

Excretion

Chapter Outline

- 8.1 Modes of Excretion
- 8.2 Human excretory system
- 8.3 Mechanism of urine formation in human
- 8.4 Regulation of kidney function
- 8.5 Micturition
- 8.6 Role of other organs in excretion
- 8.7 Disorders related to the excretory system
- 8.8 Haemodialysis



Seabirds have no problem in drinking sea water

Learning Objectives:

- Understands different modes of excretion in animals.
- Learns the structure of the human excretory system.
- Understands the structure of a nephron, mechanism of urine formation - glomerular filtration reabsorption and secretion from the renal tubules.
- Visualizes the blood supply to the kidney including the nephrons
- Learns about the possible kidney related diseases.



Earliest animal life forms arose around 700 million years ago. They were marine organisms like the modern sponges. Each cell of a modern sponge is surrounded

by sea water, but it maintains an intracellular ionic composition different from that of the sea water. Evolution led to changes in the organisation of the tissue layers followed by formation of specialized external tissue layers. This provided a barrier between the external environment and internal fluid resulting in the formation of extracellular fluid. Major changes in osmoregulation and ionic regulation occurred during the evolution of chordates. The ability to control extracellular fluid composition was essential for the diversification of animals to inhabit brackish water, fresh water and land. Animals that invaded land had the risk of desiccation and were unable to excrete metabolic waste directly into the water; hence there was a need for an alternate pathway to dispose the nitrogenous wastes.

Most animals rely on kidneys to control ionic and water balance. Some

animals depend on external tissues such as the gills, skin and digestive mucosa to collectively regulate three homeostatic processes namely, osmotic regulation, ionic regulation and nitrogen excretion. Osmotic regulation is the control of tissue osmotic pressure which acts as a driving force for movement of water across biological membranes. Ionic regulation is the control of the ionic composition of body fluids. The process by which the body gets rid of the nitrogenous waste products of protein metabolism is called excretion. Nitrogen excretion is the pathway by which animals excrete ammonia, the toxic nitrogenous end product of protein catabolism. The removal of ammonia or other metabolic alternatives such as urea and uric acid is linked to ionic and osmotic homeostasis.

Fresh water vertebrates maintain higher salt concentrations in their body fluids; marine vertebrates maintain lower salt concentrations in their body fluids and terrestrial animals have more water in their body than the surrounding hence tend to lose water by evaporation. Osmoconformers are able to change their internal osmotic concentration with change in external environment as in marine molluscs and sharks. Osmoregulators maintain their internal osmotic concentration irrespective of their external osmotic environment (example: Otters). Depending on the ability to tolerate changes in the external environment, animals are classified as stenohaline and euryhaline. The stenohaline animals can tolerate only narrow fluctuations in the salt concentration (example: Gold fish), whereas the euryhaline animals are able

to tolerate wide fluctuations in the salt concentrations eg., *Artemia*, *Tilapia* and salmon.

The major nitrogenous waste products are ammonia, urea and uric acid. Other waste products of protein metabolism are trimethyl amine oxide (TMO) in marine teleosts, guanine in spiders, hippuric acid, allantoin, allantoic acid, ornithuric acid, creatinine, creatine, purines, pyrimidines and pterines.

8.1 Modes of Excretion

Excretory system helps in collecting nitrogenous waste and expelling it into the external environment. Animals have evolved different strategies to get rid of these nitrogenous wastes. Ammonia produced during amino acid breakdown is toxic hence must be excreted either as ammonia, urea or uric acid. The type of nitrogenous end product an animal excretes depends upon the habitat of the animal. Ammonia requires large amount of water for its elimination, whereas uric acid, being the least toxic can be removed with the minimum loss of water, and urea can be stored in the body for considerable periods of time, as it is less toxic and less soluble in water than ammonia.

Animals that excrete most of its nitrogen in the form of ammonia are called **ammonoteles**. Many fishes, aquatic amphibians and aquatic insects are ammonotelic. In bony fishes, ammonia diffuses out across the body surface or through gill surface as ammonium ions. Reptiles, birds, land snails and insects excrete uric acid crystals, with a minimum loss of water and are called **uricoteles**. In terrestrial animals, less toxic urea and

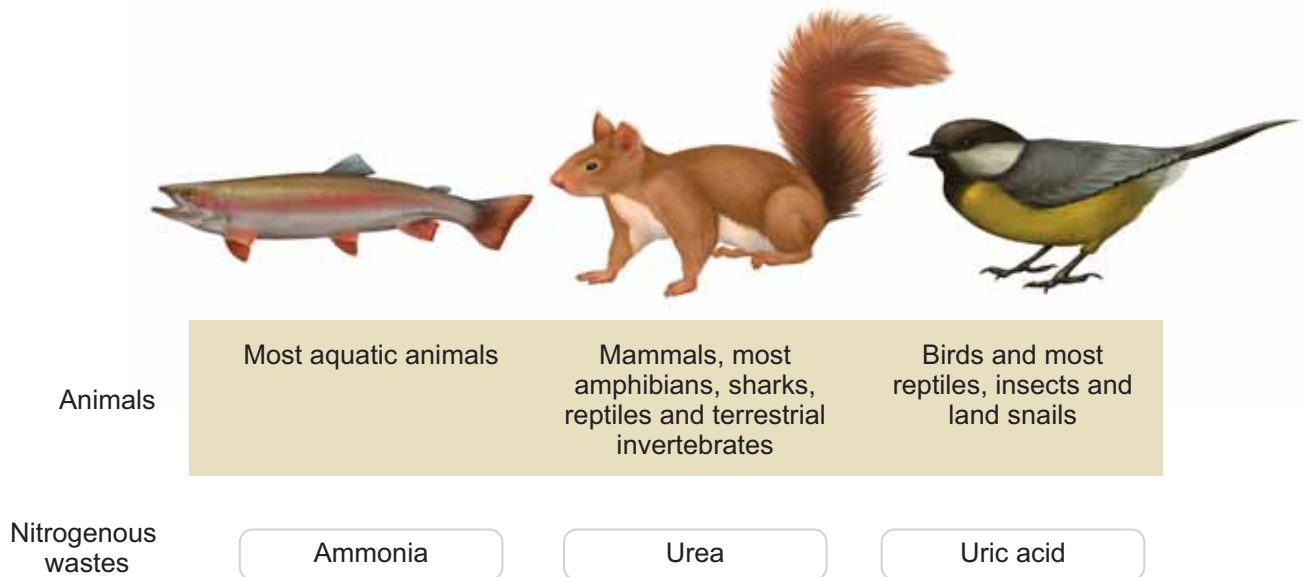


Figure 8.1 Excretory products in different groups of animals.

uric acid are produced to conserve water. Mammals and terrestrial amphibians mainly excrete urea and are called **ureoteles**. Earthworms while in soil are ureoteles and when in water are ammonoteles. Figure 8.1 shows the excretory products in different groups of animals.

The animal kingdom presents a wide variety of excretory structures. Most invertebrates have a simple tubular structure in the form of primitive kidneys called **protonephridia** and **metanephridia**. Vertebrates have complex tubular organs called kidneys. Protonephridia are excretory structures with specialized cells in the form of **flame cells** (cilia) in Platyhelminthes (example tapeworm) and **Solenocytes** (flagella) in *Amphioxus*. Nematodes have **renette cells**, **Metanephridia** are the tubular excretory structures in annelids and molluscs. **Malpighian tubules** are the excretory structures in most insects. **Antennal glands** or **green glands** perform excretory function in crustaceans like prawns. Vertebrate kidney differs among taxa in relation to the environmental conditions.

Nephron is the structural and functional unit of kidneys. Reptiles have reduced glomerulus or lack glomerulus and Henle's loop and hence produce very little hypotonic urine, whereas mammalian kidneys produce concentrated (hyperosmotic) urine due to the presence of long Henle's loop. The Loop of Henle of the nephron has evolved to form hypertonic urine. Agglomerular kidneys of marine fishes produce little urine that is isoosmotic to the body fluid. Amphibians and fresh water fish lack Henle's loop hence produce dilute urine (hyposmotic).



The average bladder holds between 300ml and 600ml of urine. If the urinary system is healthy, urine may stay in the bladder for up to about 5 hours before excretion, depending on the amount of liquid consumed. Nerves send signals to the brain when the bladder needs to be emptied, with this indication one will feel the urge to empty the bladder. The muscle in the bladder wall is called the 'detrusor' muscle. One may suffer from stress if the muscles supporting the bladder are weakened. Pelvic floor exercise helps to strengthen these muscles.

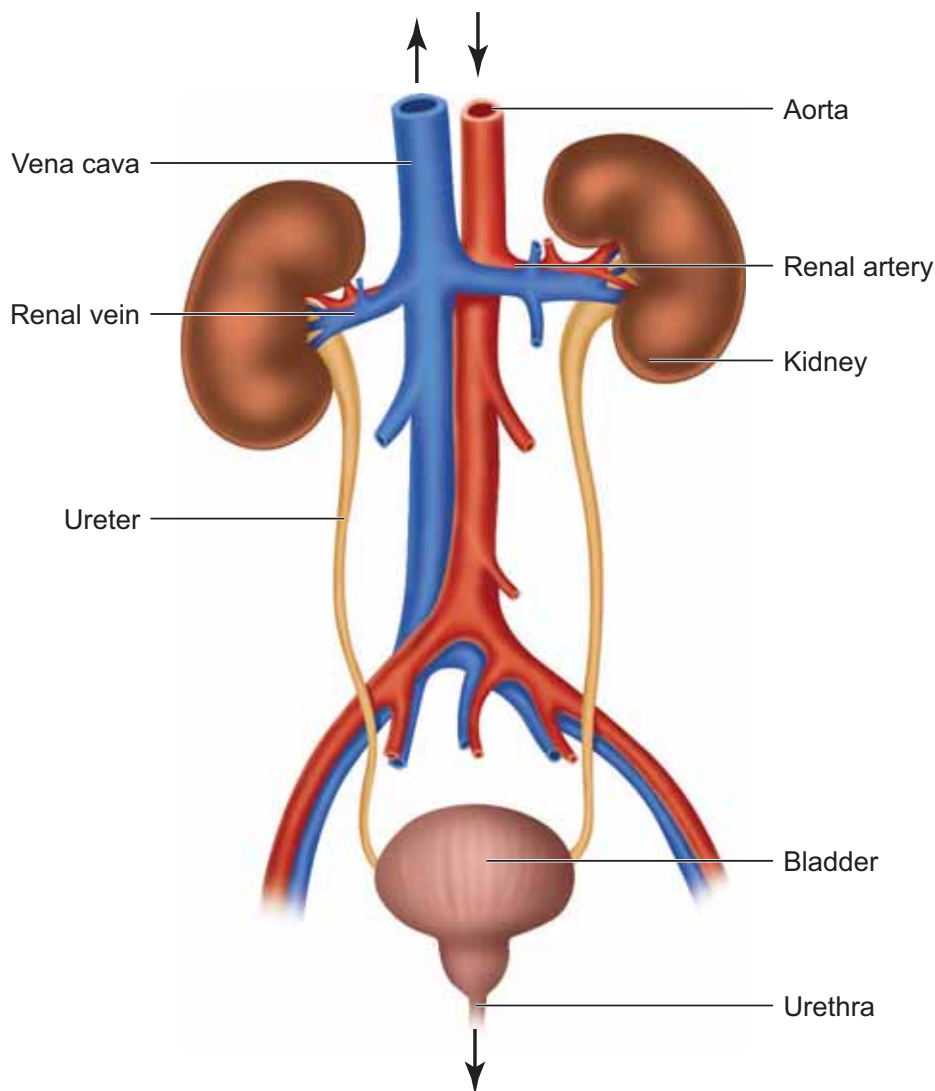


Figure 8.2 Human excretory system

8.2 Human excretory system

8.2.1 Structure of kidney

Excretory system in human consists of a pair of kidneys, a pair of ureters, urinary bladder and urethra (Figure. 8.2). Kidneys are reddish brown, bean shaped structures that lie in the superior lumbar region between the levels of the last thoracic and third lumbar vertebra close to the dorsal inner wall of the abdominal cavity. The right kidney is placed slightly lower than the left kidney. Each kidney weighs an average of 120-170 grams. The outer layer of the kidney is covered by three layers of

supportive tissues namely, renal fascia, perirenal fat capsule and fibrous capsule.

The longitudinal section of kidney (Figure. 8.3) shows, an outer cortex, inner medulla and pelvis. The medulla is divided into a few conical tissue masses called medullary pyramids or renal pyramids. The part of cortex that extends in between the medullary pyramids is the renal columns of **Bertini**. The centre of the inner concave surface of the kidney has a notch called the renal **hilum**, through which ureter, blood vessels and nerves innervate. Inner to the hilum is a broad funnel shaped space called the renal pelvis with projection called calyces. The

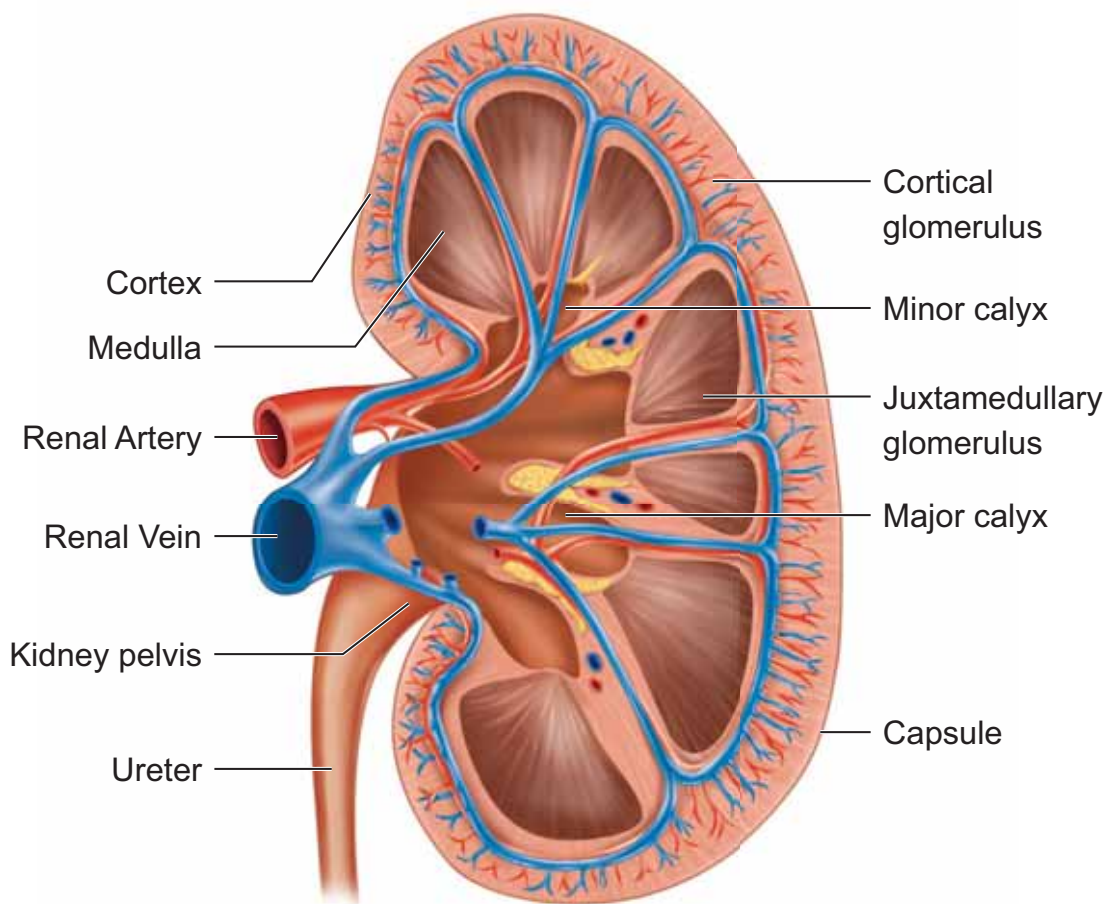


Figure 8.3 L S of kidney

renal pelvis is continuous with the ureter once it leaves the hilum. The walls of the calyces, pelvis and ureter have smooth muscles which contracts rhythmically. The calyces collect the urine and empties into the ureter, which is stored in the urinary bladder temporarily. The urinary bladder opens into the urethra through which urine is expelled out.

8.2.2 Structure of a nephron

Each kidney has nearly one million complex tubular structures called nephron (Figure 8.4). Each nephron consists of a filtering corpuscle called renal corpuscle (malpighian body) and a renal tubule. The renal tubule opens into a longer tubule called the collecting duct. The renal tubule begins

with a double walled cup shaped structure called the Bowman's capsule, which encloses a ball of capillaries that delivers fluid to the tubules, called the glomerulus (Figure 8.4). The Bowman's capsule and the glomerulus together constitute the **renal corpuscle**. The endothelium of glomerulus has many pores (fenestrae). The external parietal layer of the Bowman's capsule is made up of simple squamous epithelium and the visceral layer is made of epithelial cells called podocytes. The podocytes end in foot processes which cling to the basement membrane of the glomerulus. The openings between the foot processes are called filtration slits.

The renal tubule continues further to form the proximal convoluted tubule

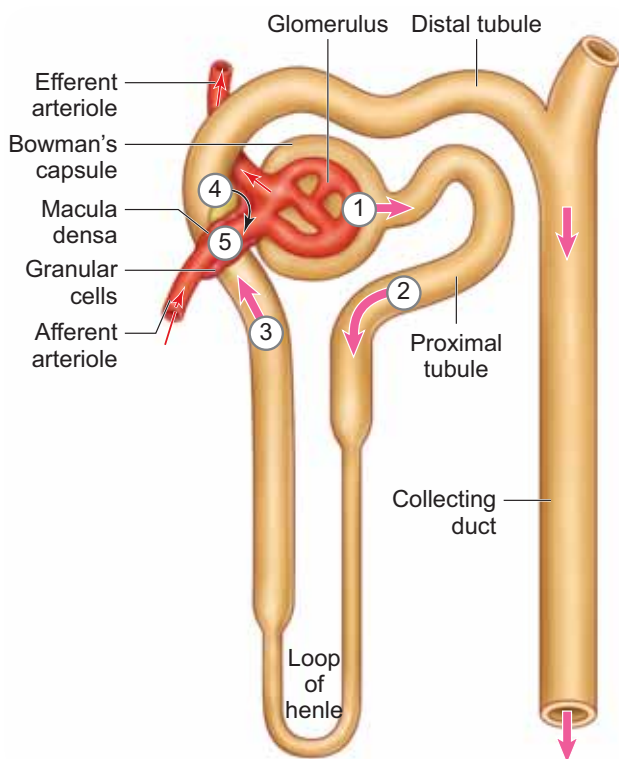


Figure 8.4 Structure of a Nephron

[PCT] followed by a U-shaped loop of Henle (Henle's loop) that has a thin descending and a thick ascending limb. The ascending limb continues as a highly coiled tubular region called the distal convoluted tubule [DCT]. The DCT of many nephrons open into a straight tube called collecting duct. The collecting duct runs through the medullary pyramids in the region of the pelvis. Several collecting ducts fuse to form papillary duct that delivers urine into the calyces, which opens into the renal pelvis.

In the renal tubules, PCT and DCT of the nephron are situated in the cortical region of the kidney whereas the loop of Henle is in the medullary region. In majority of nephrons, the loop of Henle is too short and extends

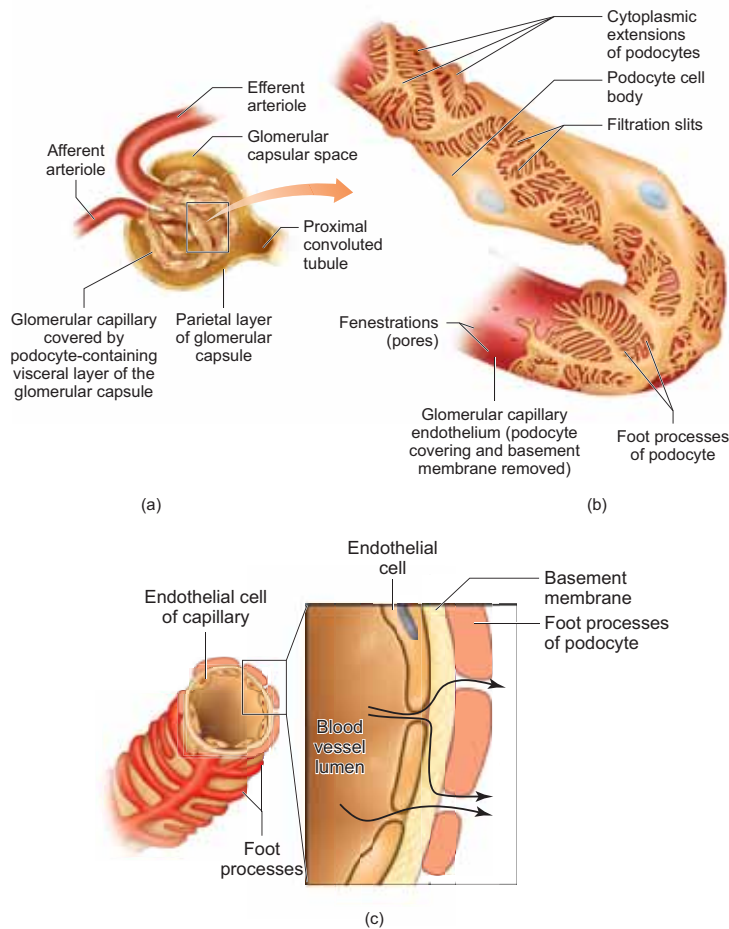


Figure 8.5 (a) Glomerulus (b) The podocytes give several foot processes that form filtration slits (c) interacts with the basement membrane to create a filter that retains blood cells and large protein in the plasma while permitting the passage of fluids through the filtration slit.

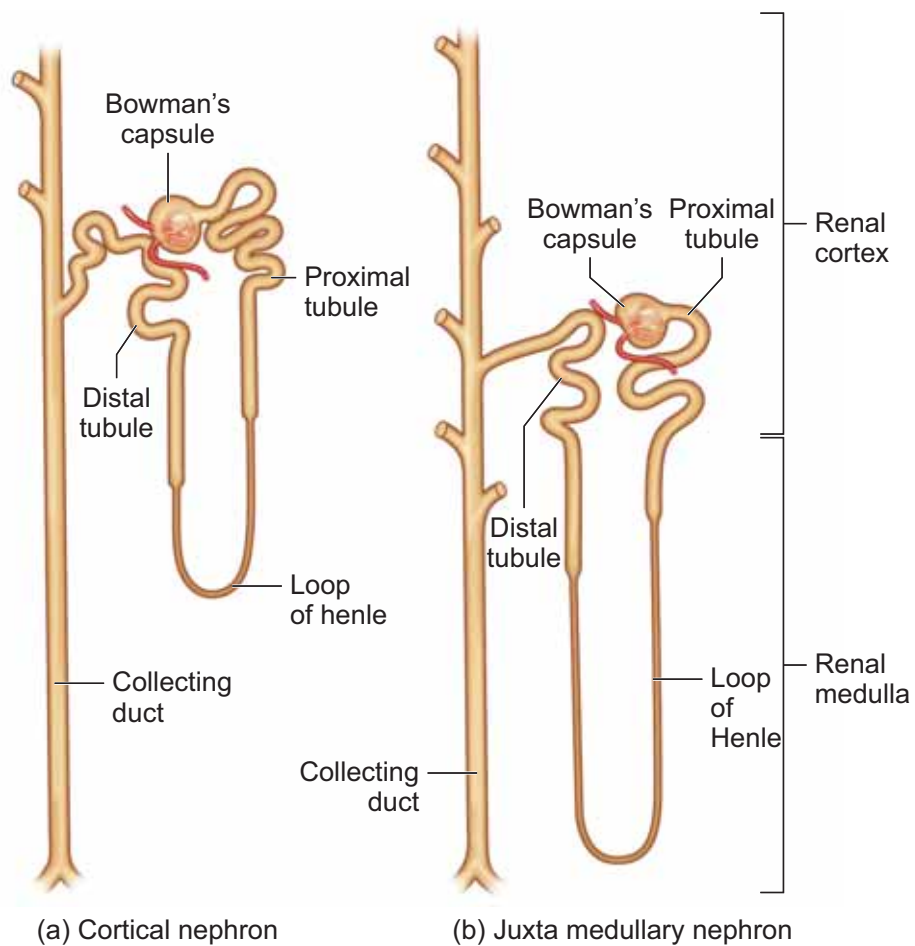


Figure 8.6 (a) Cortical nephrons are located predominantly in the outer cortex. (b) Juxtamedullary nephrons are mainly located in the inner medulla.

only very little into the medulla and are called **cortical nephrons**. Some nephrons have very long loop of Henle that run deep into the medulla and are called **juxta medullary nephrons (JMN)** (Figure 8.6 a and b)

The capillary bed of the nephrons-First capillary bed of the nephron is the glomerulus and the other is the peritubular capillaries. The glomerular capillary bed is different from other capillary beds in that it is supplied by the afferent and drained by the efferent arteriole. The efferent arteriole that comes out of the glomerulus forms a fine capillary network around the renal tubule called the peritubular capillaries. The efferent arteriole serving the juxta medullary nephron forms

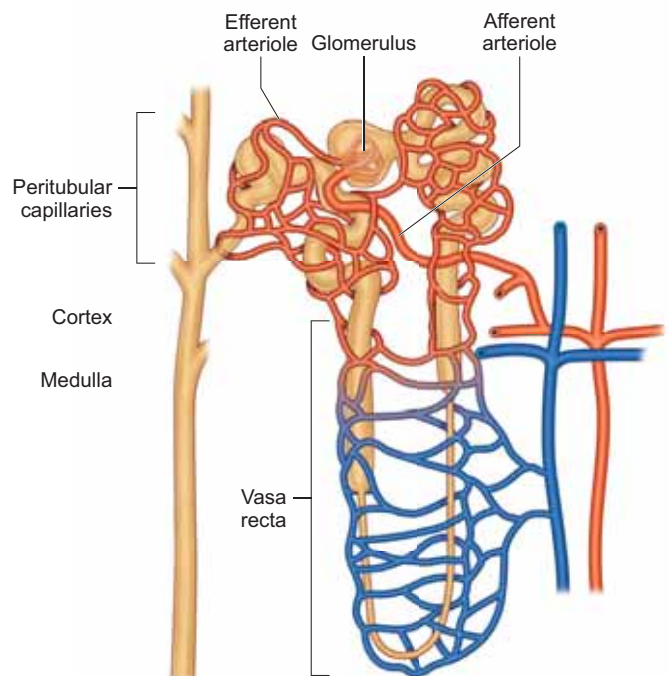
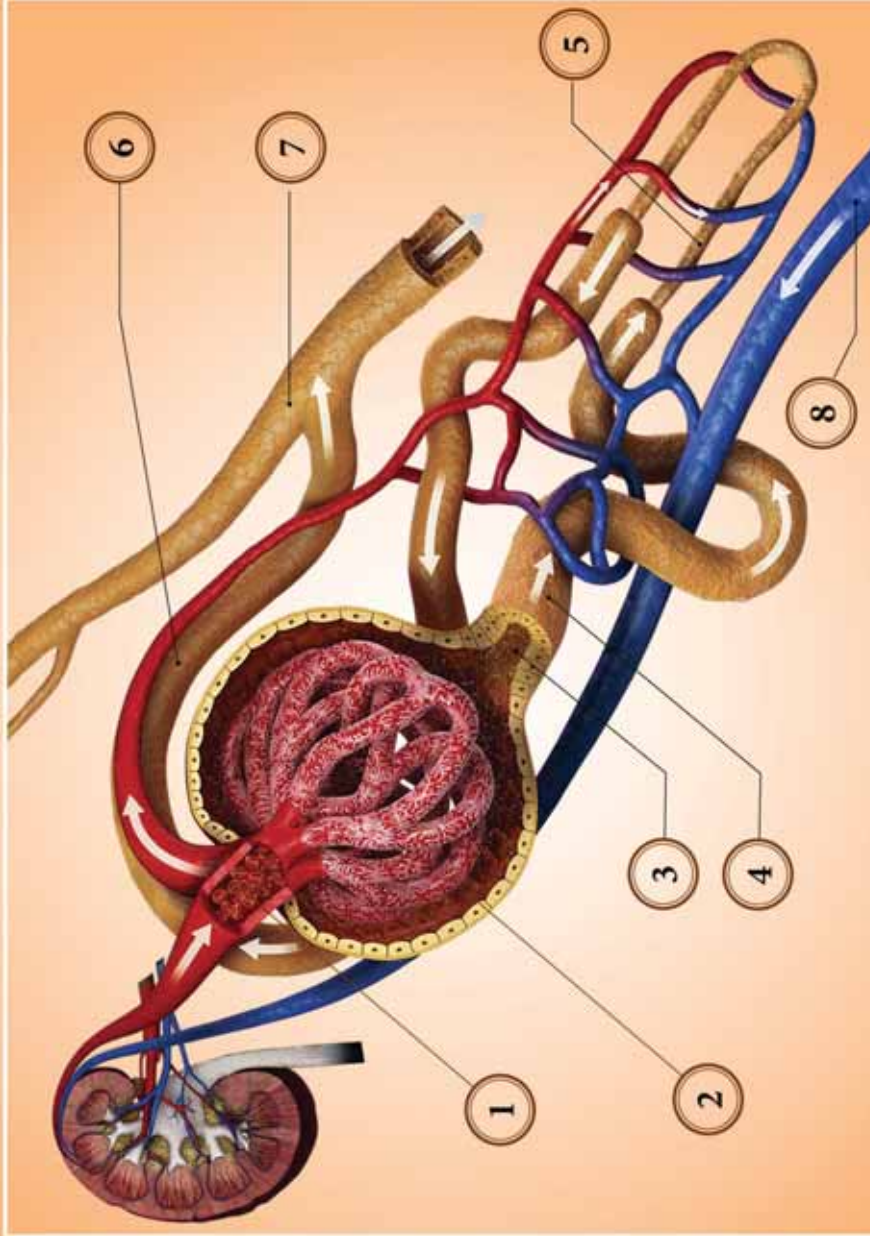


Figure 8.7 Blood vessels of the nephron.

Filtration in the Kidneys



INSIDE A KIDNEY, EACH MICROSCOPIC NEPHRON IS A COMPLEX NETWORK OF COILED CAPILLARIES AND WINDING TUBES. DOZENS OF SUBSTANCES MOVE TO AND FRO TO ELIMINATE WASTES AND FINE-TUNE URINE COMPOSITION.

1 BLOOD ENTERS THE GLOMERULUS

Blood flows from a renal arteriole into the knot of capillaries. It enters at high pressure, which will force water and other substances out of the capillaries into the capsule space.

2 CAPILLARY TO CAPSULE

Blood cells and most blood proteins are too big to cross the capillary membrane into the capsule space. But the membrane's slits and pores allow through water, mineral salts, polypeptides, and other small molecules, including wastes such as urea ammonia and creatinine.

3 PROXIMAL TUBULE

Proximal (near) to its capsule, this region allows much water to be reabsorbed into the capillaries and surrounding fluids, as well as glucose, mineral salts, and other useful substances.

4 PERITUBULAR CAPILLARIES

Also called the vasa recta, this network reabsorbs up to 99 per cent of the water in the tubule, as well as various other substances. Using active pumps, it also moves sodium from the blood to the tubule.

5 HENLE'S LOOP

As the loop of Henle dips into the renal dulla, more water moves from the tubule into the blood, as well as small amounts of mineral salts and some urea and creatinine. Some acids and amines may move into the tubule, while ammonia can go in either direction.

6 DISTAL TUBULE

Distal to (far from) its capsule, this region may see water going in or out of the tubule, depending on the concentration of water already in the tubule, while hydrogen and potassium ions move to regulate both blood and urine pH. Acids, amines, and ammonia compounds may also be transported into the tubule.

7 COLLECTING DUCT

Fine adjustment of urine composition continues into the collecting-duct system. About 5 per cent of all the water and sodium being reabsorbed into the blood is recovered here.

8 VENOUS FLOW

Blood flowing away from the nephrons carries 99 per cent of its original water, 98 per cent of its sodium, calcium, and chloride, and about 40 per cent of its urea.

bundles of long straight vessel called vasa recta and runs parallel to the loop of Henle. Vasa recta is absent or reduced in cortical nephrons (Figure 8.7).

What is the importance of having a long loop of Henle and short loop of Henle in a nephron?

8.3 Mechanism of urine formation in human

The nitrogenous waste formed as a result of breakdown of amino acids is converted to urea in the liver by the Ornithine cycle or urea cycle (Figure 8.8).

Urine formation involves three main processes namely, glomerular filtration, tubular reabsorption and tubular secretion.

i) **Glomerular Filtration:** Blood enters the kidney from the renal artery, into the glomerulus. Blood is composed of large quantities of water, colloidal proteins, sugars, salts and nitrogenous end product. The first step in urine formation is the filtration of blood that takes place in the glomerulus. This is called glomerular filtration which is a passive process. The fluid that leaves the glomerular capillaries and enters the Bowman's capsule is called the glomerular filtrate. The glomerular membrane has a large surface area and is more permeable to water and small molecules present in the blood plasma. Blood enters the glomerulus

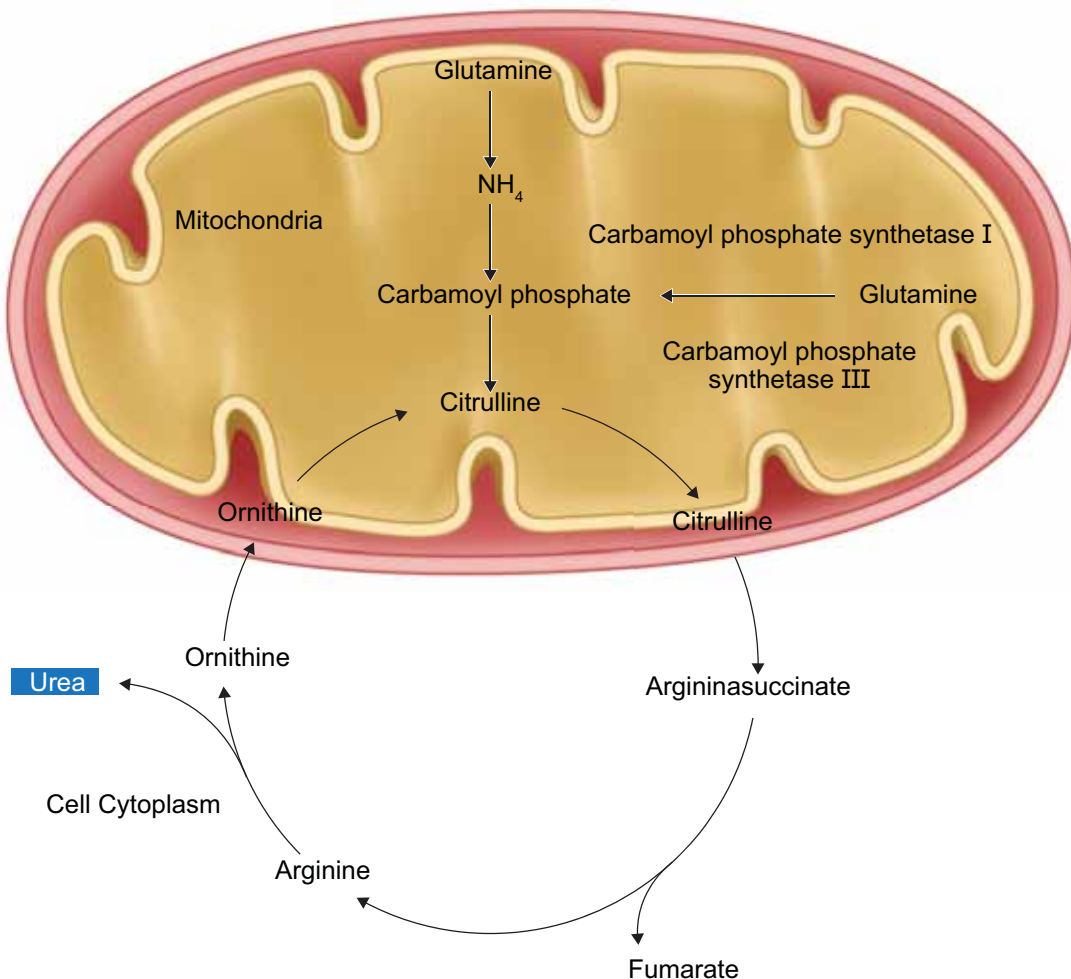


Figure 8.8 Ornithine cycle

faster with greater force through the afferent arteriole and leaves the glomerulus through the efferent arterioles, much slower. This force is because of the difference in sizes between the afferent and efferent arteriole (afferent arteriole is wider than efferent arteriole) and glomerular hydrostatic pressure which is around 55mm Hg.

Kidneys produce about 180L of glomerular filtrate in 24 hours. The molecules such as water, glucose, amino acids and nitrogenous substances pass freely from the blood into the glomerulus. Molecules larger than 5nm are barred from entering the tubule. Glomerular pressure is the chief force that pushes water and solutes out of the blood and across the filtration membrane. The glomerular blood pressure (approximately 55 mmHg) is much higher than in other capillary beds. The two opposing forces are contributed by the plasma proteins in the capillaries. These includes, colloidal osmotic pressure (30 mmHg) and the capsular hydrostatic pressure (15 mmHg) due to the fluids in the glomerular capsule. The net filtration pressure of 10 mmHg is responsible for the renal filtration.

Net filtration Pressure = Glomerular hydrostatic pressure – (Colloidal osmotic pressure + Capsular hydrostatic pressure).

Net filtration pressure = 55 mmHg – (30 mmHg + 15 mmHg) = 10mmHg

The effective glomerular pressure of 10 mmHg results in **ultrafiltration**. Glomerular filtration rate (GFR) is the volume of filtrate formed min^{-1} in all nephrons (glomerulus) of both the kidneys. In adults the GFR is approximately 120-125mL/min. Blood from the glomerulus is passed out through the efferent arteriole. The smooth muscle

of the efferent arteriole contract resulting in vasoconstriction. Table 8.1 shows the relative concentrations of substances in the blood plasma and the glomerular filtrate. The glomerular filtrate is similar to blood plasma except that there are no plasma proteins.

Renal clearance is a parameter that reflects the amount of solute passing from the plasma to the urine in a given period of time. If the renal clearance is equal to the GFR it means that there is efficient filtration with little reabsorption and secretion. It is one of the parameters used to identify the efficiency of the kidney.

Table 8.1 Concentration of substances in the blood plasma and in the glomerular filtrate

Substance	Concentration in blood Plasma/ g dm^{-3}	Concentration in glomerular filtrate/ g dm^{-3}
Water	900	900
Proteins	80.0	0.05
Aminoacids	0.5	0.5
Glucose	1.0	1.0
Urea	0.3	0.3
Uric acid	0.04	0.04
Creatinine	0.01	0.01
Inorganic ions (mainly Na^+ , K^+ and Cl^-)	7.2	7.2

A person with cirrhosis of the liver has lower than normal levels of plasma proteins and higher than normal GFR. Explain why a decrease in plasma protein would increase GFR.

In cortical nephrons, blood from efferent arteriole flows into peritubular capillary beds and enters the venous system carrying with it recovered solutes and water from the interstitial fluid that surrounds the tubule.



ii) Tubular Reabsorption

This involves movement of the filtrate back into the circulation. The volume of filtrate formed per day is around 170-180 L and the urine released is around 1.5 L per day, i.e., nearly 99% of the glomerular filtrate that has to be reabsorbed by the renal tubules as it contains certain substances needed by the body. This process is called selective reabsorption. Reabsorption takes place by the tubular epithelial cells in different segments of the nephron either by active transport or passive transport, diffusion and osmosis.

Proximal convoluted Tubule (PCT)- Glucose, lactate, amino acids, Na^+ and water in the filtrate is reabsorbed in the PCT. Sodium is reabsorbed by active transport through sodium- potassium ($\text{Na}^+ \text{K}^+$) pump in the PCT. Small amounts of urea and uric acid are also reabsorbed.

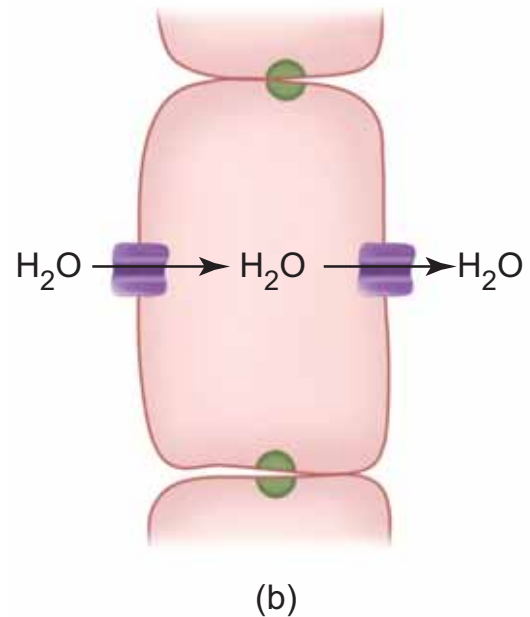


Figure 8.9 (b) Thin descending limb

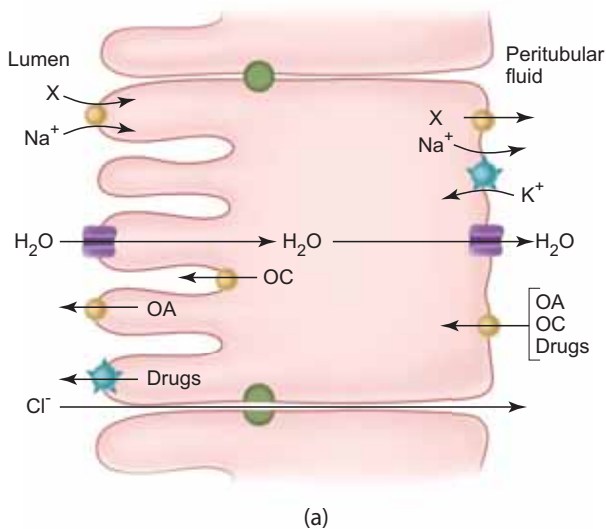


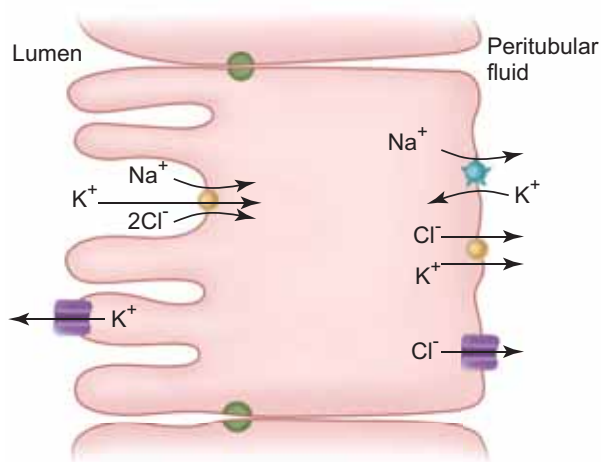
Figure 8.9 (a) Transport in the proximal convoluted tubule cells (OA: Organic anion. OC: Organic cation).

Figure 8.9 (a) shows the transport in the proximal convoluted tubule cells.

Descending limb of Henle's loop is permeable to water due the presence of aquaporins, but not permeable to salts. Water is lost in the descending limb, hence Na^+ and Cl^- gets concentrated in the filtrate (Figure 8.9(b)).

Ascending limb of Henle's loop is impermeable to water but permeable to solutes such as Na^+ , Cl^- and K^+ (Figure 8.9(c)).

The **distal convoluted tubule** recovers water and secretes potassium into the tubule. Na^+ , Cl^- and water remains in



(c)

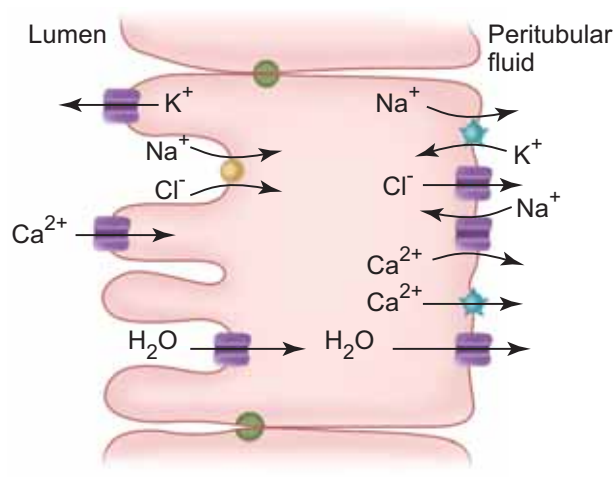
Figure 8.9 (c) Thick ascending limb

the filtrate of the DCT (Figure 8.9(d)). Most of the reabsorption from this point is dependent on the body's need and is regulated by hormones. Reabsorption of bicarbonate (HCO_3^-) takes place to regulate the blood pH. Homeostasis of K^+ and Na^+ in the blood is also regulated in this region.

Aquaporins are water-permeable channels (membrane transport proteins) that allow water to move across the epithelial cells in relation to the osmotic difference from the lumen to the interstitial fluid.

Collecting duct is permeable to water, secretes K^+ (potassium ions are actively transported into the tubule) and reabsorbs Na^+ to produce concentrated urine. The change in permeability to water is due to the presence of number of water-permeable channels called **aquaporins**.

Tubular secretion- Substances such as H^+ , K^+ , NH_4^+ , creatinine and organic acids move into the filtrate from the peritubular capillaries into the tubular fluid. Most



(d)

Figure 8.9 (d) Transport in the distal tubule

of the water is absorbed in the proximal convoluted tubule and Na^+ is exchanged for water in the loop of Henle. Hypotonic fluid enters the distal convoluted tubule and substances such as urea and salts pass from peritubular blood into the cells of DCT. The urine excreted contains both filtered and secreted substances. Once it enters the collecting duct, water is absorbed and concentrated hypertonic urine is formed. For every H^+ secreted

Osmolarity- (The solute concentration of a solution of water is known as the solution osmolarity, expressed as milliosmoles/liter (mOsm/L))

into the tubular filtrate, a Na^+ is absorbed by the tubular cell. The H^+ secreted combines with HCO_3^- , HPO_3^- and NH_3^- and gets fixed as H_2CO_4^+ , H_2PO_4^+ and NH_4^+ respectively. Since H^+ gets fixed in the fluid, reabsorption of H^+ is prevented.

Formation of concentrated urine Formation of concentrated urine is accomplished by kidneys using counter

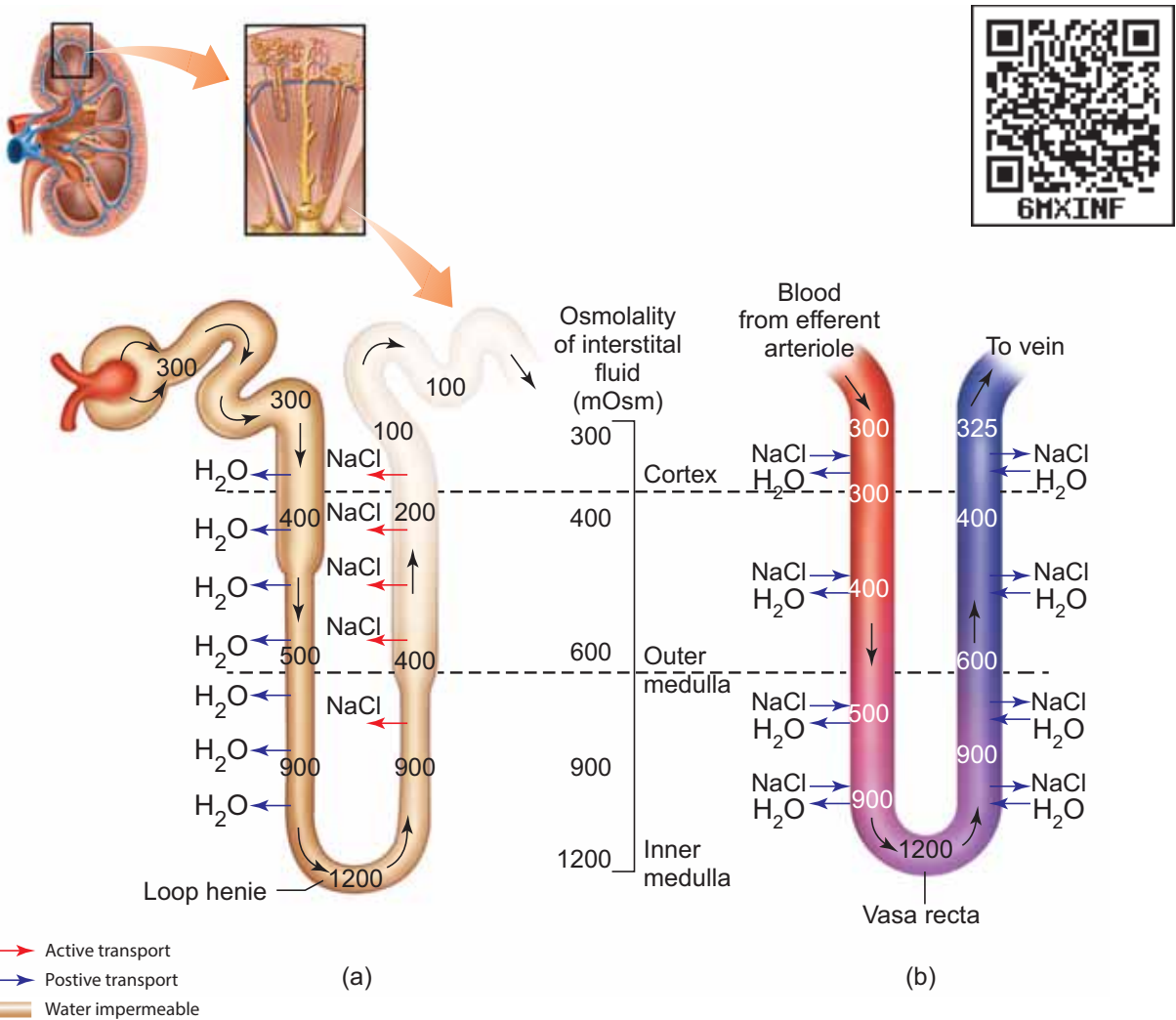


Figure 8.10 (a) Counter current multiplier – the long loops of Henle of the juxtamedullary nephrons create the medullary osmotic gradient (b) Counter current exchanger – Vasa recta preserves the medullary gradient while removing reabsorbed water and solutes.

current mechanisms. The major function of Henle's loop is to concentrate Na^+ and Cl^- . There is low osmolarity near the cortex and high osmolarity towards the medulla. This osmolarity in the medulla is due to the presence of the solute transporters and is maintained by the arrangement of the loop of Henle, collecting duct and vasa recta. This arrangement allows movement of solutes from the filtrate to the interstitial fluid. At the transition between the proximal convoluted tubule and the descending loop of Henle the osmolarity of the interstitial fluid is similar to that of

the blood – about 300mOsm. Ascending and descending limbs of Henle, create a **counter current multiplier** (interaction between flow of filtrate through the limbs of Henle's and JMN) by active transport. Figure 8.10 (a) shows the counter current multiplier created by the long loops of Henle of the JM nephrons which creates medullary osmotic gradient. As the fluid enters the descending limb, water moves from the lumen into the interstitial fluid and the osmolarity decreases. To counteract this dilution the region of the

ascending limb actively pumps solutes from the lumen into the interstitial fluid and the osmolarity increases to about 1200mOsm in medulla. This mismatch between water and salts creates osmotic gradient in the medulla. The osmotic gradient is also due to the permeability of the collecting duct to urea.

The vasa recta, maintains the medullary osmotic gradient via **counter current exchanger** (the flow of blood through the ascending and descending vasa recta blood vessels) by passive transport. Figure 8.10 (b) shows counter current exchanger where the vasa recta preserves the medullary gradient while removing reabsorbed water and solutes. This system does not produce an osmotic gradient, but protects the medulla by removal of excess salts from the interstitial fluid and removing reabsorbed water. The vasa recta leave the kidney at the junction between the cortex and medulla. The interstitial fluid at this point is iso-osmotic to the blood. When the blood leaves the efferent arteriole and enters vasa recta the osmolarity in the medulla increases (1200mOsm) and results in passive uptake of solutes and loss of water. As the blood enters the cortex, the osmolarity in the blood decreases (300mOsm) and the blood loses solutes and gains water to form concentrated urine (hypertonic). Human kidneys can produce urine nearly four times concentrated than the initial filtrate formed.

List the pathways involved in the homeostatic compensation in case of severe dehydration.

8.4 Regulation of kidney function

ADH and Diabetes insipidus

The functioning of kidneys is efficiently monitored and regulated by hormonal feedback control mechanism involving the hypothalamus, juxta glomerular apparatus and to a certain extent the heart. Osmoreceptors in the hypothalamus are activated by changes in the blood volume, body fluid volume and ionic concentration. When there is excessive loss of fluid from the body or when there is an increase in the blood pressure, the osmoreceptors of the hypothalamus respond by stimulating the neurohypophysis to secrete the antidiuretic hormone (ADH) or vasopressin (a positive feedback). ADH facilitates reabsorption of water by increasing the number of aquaporins on the cell surface membrane of the distal convoluted tubule and collecting duct. This increase in aquaporins causes the movement of water from the lumen into the interstitial cells, thereby preventing excess loss of water by diuresis. When you drink excess amounts of your favourite juice, osmoreceptors of the hypothalamus is no longer stimulated and the release of ADH is suppressed from the neurohypophysis (negative feedback) and the aquaporins of the collecting

Angiotensin Converting Enzyme inhibitors (ACE inhibitors) are used to treat high blood pressure. Using a flow chart, explain why these drugs are helpful in treating hypertension.

ducts move into the cytoplasm. This makes the collecting ducts impermeable to water and the excess fluid flows down the collecting duct without any water loss. Hence dilute urine is produced to maintain the blood volume. Vasopressin secretion is controlled by positive and negative feedback mechanism. Defects in ADH receptors or inability to secrete ADH leads to a condition called diabetes

insipidus, characterized by excessive thirst and excretion of large quantities of dilute urine resulting in dehydration and fall in blood pressure.

Consider how different foods affect water and salt balance, and how the excretory system must respond to maintain homeostasis.

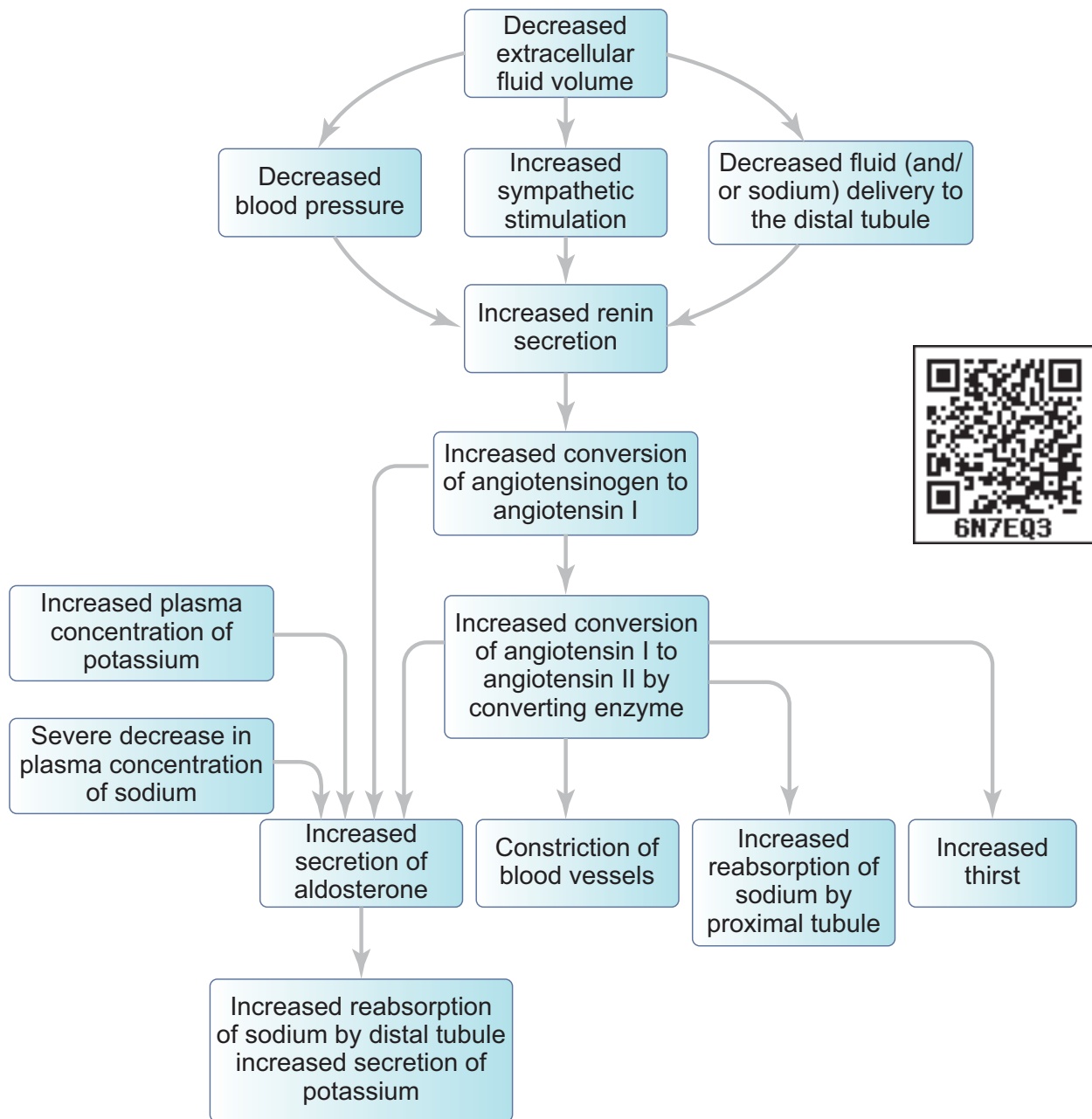


Figure 8.11 Schematic representations of the various hormones in the regulation of body fluid concentration

Renin angiotensin

Juxta glomerular apparatus (JGA) is a specialized tissue in the afferent arteriole of the nephron that consists of macula densa and granular cells. The macula densa cells sense distal tubular flow and affect afferent arteriole diameter, whereas the granular cells secrete an enzyme called renin. A fall in glomerular blood flow, glomerular blood pressure and glomerular filtration rate, can activate JG cells to release renin which converts a plasma protein, angiotensinogen (synthesized in the liver) to angiotensin I. Angiotensin converting enzyme (ACE) converts angiotensin I to angiotensin II. Angiotensin II stimulates Na^+ reabsorption in the proximal convoluted tubule by vasoconstriction of the blood vessels and increases the glomerular blood pressure. Angiotensin II acts at different sites such as heart, kidney, brain, adrenal cortex and blood vessels. It stimulates adrenal cortex to secrete aldosterone that causes reabsorption of Na^+ , K^+ excretion and absorption of water from the distal convoluted tubule and collecting duct. This increases the glomerular blood pressure and glomerular filtration rate. This complex mechanism is generally known as **Renin- Angiotensin- Aldosterone System (RAAS)**. Figure 8.11 shows the schematic representation of the various hormones in the regulation of body fluid concentration.

Atrial natriuretic factor

Excessive stretch of cardiac atrial cells cause an increase in blood flow to the atria of the heart and release Atrial Natriuretic Peptide or factor (ANF) travels to the kidney where it increases Na^+

excretion and increases the blood flow to the glomerulus, acting on the afferent glomerular arterioles as a vasodilator or on efferent arterioles as a vasoconstrictor. It decreases aldosterone release from the adrenal cortex and also decreases release of renin, thereby decreasing angiotensin II. ANF acts antagonistically to the renin-angiotensin system, aldosterone and vasopressin.

8.5 Micturition

The process of release of urine from the bladder is called micturition or urination. Urine formed by the nephrons is ultimately carried to the urinary bladder where it is stored till it receives a voluntary signal from the central nervous system. The stretch receptors present in the urinary bladder are stimulated when it gets filled with urine. Stretching of the urinary bladder stimulates the CNS via the sensory neurons of the parasympathetic nervous system and brings about contraction of the bladder. Simultaneously, somatic motor neurons induce the sphincters to close. Smooth muscles contract resulting in the opening of the internal sphincters passively and relaxing the external sphincter. When the stimulatory and inhibitory controls exceed the threshold, the sphincter opens and the urine is expelled out.

An adult human on an average excretes 1 to 1.5 L of urine per day. The urine formed is a yellow coloured watery fluid which is slightly acidic in nature (pH 6.0), Changes in diet may cause pH to vary between 4.5 to 8.0 and has a characteristic odour. The yellow colour of the urine is due to the presence of a pigment,

Hypotonic urine is formed when osmotic pressure of the body fluid is decreased due to water retention or solute loss when ADH secretion is lowered. If you drink large volume of water without eating anything salty, the total body fluid volume increases quickly and the osmolarity decreases. The kidneys increase the volume of urine excreted. The reverse happens when you eat salty food without drinking water.

urochrome. On an average, 25-30 gms of urea is excreted per day. Various metabolic disorders can affect the composition of urine. Analysis of urine helps in clinical diagnosis of various metabolic disorders and the malfunctioning of the kidneys. For example the presence of glucose (glucosuria) and ketone bodies (ketonuria) in the urine are indications of diabetes mellitus.

8.6 Role of other organs in excretion

Apart from kidneys, organs such as lungs, liver and skin help to remove wastes. Our lungs remove large quantities of carbon dioxide (18 L/day) and significant quantities of water every day. Liver secretes bile containing substances like, bilirubin and biliverdin, cholesterol, steroid hormones, vitamins and drugs which are excreted out along with the digestive wastes.

Sweat and sebaceous glands in the skin eliminate certain wastes through their secretions. Sweat produced by the sweat

glands primarily helps to cool the body and secondarily excretes Na^+ and Cl^- , small quantities of urea and lactate. Sebaceous glands eliminate certain substances like sterols, hydrocarbons and waxes through sebum that provides a protective oily covering for the skin. Small quantities of nitrogenous wastes are also excreted through saliva.

8.7 Disorders related to the Excretory System

Urinary tract infection

Female's urethra is very short and its external opening is close to the anal opening, hence improper toilet habits can easily carry faecal bacteria into the urethra. The urethral mucosa is continuous with the urinary tract and the inflammation of the urethra (urethritis) can ascend the tract to cause bladder inflammation (cystitis) or even renal inflammation (pyelitis or pyelonephritis). Symptoms include dysuria (painful urination), urinary urgency, fever and sometimes cloudy or blood tinged urine. When the kidneys are inflamed, back pain and severe headache often occur. Most urinary tract infections can be treated by antibiotics.

Renal Failure (Kidney Failure)- Failure of the kidneys to excrete wastes may lead to accumulation of urea with marked reduction in the urine output. Renal failure are of two types, Acute and chronic renal failure. In acute renal failure the kidney stops its function abruptly, but there are chances for recovery of kidney functions. In chronic renal failure there is a progressive loss of function of the

nephrons which gradually decreases the function of kidneys.

Females are prone to recurring urinary tract infections as they have shorter urethras. With age prostate in males may enlarge which forces urethra to tighten restricting a normal urinary flow.

Uremia - Uremia is characterized by increase in urea and other non-protein nitrogenous substances like uric acid and creatinine in blood. Normal urea level in human blood is about 17-30mg/100mL of blood. The urea concentration rises as 10 times of normal levels during chronic renal failure.

Renal calculi- Renal calculi, also called renal stone or kidney stone or nephrolithiasis, is the formation of hard stone like masses in the renal tubules of renal pelvis. It is mainly due to the accumulation of soluble crystals of salts of sodium oxalates and certain phosphates. This result in severe pain called “renal colic pain” and can cause scars in the kidneys. Renal stones can be removed by techniques like pyleothotomy or lithotripsy.

Glomerulonephritis- It is also called Bright’s disease and is characterized by inflammation of the glomeruli of both kidneys and is usually due to post-streptococcal infection that occurs in children. Symptoms are haematuria, proteinuria, salt and water retention, oligouria, hypertension and pulmonary oedema.

8.8 Haemodialysis

Malfunctioning of the kidneys can lead to accumulation of urea and other toxic substances, leading to kidney failure. In such patients toxic urea can be removed from the blood by a process called haemodialysis. A dialyzing machine or an artificial kidney is connected to the patient’s body. A dialyzing machine consists of a long cellulose tube surrounded by the dialysing fluid in a water bath. The patient’s blood is drawn from a convenient artery and pumped into the dialyzing unit after adding an anticoagulant like heparin. The tiny pores in the dialysis tube allows small molecules such as glucose, salts and urea to enter into the water bath,

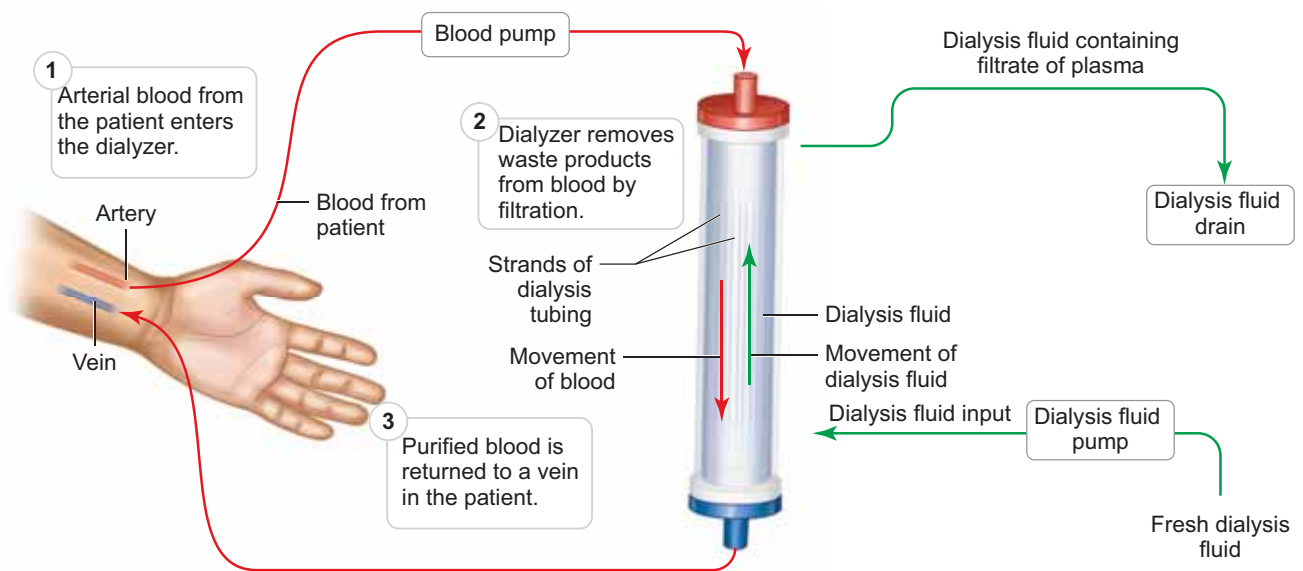


Figure 8.12 Simplified diagram of hemodialysis

whereas blood cells and protein molecules do not enter these pores. This stage is similar to the filtration process in the glomerulus. The dialysing liquid in the water bath consists of solution of salt and sugar in correct proportion in order to prevent loss of glucose and essential salts from the blood. The cleared blood is then pumped back to the body through a vein.

Kidney Transplantation

It is the ultimate method for correction of acute renal failures. This involves transfer of healthy kidney from one person (donor) to another person with kidney failure. The donated kidney may be taken from a healthy person who is declared brain dead or from sibling or close relatives to minimise the chances of rejection by the immune system of the host. Immunosuppressive drugs are usually administered to the patient to avoid tissue rejection.

Activity

Visit a nearby health center to observe the analysis of urine. Dip strips can be used to test urine for a range of different factors such as pH, glucose, ketones and proteins. Dip sticks for detecting glucose contain two enzymes namely, glucose oxidase and peroxidase. These two enzymes are immobilized on a small pad at one end of the stick. The pad is immersed in urine. If the urine contains glucose, a brown coloured compound is produced. The resulting colour pad is matched against a colour chart. The colour does not indicate the current blood glucose concentrations.



The world's first successful human kidney transplantation was performed from one twin to another by Joseph E. Murray and his colleagues at Peter Bent Brigham Hospital, Boston in 1954. The first ever human kidney transplant performed in India was done at the King Edward Memorial Hospital at Mumbai in May 1965, using a cadaver donor in a non-renal failure patient who had had hypernephroma. The first successful live donor kidney transplant in India was done at Christian Medical College Hospital, Vellore in January 1971 by Dr. Johnny and Dr. Mohan Rao.

Summary

Epithelial tissues are the interface between internal fluids and the external environment, creating osmotic barriers in lower organisms. Other specialized epithelial tissues that mediate osmotic and ionic regulation are gills, digestive tract and specialized excretory tissues in different animal groups. Animals remove toxic ammonia to less toxic forms by excretion. Three main strategies of nitrogen excretion are ammonotelic (ammonium), Uricotelic (uric acid) and Ureotelic (Urea). Most aquatic animals are ammonotelic, whereas terrestrial animals are uricotelic (reptiles and birds) or ureotelic (mammals). Urea is produced by the Ornithine cycle/Urea cycle in the liver.

Invertebrates have primitive kidneys such as protonephridia and metanephridia. Water balance in insects is regulated by Malpighian tubules. Ion and water regulation in vertebrates are carried out by the kidneys. The functional units of kidney is the nephron. Urine is formed by 3 processes, Glomerular filtration, tubular reabsorption and tubular secretion. Filtration occurs at the glomerulus, a ball of capillaries surrounded by the Bowman's capsule. From the Bowman's capsule the primary urine enters the proximal tubule, and proceeds to the loop of Henle, with its ascending and descending limbs. The hypertonic fluid then flows to the distal tubule and through the collecting duct into the ureters, the urinary bladder, after a short storage it is sent out of the urethra. Central to the nephron is the counter current system set up between the loop of Henle and the collecting duct along with the capillaries that serve the nephron.

Kidney function is regulated at different levels. GFR is affected by colloidal osmotic pressure and capsular hydrostatic pressure between the glomerulus and Bowman's capsule, surface area available for filtration are the factors that affect filtration pressure. The kidneys act only on the plasma, yet the extra cellular fluid consists of both plasma and interstitial fluid. The interstitial fluid is the true internal fluid environment of the body. Interstitial fluid is the only component that comes in direct contact with the cells. Thus by performing regulatory and excretory roles on the plasma, the kidneys maintains the proper interstitial fluid environment for optimum cell functioning.

Various hormones control diuresis. Vasopressin alters the permeability of the collecting duct, the renin- angiotensin system, sympathetic system and aldosterone act together to regulate Na^+ , K^+ , water and pressure balance.



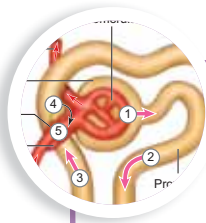
CASE STUDY

Both the kidneys of Ravi (28 years) were not functioning and he was undergoing dialysis. He was admitted to a hospital with renal failure. His mother Suganthi (47 years) was willing to donate one of her kidneys to her son after she was given counseling. Their blood groups were matching and later approval was obtained from transplant committee and technical committee. Operation was performed for 5 hrs. He was administered with immunosuppressive drugs and anti inflammatory drugs. He recovered from the operation and returned home.

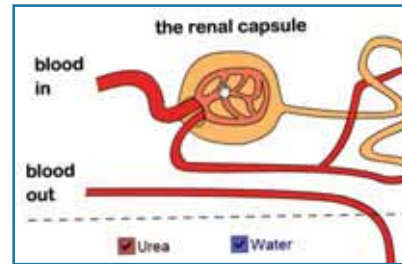
1. Name the disease Ravi was suffering from.
2. What relation is the donor of the kidney
3. Name the type of matching done to perform the transplant.
4. Why approval has to be got from transplant committee and technical committee?
5. What do you think about Suganthi donating her kidney?



Let go away



Let's explore the Biomed Heads-Kidney and understand the **functions of the nephron.**



Step – 1

Use the URL to land in 'Biomed heads-Kidney' page. Click 'Continue' button near the kidney diagram to download an interactive flash file.

Step – 2

Open the flash file and then click 'Continue' button to start the interactive activity.

Step – 3

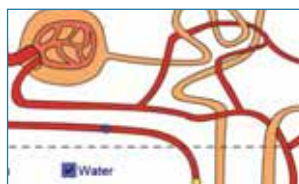
By selecting the molecules given in the list, you can understand how the nephrons process these molecules in accordance to their properties.

Step – 4

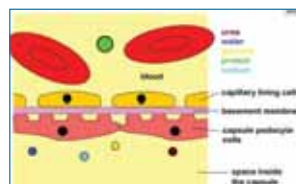
Use the drop-down menu on the top right corner of the window to understand the parts of the nephron and their functions.



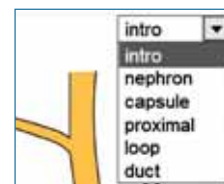
Step 1



Step 2



Step 3



Step 4

Biomed heads-Kidney function's URL:

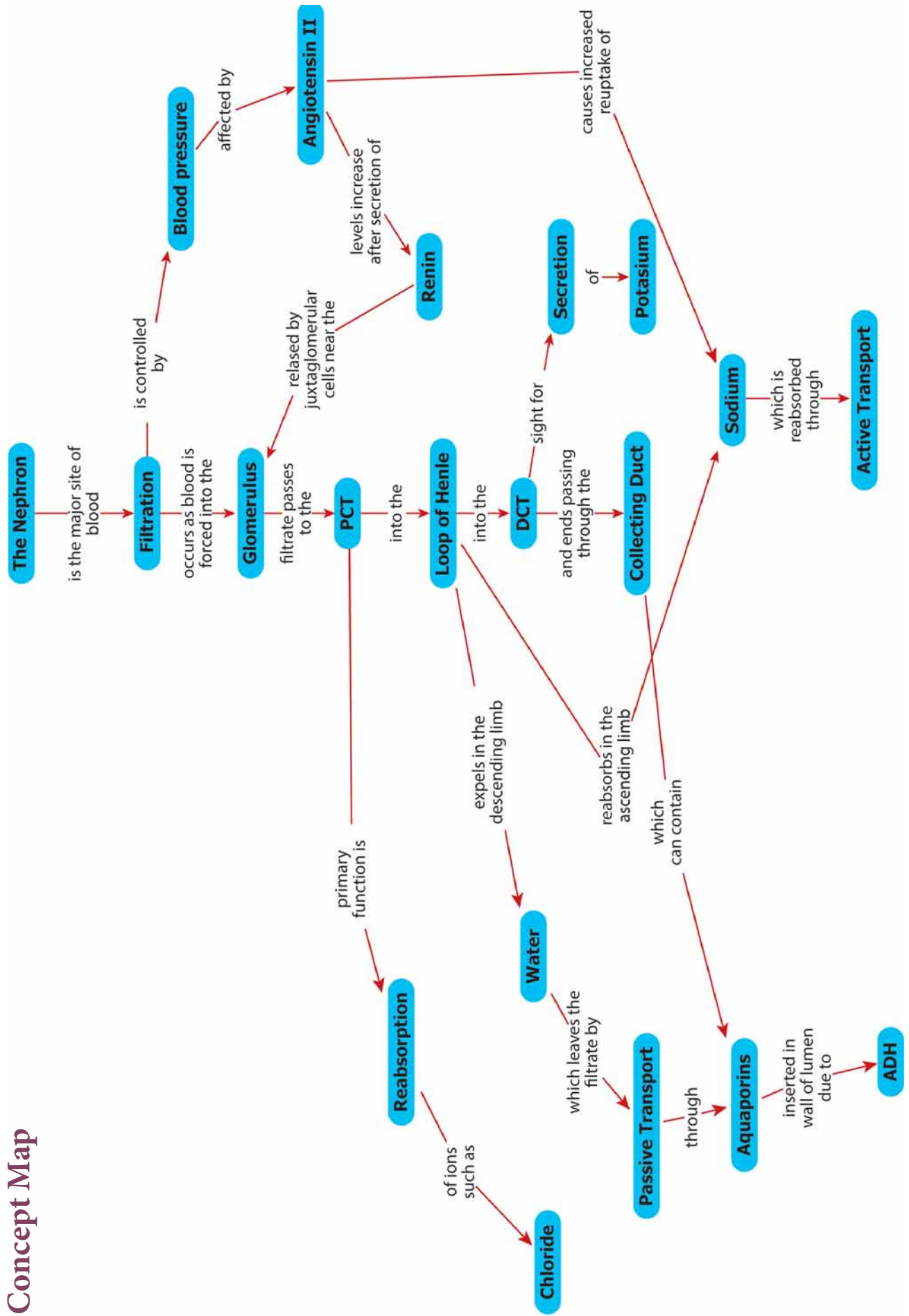
<http://www.biomedheads.com/kidney--nephrons.html>



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* Pictures are indicative only

Concept Map



Glossary

Atrial natriuretic peptide – is a polypeptide hormone released by atrial myocytes (muscle cells) from the granules of the atria of the heart in response to high blood pressure, hypervolemia and exercise. It is involved in the homeostatic control of body water and sodium.

Aquaporins – or water channels are formed by specific plasma membrane proteins in the tubular cells. These water channels of the proximal convoluted tubules are always open accounting for the high water permeability in this region. In contrast the water channels in the distal convoluted tubule are regulated by the hormone vasopressin accounting for the variable water re-absorption in that region.

Bowman's capsule hydrostatic pressure – The pressure exerted by the fluid in the Bowman's capsule. This pressure tends to push fluid out of Bowman's capsule, opposes the filtration of fluid from the glomerulus into Bowman's capsule.

Cortical nephrons – All nephrons originate in the cortex, but the glomeruli of the cortical nephrons lie in the outer layer of the cortex. Peri tubular capillaries do not form vasa recta.

Glomerular filtration – this is the first step in urine formation where 20% of the plasma that enters the glomerulus is filtered. The glomerular filtrate that comes out of the glomerulus into the Bowman's capsule is the protein – free plasma.

Glomerular capillary pressure – It is the fluid pressure exerted by the blood within the glomerular capillaries.

Glomerulus – a tuft of capillaries that filters protein – free plasma into the tubular component

Juxtaglomerular apparatus – The ascending limb of Henle returns to the glomerular

region of its own nephron, where it passes through the fork formed by the afferent and efferent arterioles. Both the tubular and vascular cells at this point are specialized to form juxtaglomerular apparatus that lie next to the glomerulus. (Juxta means “next to”).

Juxtamedullary nephrons – the glomeruli of the juxtaglomerular nephrons lie in the inner layer of cortex next to the medulla and the loops of Henle plunges through the entire depth of the medulla Concentrated urine is formed in these nephrons.

Filtration slits - The narrow slits between adjacent foot process that provides a pathway through which the fluid leaving the glomerular capillaries can enter the lumen of Bowman's capsule.

Peritubular capillaries -supply the renal tissue, involved in exchanges with the fluid in the tubular region.

Podocytes – The glomerular membrane consists of octopus like cells called podocytes that entangles the glomerular tuft. Each podocyte bears many foot processes.

Vasa recta – (straight vessels) The peritubular capillaries of the juxtaglomerular nephrons forms vascular loops which run in close association with the loops of Henle.

Evaluation

1. Arrange the following structures in the order that a drop of water entering the nephron would encounter them.
 - a. Afferent arteriole
 - b. Bowman's capsule
 - c. Collecting duct
 - d. Distal tubule
 - e. Glomerulus
 - f. Loop of Henle
 - g. Proximal tubule
 - h. Renal pelvis

2. Name the three filtration barriers that solutes must come across as they move from plasma to the lumen of Bowman's capsule. What components of the blood are usually excluded by these layers?
3. What forces promote glomerular filtration? What forces opposes them? What is meant by net filtration pressure?
4. Identify the following structures and explain their significance in renal physiology?
 - a. Juxtaglomerular apparatus
 - b. Podocytes
 - c. Sphincters in the bladder
 - d. Renal cortex
5. In which segment of the nephron most of the re-absorption of substances takes place?
6. When a molecule or ion is reabsorbed from the lumen of the nephron, where does it go? If a solute is filtered and not reabsorbed from the tubule, where does it go?
7. Match each of the following substances with its mode of transportation in proximal tubular reabsorption.

a. Na ⁺	-	simple diffusion
b. Glucose	-	primary active transport
c. Urea	-	indirect active transport
d. Plasma	-	paracellular movement
e. proteins	-	facilitated diffusion
f. Water	-	endocytosis
8. Which segment is the site of secretion and regulated reabsorption of ions and pH homeostasis?
9. What solute is normally present in the body to estimate GFR in humans?
10. Which part of the autonomic nervous system is involved in micturation process?
11. Match the following terms.

a. α-receptor arteriole	-	afferent
b. Autoregulation	-	basal lamina
c. Bowman's capsule	-	capillary blood pressure
d. Capsule fluid	-	colloid osmotic pressure
e. Glomerulus	-	GFR
f. Podocyte	-	JG cells
g. Vasoconstriction	-	plasma proteins Norepinepherine
12. If the afferent arteriole of the nephron constricts, what happens to the GFR in that nephron? If the efferent arteriole constricts what happens to the GFR in that nephron? Assume that no auto regulation takes place.
13. How is the process of micturition altered by toilet training?
14. Concentration of urine depends upon which part of the nephron
 - a. Bowman's capsule
 - b. length of Henle's loop
 - c. P.C.T.
 - d. net work of capillaries arising from glomerulus
15. If Henle's loop were absent from mammalian nephron, which one of the following is to be expected?
 - a. There will be no urine formation
 - b. There will be hardly any change in the quality and quantity of urine formed
 - c. The urine will be more concentrated
 - d. The urine will be more dilute
16. A person who is on a long hunger strike and is surviving only on water, will have
 - a. Less amino acids in his urine

- b. Macula densa cells
 - c. Less urea in his urine
 - d. More sodium in his urine
17. What will happen if the stretch receptors of the urinary bladder wall are totally removed?
- a. Micturition will continue
 - b. Urine will be continue to collect normally in the bladder
 - c. there will be micturition
 - d. urine will not collection the bladder
18. The end product of Ornithine cycle is
- a. carbon dioxide b. uric acid
 - c. urea d. ammonia
19. Identify the wrong match
- a. Bowman's capsule - Glomerular filtration
 - b. DCT - Absorption of glucose
 - c. Henle's loop - Concentration of urine
 - d. PCT - Absorption of Na^+ and K^+ ions
20. Podocytes are the cells present on the
- a. Outer wall of Bowman's capsule
 - b. Inner wall of Bowman's capsule
 - c. neck of nephron
 - d. Wall glomerular capillaries
21. Glomerular filtrate contains
- a. Blood without blood cells and proteins
 - b. Plasma without sugar
 - c. Blood with proteins but without cells
 - d. Blood without urea
22. Kidney stones are produced due to deposition of uric acid and
- a. silicates
 - b. minerals
 - c. calcium carbonate
 - d. calcium oxalate
23. Animal requiring minimum amount of water to produce urine are
- a. ureotelic b. ammonotelic
 - b. uricotelic d. chemotelic
24. Aldosterone acts at the distal convoluted tubule and collecting duct resulting in the absorption of water through
- a. Aquaporins b. spectrins
 - c. GLUT d. Chloride channels
25. The hormone which helps in the reabsorption of water in kidney tubules is
- a. cholecystokinin
 - b. angiotensin II
 - c. antidiuretic hormone
 - d. pancreaseozym
26. Malpighian tubules remove excretory products from
- a. mouth b. oesophagus
 - c. haemolymph d. alimentary canal.
27. Identify the biological term
- Homeostasis, excretion, glomerulus, urea, glomerular filtration, ureters, urine, Bowman's capsule, urinary system, reabsorption, micturition, osmosis, glomerular capillaries via efferent arteriole, proteins.
- a. A liquid which gathers in the bladder.
 - b. Produced when blood is filtered in a Bowman's capsule.
 - c. Temporary storage of urine.
 - d. A ball of inter twined capillaries.
 - e. A process that changes glomerular filtrate into urine.
 - f. Removal of unwanted substances from the body.
 - g. Each contains a glomerulus.
 - h. Carry urine from the kidneys to the bladder.
 - i. Contains urea and many useful substances.

- j. Bloods is filtered through its walls into the Bowman's capsule.
 - k. Scientific term for urination.
 - l. Regulation of water and dissolved substances in blood and tissue fluid.
 - m. Carry urine from the kidneys to the bladder.
 - n. Consists of the kidneys, ureters and bladder.
 - o. Removal of useful substances from glomerular filtrate.
 - p. The process by which water is transported in the proximal convoluted tubule.
 - q. Where has the blood in the capillaries surrounding the proximal convoluted tubule come from?
 - r. What solute the blood contains that are not present in the glomerular filtrate?
28. With regards to toxicity and the need for dilution in water, how different are ureotelic and uricotelic excretions? Give examples of animals that use these types of excretion?
29. Differentiate protonephridia from metanephridia
30. What is the nitrogenous waste produced by amphibian larvae and by the adult animal?
31. How is urea formed in the human body?
32. Differentiate cortical from medullary nephrons
33. What vessels carry blood to the kidneys? Is this blood arterial or venous?
34. Which vessels drain filtered blood from the kidneys?
35. What is tubular secretion? Name the substances secreted through the renal tubules
36. How are the kidneys involved in controlling blood volume? How is the volume of blood in the body related to arterial pressure?
37. Name the three main hormones are involved in the regulation of the renal function?
38. What is the function of antidiuretic hormone? Where is it produced and what stimuli increases or decreases its secretion?
39. What is the effect of aldosterone on kidneys and where is it produced?
40. What evolutionary hypothesis could explain the heart's role in secreting a hormone that regulates renal function? What hormone is this?

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