood flow:* A large proportion of blood flows into the glomerulus. The greater the rate of flow of blood into the glomerulus, the greater will be the GFR.
2) *Sympathetic stimulation:* If there is a mild or moderate sympathetic stimulation of the kidney, the GFR decreases. But if there is a strong sympathetic stimulation, glomerular pressure is reduced and the GFR falls to zero.
3) *Afferent arteriolar constriction:* Afferent arteriolar constriction decreases the rate of blood flow into the glomerulus, decreases the glomerular pressure and the GFR.
4) *Efferent arteriolar constriction:* Constriction of the efferent arteriole increases the glomerular pressure and the GFR.
5) *Arterial pressure:* Though an increase in the arterial pressure causes an increase in GFR but the effect is minimized because of autoregulation of the kidney. Rise of arterial pressure increases constriction of afferent arteriole. This prevents a major rise in glomerular pressure causing the GFR to increase to only 15 to 20 percent.

Before we proceed to the second phase, i.e. selective reabsorption, let us get to know a few important terms associated with the mechanism of urine formation that might be of help to us to understand the process better. These are presented in Box 7.1.

Box 7.1: Important terms associated with the mechanism of urine formation
Maximum Tubular Secretory Capacity: The maximum rate at which tubules can transport a substance from the blood vessel to the lumen or from the lumen to the blood vessel is limited by the *carrier system*. The maximum rate is known as the *tubular maximum* and is usually expressed as milligram per minute.

Box Contd..

Active transport: When the substances are transported through a cell membrane against a concentration gradient, that is, from a dilute solution to a concentrated solution, energy must be imported to the molecules. This process of transport is called as the *active transport.*

Active transport of sodium occurs from inside the epithelial cells into the spaces between the cells. This transport from the cell diminishes the sodium concentration inside the cell. Other substances, besides sodium, that are actively absorbed through the tubular epithelial cells include glucose, amino acids, phosphate ions and others.

Hydrogen ions and potassium ions are actively secreted into all or some portions of the tubules. Active secretion occurs in the same way as active absorption. Here, the cell membrane transports the secreted substances in the opposite direction i.e. from a low concentration to a high concentration, against a gradient.

Passive transport or diffusion: Diffusion means *the random movement of particles in a fluid.* The movement of particles from a high concentration area to a low concentration area takes place till the concentration is uniform. Although the particles move at random in all directions, a greater number of them move from a region of higher concentration to that of a lower concentration. When water is reabsorbed, the concentration of urea in the tubular fluid rises. This, in turn, causes urea to diffuse from the tubular fluid to the peritubular fluid (fluid surrounding the tubule). Chloride, phosphate and bicarbonate ions are attracted from the tubular fluid towards the peritubular fluid.

A few substances are secreted by diffusion in the same manner. For example, ammonium ions are synthesized inside the epithelial cells and diffuse into the tubular lumen. They help to control the degree of acidity of tubular fluid.

Now, let us get back to the second phase i.e. selective reabsorption and try to understand what role does this phase has in the formation of urine.

2) *Selective reabsorption:* The purpose of this process is to reabsorb those constituents of the filtrate which are essential to the body. By this reabsorption, the composition and volume of the filtrate is altered, fluid and electrolyte balance of the body is maintained.

   The specialized cells of the tubules selectively reabsorb the constituents of the filtrate as they pass through the tubule. Plasma substances like glucose, amino acids and vitamin C are reabsorbed under normal circumstances. They have a *high threshold value*. But there is a limit to it. If the blood glucose is within 120 mg per 100 ml of blood then all the glucose in the filtrate is reabsorbed. If it exceeds 180 mg per 100 ml of blood, some glucose appears in the urine. This occurs in the case of *diabetes mellitus*. A major portion of the waste products like ammonia, creatinine and sulphates are not reabsorbed but excreted. These substances have *low threshold values*. In between these high threshold substances and low threshold substances, there are some substances which are reabsorbed according to the need of the body. For example, the reabsorption of inorganic salts depends upon the plasma level of the substances.

Let us briefly look at the few important aspects that might help us in understanding and remember the process of selective reabsorption. These are presented in Box 7.2.

Box 7.2: Selective Reabsorption Process

- Specialized proteins called 'transporters' are located on the membranes of the various cells of the nephron.
- These transporters grab the small molecules from the filtrate as it flows by them.
- Some transporters require energy, usually as ATP (active transport), while others don't (passive transport).
- Water gets reabsorbed passively by osmosis in response to the build up of reabsorbed Na in spaces between the cells that form the walls of the nephron.
- Other molecules get reabsorbed passively when they are caught up in the flow of water (solvent drag).
- Reabsorption of most substances is related to the reabsorption of Na, either directly, via sharing a transporter or indirectly through a solvent drag.

Both passive and active reabsorption of molecules from the nephron to the blood occurs at the PCT. Cells lining the PCT are anatomically adapted for active re-absorption. There are other features as well which play a role in the re-absorption. These are:

a) Microvilli: Lots of microvilli, i.e. minute, hair-like projections of the cell membranes increase the surface area for reabsorption.

b) Mitochondria: Lots of mitochondria make ATP needed for active transport.

c) Active transport is selective re-absorption.

There are also two major factors that affect the reabsorption process. These include:

1) *Concentration of small molecules in the filtrate* - the higher the concentration, the more molecules can be reabsorbed.

2) *Rate of flow of the filtrate*- the flow rate affects the time available for the transporters to reabsorb molecules.

The useful products return to the blood and the water is passively reabsorbed. Sodium and chloride ions are actively reabsorbed, which encourages the water to follow. Amino acids and glucose are reabsorbed to blood. The reabsorption rate is *400 mg/100ml plasma.* The rest of the glucose is in the urine. In diabetes mellitus, the excess glucose is present in the blood. A part in the filtrate is reabsorbed, part is not.

Next, we move on to the third and last phase in the process of urine formation, that is, secretion.

3) *Secretion*: In the process of filtration through the glomerulus, the non-threshold substances and drugs are not cleared from the blood because the blood does not remain for a long time in the glomerulus. Such substances are secreted into the convoluted tubules and cleared from the blood. These substances include para-amino hippuric acid (PAH) and penicillin *(a group of broad-spectrum antibiotic drugs obtained from penicillium molds or produced synthetically, used to treat various infections and diseases)* etc. They pass from the blood into the urine.

Having learnt about the urine formation function, we move on to the water balance function of the kidney.

B) *Water Balance Function of the Kidney*

Water is one of the most important constituent in the daily diet. You are already aware of the roles it plays in our body. Maintenance of water and electrolyte balance in the body is an equally important consideration. Let us see how kidneys help to regulate and maintain water balance. The body excretes excess water through the kidneys. The balance between intake and output is maintained by the posterior pituitary hormone *ADH* or *anti-diuretic hormone* or *vasopressin.* Substances that stimulate the formation of urine are termed as *diuretics.* The hormone ADH causes the suppression of urine. The minimum urinary output is about 500 ml per day average being 1500 ml.

There are cells in the hypothalamus (in the brain) which are sensitive to the changes in the osmotic pressure of the blood. These sensory receptors sensing the osmotic pressure are called as *osmoreceptors.*

When the concentration of sodium and other osmotically active substances in the extracellular fluid rises, there is an increased osmotic pressure in the fluid. Osmoreceptors (supraoptic nucleus) in the hypothalamus are stimulated. The hypothalamus sends message to the posterior pituitary gland and it secretes ADH. The ADH acts on the *distal convoluted tubules* and *collecting ducts of the kidney* to cause an increase in the permeability resulting in an increased reabsorption of water which reduces osmotic pressure of the blood. The pore size of the epithelial cell is increased. This is enough for the water molecules to diffuse through, but does not allow most other substances in the tubular fluid to pass through. Thus water is returned to the body fluids whereas the sodium and other solutes are lost in the urine. In this way, the osmotic and water balance is maintained.

If there is an increased concentration of dissolved substances in the blood, there is an increased ADH production. The water reabsorption under ADH influence in the DCT and collecting duct is known as *facultative absorption.* In deficiency of ADH, there is less facultative absorption, hence urine output is increased. This condition is called as *diabetes insipidus.* On the other hand, if the osmotic pressure of the blood is reduced due to increased plasma volume, the amount of ADH secretion is reduced and *diuresis* occurs. Two mechanisms that are involved in this process are:

- the structure and transport properties of the *loop of Henle* in the nephron, and
- the *anti-diuretic hormone (ADH),* also called as *vasopressin,* secreted by the pituitary gland.

Let us begin first by understanding the structure and transport properties of the Loop of Henle.

Transport properties of Loop of Henle: The loop of Henle, as shown in Figure 7.5, has a descending limb and an ascending limb. As the filtrate moves down the loop of Henle, water is reabsorbed, but the ions (Na, Cl) are not. The removal of water serves to concentrate the Na and Cl ions in the lumen. Now, as the filtrate moves up the other side (ascending limb), Na and Cl ions are reabsorbed but the water is not. What these two transport properties do is set up a concentration difference in NaCl along the length of the loop with the highest concentration at the bottom and lowest concentration at the top. The loop of Henle can then concentrate NaCl in the medulla. The longer the loop, the bigger the concentration gradient. This also means that the medulla tissue tends to be saltier than the cortex tissue. This property of loop of Henle to improve osmolarity of filtrate in a counter current flow - is known as Counter current Multiplier System – where Na is multiplied every time it passes through loop of Henle. That is the reason why filtrate is isotonic in PCT, becomes hypertonic as it passes through loop of Henle, hypo as it goes to DCT and finally hypertonic as it leaves collecting duct (Figure 7.5). So normally urine is highly concentrated and hypertonic as compared to blood.

Now, as the filtrate flows through the collecting ducts, which go back down through the medulla, water can be reabsorbed from the filtrate by osmosis. Have a look at the Figure 7.5. Here you will notice that water moves from an area of low Na concentration (high water concentration) in the collecting ducts to an area of high Na concentration (low water concentration) in the medullary tissue. If you remove water from the filtrate at this final stage, you can concentrate the urine.

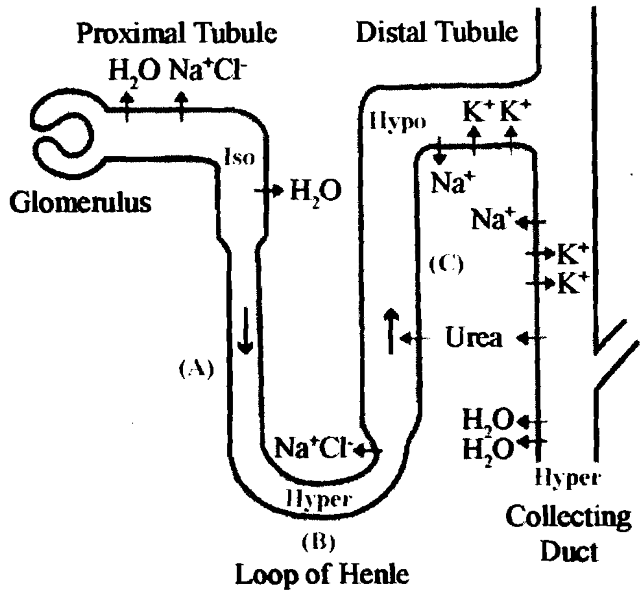

Figure 7.5: Transport in loop of Henle

Now let us study about the hormone ADH (anti-diuretic hormone) or vasopressin and its role in maintaining water balance.

Anti-Diuretic Hormone (ADH): It is secreted by the pituitary gland and controls the ability of water to pass through the cells in the walls of the collecting ducts. If ADH is not present, then water cannot pass through the walls of the ducts. The more the ADH present, the more water can pass through.

Just now we have studied about the specialized nerve cells called as *osmoreceptors* that are present in the hypothalamus of the brain. These cells, as you would recall, sense the Na concentration of the blood. The nerve endings of these osmoreceptors are located in the posterior pituitary gland and secrete ADH. If the Na concentration of the blood is high, the osmoreceptors secrete ADH. If the Na concentration of the blood is low, they do not secrete ADH. In reality, there is always some very low level of ADH secreted from the osmoreceptors. Thus we can see that the electrolyte balance is always maintained by the kidneys. This function is further elaborated next.

C) *Maintenance of Electrolyte Balance*

In the process of formation of urine, the kidneys also maintain electrolyte balance. Sodium is the most important cation that exists in the extra-cellular fluid of the body. It comes from the diet and common salt. It is lost through the skin as a constituent of sweat and through kidneys as a constituent of urine. The kidneys maintain sodium balance by the help of adrenocortical hormone, aldosterone and also by the renin-angiotensin system. When there is a decreased concentration of sodium, aldosterone secretion increases. It increases the re-absorption of sodium from the *glomerular filtrated* and the level of sodium is increased in blood. A fall in the concentration of sodium stimulates *renin* secretion from the *kidneys*. Renin acts on the serum globulin to form angiotensin. Renin-angiotensin system stimulates aldosterone which helps in increasing sodium reabsorption from the tubules and maintain its concentration in the blood.

Levels of other ions like potassium, chloride, bicarbonate are also maintained along with sodium. When sodium ion reabsorption from the filtrate is increased, potassium ion excretion is increased. Along with potassium ions, hydrogen ions are also secreted into the tubules as illustrated in Figure 7.5. When hydrogen ions are secreted, the bicarbonate ions are accumulated in the blood and extra-cellular fluid, as hydrogen comes from carbonic acid (H_2CO_3). Aldosterone causes an enhanced reabsorption of chloride ions.

Like maintaining the electrolyte balance, the kidneys also maintain the pH balance in the body. Let us learn how.

D) *Maintaining pH Balance*

You must be aware of the term pH. pH we know provides a measure on a scale from 0 to 14 of the acidity or alkalinity of a solution (where 7 is neutral and greater than 7 is basic (alkaline) and less than 7 is acidic). It is essential that the body maintains an optimum pH of 7.4 and kidneys do play a major role in ensuring that. Let us see how.

The kidneys can correct any imbalances by removing excess acid (hydrogen ion) or base (bicarbonate) in the urine and restoring the bicarbonate concentration in the blood to normal. The tubular cells produce a constant amount of hydrogen ions and bicarbonate ions because of their own cellular metabolism (production of carbon dioxide). Through a carbonic anhydrase reaction similar to the red blood cells, hydrogen ions get produced and secreted into the lumen of the nephron. Also, bicarbonate ions get produced and secreted into the blood. In the lumen of the nephron, filtered bicarbonate combines with the secreted hydrogen ions to form carbon dioxide and water (carbonic anhydrase is also present on the luminal surface of the kidney cells). Whether the kidney removes hydrogen ions or bicarbonate ions in the urine depends upon the amount of bicarbonate filtered in the glomerulus from the blood relative to the amount of hydrogen ions secreted by the kidney cells. When the amount of filtered bicarbonate is greater than the amount of secreted hydrogen ions, then bicarbonate is lost in the urine. Likewise, if the amount of secreted hydrogen ion is greater than the amount of filtered bicarbonate, then hydrogen ions will be lost in the urine (i.e. acidic urine).

Now, this acid/base balance of our blood changes in response to many things. These include:

- *Diet:* the diets that are rich in meats provide acids to the blood when digested. In contrast, the diets rich in fruits and vegetables make our blood more alkaline because they are rich in bicarbonates.
- *Exercise:* exercising muscles produce lactic acid that must be eliminated from the body or metabolized.
- *Breathing:* a high altitude causes rapid breathing that makes our blood alkaline. In contrast, certain lung diseases that block the diffusion of oxygen can cause the blood to be acidic.

Let us further study the effect of diet on the acid/base balance by taking the example of acid diet and alkaline diet. We must, however, first understand what we mean by an *acid diet* and *alkaline diet.* A diet which is rich in proteins (meat, fish, eggs, cheese) and when catabolised leave an acidic residue to be excreted in the urine is referred to as *acid diet.* On the other hand, a diet consisting mainly of fruits, vegetables and milk, which when catabolised leave an alkaline residue to be excreted in the urine is *alkaline diet.*

Let us first see how the acid/base balance is maintained in a acid diet.The sequence of steps involved include:

1) Hydrogen ions added to the blood by breaking down a meat-rich diet combine with the bicarbonate ions in the blood and form carbon dioxide and water.
2) This reaction reduces the bicarbonate concentration and the pH in the blood.
3) The decreased bicarbonate concentration in the blood reduces the amount of bicarbonate filtered in the glomerulus.
4) All of the filtered bicarbonate combines with the hydrogen ion secreted by the kidney cells in the lumen to form carbon dioxide and water.
5) Because the filtered load of bicarbonate was less than the amount of hydrogen ion secreted by the kidney cells, there is an excess of hydrogen ions in the urine.
6) The amount of bicarbonate secreted from the kidney cells into the blood was equal to the hydrogen ion secreted into the lumen and greater than the filtered load of bicarbonate from the blood, therefore, the blood has a net gain of bicarbonate.
7) This process continues to lose hydrogen ions in the urine and gain bicarbonate in the blood until the concentration of hydrogen (pH) and bicarbonate ions in the blood are restored to normal.

Next we shall see how acid/base balance is maintained in case of an alkaline diet.

1) Bicarbonate ions added to the blood from the fruit or vegetable-rich diet combines with hydrogen ions to form carbon dioxide and water.
2) This reaction reduces the hydrogen ion concentration and increases the pH.
3) The increased bicarbonate concentration increases the amount of bicarbonate filtered in the glomerulus.
4) The filtered bicarbonate exceeds the amount of hydrogen ion secreted by the kidney cell, and excess bicarbonate is lost in the urine.
5) The amount of bicarbonate secreted from the kidney cells into the blood was equal to the hydrogen ions secreted into the lumen and less than the filtered load of bicarbonate from the blood, therefore, the blood has a net loss of bicarbonate.
6) This process continues to lose bicarbonate in the urine and reduce the bicarbonate in the blood until the concentrations of hydrogen (pH) and bicarbonate ions in the blood are restored to normal.

The discussion above must have given you a clear idea about the functions of kidney in maintaining the acid/base balance in the blood. Finally, let us get to know the regulatory function of the kidney.

E) *Regulation of Blood Composition*

Each part of the nephron has different types of cells with different properties. An understanding of this is important to know how the kidneys regulate the composition of the blood. The nephron has a unique blood supply as compared to the other organs. Let us now study what is the unique blood supply of the nephrons and ultimately play a major role in regulating the blood composition:

- *Afferent arterioles:* Look at Figure 7.4 and identify the afferent arterioles. These connect the renal artery with the glomerular capillaries.
- *Glomerular capillaries:* There are the coiled capillaries that are inside the Bowman's capsule.
- *Efferent arterioles:* Identify the efferent arterioles in Figure 7.4. As you would have noticed, these connect the glomerular capillaries with the peritubular capillaries.

- *Peritubular capillaries:* These are located after the glomerular capillaries and surrounding the PCT, loop of Henle and the DCT.
- *Interlobular veins:* These are the veins that drain the peritubular capillaries into the renal vein.

The above mentioned blood vessels (forming portal circulation) help in the regulation of blood composition by the kidneys. Kidney is the only organ of the body in which the two capillary beds, in a series, connect arteries with the veins. This arrangement is important for maintaining a constant blood flow through and around the nephron despite fluctuations in the systemic blood pressure.

Check Your Progress Exercise 2

1) Give a few important physiological functions of kidneys.

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2) What do you understand by the term GFR? What are the factors affecting GFR?

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3) What are the three steps involved in urine formation?

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4) Name the hormone that contribute to the regulation of water reabsorption. How does it maintain osmotic and water balance?

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5) List the portal vessels (vessels having two sets of capillaries i.e. glomerular and peritubular capillaries) supplying blood to the nephrons.

   ....

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Our study of the kidney and its function in urine formation would not be complete without a discussion on the counter current mechanism. Let us now understand what do we mean by counter current mechanism and what is its significance in maintaining the concentration of the filtrate.

7.3.4 Counter Current Mechanism

What is counter current mechanism? Counter current mechanism is *the mechanism by which the kidneys produce osmotically concentrated urine.* Let us see how.

In the proximal convoluted tubule (PCT), the substances like glucose and amino acids are reabsorbed mainly as isotonic solution. Most of the reabsorption occurs here and this is the obligatory absorption. If more solute is to be absorbed, more water is reabsorbed and vice versa. This process mainly occurs in the PCT. When the filtrate reaches the loop of Henle, it is still isotonic (having the same or equal osmotic pressure) with the blood plasma.

According to *Wirz*, the filtrate becomes concentrated as it passes down the descending limb of the loop. This portion of the loop lies in the renal medulla and is hyperosmotic with respect to the plasma. Hence, water is lost from the descending limb to make the tubular fluid also hyperosmotic. In the ascending limb, a reverse set of actions occurs as you have already studied earlier under the water balance function of kidneys. The tubule passes from a hyperosmotic zone to a hypoosmotic zone. To maintain the balance, there is an active secretion of sodium chloride unaccompanied by water in the ascending limb, so that the tubular fluid becomes hypoosmotic with the plasma. This mechanism is known as the hair pin *counter current multiplier mechanism.* The filtrate as it passes down the descending limb of the loop of Henle, gets multiplied in its content of sodium which is through the interstitium and to descending limb through the secretion in the ascending limb. The *vasa recta* (arterial capillary) act as a counter current exchanger system, faithfully exchanging ions with the interstitium. Through this countercurrent mechanisms, kidney can maintain osmolarity between 300 mOsm/L to 1200 mOsm/L.

So far we studied about the contribution of the kidneys in urine formation and its role in maintaining the pH and performing other regulatory functions. Besides these, did you know that the kidneys also have non-excretory functions? The next sub-section focuses on these non-excretory functions of the kidney.

7.3.5 Non-Excretory Functions of Kidney

Though the major contribution of the kidneys, as you have learnt so far, is to form urine and to maintain the constancy of internal environment, certain functions are sub-served by the kidneys apart from excretion (non-excretory function). These are the non-excretory roles of kidney. The kindey serves:

- as an endocrine gland
- in metabolic activities, and
- in autoregulation.

Let us now discuss each of these roles of kidneys, in a greater detail.

Kidney as an *endocrine gland:* The kidney produces substances that can be described as hormones. Hormones are the chemicals produced by glands in the body and circulate in the bloodstream.

Erythropoietin, a glycoprotein, is released from the kidneys in response to the tissue hypoxia. It stimulates the production of red blood cells by the bone marrow. The cellular site of production of erythropoietin is not clearly known, but acts as a hormone.

The liver converts vitamin D (cholecalciferol) to 25-hydroxycholecalciferol. This 25-hydroxy compound is then converted into 1,25-dihydroxycholecalciferol by the kidney when the plasma calcium level is below normal. This di-hydroxy compound of vitamin D is much more active than the original vitamin in bringing about the absorption of calcium from the intestine and can be considered a hormone produced by the kidney.

An inadequate blood flow to the kidneys leds to the release of a protease enzyme called *renin.* Renin is secreted from juxtaglomerular apparatus (a group of cells located between afferent and efferent arterioles). It combines with angiotensinogen to form angiotensin I and angiotensin II, which is a powerful vasoconstrictor and increases the blood pressure. It also stimulates aldosterone (mineralocorticoid) secretion of the adrenal cortex.

Metabolic activities of the kidney: For synthesis of creatine, three amino acids glycine, arginine and methionine are involved directly. The first reaction is to form glycocyamine from arginine and glycine. This occurs in the *kidneys*. The synthesis is completed by methylation of glycocyamine in the liver. Creatinine is an anhydride of creatine.

The kidney is also involved in carbohydrate metabolism. Glucose-6-phosphate is present in the renal cortex. This enables the kidney to contribute some glucose to the blood of glycogenolysis (the breaking down or catabolism of the polysaccharide glycogen into molecules of the sugar glucose and molecules of glucose – 1-phosphate within the body by enzymes). Kidneys also contribute glucose to the blood by gluconeogenesis (the production of glucose from non-carbohydrate precursors, such as amino acids, within the liver).

Autoregulation function of kidneys: The kidneys possess the property of autoregulation. This means that the blood flow in the kidneys remain constant. It is independent of the blood pressure changes, provided this pressure is within the range of 80-120 mm Hg. The glomerular blood flow and GFR are not affected by the small changes in blood pressure. But if after haemorrhage or due to any other reason, the blood pressure falls to a very low level, the autoregulation is lost. The glomerular filtration rate is reduced and may stop, resulting in anuria (no urine).

With this, we come to an end of our discussion on the organ responsible for urine formation i.e. the kidney and its functions, both excretory and non-excretory, in our body.

Let us now follow the path which the urine takes in the urinary system in its way out of the body. Once the urine is formed, it enters the ureters. Let us get to know more about the ureters.

7.4 URETERS

Ureters, as can be seen in Figure 7.1, are *the two tubes which convey the urine from the kidneys to the urinary bladder*. Each tube measures approximately 10 to 12 inches in length. They start from the pelvis of the kidney and pass downwards.

What is the structure of the ureters?

The outer coat of the ureter consists of *fibrous tissue*. The middle layer is *a muscle layer* consisting of smooth muscle (outer longitudinal and inner circular). The inner lining is a *mucous membrane* consisting of transitional epithelium.

What is the main function of the ureters?

The ureters propel the urine from the kidney into the bladder by contraction of the muscle layer. On the other hand, as the urinary bladder contracts, the walls of the ureters are pressed together. This prevents the urine to be forced back to the ureter.

So by the simple contraction of the muscle, the urine is passed from the ureter to the urinary bladder. Let us get to know about the urinary bladder now.

7.5 THE URINARY BLADDER

The urinary bladder is a sac, which acts as a reservoir for urine. Look at Figure 7.1 for a view of the urinary bladder. You would realize that the size and position of the urinary bladder varies depending on the amount of urine content. It is roughly pear shaped, but becomes more oval in shape as it fills with urine. It lies in the *pelvic cavity* (a cavity extending from the lower end of abdominal cavity). But when the bladder is grossly distended, it rises to the *abdominal cavity* (largest cavity that is situated in the main part of the trunk below the diaphragm).

What is the structure of the urinary bladder?

The bladder is composed of four layers of tissues. The outermost *serous membrane* is a thin membrane lining the closed cavities of the body and has two layers with a space in-between that is filled with the serous fluid which covers only the superior surface of the bladder. Next layer is a *muscle layer* composed of longitudinal and circular muscle fibre. The third layer is a *sub-mucous layer* containing blood vessels, lymphatics, sympathetic and parasympathetic nerves. The innermost layer is a *mucous layer* composed of transitional epithelium. There are three orifices in the bladder. The upper two orifices are the openings of the two ureters as illustrated in Figure 7.6. The inferior orifice is the point of origin of the urethra. These three orifices form a triangle described as the *trigone* of the bladder.

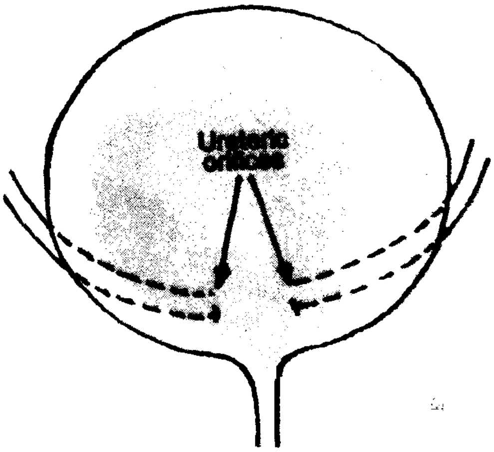

Figure 7.6: Orifices of the bladder

What is the role of the urinary bladder?

As mentioned earlier, the urinary bladder acts as a reservoir for urine. When the urine gradually accumulates in the bladder, there is a change in the volume but there is a little change in pressure upto a certain limit. When the volume reaches upto 200 to 300 ml, the pressure stimulates the nerve endings in the bladder wall and initiates the process of micturition (to urinate) through spinal reflex in which the parasympathetic are the efferents to the bladder.

In simple terms, when the urinary bladder becomes filled with urine, it stretches out. When it stretches beyond a certain point, nerves in the wall of the bladder send a message to the spine. The spine sends a message to the brain, which is experienced by the body as discomfort. This signals to the person that it is time to urinate. Coinciding with the urge to urinate, the nerve centers in the spinal cord cause the muscle around the urethra (the tube leaving from the bladder) to relax. This causes the main bladder muscle to shorten, which pushes urine outside of the body through the urethra.

You may have experienced that at times we can inhibit the urge to urinate until it is convenient to micturate. How is this possible? The brain can inhibit the spinal micturition reflex (the process of urination) for a limited period of time. Over-distension of the bladder causes an involuntary relaxation of the sphincters and a small amount of urine escapes. Micturition occurs when the muscular wall of the bladder contracts and the urethral sphincters relax.

In the infants, the nervous system is not fully developed. Micturition occurs simply by the reflex action and cannot be controlled voluntarily. In spinal cord injury, bladder disturbances are common.

Now we are familiar with the structure, role of urinary bladder. The last organ in the urinary system is the *urethra.* We shall now get to know the physiology of this organ.

7.6 THE URETHRA

The urethra is a canal which extends from the bladder to the exterior as illustrated in Figure 7.1. The length of the urethra varies between male and female. Where the urethra commences, there is a sphincter muscle i.e. a ring of muscle that contracts to close an opening, controls the passage of urine. The urethra opens at the external orifice guarded by a sphincter muscle, which is under the control of the will.

What is the structure of the urethra?

The urethra is composed of three layers of tissue. The muscle coat consists of longitudinal and circular muscle. The second layer is a thin spongy coat containing large number of blood vessels and the innermost mucous membrane consists of stratified squamous epithelial cells.

What is the function of urethra?

The urethra discharges urine from the urinary bladder to the exterior.

We hope the discussion above must have given you a good insight into the structure and functioning of the urinary system. Starting with the kidney, we saw that the urinary system includes kidneys also the ureters, urinary bladder and the urethra. All these organs play a significant role either in urine formation or discharge of urine from the body. Do you know what are the constituents of urine? The next section focuses on this and on the examination of urine. Before we move on this topic let us recapitulate what we have learnt so far.

Check Your Progress Exercise 3

1) What do you understand by counter current mechanism?

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....

2) Explain the role of kidney as:

   a) an endocrine gland

   ....

   ....

   b) autoregulator

   ....

   ....

3) Enumerate the functions of ureters and urinary bladder.

....

....

7.7 CONSTITUENTS AND EXAMINATION OF URINE

The quantity of urine in 24 hours in adult normal individual varies from 600 ml to 2500 ml. It is pale yellow in colour, hypertonic, acidic with a specific gravity of 1.007-1.012. The urine comprises of various constituents. Let us get to know them.

7.7.1 Normal and Abnormal Constituents of Urine

The urine comprises of various constituents. These may be either normal or abnormal ones. Let us see what these are. We start with the normal constituents.

Normal constituents of urine: The normal constituents of urine are of two types. These are the organic substances and the inorganic substances as listed herewith.

- *Organic substances:* Urea, creatinine, ammonia, uric acid, hippuric acid, amino acid, urine pigments, vitamins, hormones and their degraded products, and enzymes.
- *Inorganic substances:* Chlorides, phosphates and sulphates of sodium, potassium, calcium, magnesium etc.

Sometimes, certain abnormal constituents are detected in urine. We call them abnormal because normally they are not present in the urine. What are these constituents and under what conditions do they occur? Let's find out.

Abnormal constituents of urine: The detection of abnormal constituents in urine indicates the presence of certain metabolic disorders in the body. These abnormal constituents include:

1) *Glucose:* Presence of detectable amounts of glucose occurs in diabetes mellitus, Cushing syndrome, gigantism etc.

2) *Fructose:* Excretion of fructose in urine occurs as a metabolic defect in the liver.

3) *Galactose:* Galactose is present in the urine in the conditions of *galactosemia*, a metabolic defect caused due to the deficiency of the enzyme galactose-1-phosphate uridyl transferase.

4) *Proteins:* Abnormal amounts of proteins are excreted in certain inflammatory diseases like *glomerulonephritis* (inflammation of the glomerulus of the kidney, characterized by the decreased production of urine and by the presence of blood and protein in the urine and by edema) and *nephrotic syndrome* (a collection of symptoms that indicate kidney damage, such as high levels of protein in the urine, lack of protein in the blood and high blood cholesterol).

5) *Bence-Jones Protein:* Bence-Jones proteins are the small proteins (dimers of immunoglobulin light chains) normally produced by the plasma cells and are found in the urine. Bence-Jones proteins are sufficiently small to be excreted by the kidney. Persons suffering from *multiple myeloma* (a tumor of the bone marrow, usually malignant), *leukemia* (cancer of the blood) and *Hodgkin's disease* (a cancer in the lymphatic system) excrete large amount of protein in urine called *Bence-Jones protein.*

6) *Ketone bodies:* Ketone body is *an intermediate breakdown product of fats in the body*. It can be any of three compounds (acetoacetic acid, acetone and/ or beta-hydroxybutyric acid) found in excess in blood and urine of persons with metabolic disorders. These three compounds may be excreted in the urine in severe diabetes mellitus or in prolonged starvation due to the impairment of the carbohydrate metabolism. You may also recall reading about ketone bodies in Nutritional Biochemistry Course, Unit 7.

7) *Bile pigments and bile salts:* These occur in urine in conditions of hepatic and obstructive jaundice i.e. obstruction to the flow of bile into the duodenum, whether intra or extra hepatic.

8) *Blood:* In acute inflammation and trauma, blood may be present in the urine. This condition is known as *haematuria*. Blood may be present in cancer, renal stone and tuberculosis, which you already know is an infectious disease caused by the bacteria – *Mycobacterium tuberculosis* – which may affect almost any tissue or organ of the body. The most common target of the disease, however, is the lungs.

9) *Calculi and casts:* An abnormal concretion in the body usually formed of mineral salts and found in the gall bladder, kidney or urinary bladder, for example, is referred to as *calculi* while *casts* refer to the small tubules. These may be present in urine due to the formation of renal stones in any part of the urinary system.

10) *Pus:* Pus cells are found in the urine in infections of urinary tract. Pus is actually a viscous, yellowish-white fluid formed in infected tissue, consisting chiefly of leucocytes, cellular debris and liquefied tissue elements.

So that was an exhaustive list. Some normal and some abnormal constituents can be present in the urine. How can we detect these constituents? Well, simply by examination of the urine. Let us get to know about this process next.

7.7.2 Examination of Urine

Examination of urine is done to detect the presence of any abnormal constituent(s) and hence can be used as an important screening test for identifying metabolic disorders. Let us see what does the clinical examination involves and how does it help. We shall begin with general examination.

1) *General examination:* This includes general appearance, volume and specific gravity together with the simple chemical tests for reaction, albumin, sugar, ketones and blood. Let us learn about this examination in more details.

- *General appearance:* Dilute urine is usually pale and straw-colored while the concentrated urine is dark and acid urine is darker. Blood may cause the urine to be red or brown. In obstructive jaundice, the presence of bile pigments in the urine causes it to be dark orange changing to green. Freshly passed normal urine is clear but may become cloudy due to the presence of phosphates. Hence depending on the general appearance of the urine, some judgment can be made.

- *Volume:* Measurement of the volume of each urine specimen passed is necessary for the conditions in which the fluid balance is affected, for example, operation, oedema (swelling caused by an abnormal accumulation of fluid in the body tissues), dehydration (excessive loss of water from the body) and kidney failure (a chronic condition in which the body retains fluid and harmful wastes build up because the kidneys no longer work properly) etc.

- *Specific gravity* and *pH:* Normally, the first morning urine has a specific gravity of 1.015 to 1.020. Normal urine is usually slightly acidic with a pH of about 6.0.

- *Albumin:* Albumin in the urine generally means leaking of the plasma albumin through the inflamed renal glomerulus (glomerulonephritis). It may also be present in violent exercise, during fever and in certain forms of chemical poisoning.

- *Glucose:* Detectable amount of glucose is only found in the urine when the blood level exceeds a certain threshold value i.e., 180 mg/100 ml. In untreated diabetes mellitus, the blood level will exceed this value, especially after a carbohydrate meal. The result is that the glucose appears in the urine. This condition is called *glycosuria.* If the patient is treated with insulin, then also glucose may appear in the urine because some residual urine is left in the bladder. Higher the blood sugar level, greater the glycosuria.

- *Ketones:* The ketone bodies accumulate in the blood in impaired glucose metabolism as in starvation and diabetes mellitus. The high levels of ketone bodies are excreted in the urine. Ketone bodies include acetone, acetoacetic acid and beta-hydroxybutyric acid.

After general examination, we move on to the microscopic and specific examination of urine. Let us see what is done in these examinations.

2) *Microscopical examination:* By microscopical examination, the pus cells, RBC and cast cells are found if the infection is present. Microscopical examination also reveals the presence of crystals of chemical substances in the urine, for example, uric acid, urates, oxalates, phosphates etc.

3) *Special examination:* The special examination requires the determination of various chemical substances in the urine including amino acids, bile pigments and salts, calcium, creatinine, drugs, electrolytes, hormones and porphyrin. Why are these chemicals examined in the urine? Let's find out.

- *Amino acids:* Normal urine contains only small amount of certain amino acids, for example, glycine and glutamine. Abnormal amounts and types of amino acids are found in liver failure and in a number of congenital disease i.e., a disease or disorder that is inherited genetically.

- *Bile pigments and salts:* The bile pigment, bilirubin (a pigment formed from the destruction of red blood cells), is altered in the intestine to urobilinogen, a coloured substance formed in the intestine from the breakdown of bilirubin. In the urine, the urobilinogen gradually changes to urobilin. In haemolytic jaundice (jaundice due to the breakdown of red blood cells), excretion of urobilin, a brown bile pigment, is increased upto 10 mg daily and in obstructive jaundice (jaundice caused by something blocking the bile duct, for example, gallstones and tumors), it is reduced usually to less than 0.3 mg daily.

  Bilirubin appears in the urine when there is an appreciable amount of conjugated bilirubin present in the plasma.

- *Calcium:* Normally 100 to 300 mg of calcium is excreted in the urine daily. Urine calcium is low in intestinal malabsorption and rickets – a childhood disease caused by deficiency of vitamin D and sunlight, associated with impaired metabolism of calcium and phosphorus. It is high in hyperparathyroidism.

- *Creatine:* Normal urine contains little or no creatine. Some may be found during menstruation, pregnancy and childhood. Urine creatine is considerably increased in conditions involving muscular wasting.

- *Creatinine:* It is an end-product of protein metabolism, an anhydride of creatine, found in the blood and urine that can be used to help assess if the kidneys are working adequately. Normally 1.1 to 3.4 g of creatinine is excreted daily.

- *Drugs:* Levels of alcohol and barbiturates (a group of drugs derived from barbituric acid that is used to sedate, to control convulsions or to induce sleep) are estimated in the urine samples. In cases of suspected intoxication, they may provide valuable information, especially when the blood samples are not available.

- *Electrolytes:* Estimation of urine chloride, sodium, potassium is of significant importance when the electrolyte balance is disturbed.

- *Hormones:* Increased or decreased production of a hormone in the body alters the amount of hormone or its degraded products excreted in the urine. For example, pregnancy tests are based on increased chorionic gonadotrophin present in the urine. Corticosteroid hormones are reduced in Addison's disease, which is due to a failure of the adrenal cortex.

- *Porphyrins:* Porphyrins (a group of compounds containing the porphin structure, four pyrrole rings connected by methine bridges in a cyclic configuration to which a variety of side chains are attached) are the intermediates in haemoglobin synthesis. In haemolytic anaemia, when the red blood cells are broken down excessively, the body tries to form more red blood cells and consequently the rate of haemoglobin synthesis increases. Excess porphyrins are produced and so are excreted in the urine.

In the section above, we have studied about the general, microscopic and specific examination of urine to detect abnormal constituents. In addition there are certain tests and procedures used to evaluate renal function. Let us learn about them.

7.8 RENAL FUNCTION TESTS

Renal function tests are the common tests and procedures used to evaluate renal function and for this, the analysis of blood and urine samples is essential. The purpose of these tests is to determine if the kidneys are performing their tasks adequately. These tasks, as you are already aware of, involve many vital functions such as removing metabolic waste products from the bloodstream, regulating body's water balance and maintaining the pH. The following are some of the basic renal function tests:

1) *Blood urea nitrogen (BUN):* It is a test that measures the amount of urea nitrogen in the blood. Urea is formed in the liver as an end product of protein metabolism and is carried to the kidneys for excretion.

During digestion, protein is broken down to amino acids. Amino acids contain nitrogen, which is removed as NH_4^+(ammonium ion), while the rest of the molecule is used to produce energy or other substances needed by the cell. The ammonia combines with other small molecules to produce urea. The urea makes its way into the blood and is ultimately eliminated in the urine by the kidneys. You may recall reading about this aspect in the Nutritional Biochemistry Course in Unit 8.

Nearly all kidney diseases cause an inadequate excretion of urea, elevating BUN levels in the blood. Other causes of high BUN levels include dehydration, gastrointestinal bleeding, steroid treatment and use of many other drugs compete with urea for elimination by the kidneys.

The *normal values* for the test are: 7 to 20 mg/dl and the abnormal results indicate many diseases.

2) *Serum creatinine test:* Creatinine is a breakdown product of creatine, an important component of muscle. A serum creatinine test measures the amount of creatinine in the blood. The production of creatinine depends on person's size and the muscle mass, which varies very little. Creatinine is excreted exclusively by the kidneys, and its level in the blood is proportional to the glomerular filtration rate.

The serum creatinine level provides a more sensitive test of kidney function than BUN because kidney impairment is the most common cause of elevated creatinine.

The normal (usual) value for this test is 0.8 to 1.4 mg/dl. Females have a lower creatinine than males due to decreased muscle mass. The greater-than-normal and lower than normal values indicate various diseases.

3) *Urine creatinine test:* This test measures the amount of creatinine in urine. A measurement of the serum creatinine level is often used to evaluate kidney function. Urine creatinine levels can be used as a screening test to evaluate kidney function, or can be a part of the creatinine clearance test.

Creatinine, as you would know, is a breakdown product of creatine, which is an important constituent of muscle. By far, the most important source of energy inside cells are the high-energy phosphate bonds of the ATP molecule.When one of these bonds is broken, energy is released and ATP becomes ADP. Creatine phosphate represents a backup energy source for ATP because it can quickly re-convert ADP to ATP.

The creatine molecule gradually degrades to creatinine with time. Creatinine is a waste product, that is, it cannot be used by the cells for any constructive purpose. The daily production of creatine, and subsequently creatinine, depends on the muscle mass, which fluctuates little in most normal people over long ranges of time.

Creatinine is excreted from the body entirely by the kidneys. With normal kidney function, the serum (blood) creatinine level should remain constant and normal. In normal human adult, the value is relatively constant. The average value is 15 ml/ minute. Normal values are highly dependent on the age and lean body mass of the person from whom the urine is being collected from. Urine creatine (24 hour sample) values may, therefore, be quite variable and can range from 500 mg/day to 2000 mg/ day.

The abnormal values of urine creatinine and creatinine clearance are often non-specific.

4) *Urine osmolality test:* Urine osmolality is a measurement of the number of dissolved particles in urine. It is a more precise measurement than specific gravity for evaluating the ability of the kidneys to concentrate or dilute the urine. Kidneys that are functioning normally will excrete more water into the urine as fluid intake is increased, diluting the urine. If the fluid intake is decreased, kidneys excrete less water and the urine becomes more concentrated.

The test may be done on a urine sample collected first in the morning, on multiple timed samples, or on a cumulative sample collected over a twenty-four hour period. The patient will typically be prescribed a high-protein diet for several days before the test and asked to drink no fluids the night before the test. The normal values for the test, in case of restricted fluid intake is 800 mOsm/Kg of water and with increased fluid intake, osmolality should be less than 100 mOsm/Kg.

5) *Urine protein test:* Healthy kidneys filter small molecules of proteins from the bloodstream and then reabsorb them, allowing no protein, or only slight amounts of protein into the urine. The persistent presence of significant amounts of protein in the urine, then, is an important indicator of kidney disease. A positive screening test for protein (included in a routine urinalysis) on a random urine sample is usually followed-up with a test on a 24-hour urine sample that more precisely measures the quantity of protein. Such a sample should not contain more than 150 mg protein.

The best tests for assessing renal function are the *renal clearance tests*. The term 'plasma clearance' is used to express the ability of the kidneys to clean or clear the plasma of various substances. The following clearance tests are commonly used:

i) *Creatinine clearance test:* It determines how efficiently the kidneys are clearing creatinine from the blood and serves as an estimate of kidney function. It compares the level of creatinine in urine with the creatinine level in the blood. For this test, urine and serum levels of creatinine are measured, as well as the volume of urine excreted over a 24-hour period. The creatinine clearance rate is then calculated and expressed as the volume of blood, in milliliters, that can be cleared of creatinine in one minute. The normal results for the test are 90-139 ml/min for adult males less than 40 years old and 80-125 ml/min for adult females less than 40 years old. For people above 40, the values decrease by 6.5 ml/min for each decade of life. A low creatinine clearance value indicates abnormal kidney function.

Because creatinine is found in stable plasma concentrations, is freely filtered and not reabsorbed, and is minimally secreted by the kidneys, creatinine clearance is used to estimate the glomerular filtration rate (GFR). The GFR, in turn, is the standard by which kidney function is assessed.

ii) *Inulin clearance test:* Inulin is *a complex polysaccharide found in certain plant roots.* In the test, a known amount of inulin is infused into the blood at a constant rate. The inulin is filterable, that is, it passes freely through the glomerular membranes, so that its concentration in the glomerular filtrate equals that of the plasma. In the renal tubule, inulin is not reabsorbed to any significant degree nor is it secreted by the tubules. It does not alter the renal function and is easily estimable. Consequently, the rate at which it appears in the urine can be used to calculate the rate of glomerular filtration. Inulin clearance can be calculated from the following formula,

$$C_{In} = \frac{U_{In} \times V}{P_{In}} \text{ ml/minute}$$

where, C_{In} = inulin clearance in ml/minute

U_{In} = inulin concentration in mg per 1.0 ml of urine

V = volume of urine in ml/minute

P_{In} = inulin concentration in mg per 1.0 ml of plasma

The normal inulin clearance value is 125 ml per minute.

iii) *Urea clearance test:* A test of renal function based on urea clearance. Urea is a waste product that is created by protein metabolism and excreted in the urine. The urea clearance test requires a blood sample to measure the amount of urea in the bloodstream and two urine specimens, collected one hour apart, to determine the amount of urea that is filtered, or cleared by the kidneys into the urine. The normal value of this test is 64-99 ml/min. The formula for urea clearance is given below:

$$Cu = \frac{Uu \times V}{Pu}$$

where, Cu = urea clearance in ml/minute

Uu = urine urea in mg/ml

V = volume of urine in ml

Pu = urea in mg per ml of plasma

iv) *Other blood tests:* Measurement of the blood levels of other elements regulated in part by the kidneys can also be useful in evaluating the kidney function. These include sodium, potassium, chloride, bicarbonate, calcium, magnesium, phosphorus, protein, uric acid and glucose. Apart from these, certain additional tests such as renal imaging (IVP, ultrasound, CT scan, MRI scan) and renal biopsy can be done to identify the cause of kidney problem.

You have been introduced to various tests, procedures used in the examination and assessment of renal functioning, in the discussion above. We hope this information will be of use to you in dietetic practice. Another aspect which we should know about is the consequences of abnormal kidney functioning. The next section focuses on this topic. But now let us take a break and recapitulate what we have learnt so far.

Check Your Progress Exercise 4

1) Fill in the blanks:

   a) BUN measures the amount of.. in the blood.

   b) The level of .... in the blood is proportional to GFR.

   c) A screening test to evaluate kidney function is .... test.

   d) A .... creatinine clearance value indicates .. ..kidney function.

   e) The normal inulin clearance value is ....

2) List the abnormal constituents of urine.

   ....

   ....

3) Why is clinical examination of urine necessary? Which chemical substances in the urine can be revealed by the special examination?

   ....

   ....

   ....

   ....

4) What do you understand by term renal function test? Name any two renal function tests.

   ....

   ....

   ....

7.9 PATHOPHYSIOLOGY OF KIDNEY

Let us start by first understanding what we mean by pathophysiology of kidney. The functional changes associated with or resulting from disease or injury of the kidneys is pathophysiology of kidney.

Now, let us study about the pathophysiology of kidney. The conditions associated with the abnormal kidney functioning include:

- *Acute glomerulonephritis:* Glomerulonephritis is a disease of the kidneys that results in the inflammation of the glomeruli of the nephrons. Acute glomerulonephritis is a common kidney disease, caused by toxins of certain streptococcal bacteria and occurs approximately 2 weeks after a severe streptococcal infection. It occurs mostly in children 3-10 years of age. The glomeruli becomes inflammed and swollen. Protein and red blood cells leak in larger quantities into the urine.

- *Chronic glomerulonephritis:* The repeated occurrence of acute glomerulonephritis, persisting proteinuria, hypertension and chronic renal failure may damage more and more nephrons, causing chronic glomerulonephritis. This may continue for a few too many years leading to oedema and coma.

- *Nephrotic syndrome:* A type of nephritis (an inflammation of the kidneys) that is characterized by low serum albumin, proteinuria and swelling (oedema). Swelling, weight gain, high blood pressure and anorexia are the key features. Nephrotic syndrome can be seen with a number of illnesses that could cause damage to the kidney glomerulus. This may be due to the progressive glomerulonephritis, diabetes mellitus, malaria or certain drugs and toxic venom. It refers to the presence of proteinurea and oedema. We will learn about dietary management of nephrotic syndrome in the Therapeutic and Clinical Nutrition Course.

- *Renal failure:* It is the inability of the kidneys to manufacture and excrete urine causing the waste products to accumulate in the blood plasma. If the kidneys do not function, waste products like urea, uric acid, creatinine and sulphuric acid will accumulate in the blood. In kidney failure, the urea level rises from 30 mg/100 ml to 150 mg/100 ml or more. The GFR falls and the kidneys cannot maintain the electrolyte balance. Symptoms appear when the glomerular filtration rate has fallen from 12 ml/minute to 30 ml/minute. In this case, the water and electrolyte balance is maintained to some extent by a careful choice of diet. Protein is severely restricted to minimize the production of sulphuric acid. Your skills as a dietitian will be tested here for planning low protein diets. When the GFR is below 3 ml/minute, dialysis is needed to maintain life.

What is dialysis? The next section presents a review on dialysis.

7.10 DIALYSIS

By now, you must have well understood the functions of kidney and the implications of abnormal kidney functioning as well. Here in this section, we shall be focusing on a alternate strategy in case of kidney failure or improper kidney function. This process is referred to as *dialysis*. The word dialysis means a form of diffusion i.e., a form of filtration to separate the macromolecules from ions and low molecular weight compounds in a solution through a semi-permeable membrane. In simple terms, dialysis is *a therapy which eliminates the toxic wastes from the body when the kidney fails, and cannot do its job of eliminating these toxic wastes.*

An artificial kidney can be made by using a semi-permeable membrane between the blood and the dialyzing fluid. The artificial kidney uses the cellulose membranes in place of the phospholipid-bilayer membranes used by real kidneys to separate the components of blood. Parallel chains form linkages with one another by hydrogen bonding to make strong fibers. These fibers in turn, interact to form the strong, sheet-like structure of the membrane. It requires the cannulation (insertion of a tube) of an artery and a vein to enable the blood to be passed through the dialyzing apparatus.

When the kidneys do not function properly, dialysis must be performed artificially. Without this artificial kidney dialysis, toxic wastes build up in the blood and tissues and cannot be filtered out by the ailing kidneys. This condition is known as *uremia*, which literally means *urine in the blood.* Eventually, this waste build-up leads to death.

The composition of a dialyzing fluid is adjusted so as to restore the blood to its correct composition. Such a technique, if carried out every few days, helps a patient with kidney failure to survive. The main functions of dialysis include *clearing wastes from the blood, restoring proper balance of certain electrolytes in the blood and eliminating extra fluid from the body.*

How is dialysis done? Let's find out.

Types of artificial kidney dialysis: Two types of artificial kidney dialysis are used clinically – *hemodialysis* and *peritoneal dialysis*. Let us briefly study about both of these processes.

- *Hemodialysis:* In hemodialysis, the process takes place inside a machine. Blood is taken from the body, pumped into the dialysis machine, cleaned and pumped back into the body. Hemodialysis uses a cellulose-membrane tube that is immersed in a large volume of fluid. The blood is pumped through this tubing and then back into the patient's vein as shown in the Figure 7.7. The membrane has a molecular weight cut-off that will allow most of the solutes in the blood to pass out of the tubing but retain the proteins and cells. The external solution in which the tubing is immersed is a salt solution with ionic concentrations near or slightly lower than the desired concentrations in the blood. Recall that if the external concentration of a particular species is lower than the internal concentration, then that species will pass through the cellulose membrane by diffusion into the external solution. In this manner, excess substances in the blood are removed from the body. To maintain the blood's concentration of a species, the external solution is made to have the same concentration of that species as the blood. In such a case, the two solutions are in dynamic equilibrium and so the blood's concentration does not change.

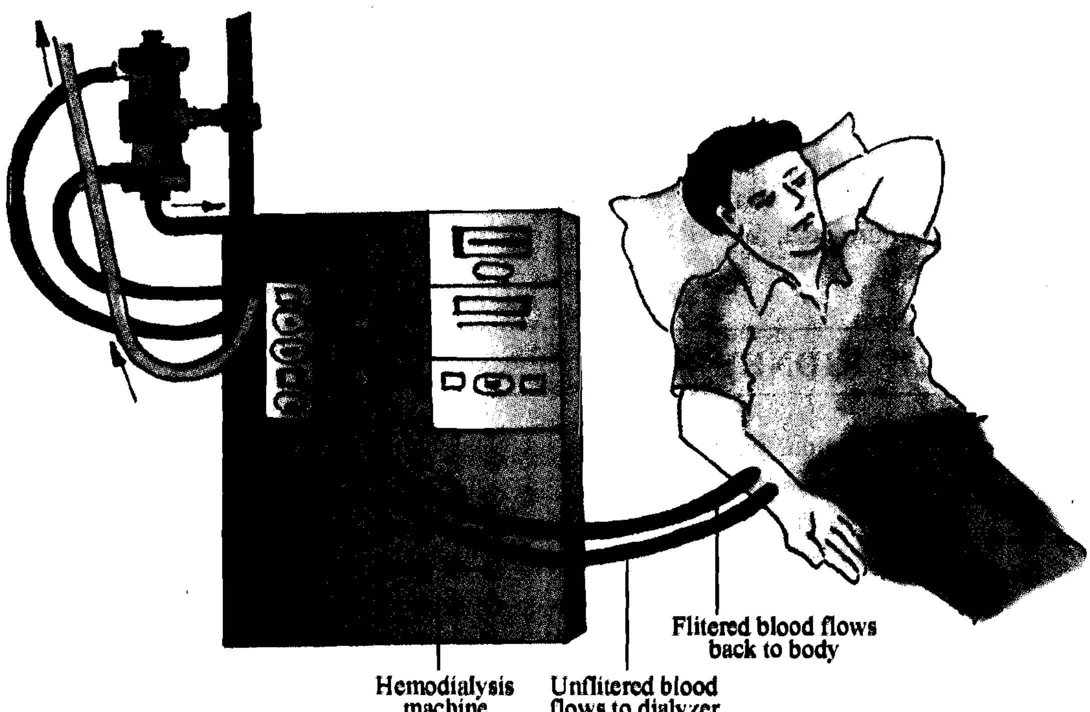

Figure 7.7: Hemodialysis

- *Peritoneal dialysis:* In peritoneal dialysis, the process of dialysis takes place inside the body. Peritoneal dialysis does not use an artificial membrane, but rather uses the lining of the patient's abdominal cavity, known as the *peritoneum*, as a dialysis membrane. As illustrated in the Figure 7.8, a tube (catheter) is inserted into the abdomen during an operation. Special dialysis fluid is injected into the abdominal cavity and solutions diffuse from the blood into this fluid. Excess waste and water pass from the blood into the fluid. After several hours, the fluid is removed with a needle and replaced with a new fluid. The patient is free to perform normal activities between fluid change.

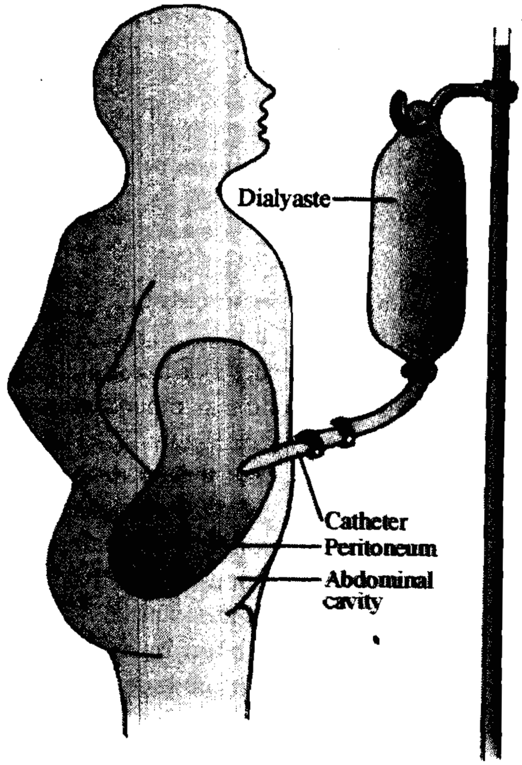

Figure 7.8: Peritoneal dialysis

Thus, artificial kidney dialysis uses the same chemical principles that are used naturally in the kidneys to maintain the chemical composition of the blood. Diffusion across semi-permeable membranes, polarity and concentration gradients are central to the dialysis process for both natural and artificial kidneys.

Other than renal dialysis, there is yet another alternative for patients with renal failure or end stage renal disease. This is *kidney transplant*. Let us learn about this procedure next. With this topic we shall end our study of the physiology of renal system.

7.11 KIDNEY TRANSPLANT

In this section, we will learn about what is kidney transplant and which are the conditions in which it becomes a necessity. So let us get started with what is kidney transplant.

What is kidney transplant?

Kidney transplant is a surgical procedure to implant a healthy kidney into a patient with kidney disease or kidney failure. The kidney transplant may be taken from a living donor or from a recently deceased donor.

The kidney of a donor may be transplanted into the pelvis of the recipient (whose kidney has been damaged). A donated kidney may come from an anonymous donor who has recently died or from a living person, usually a relative. But there may be an immunological problem. So the kidney that is transplanted must be a good match for the recipient's body. The transplanted kidney tends to be rejected by the body of the recipient, if the body's immune system doesn't recognizes it as a normal body part. Red cell and white cell (HLA typing) and tissue matching are carried out between the recipient and possible donors before this procedure is carried out.

Why is a renal transplant necessary?

A number of diseases can directly damage the kidney, which can seriously affect the removal of water and waste products, production of red blood cells, regulation of blood pressure and balance of electrolytes such as potassium, calcium and phosphorus. A kidney transplant may be recommended for patients with kidney failure caused by severe, uncontrollable high blood pressure, infections, diabetes, glomerulonephritis (a type of kidney disease caused by inflammation of the internal kidney structures, the glomeruli).

If the damage is severe enough, transplantation may be necessary. A transplant provides a patient with a kidney that can keep up with the demands of a full, active life.

You might think of a transplant as involving the removal of the old organ for replacement with the new, but in a kidney transplant, the original kidneys are left in place. The new kidney is placed lower down as you can see in the Figure 7.9. The new kidney's blood vessels are joined to the blood vessels that supply the leg and its ureter is attached to the bladder. (A small plastic tube is often inserted into the ureter to prevent it from getting blocked).

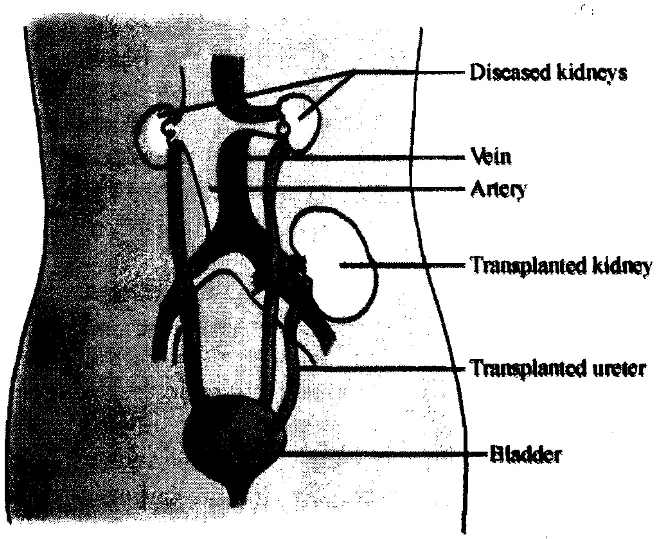

Figure 7.9: Renal transplant

With renal transplant we end our study of physiology of renal system.

Check Your ProgressExercise 5

1) What do you understand by the following terms:

a) Nephrotic Syndrome

....

....

....

b) Renal failure

....

....

....

....

c) Dialysis

....

....

2) Enumerate the types of artificial kidney dialysis.

....

....

....

3) What is a kidney transplant? What is the major problem in this process?

....

....

....

7.12 LET US SUM UP

In this unit, we learnt about the renal system, the organs involved and their major roles. We saw that there are two kidneys in our bodies which act as excretory organs. Kidneys form urine by filtration, reabsorption and secretion. In forming the urine, the water and electrolyte balance is also maintained. We learnt about excretory functions of the kidneys besides other non-excretory functions. The kidney acts as an endocrine gland and sometimes involved in metabolism.

Next we studied about the other organs in the urinary system i.e. the ureters, urinary bladder and the urethera. We studied their structure and the functions.

The unit also focused on the various diagnostic tests that are used to asses the functional status of kidneys. We studied about disorders that affect the kidney functioning. Finally, we studied about the preventive strategies which are being adopted for patients with renal failure. We learnt that the failure of kidney needs dialysis for maintaining life and in severe cases, kidney transplant is the only resort of saving one's life. The processes of dialysis and kidney transplant was discussed briefly.

7.13 GLOSSARY

Acute Glomerulonephritis : an inflammation of the glomerular nephrons caused by toxins of certain streptococcal bacteria.

Autoregulation : the intrinsic tendency of an organ or a tissue to maintain blood flow.

Calculi : an abnormal concretion in the body usually formed of mineral salts and found in the gall bladder, kidney, or urinary bladder.

Casts : the small tubules.

Chronic Glomerulonephritis: damage of a large number of nephrons caused by the repeated occurrence of acute glomerulonephritis, persisting proteinuria, hypertension and chronic renal failure.

Congenital disease : a disease or disorder that is inherited genetically.

Diuretics : the substances that stimulate the formation of urine.

Glomerulonephritis : an inflammation of the glomerulus of the kidney, characterized by the decreased production of urine and by the presence of blood and protein in the urine and oedema.

Hemolytic jaundice : jaundice due to the excessive breakdown of red cells.

Hodgkin's disease : a type of lymphoma, a cancer of the lymphatic system. It causes the cells in the lymphatic system to abnormally reproduce, eventually making the body less able to fight infection along with the steady enlargement of lymph glands, spleen and other lymphatic tissue.

Hyperosmotic : describes a cell or other membrane-bound object which has a higher concentration of solutes than its surroundings. For example, a cell which has a higher salt concentration than the salt concentration of the surrounding medium is hyperosmotic. Water is more likely to move into the cell through osmosis as a result. This is the opposite of hypoosmotic.

Hypoosmotic : describes a cell or other membrane-bound object which has a lower concentration of solutes than its surroundings. For example, a cell in a high-salt concentration medium is hypoosmotic. Water is more likely to move out of the cell by osmosis as a result. This is the opposite of hyperosmotic.

Juxtaglomerular cells : a group of cells located between afferent and efferent arterioles.

Myeloma : a tumor of the bone marrow; usually malignant and composed of cells normally found in the bone marrow.

Orifice : an entrance or outlet of any body cavity.

Osmolality : a measurement of urine concentration that depends on the number of particles dissolved in it. Values are expressed as milliosmols per kilogram (mOsm/Kg).

Porphyrins : a group of compounds containing the porphin structure, four pyrrole rings connected by methine bridges in a cyclic configuration to which a variety of side chains are attached.

Renal acidosis : an abnormal excretion of acid from the distal tubule of each nephron.

Renal failure : the inability of the kidneys to manufacture and excrete urine causing the waste products to accumulate in the blood plasma.

Transitional Epithelium : an epithelium with large polyploid superficial cells, cuboidal in the relaxed state but broad and squamous in the distended state.

Urobilinogen : a coloured substance formed in the intestine from the breakdown of bilirubin.

7.14 ANSWERS TO CHECK YOUR PROGRESS EXERCISES

Check Your Progress Exercise 1

1) The various parts of the urinary system are: 2 kidneys, 2 ureters, 1 urinary bladder and a urethra.

2) The functional unit of kidney is nephron. Its basic parts include a renal corpuscle comprising of glomerulus associated with glomerular or Bowman's capsule which serves as a filter to remove organic wastes, excess inorganic salt and water. The other part is the renal tubule which comprises PCT, loop of Henle which is responsible for carrying urine out of nephron, and DCT.

Check Your Progress Exercise 2

1) The physiological functions of kidneys are:
   - keep the concentrations of various ions and other important substances constant
   - keep the volume of water in the body constant
   - regulate the osmotic pressure of extra-cellular fluid
   - removal of wastes
   - keep the acid/base concentration of the blood constant and regulate the blood pressure
   - stimulate the RBC production, and
   - maintain calcium levels.

2) GFR or Glomerular Filtration Rate is the volume of filtrate produced per minute. Renal blood flow, sympathetic stimulation, afferent arteriolar constriction, efferent arteriolar constriction and arterial pressure are the factors affecting GFR.

3) The three steps involved in process of urine formation are simple filtration, selective reabsorption and secretion.

4) The hormone which is responsible for the regulation of water re-absorption is ADH or vasopressin. In case of increased concentration of dissolved substances and osmotic pressure in the blood, the osmoreceptors in the hypothalamus are stimulated to secrete ADH. ADH acts on the DCT and collecting ducts to cause an increase in the permeability resulting in an increased reabsorption of water, which reduces the osmotic pressure of the blood. In this way, osmotic and water balance are maintained.

5) The vessels that supply blood to the nephrons are afferent arterioles, glomerular arterioles, peritubular capillaries and interlobular veins.

Check Your Progress Exercise 3

1) Counter current mechanism is the mechanism by which the kidneys produce osmotically concentrated urine. The substances like glucose and amino acid are reabsorbed in the proximal convoluted tubule. As the solution passes down the descending limb of the loop, it becomes concentrated due to loss of water. In the ascending limb, a reverse set of actions occurs. To maintain the balance, there is an active secretion of NaCl in the ascending limb so that the tubular fluid becomes hypoosmotic with the plasma.

2) a) Kidneys act as an endocrine gland as they produce hormones such as erythropoietin which stimulates the production of RBCs in the bone marrow. It helps in the conversion of 25-hydroxycholecalciferol to the active form and secretes renin from juxtaglomerular apparatus, which through production of angiotensin stimulates aldosterone secretion.

b) Kidneys possess the property of autoregulation. This means that the blood flow in the kidneys remains constant. It is independent of the blood pressure changes, provided this pressure is within the range of 80-120 mm Hg. The glomerular blood flow and GFR are not affected by the small changes in blood pressure.

3) The ureters propel the urine from the kidney into the bladder by contraction of the muscle layer. The urinary bladder acts as a reservoir for urine.

Check Your Progress Exercise 4

1) a) urea nitrogen

b) creatinine

c) urine creatinine

d) low, abnormal

e) 125 ml/minute

2) The abnormal constituents of urine are glucose, fructose, galactose, proteins, Bence-Jones proteins, ketone bodies, bile pigments and bile salts, blood calculi, casts and pus cells.

3) Clinical examination of urine is done to detect the presence of any abnormal constituent(s) and hence can be used as an important screening test for identifying metabolic disorders. The substances in urine which can be revealed by special examination include amino acid, bile pigments and salts, clacium, creatine, creatinine, drugs, electrolytes, hormones and porphyrins.

4) Renal function tests are the common test and procedures used to evaluate renal function. These functions include removal of metabolic waste products from the bloodstream, regulatin of body's water balance and maintenance of pH. BUN and serum creatine test are the two renal function tests.

Check Your Progress Exercise 5

1) a) Nephrotic syndrome is a type of inflammation of the kidneys, that is characterized by low serum albumin, proteinuria and edema. It can be seen with a number of illnesses that could cause damage to the kidney glomerulus such as glomerulonephritis, diabetes mellitus, malaria or certain drugs and toxic venom.

b) Renal failure is the inability of the kidneys to manufacture and excrete urine causing the waste products such as urea, uric acid, creatinine and sulphuric acid to accumulate in the blood. The GFR falls and the kidneys cannot maintain the electrolyte balance.

c) Dialysis is a form of diffusion/filtration process to separate the macromolecules from ions and low molecular weight compounds in a solution through a semi-permeable membrane between the blood and the dialyzing fluid. The cellulose membranes are used in place of the phospholipid-bilayer membranes to separate the components of blood.

2) There are two types of artificial kidney dialysis.

a) Hemodialysis: A method of dialysis in which the blood is purified by circulating through an apparatus outside the body.

b) Peritoneal dialysis: A method of purifying the blood by flushing the abdominal cavity with dilute salt solution. The solution is removed with the needle and replaced with new fluid.

3) Kidney transplant is a surgical procedure to implant a healthy kidney into a patient with kidney disease or kidney failure. The transplanted kidney tends to be rejected by the body of the recipient, if the body's immune system doesn't recognizes it as a normal body part.