19.3. MECHANISM OF URINE FORMATION

The whole process of urine formation occurs in three stages and these are—

(*i*) Glomerular ultrafiltration

(*ii*) Tubular reabsorption

(*iii*) Tubular secretion.

The first step in urine formation is the glomerular filtration. The water, inorganic and organic compounds of low molecular weight present in the plasma are filtered by the wall of the capillaries of the glomerulus as the capillaries are highly permeable. The filtration occurs through three layers *i.e.* the endothelium of glomerular capillaries, the epithelium of Bowman's capsule and the basement membrane between these two layers. Water, inorganic salts *viz.* Na^+, K^+, Cl^-, HCO_3^- and organic compounds such as urea, uric acid, glucose, amino acids can pass through the wall of the capillaries very easily except plasma protein, RBC and WBC. This is called the glomerular filtrate. Chemically this fluid has almost similar components of plasma but without any plasma protein.

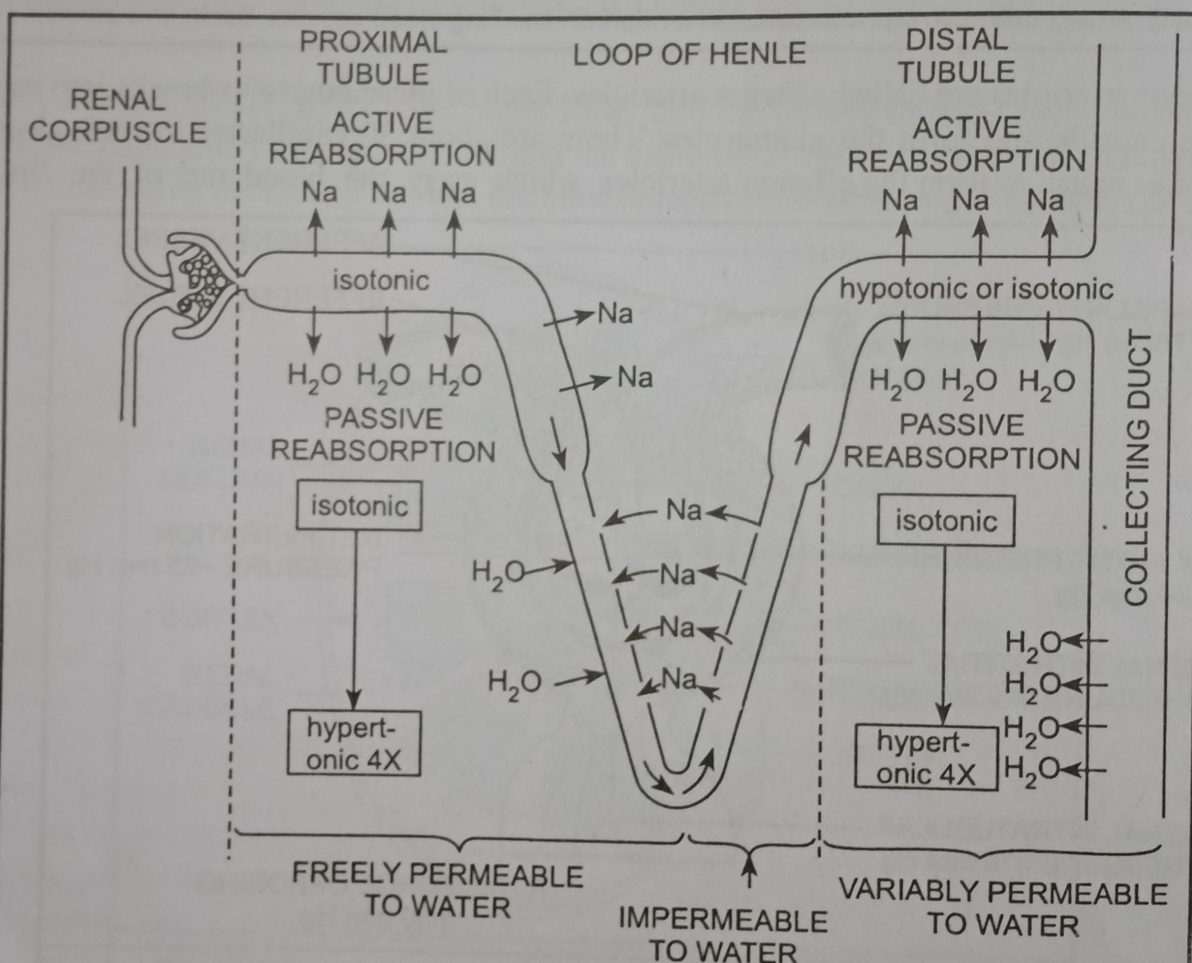

Fig 19.5. Mechanism of urine formation

The glomerular filtrate is formed mainly due to hydrostatic pressure of the glomerular capillaries which is 70-90 mm. Hg. It also depends upon the oncotic pressure of the plasma which is about 30 mm. Hg. and the volume of fluid pressure within the glomerular capsules is about 15 mm. Hg. Therefore, the pressure realizing the glomerular filtration is the difference between glomerular capillary pressure and sum total of oncotic pressure and intracapsular pressure of fluid. Hence the filtration pressure is $70 - (30 + 15) = 25$ mm. Hg.

The amount of filtrate formed by the kidneys per minute is called **glomerular filtration rate (GFR)**. About 130 ml. of glomerular filtrate is formed per minute in both the kidneys which amounts to 170-180 litres in a day. This large filtration capacity is possible because of rich blood supply to the kidneys, the specialized structure and the large filtration surface of the glomerular capillaries and also the relatively high blood pressure within them. However, this fluid is greatly reduced and modified and the amount of urine excreted per day is only 1.5 litres. Nearly 99 per cent of the filtrate has been reabsorbed by the renal tubules before it reaches the ureter. This is possible because large amount of water of the filtrate with some inorganic and organic ions are reabsorbed as the fluid passes through the tubule. This is called **reabsorption.** Glucose, amino acids, Na^+ etc. of the filtrate are reabsorbed in the renal tubules by active absorption while nitrogeneous wastes and to some extent water are absorbed passively in the initial segments of the renal tubule.

The kidneys have an elaborate mechanism of controlling the glomerular filtration rate. Juxta glomerular apparatus (JGA), a special sensitive region formed by the cellular modifications in the distal convoluted tubules and the afferent arterioles control the glomerular filtration rate. These cells of JGA stimulate the secretion of renin if the GFR falls below normal which causes more blood flow to the glomerular and thereby increasing the glomerular filtration rate.

To reduce the volume of the urine as mentioned above, most of the glomerular filtrate is absorbed in the renal tubules. The epithelial cells of the different parts of the renal tubule reabsorbed the filtrate either by active or passive mechanisms. Glucose, amino acids, Na^+ etc. are reabsorbed actively while the nitrogenous wastes and water are absorbed by passive mechanism. The reabsorption of substances from the glomerular filtrate into the blood differs in different segments of the nephron. Some parts of the tubule also secrete H^+, K^+ and ammonia into the filtrate and thereby maintaining the ionic and acid balance of the body.

9.4. FUNCTIONS OF THE TUBULES

Proximal Convoluted Tubule (PCT). The cavity of the Bowman's capsule continues into proximal convoluted tubule (PCT). It is a coiled structure and lined by free brush bordered cuboidal epithelium. Because of the presence of microvilli, the absorptive power is increased. The functions of PCT are to reabsorb 70-80 per cent electrolytes and water from the glomerular filtrate. It also maintains the pH and ionic balance of the body fluid by secreting the H^+ ions, K^+ ions and ammonia into the filtrate and by absorbing HCO_3^- from the filtrate.

Henle's loop. The proximal convoluted tubule merges with descending loop of Henlee and it ultimately forms the ascending limb of the loop. The descending limb consists of squamous epithelium and the ascending limb consists of cuboidal and columnar epithelium. The Henle's loop plays important role in maintaining the osmolarity of interstitial cells. The descending loop of Henlee is permeable to water but impermeable to electrolytes and so absorption of electrolytes does not occur here but the filtrates is concentrated due to the absorption of water. On the other hand the ascending loop is impermeable to water but allows the transport of electrolytes either by active or passive mechanisms., As a result the concentrated filtrate moves upward and gets diluted due to the passage of electrolytes into the medullary fluid.

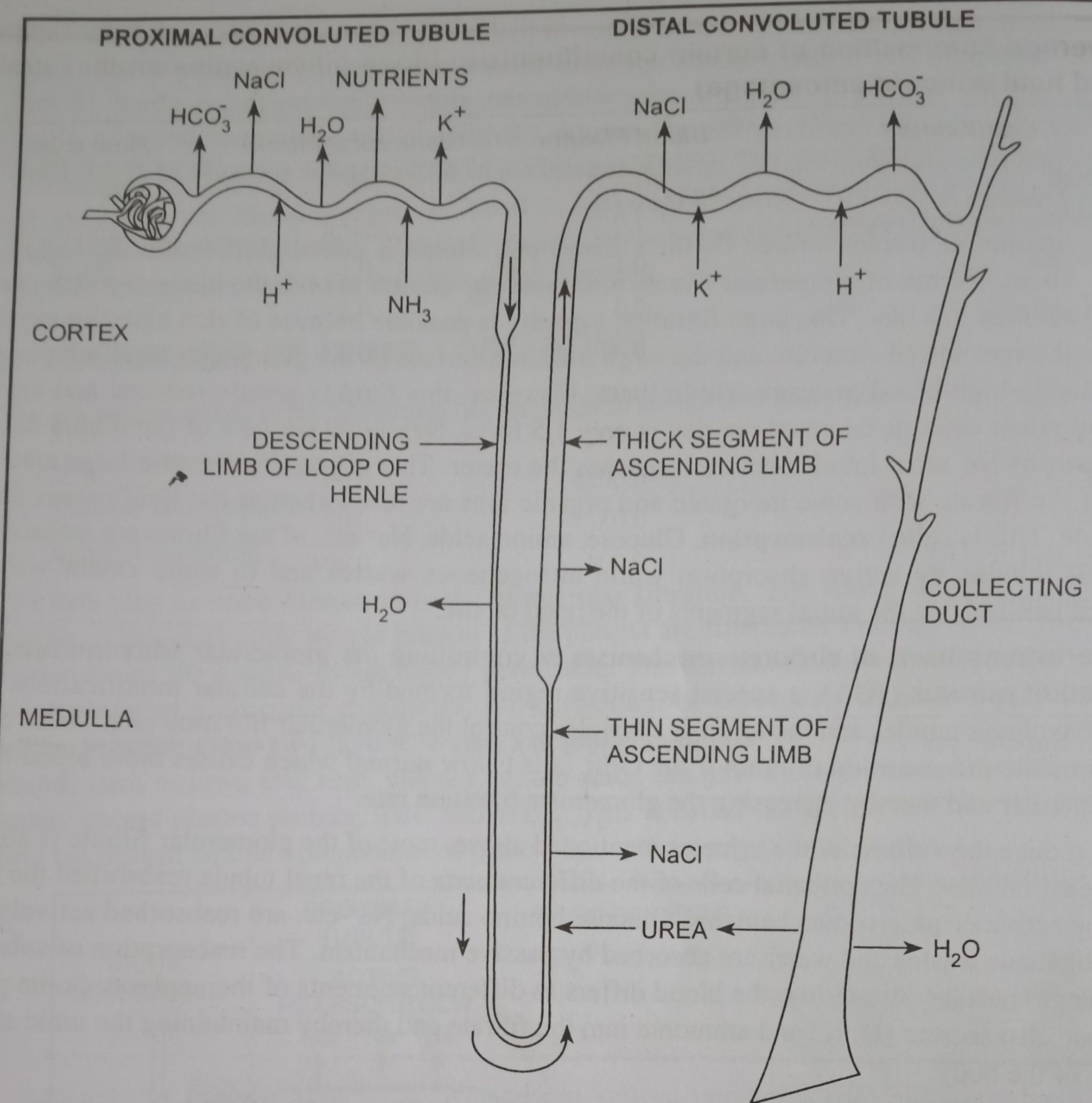

Fig. 19.6. Reabsorption and secretion of major substances at different parts of the nephron showing the direction of movement of materials.

Distal convoluted tubule (DCT). It is the continuation of the ascending limb of Henle. It is lined by cuboidal epithelium which has no brush border and possess less number of microvilli. The wall of the distal convoluted tubules further absorb water, sodium, potassium and HCO_3^- ions from the filtrate. Moreover, this part of the renal tubule secretes hydrogen and potassium ions and NH_3 to maintain the pH and sodium-potassium balance in blood.

Collecting duct. Many of the distal convoluted tubules open into the collecting tubules or collecting ducts. All the collecting ducts join together to constitute the large duct known as duct of Bellini which ultimately forms the ureter. More water is absorbed in this region to produce concentrated urine. This duct is also responsible for maintenance of pH and ionic balance of blood by the selective secretion of H^+ and K^+ ions.

19.5. MECHANISM OF CONCENTRATION OF THE FILTRATE

Mammals and birds produce hypertonic urine which is an adaptation of land vertebrates for the conservation of water.

(A) Average composition of certain constituents in blood plasma, glomerular filtrate and final urine (in percentage)

Constituents	*Blood Plasma*	*Glomerular filtrate*	*Final urine*
1. Water	90—92	99	98—99
2. Proteins, Fats and Glycogen	7.9	absent	absent
3. Glucose	0.1	0.1	absent
4. Na^+	0.3	0.3	0.4
5. Cl^-	0.37	0.37	0.7
6. K^+	0.02	0.02	0.15
7. SO_4	0.002	0.002	0.18
8. Mg^{++}	0.0025	0.0025	0.006
9. Urea	0.03	0.02	2.0
10. Uric acid	0.004	0.004	0.05
11. Creatinine	0.001	0.001	0.075

(B) Average amount of various substances of glomerular filtrate and urine in one day in adult human.

Substances	*Amount present in glomerular filtrate*	*Amount passed in urine*
1. Na^+	600 gm	6 gm
2. K^+	35 gm	2 gm
3. Ca^{++}	5 gm	0.2 gm
4. Glucose	200 gm	Traces or absent
5. Water	180 litres	1.5 litre
6. Urea	60 gm	35 gm

This is only possible for the counter-current mechanism. The Henle's loop and vasa recta play significant role for concentration of urine and thus forming the hypertonic urine.

To make the hypertonic urine, 90 to 99 per cent of water and other useful substances are absorbed by the tubular part of the nephron and passed on to the blood. Due to the presence of microvilli in the epithelial lining and more surface area of absorption in the proximal convoluted tubule most of the water, glucose, amino acids etc. are absorbed in this part of renal tubule. Absorption of all these substances make the tubular fluid isotonic. The concentrated tubular fluid passes along the descending limb of loop of Henle. As the descending limb is permeable to water but impermeable to sodium the water moves out and so tubular fluid becomes more hypertonic by the time it reaches the tip of the loop of Henle. Due to impermeability of sodium, osmotic concentration of sodium rises. The passage of water through the descending limb of Henle is passive and it is possible only because of the active reabsorption of sodium in the ascending limb which then passes to the interstitial fluid. As a result the interstitial fluid becomes hypertonic and so it attracts more water from the descending limb. The passage of water from the urine in descending limb facilitates the reabsorption of sodium in the ascending limb while the reabsorption of sodium facilitates passage of water from the descending limb. Both the processes are coupled and so operate together. The counter current mechanism changes the isotonic nephritic filtrate to hypertonic urine. The increase in the length of the limbs of Henle's loop leads to more concentration of urine *i.e.* hypertonic urine. Desert animals are having long loops of

Henle and so they can conserve more water by eliminating concentrated urine. The human urine is four times concentrated than the glomerular filtrate that are produced initially.

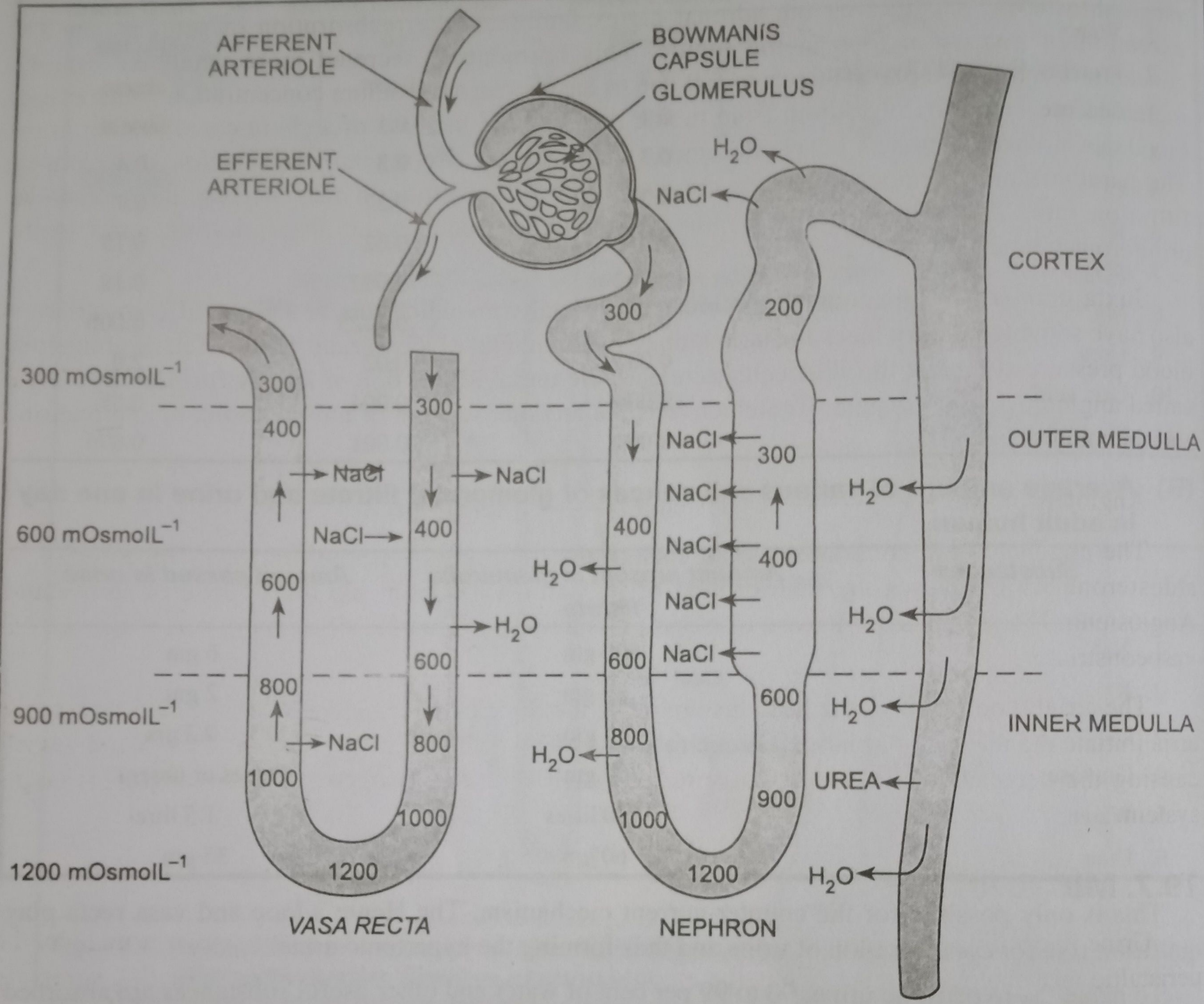

Fig. 19.7. Diagrammatic representation of a nephron and vasa recta showing counter-current mechanism.

19.6. REGULATION OF KIDNEY FUNCTION

The function of the kidney is regulated by nervous system, hormonal feedback mechanisms, JGA and by heart.

The autonomic nervous system controls the glomerular filtration and tubular reabsorption. The kidneys are innervated y the sympathetic nerves. The nerve impulses cause the constriction or dilation of the renal blood vessels. It increases the permeability of the glomerular wall and also effect the tubular reabsorption.

The rate of urine formation and its concentration are controlled by the hormonal mechanism. Changes of blood volume, body fluid volume and the ionic concentration in the body fluid activate the osmoreceptors of the body which in turn stimulate the neorohypophysis to release the antidiuretic hormone (ADH). The ADH stimulates the water reabsorption in the tubule and thereby preventing the diuresis. On the other hand the increase of body fluid volume prevents the release of ADH. ADH or vasopressin also effect the functioning of the kidney by constricting the blood vessels which causes the increase of blood pressure. Increase blood pressure causes the more formation of glomerular filtration rate. Aldosterone secreted by the adrenal cartex facilitates the reabsorption of sodium ions and excretion of potassium ions in the tubule. This hormone is secreted more when the osmotic concentration of blood plasma tends to fall due to the decrease of sodium concentration which causes increased reasbsorption of sodium from tubule resulting the increase of sodium concentration in the blood. Two other hormones, *i.e.* parathormone and thyroxine also regulate the function of the kidney. The parathormone hormone enhances the absorption of calcium and also increase the glomerular filtration rate. Thyroxine secreted by the thyroid gland reduces the absorption of water in the uriniferous tubules.

Juxta glomerular apparatus (JGA) located in distal convoluted tubule and the afferent arteriole also have some regulatory mechanism in kidney function. Fall of glomerular fluid or fall of glomerular blood pressure stimulate the JGA cells to release the renin. Regulation of kidney function by JGA is called angiotensinogen system. Renin converts the angiotensinogen of blood plasma to angiotensin I and then angiotensin II.

$$\text{Angiotensinogen} \xrightarrow{\text{Renin}} \text{Angiostenin I} \longrightarrow \text{Angiostenin II.}$$

The angiostenin II stimulates the adrenal cortex of adrenal gland to secrete more secretion of aldosterone which causes the reabsorption of Na^+ and water from the distal parts of the tubule. Angiostenin II also leads to increase of blood pressure and glomerular filtration rate as it also acts as vasoconstrictor.

The atrial blood flow of the heart also regulate the function of the kidney. More blood flow to the atria initiate the release of atrial-natriuretic factor (ANF) which results the dilation of the blood vessels causing the decrease of the blood pressure. So, ANF system acts opposite to the angiotensinogen system.

19.7. MICTURITION

Urine is continuously formed and transported to the urinary bladder for temporary storage by the peristaltic movement of ureter. When the amount of urine in the bladder is about 300 cc. a voluntary signal is given by the central nervous system which causes the initiation of stretching of the urinary bladder. Then the stretch receptors present in the wall of the urinary bladder send a signal to the central nervous system which on turn passes the motor messages to the urinary bladder. Then the smooth muscles of the bladder contracts and relaxation of the sphincter surrounding the urethra occurs. Due to this increased pressure in the bladder, urine is forced out through the urethra. The process of expulsion of urine is called micturition. The act of urination is naturally an unconscious reflex which however, is subjected to voluntary control. Voluntary restraint of urination is effected by maintaining the contraction of the sphincter. The total amount excreted by a normal adult man varies from 1000—1800 ml in a day with an average of about 1500 ml. The normal urine is transparent and straw-yellow or amber coloured liquid having acidic in nature. It contains a pigment called urochrome and the characteristic aromatic odour of urine is due to the presence of some volatile substances called urinod. Various conditions can affect the characteristics of urine. The volume and composition of urine are directly related to the amount and composition of food, amount of water taken into the body, environmental condition, physical condition, etc. Urine is used for clinical diagnosis of many metabolic disorders of the body. The diabetes mellitus can be easily diagnosed by the presence of glucose (*i.e.* Glycosoria) and ketone bodies (*i.e.* ketonuria) in the urine.

Functions of the Kidney

The kidney of vertebrates performs the following functions :

1. Kidney removes the nitrogeneous substance, *i.e.*, urea and uric acid from the blood.
2. Kidney maintains the fluid balance of the body by removing the excess of water.
3. Kidney regulates the pH of the blood by removing the acidic substances from the blood.
4. Kidney regulates the ionic balance of the body fluid and thereby maintaining the osmotic concentration of the cell and interstitial fluid.
5. Kidney also removes the pigments, drugs, poisons and excess vitamin from the blood.
6. Kidney regulates the blood pressure.
7. Kidney secretes the enzyme renin which plays an important role in absorption of Na^+ ion.

19.8. ROLE OF OTHER ORGANS IN EXCRETION (ACCESSORY EXCRETORY ORGANS)

In addition to the kidney, vertebrates possess other excretory organs to remove the excretory products from the body. These are :

1. Skin or integument. In number of aquatic animals where excretory organs are not well developed, excretory substance are removed from the body by diffusion through the general body surface. Ammonia is mainly diffused from the body through the integument. Higher animals like mammals including man possess two types of glands namely **sebaceous glands** and **sweat glands** in their skin.

Average Composition of Urine
(of an adult normal man taking a mixed diet in 24 hours)

Organic constituents		*Inorganic constituents*	
1. Nitrogen (total)	23—35 gm	1. Chloride (As NaCl)	10—15 gm
2. Urea	25—30 gm	2. Chloride	6—9 gm
3. Creatine	60—150 gm	3. Phosphate	0.8—1.3 gm
4. Creatinine	1.2—1.7 gm	4. Sulphate	0.8—1.3 gm
5. Uric acid	0.5—0.8 gm	5. Sodium	4-5 gm
6. Ammonia	0.3–1.0 gm	6. Potassium	2.5—3.00 gm
7. Hippuric acid	0.1—1.0 gm	7. Calcium	0.1—0.3 gm
8. Amino acid	150—200 mg	8. Magnesium	0.1–0.2 gm
9. Vitamins, hormones and enzymes	traces	9. Iodine	50—200 mgm
10. Allantoin	traces	10. Lead	50 μgm
		11. Arsenic	50 μgm
		12. Iron	0.006 gm
		13. Water	1000—1500 ml

The **sebaceous glands** of the skin are located near the hairs, the duct of which opens into the hair follicles. These are holocrine glands and composed of stratified epithelium. It secretes the sebum which mixes with the sweat on the surface and making the skin softer and lubricating the hair. Some excretory substances like waxes, fatty acids, sterols are excreted from the body in the form of sebum.

The **sweat glands** are embedded in the sub-cutaneous layer of the skin and are distributed evenly over the body surface. The glands secrete sweat. The sweat is responsible for elimination of certain breakdown products of metabolism, help in the loss of body heat and maintaining the osmotic concentration of the body fluid by eliminating the water and salts. However, small amount of sodium chloride, urea, lactic acid are also eliminated form the body along with the sweat.

The **liver** removes the bile pigments namely biliverdin and bilirubin formed by the decomposition of the haemoglobin of the worn out RBC through the bile. These pigments pass into the alimentary canal along with the bile and finally removed with the foecal matter. The liver eliminates cholesterol, steroid hormones, some vitamins and drugs via bile. Moreover, ammonia produced from the deamination of amino acids combines with carbon dioxide to form urea. The process is known as ornithine cycle. Uric acid is also produced in liver in uricotelic animals. The damaged liver cannot remove the bile pigments and so the pigments accumulate in the blood and cause jaundice. The excess pigments import yellowish tinge to the skin.

Lungs eliminate carbon dioxide (18 litres/day) and water in the form of water vapour formed during respiration. Water vapour and CO_2 are removed by the lungs during expiration.

Calcium, magnesium and iron ions are excreted internally by the epithelial cells of the **intestine** which are later excreted along with the faecal matter.

19.9. DISORDERS OF THE EXCRETORY SYSTEM

In *uremia*, urea level of the blood rises abnormally which may cause the failure of the kidney function. As a result metabolic waste are accumulating in the blood which may cause many physiological disorders. In such conditions, artificial measures are adopted to remove all these waste products from the blood. The process is called **hemodialysis** and the apparatus used for this is known as **hemodialiser** or **artificial kidney.** In hemodialysis, the blood of the patient is taken out from a convenient artery and cooled to 0°C. Then an anticoagulant (like heparin) is added to the blood to prevent coagulation. The blood is then pumped into the hemodialiser. The blood flows in the apparatus through tubes bounded by collophane membrane. This membrane is impermeable to protein but permeable to urea, uric acid, creatine. Thus the membrane filters the permeable substances from the blood into a salt solution where the tubes are immersed. Then the blood free from these metabolic wastes is warmed to body temperature and are mixed with antiheparin to restore its normal coagulability. This purified blood is then pumped back into the body of the patient through a vein. The whole process is commonly known as dialysis.

The acute renal failure in human can be corrected by transplantation of damaged kidney by a functional kidney. A kidney from a donor, preferably a close relative having the same blood group may be used for transplantation to minimise its chances of rejection by the immune system of the host.

Formation of stone calculi is another problem that occurs in most of the cases. The stone in the kidney is mainly formed by the oxalate and phosphate crystallised salts within the kidney. The calculi in the kidney are mostly removed by surgical procedure.

Inflammation or malfunctioning of the glomerulus of the kidney may lead to a condition known as glomerulonephritis which ultimately results severe metabolic disorder within the body.

Salient Points to Remember

1. Metabolic waste products are removed from the body by excretion. Separation and elimination of water ...of cellular metabolism are carried out by excretion. ...products, water, carbon dioxide, inorganic salts, excess ... are removed by lungs but