Human Physiology

Excretory Products and Their Elimination

Homeostasis

Homeostasis (Gr. *homoior* = same, *stasis* = standing) simply means maintenance of the constant internal environment of the body. Maintenance of **homeostasis** or the steady state is an utmost necessity for normal life processes. Homeostatic mechanisms maintain conditions within a range, in which the animal's metabolic processes can occur. Moreover, the cells of an animal cannot survive even a change in water content beyond the range. Therefore, animals, whether they inhabit land, or freshwater, or marine, or migrate between these environments, have an impervious coat to resist water entry or exit, for example, scales are present in fish and reptiles, feathers in birds and hairs in mammals. However, all possess readily permeable membranes, such as respiratory surfaces (lungs, trachea, and gill) and oral membranes. These surfaces can neither be waterproof, nor can resist ionic diffusion. Similarly, accumulation of toxic metabolic wastes in the cellular environment is dangerous. Both osmoregulation and excretion help in maintaining chemical and fluid homeostasis, i.e., nearly uniform and beneficial physiological state in the body.

Osmoregulation and Osmolarity

The regulation of solute movement, and hence, water movement, through osmosis, is known as osmoregulation. **Osmosis** may be defined as a type of diffusion where the movement of water occurs selectively across a semipermeable membrane. It occurs whenever two solutions, separated by semipermeable membrane (the membrane that allows water molecules to pass but not the solutes) differ in total solute concentrations, or **osmolarity.** The total solute concentration is expressed as molarity or moles of solute per litre of solution. The unit of measurement for osmolarity is milliosmole per litre (mosm L^{-1}). If two solutions have the same osmolarity, they are said to be **isotonic**. When two solutions differ in osmolarity, the solution with higher concentration of solute is called **hypertonic,** while the more dilute solution is called **hypotonic.** If a semipermeable membrane separates such solutions, the flow of water (osmosis) takes place from a hypotonic solution to a hypertonic one.

Osmoconformers are the animals that do not actively control the osmotic condition of their body fluids. They rather change the osmolarity of body fluids according to the osmolarity of the ambient medium. All marine invertebrates and some freshwater invertebrates are strictly osmoconformers. Hagfish is the vertebrate osmoconformer. Osmoconformers show an excellent ability to tolerate a wide range to cellular osmotic environments.

Osmoregulators, on the other hand, are the animals that maintain an internal osmolarity, different from the surrounding medium in which they inhabit. Many aquatic invertebrates are strict or limited osmoregulators. Most vertebrates are strict osmoregulators, i.e., they maintain the composition of the body fluids within a narrow osmotic range. The notable exception, however, are the hagfish (*Myxine* spp., a marine cyclostome fish) and elasmobranchs (sharks and rays).

Osmoregulators must either eliminate excess water if they are in a hypotonic medium, or continuously take in water to compensate for water loss if they are in a hypertonic situation. Therefore, osmoregulators have to spend energy to move water in or out and maintain osmotic gradients by manipulating solute concentrations in their body fluids.

Water and solute regulation in freshwater environment:
Body fluids of fresh water animals (osmolarity 200– 300 m osm L^{-1}) are hypertonic to surrounding medium (ostmolarity 50 m osm L^{-1}), so there will be two problems mentioned below.

i. Gain of surplus water passively due to osmotic gradient.
ii. Loss of salts from body continuously.

To encounter the problems, fresh water animals have two adaptations as they do not drink water and also possess specialized ion absorbing cells ionocytes /chloride cells in the gill membranes to import Na^+ and Cl^- actively.

Water and solute regulation in marine environment

Marine animals have the body fluids hypotonic (300 mos mL^{-1}) to sea water (1000 mos mL^{-1}). So they loose water from gill membranes, oral canal membranes. To compensate this water loss, they drink water which leads to increase salt concentration in body. They also possess ionocytes or chloride cells in gill membrane to eject out excess of monovalent ions while excess of divalent cations are exerted with faeces.

Water and solute regulation in terrestrial environment

Land animal's continuosly loose water through oral, nasal or respiratory surface during breathing or by sweating or by micturation.The water loss is compensated by drinking water and eating moist food.

Resonate the Concept

- Kangaroo rats loose very little water, because they can recover 90 percent of the loss by using metabolic water.
- Camel generally excretes concentrate urine to secure water in body. When water is not available, the camels do not produce urine but store urea is tissues and solely depend on metabolic water.

		Kangaroo rat	Human
Water gain	**Ingested in**	**0**	**1500 (60%)**
(ml/dl)	Liquid Ingested	6 (10%)	750 (30%)
	In food Derived from metabolism	54 (90%)	250 (10%)
Total		60 (100%)	2500 (100%)
Water loss	**Evaporation**	**43.9 (73%)**	**900 (36%)**
(ml/dl)	Urine	13.5 (23%)	1500 (60%)
	Faeces	2.6 (4%)	100 (4%)
Total		60 (100%)	2500 (100%)

Excretion and excretory products

Excretion is removal of metabolic wastes from the body. CO_2 and water are metabolic wastes of carbohydrate and fat metabolism while nitrogenous wastes are formed by protein and nucleic acid metabolism.

Nitrogenous wastes products are of the following types:

1. **Ammonia:** It is first and highly toxic metabolic waste of protein metabolism which is produced in liver by the process of deamination and requires large amount of water for its excretion.
2. **Urea:** It is white crystalline solid, comparatively less toxic, produced in liver from NH_3 and CO_2. Normal blood urea level is 8-26 mg/100 ml of blood.
3. **Uric Acid:** Semisolid or crystalline excrete waste, produced in liver and its elemination, in such form, helps in conservation of body water. e.g. Insects, amphibians, reptiles and birds (as Bird droppings guano).
4. **Xanthines and Guanines:** It is metabolic waste of nucleotide metabolism. e.g. spiders and penguins.

5. **Trimethylamine oxide (TMO):** Certain marine molluscs, crustaceans and teleost fishes first form trimethylamine from their ammonia by a process known as **methylation**. Then, the trimethylamine is oxidised to trimethylamineoxide for excretion.This oxide is soluble in water, but nontoxic.
6. **Ornithuric acid:** It is a specialised product in birds which is formed as the product of fat metabolism by benzoic acid. This combines with ornithine and change into ornithuric acid for excretion.
7. **Hippuric acid:** In mammals, it is form during fat metabolism by benzoic acid. This acid combines with glycine and change into less toxic hippuric acid for excretion.
8. **Creatine and Creatinine:** It is produced from creatine phosphate present in muscles by the metabolism of 3 amino acids Glycine, Arginine and Methionine. Increased level of creatinine indicates to kidney damage.

Classification of animals on the basis of excertory products

S.No.	Ammonotelic	Ureotelic	Uricotelic
1	The animals excrete ammonia are called ammonotelic.	The animals excrete urea are called ureotelic.	The animals excrete uric acid are called uricotelic.
2	Excretion of ammonia is called ammonotelism.	Excretion of urea is called ureotelism	Excretion of uric acid is called uricotelism.
3	**Examples :** Protozoans, (e.g. *Amoeba*, *Paramoecium*), sponges (e.g. *Sycon*), cnidarians (e.g. *Hydra*), Liver fluke, Tape worm, *Ascaris, Nereis*, Earthworm, Leech, *Prawn, Pila,* Bony fishes, Salamanders, Amphibian tadpoles	**Examples :** *Ascaris,* Earthworm, (Both are ammonotelic and ureotelic), cartilagenous fishes (e.g. sharks and rays), Frogs, Toads, Turtles, Alligators, Mammals (e.g. Man)	**Examples:** Most insects (e.g. cockroach), most land crustaceans, land snails (e.g. *Helix*), land reptiles (lizards and snakes), birds.

Excretory structure in different animals

S.No.	Animal groups	Main excretory structure
1	Protozoans	Plasmalemma or general body surface
2	Porifera and cnidaria	Plasma membrane of each cell
3	Platyhelminthes (*Planaria*, Liver fluke, Tapeworm)	Protonephridia or flame cells or Solenocytes (also present in rotifers, some annelids and cephalochordata e.g. Amphioxus)
4	Aschelminthes (Round worms)	H-shaped renette cells
5	Annelids (*Nereis*, Earthworm, Leech)	Nephridia
6	Arthropods (i) Insects, centipedes and millipedes (ii) Crustaceans (e.g., Prawn) (iii) Scorpions and spiders	Malpighian tubules Antennary or Green glands Coxal glands
7	Molluscs (e.g., *Unio*)	Keber's organs and organs of Bojanus
8	Echinodermates (e.g., Star fish)	No specialised excretory organ
9	Hemichordates (e.g., *Balanoglossus*)	Proboscis gland
10	Urochordates	Neural gland
11	Cephalochordates	Solenocytes
12	Vertebrates	Kidneys

Test your Resonance with concept

1. Waste products of adenine and guanine metabolism are excreted by man as
(1) Ammonia (2) Urea (3) Uric acid (4) Allantois

2. Reptiles are
(1) Ammonotelic (2) Uricotelic
(3) Ureotelic in water and uricotelic on land (4) ureotelic

3. Correct order of excretory organs in Cockroach, Earthworm and Rabbit respectively
(1) Skin, Malpighi tubules, kidney (2) Malpighi tubules, nephridia, kidney
(3) Nephridia, Malpighi tubule, kidney (4) Nephridia, kidney, green gland

4. Two examples in which the nitrogenous wastes are excreted from body in the form of uric acid are
(1) Birds and lizards (2) Mammals and mollusc
(3) Insects and bony fishes (4) Frogs and cartilagenous fishes

Answers

1. (3) **2.** (2) **3.** (2) **4.** (1)

Excretory system of human beings

Nephrology - is the scientific study of the anatomy, physiology, and pathology of the kidneys. The branch of medicine that deals with the male and female urinary systems and the male reproductive system is called urology

Mammalian (human) urinary system consists of a pair of kidneys, a pair of ureter, a urinary bladder and a urethra.

(A) Kidneys: The kidneys are dark-red, bean-shaped organs about **10-12 cm** long, **5-7 cm** wide and **2-3 cm** thick. Each weight about **120-170 gm**. They are placed against the back wall of the abdominal cavity just below the diaphragm, one on either side opposite the last thoracic and first three lumber vertebrae **(T_{12} - L_3)**. In man left kidney occurs at a slightly higher level than the right one, because right side has prominent right liver lobe. The 11^{th} and 12^{th} pairs of ribs protect them.

Kideny is covered by 3 protective layers which are as follows:

(i) Renal Capsule: It is innermost, tough protective cover made up to dense irregular connective tissue, with few elastic fibres and few muscles. It is continuous with outer coat of ureters.

(ii) Adipose Capsule: It is the middle cover involving adipose tissue and acts as shock absorber.

(iii) Renal Fascia: It is the outer most fibrous cover linking it with the abdominal wall. Madeup of dense irregular connective tissue.

Resonate the Concept

- Nephroptosis or floating kidney, is an inferior displacement or dropping of the kidney. It occurs when the kidney slips from its normal position because it is not securely held in place by adjacent organs or its covering of fat.
- As the kidneys are fused with the body wall on the dorsal side, peritoneal cover is present only on the ventral side. This arrangement is called **retroperitoneal arrangement**.

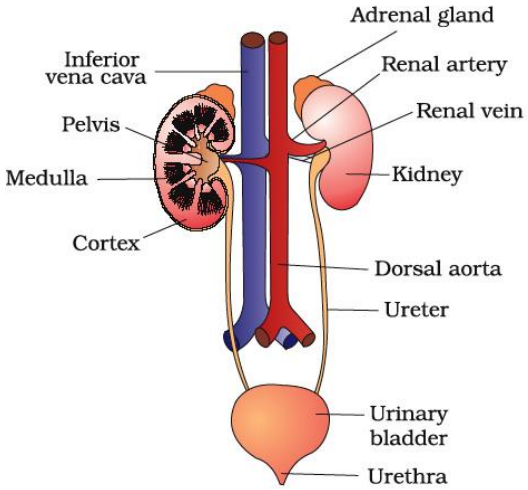


Fig. Human Urinary system

In mammals, the kidney is concavo convex. The center of concave inner surface is called as hilum or hilus.

From this hilus surface, the renal artery & renal nerves enter into the kidney and the renal vein & the ureter come out.

- **Histology of kidney:** The kidneys are metanephric in mammals. It is divisible into two parts outer-cortex and inner-medulla.The cortex extends into the medulla, between the pyramids, and forms **renal columns of Bertini**. Similarly, the medulla is subdivided into 8 to 18 conical masses called as the renal pyramids. Each pyramid having broad base towards the cortex and a narrow end called renal papilla towards the pelvis. Each renal papilla projects into the cavity of a minor calyx. Which open into 2 - 3 major calyces join to form major calyx. The major calyces open into a wide funnel like structure, the **pelvis**. The latter leads into the ureter.

  The functional unit of kidney is called **uriniferous tubule or nephron** which is thin, long, much onvoluted tubular unit. One human kidney may contain about **one million (10 lac)** nephrons. Number of nephron decrease at rate of 10% every decade after 40 year of age.

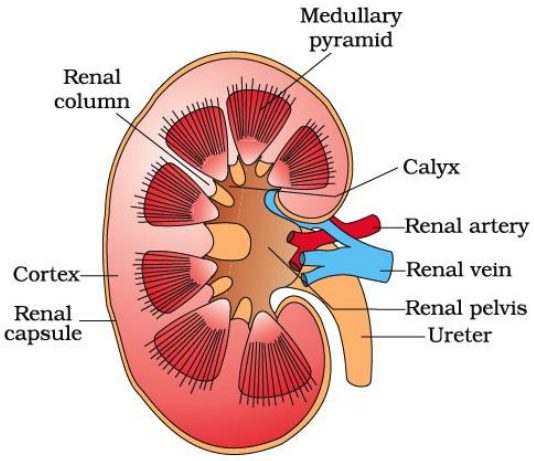


Fig. Longitudinal section (Diagrammatic) of Kidney

(B) Ureters: From the hilum of each kidney emerges a whitish tube the ureter. The ureters are about 28 cm long and 3 mm in diameter. Their wall consists of **transitional epithelium** surrounded by a layer of muscle fibres. Openings of the two ureters in the bladder are separate, but closely placed. **These are oblique, so that the urine can not regurgitate into the ureters when the bladder contracts.** Peristalsis of ureters also checks regurgitation of urine. Like kidneys, the ureters are also retroperitoneal.

(C) Urinary bladder: The urinary bladder is pear-shaped hollow muscular organ situated in pelvic cavity, which is made up of smooth and involuntary muscles. The muscles are also known as **detrusor muscles** (muscles that has the action of expelling a substance). The lower part or neck of the bladder leads into the urethra.

The lumen of the urinary bladder is lined by transitional epithelium which has great power of streching. The neck of bladder is guarded by two sphincters, inner is involuntary controlled by spinal reflex and outer is voluntary controlled by cerebral cortex. Mucosa of bladder with folds called rugae. (Rugae also present is stomach and vagina).

(D) Urethra: The urinary bladder leads to the urethra. In a female, it is quite short, only about 3 to 5 cm long, and carries only urine while in a male, it is much longer, about 20 cm and carries urine as well as spermatic fluid. It passes through the prostate gland and the penis. It opens out at the tip of the penis by urinogenital aperture.

Resonate the Concept

- Path of urinary drainage: Collecting duct → Papillary duct in renal pyramid → Minor calyx → Major calyx → Renal pelvis → Ureter → Urinary bladder

Structure of nephron

A nephron or uriniferous tubule consists of two parts:

(A) Malpighian body / Renal corpuscles: Malpighian body or Malpighian corpuscles (after the Italian microscopist **Marcello Malpighi)** is composed of two structures Bowman's capsule and glomerulus.

(i) Bowman's capsule: The proximal end of each nephron forms a blind or closed, enlarged and double walled cup, the Bowman's capsules in the cortex. (Name Bowman's capsule is based on English physiologist and histologist **William Bowman**). The two walls of Bowman's capsule are inner visceral and outer parietal. Both are single layered and are supported over basement membrane. The podocytes forming the inner wall of the Bowman's capsule. A podocyte has number of interdigitated evaginations called pedicets or feet. The pedicels rest over the basement membrane. They enclose about 25 nm wider gaps called slit pores or filtration slits. The outer wall of the Bowman's capsule consists of unspecialized squamous (flattened) epithelium.

(ii) Glomerulus: Each capsule contains a network of blood capillaries the **glomerulus** which receives blood through **afferent arteriole** and the blood comes out through the **efferent arteriole**. The diameter of the efferent arteriole is comparatively lesser. Glomerulus is a network of up to 50 parallel branching and anastomosing capillaries covered by endothelium, basement membrane and epithelium made of **podocytes** which has slit pores that restrict passage of colloids. Small molecules and water can easily pass through them in to the PCT.

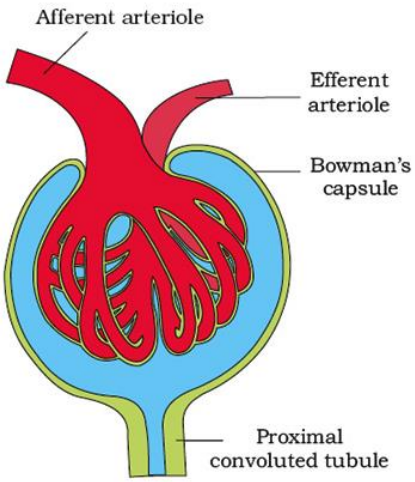


Fig. Malpighian body (renal corpuscle)

Resonate the Concept
• Bowman's capsule and glomerulus receives about 20 – 25% of the cardiac out put (blood) at rest.

(B) Tubule: The Bowman's capsule opens into a coiled tubule which opens into U shape tube which leads to another coiled tube.

(i) Proximal convoluted tubule (PCT): Lower part of Bowman's capsule leads into proximal convoluted tubule. The latter is present in the cortex. The anterior part of the PCT is more coiled where as its posterior part is almost straight. Its twisted part is surrounded by peritubular blood capillaries. PCT is lined by cuboidal epithelium having brush borders with long microvilli for increasing absorptive area. The cells contain abundant mitochondria and food reserve for providing energy to perform active absorption and secretion.

(ii) Loop of Henle: It is hair-pin loop like tubular part of nephron which descends into renal medulla. It is less developed in reptiles, incompletely developed in Aves and most developed in Mammals.

Loop of Henle is made of two parallel limbs, called as descending limb and ascending limb, they are joined by curved base.

(a) Descending limb: Descending limb is in continuation with the proximal convoluted tubule and has two parts, thick segment and thin segment. Thick segment constitutes about four-fifth of the descending limb. It is lined by cuboidal cells. They have sparse microvilli and fewer mitochondria indicating that active absorption and secretion are absent. Thin segment is narrow part of descending limb. It lies in the medulla is lined by flat epithellal cells having sparse microvilli and few mitochondria. Thin segment gets curved to become part of ascending limb.

(b) Ascending limb: Ascending limb consists of thin segment in the proximal part and thick segment afterwards. Thin segment is lined by flat epithellal cells which allow passive diffusion of some solutes (e.g. Na^+, Cl^-) depending upon their concentration gradient. Thick segment of ascending limb is wider and lined by cuboidal cells having microvilli as well as mitochondria. Thick ascending segment is involved in active secretion of NaCl in the medulla.

Resonate the Concept

- **Vasa recta:** Loop of Henle is covered by a stair case of network of blood capillaries arising from Efferent glomerular arteriole called vasa recta. It forms a counter-current system with the loop of Henle and has ascending branch in the area of descending limb and descending branch in the area of ascending limb.

(iii) Distal convoluted tubule (DCT): Distal convoluted tubule is another coiled part of nephron. The epithelial lining of the distal convoluted tubule consists of cuboidal cells having sparse microvilli and deep mitochondria. Distal convoluted tubule is covered by peritubular blood capillaries. The last part of nephron is nearly straight, called connecting or junction tubule and opens into the collecting ducts.

Resonate the Concept

- Collecting ducts: Each nephron opens into a wider collecting tubule in the area of cortex. Collecting tubules are lined by speciallized cuboidal epithelium with very few microvilli. They open into still wide collecting ducts. The collecting ducts enter medulla and form ducts of Bellini. The ducts run through renal pyramids.

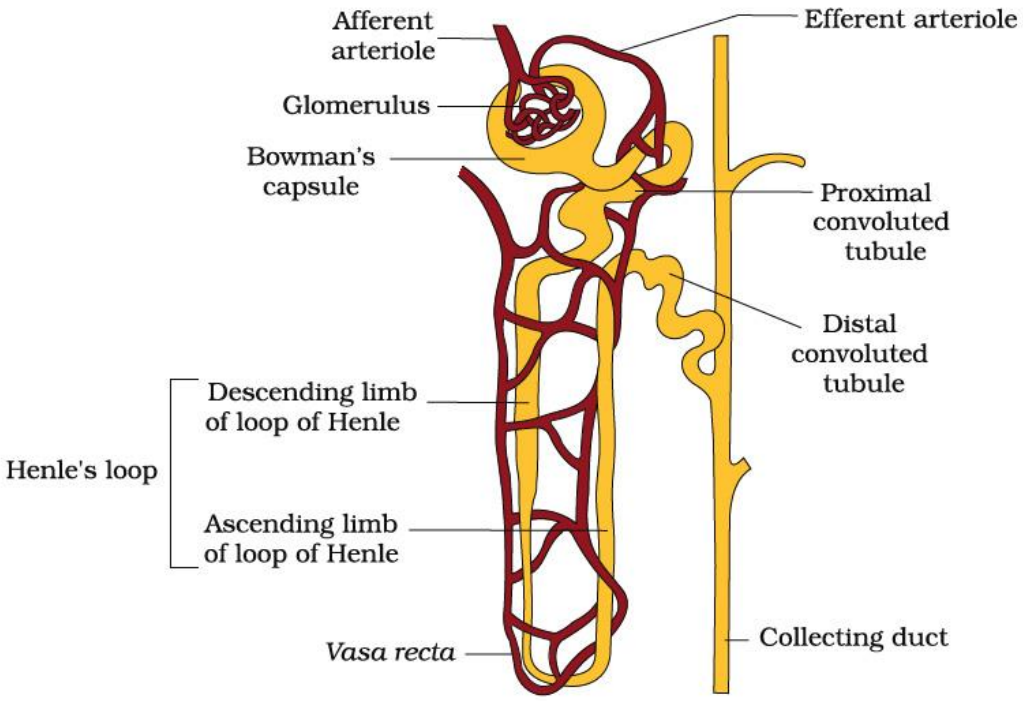
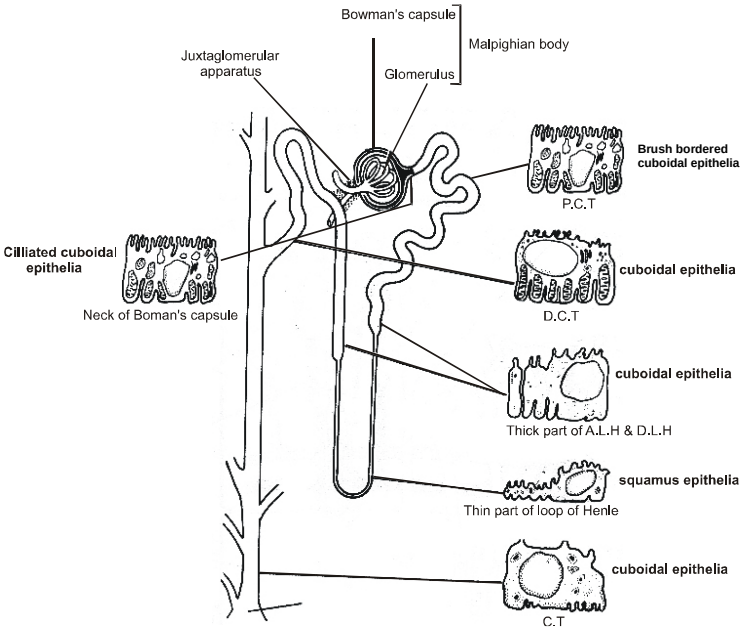


Diagram showing structure of Nephron

Histology of nephron



Types of nephron

Nephrons are of two types cortical and juxtamedullary, with regard to their location in the kidney.

S.No.	Juxtamedullary Nephrons	Cortical Nephrons
1	They are about 15 per cent of total nephrons.	They are about 85 per cent of total nephrons.
2	Their glomeruli lie close to the inner margin of the cortex.	Their glomeruli lie in the outer cortex.
3	They are larger in size.	They are smaller in size.
4	Loops of Henle are very long and extend deep into the medulla.	Loops of Henle are very short and extend only a little into the medulla.
5	They control plasma volume when water supply is short.	They control plasma volume when water supply is normal.

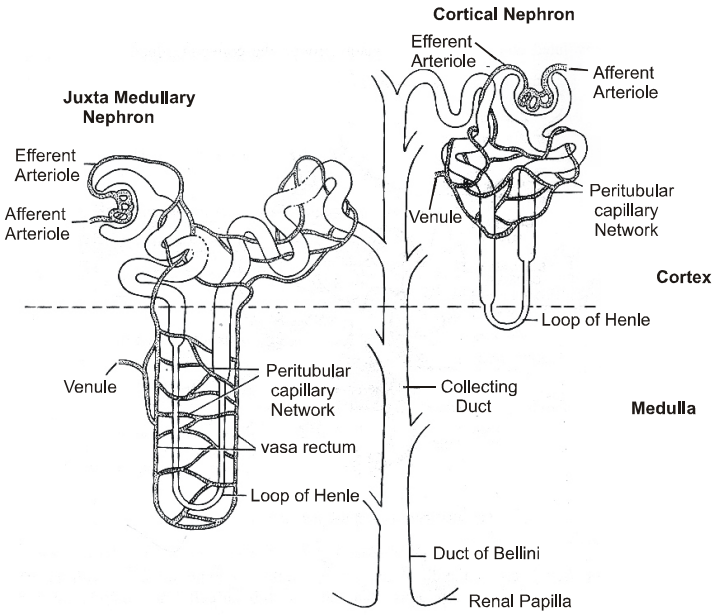


Fig : Juxtamedullary and cortical nephrons

Test your Resonance with concept

1. "Columns of Bertini" in the kidney of mammals are formed as the extension of
(1) Medulla into cortex (2) Cortex into medulla
(3) Medulla into pelvis (4) Pelvis into ureter

2. Each human kidney has nearly
(1) 10,000 nephrons (2) 50,000 nephrons
(3) 1,00,000 nephrons (4) 1 million nephrons

3. Which one of the four parts mentioned below does not constitute a part of a single uriniferous tubule
(1) Bowman's capsule (2) Distal convoluted tubule
(3) Loop of Henle (4) Collecting duct

4. If kidneys fail to reabsorb water the effect on tissue would
(1) Remain unaffected (2) Shrink and shrivel
(3) Absorb water from blood plasma (4) Take more O_2 from blood

5. Solenocytes are the main excretory structures in
(1) Annelids (2) Molluscs
(3) Echinodermates (4) Platyhelminthes

Answers

1. (2) **2.** (4) **3.** (4) **4.** (2) **5.** (4)

Urine Formation

It involves three processes glomerular filtration, reabsorption and tubular secretion.

(A) Ultra filtration (Starling's hypothesis): It is passive process which takes place from the glomerulus into the Bowman's capsule. The glomerular epithelium has various micropores (diameter = 50 – 100 nm or 0.05 – 0.1 μm) which increase the rate of filtration. The glomerular capillary blood pressure causes filtration of blood through 3 layers, i.e., the endothelium of glomerular blood vessels, the epithelium of Bowman's capsule and a basement membrane between these two layers. The non colloidal part of the plasma as urea, water, glucose, salts, vitamins, minerals, nitrogenous waste are forced out from the glomerular capillaries into the Bowman's capsule by the high pressure of the blood in the glomerular capillaries. The pressure and resistence is high because the glomerular capillaries are narrower than the afferent renal arteries. Glomerular capillaries are about 50 times more permeable than capillaries elsewhere. Pressure highest in glomerular capillaries than in capillaries else where, produce more filtrate. The effective filtration pressure that causes ultrafiltration is determined by three pressures.

(i) Glomerular blood hydrostatic pressure (GBHP): Hydrostatic pressure is the force that a fluid exerts against the walls of its container under pressure.
GBHP = +60 mm Hg

(ii) Blood colloidal osmotic pressure (BCOP): The BCOP is the osmotic pressure created in the blood of glomerular capillaries due to plasma proteins albumin, globulin, and fibrinogen. It resists the filtration of fluid from the capillaries.
BCOP = 32 mm Hg
BCOP in other body capillaries is 25 mm Hg

(iii) Capsular hydrostatic pressure (CHP): CHP is the pressure caused by fluid (filtrate) that reaches into Bowman's capsule and resists filtration.
CHP = 18 mm Hg

Effective filtration pressure (EFP)/Net filtration pressure (NFP): EFP is glomerular blood hydrostatic pressure minus the colloidal osmotic pressure of blood and capsular hydrostatic pressure.

EFP = GBHP – (BCOP + CHP) = 60 mmg – (32 mmg Hg + 18 mm Hg) = 60 – 50 = 10 mm Hg

As there is net filtration pressure of 10 mm Hg. in the lumen of glomerular capillaries as compared to lumen of Bowman's capsule, the filterable components of blood are passed out of the glomerular capillaries. They pass through endothelial fenestrations, basement membranes and filtration slits of podocytes to enter the lumen of Bowman's capsule. The phenomenon is called nephric or glomerular filtration.

Resonate the Concept

- About 1100 - 1200 ml of blood is put to filtration in the two kidneys every minute which consititues roughly 1/5th of the blood pumped out by each ventricle of the heart in a minute. It produces a glomerular or nephric filtrate of about 125 ml/min or 180 l/day. The rate of filtration is called glomerular filtration rate (GFR).

(B) Selective reabsorption: Nearly **99 percent** of the filtrate has to be reabsorbed by the renal tubules.

(i) Proximal convoluted tubule: PCT is the pivotal site for reabsorption. Nearly all of the essential nutrients and 70-80 per cent of electrolytes and water are reabsorbed by this segment. Glucose, amino acid and Na^+, K^+ ions are reabsorbed by active transport. Cl^- ions are reabsorbed by passive transport following the positively charged ions. Active uptake of ions reduces the concentration of the filtrate and an equivalent amount of water passes into the peritubular capillaries by osmosis. Here 65% water is reabsorbed by passive transport. It is also known as obligatory water reabsorption.

Most of the important buffer bicarbonate (HCO_3^-) is also reabsorbed from the filtrate. PCT absorb nearly 80–90% of filtered bicarbonate. 50% urea is reabsorbed by diffusion. The rest remain in the filtrate for removed in the urine.

Resonate the Concept

- PCT also helps to maintain the pH and ionic balance of the body fluids by selective secretion of hydrogen ions, ammonia and potassium ions into the filtrate and by absorption of from it.

(ii) Henle's loop: Reabsorption in its ascending segment is minimum. However, this region plays a significant role in the maintenance of high osmolarity of medullary interstitial fluid. The descending limb of loop of Henle is permeable to water but almost impermeable to electrolytes. This concentrates the filtrate as it moves down. The ascending limb is impermeable to water but allows transport of electrolytes actively or passively. Therefore, as the concentrated filtrate passes upward, it gets diluted due to the passage of electrolytes to the medullary fluid.
15% water, 20-30% $Na^+ + K^+$, 35% Cl^-, 10-20% HCO_3^-.

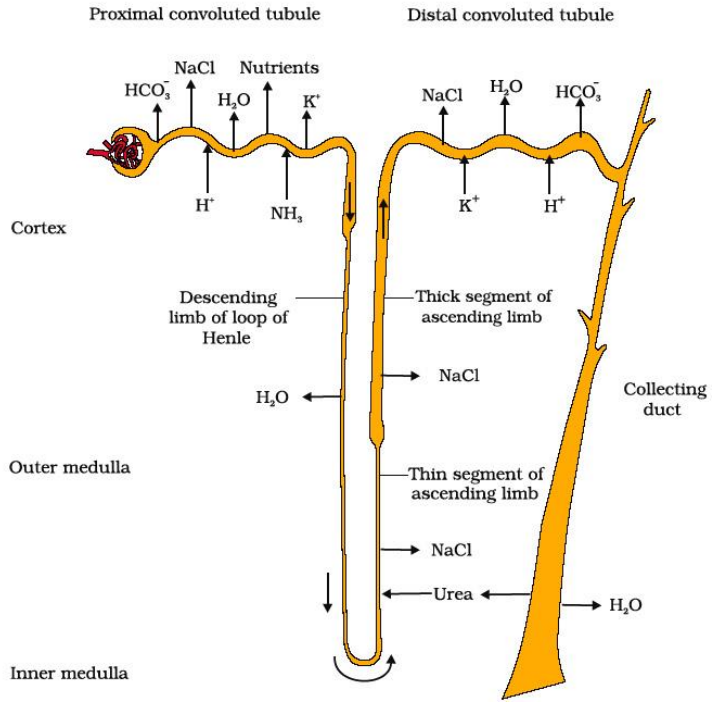


Fig. Reabsorption and secretion of major substances at different parts of the nephron (Arrows indicate direction of movement of materials.)

(iii) Distal convoluted tubule (DCT): Conditional reabsorption of Na+ and water takes place in this segment. DCT is also capable of reabsorption of and selective secretion of hydrogen and potassium ions and NH_3 to maintain the pH and sodium-potassium balance in blood.

(iv) Collecting duct (CD): This long duct extends from the cortex of the kidney to the inner parts of the medulla. Large amounts of water could be reabsorbed from this region to produce a concentrated urine. This segment allows passage of small amounts of urea into the medullary interstitium to keep up the osmolarity. It also plays a role in the maintenance of pH and ionic balance of blood by the selective secretion of H^+ and K^+ ions

(C) Tubular secretion: Tubular secretion probably plays only a minor role in the function of human kidneys, but in animals, such as marine fish and desert amphibians which lack glomeruli and Bowman's capsules, tubular secretion is the only mode of excretion.

It occurs as under –

(i) Creatinine, hippuric acid and foreign substances (pigments, drugs including penicillin) are actively secreted into the filtrate in the PCT from the interstitial fluid. Hydrogen ions and ammonia are also secreted into the PCT.

(ii) Potassium, hydrogen, NH_4^+ and HCO_3^- ions are secreted by active transport, into the filtrate in the DCT.

(iii) Urea enters the filtrate by diffusion in the thin region of the ascending limb of Henle's loop.

(iv) Removal of H^+ and NH_4^+ from the blood in the PCT and DCT helps to maintain the pH of the blood between 6 to 8. Any variation from this range is dangerous. Active secretion of H^+ at PCT is responsible for acidic pH of urine.

Resonate the Concept
• When the blood pressure, and consequently the filtration pressure, drop below a certain level, filtration stops and urine is formed by tubular secretion only.

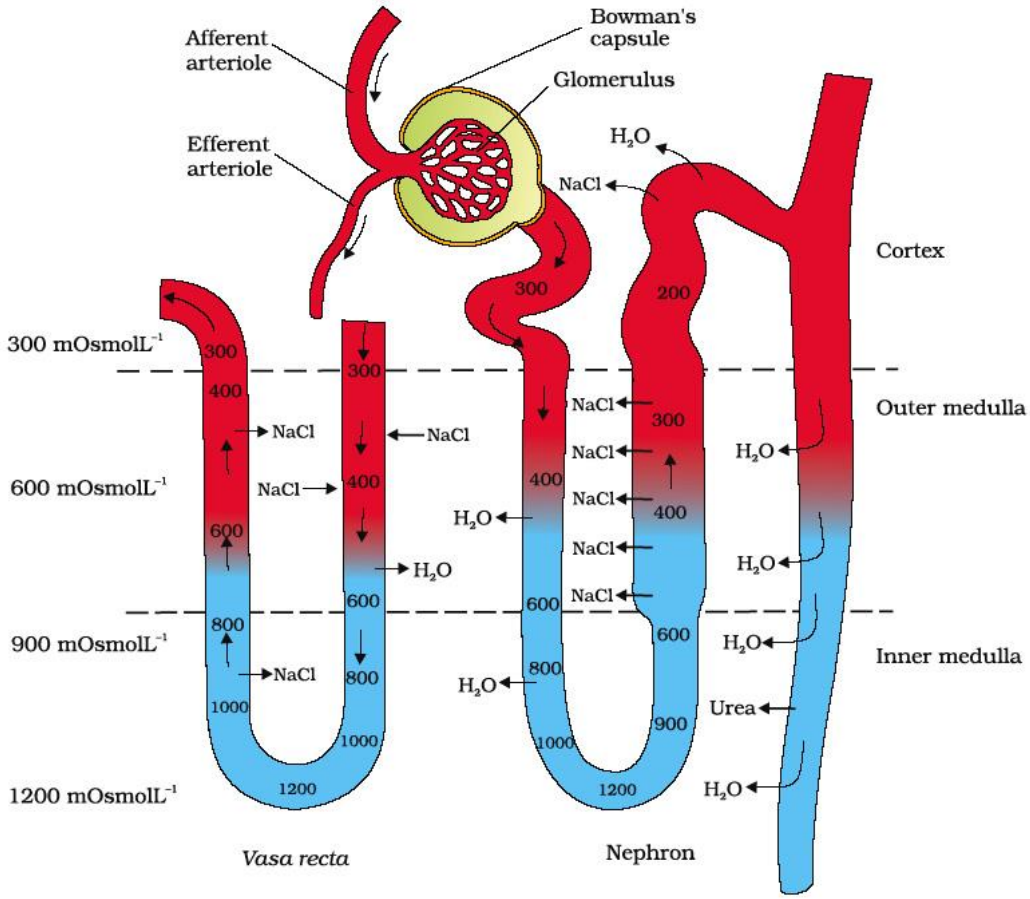
Counter current mechanism

Mammals have the ability to produce a concentrated urine. The Henle's loop and vasa recta play a significant role in this. The flow of filtrate in the two limbs of Henle's loop is in opposite directions and thus forms a counter current. The flow of blood through the two limbs of vasa recta is also in a counter current pattern. The proximity between the Henle's loop and vasa recta, as well as the counter current in them help in maintaining an increasing osmolarity towards the inner medullary interstitium, **i.e., from 300 mosmol/l in the cortex to about 1200 mosmol/l in the inner medulla**. This gradient is mainly caused by **NaCl and urea**. NaCl is transported by the ascending limb of Henle's loop which is exchanged with the descending limb of vasa recta. NaCl is returned to the interstitium by the ascending portion of vasa recta. Similarly, small amounts of urea enter the thin segment of the ascending limb of Henle's loop which is transported back to the interstitium by the collecting tubule.

The above described transport of substances facilitated by the special arrangement of Henle's loop and vasa recta is called the counter current mechanism. This mechanism helps to maintain a concentration gradient in the medullary interstitium. Presence of such interstitial gradient helps in an easy passage of water from the collecting tubule thereby concentrating the filtrate (urine).

Resonate the Concept

- Human kidneys can produce urine nearly four times concentrated than the initial filtrate formed.



Diagrammatic representation of a nephron and vasa recta showing counter current mechanisms

Micturition

Urine formed by the nephrons is ultimately carried to the urinary bladder where it is stored till a voluntary signal is given by the central nervous system (CNS). This signal is initiated by the stretching of the urinary bladder as it gets filled with urine. In response, the **stretch receptors** on the walls of the bladder send signals to the CNS. The CNS passes on motor messages to initiate the contraction of smooth muscles of the bladder and simultaneous relaxation of the urethral sphincter causing the release of urine. The process of release of urine is called micturition. Relaxation and contraction of the urinary bladder are caused by impulses from the sympathetic and parasympathetic nerve fibres. So, it is self generated reflex.

Resonate the Concept

Incontinence (Enuresis) also known as involuntary urination, is any leakage of urine. It is a common and distressing problem, whic may have a large impact on quality of life.
There are three main types of incontinence:

- Urge incontinence due to an overactive bladder
- Stress incontinence due to poor closure of the bladder
- Overflow incontinence due to either poor bladder contraction or blockage of the urethra.d urine is formed by tubular secretion only.

Urine

The fluid and dissolved waste substances excreted by the kidneys constitute urine.

(a) Quantity: An adult man normally passes about 1 to 1.5 litres of urine in 24 hours. The volume of urine depends upon the fluid intake, level of physical activity, type of food taken and environmental temperature.

Less fluid intake and profuse sweating due to heavy physical work and high temperature reduce urine output. Certain substances, such as tea, coffee and alcohol, increase urine output. These are said to be diuretics.

(b) Physical properties: Urine is transparent yellowish fluid, but becomes turbid (cloudy) on standing, its colour depending on its concentration. Its colour is due to a pigment **urochrome** derived from the breakdown of haemoglobin from the worn-out RBCs. Colour of the urine is altered by certain materials taken such as beet, vitamin B complex and some drugs. It is hypertonic to blood plasma. Its specific gravity ranges between 1.001 to 1.035, being slightly higher than that of water. Its pH is 6. It depends on the diet. High protein food and fruits increase acidity whereas vegetables increase alkalinity. Urine has a characteristic unpleasant odour. If allowed to stand, urea is degraded by bacteria to ammonia which imparts a strong smell to urine.

(c) Chemical composition: Urine consists of water and organic and inorganic substances. Water alone forms about 95% of it, other substances form only 5%. The organic substances are mainly nitrogenous organic compounds include urea, uric acid, creatinine and hippuric acid. Of these, urea is the principal component of human urine. The non nitrogenous organic compounds include vitamin C, oxalic acid, phenolic substances include ammonia, and mineral salts such as chlorides, sulphates and phosphates of sodium, potassium, calcium and magnesium. Sodium chloride is the principal mineral salt of the urine. Urine also contains some other substances, such as pigments and drugs, and some epithelial cells, leucocytes, mucin, enzymes, and hormones.

1. Water 95% to 96%
2. Urea 2%
3. Uric acid 0.2%
4. NH_3 0.25%
5. Creatinine 0.5%
6. Hippuric acid 0.025%
7. Salts 1%

Homeostatic regulatory functions of kidneys

By continuously eliminating metabolic wastes and other impurities, and even the surplus quantity of useful materials from blood plasma in the form of urine, kidneys play a vital role in homeostasis. Kidneys also operate certain other homeostatic regulatory mechanisms. Proper maintenance of the internal environment is knows as homeostasis. All regulatory functions of kidneys can be enumerated as follows –

(A) Osmoregulation: Being the universal solvent, water is the actual vehicle in ECF to transport materials between various parts of body. Water volume in ECF tends to vary considerably due to several reason, such as drinking, perspiration, diarrhoea, vomiting, etc. As described in previous pages, the kidneys maintain the water balance in ECF by diluting or concentrating urine.

(B) Regulation of osmotic pressure: Osmolality of cytoplasm is mainly due to proteins and potassium and phosphate ions, whereas that of the ECF is mainly due to sodium, chloride and bicarbonate ions. Inspite of marked difference in chemical composition, the two fluids – intracellular (cytoplasm) and extracellular (interstitium) – must be isotonic, because if ECF becomes hypotonic, cells will absorb water, swell. By retaining apropriate number, mainly of sodium and chloride ions, kidneys maintain the normal osmolality of ECF.

(C) Regulation of pH: Concentration of hydrogen ions (NaH_2 PO_4) in ECF is to be regulated at a constant value usually expressed as pH (minus log of H^+ concentration). The normal pH of ECF is about 7.4. A low pH i.e. a high H^+ concentration causes acidosis, while a high pH i.e. a low H^+ concentration causes alkalosis. Both of these conditions severely affect cellular metabolism. Several special control systems, therefore, operate in the body to prevent acidosis and alkalosis. These systems are called acid-base buffer systems.
Kidneys play a key role in maintenance and operation of these systems. Further, the kidneys regulate hydrogen ion concentration in ECF by excreting acidic or basic urine.

(D) Regulation of electrolyte concentrations in ECF: The kidneys regulate, not only the total concentrations of water and electrolytes in ECF, but also the concentrations of individual electrolytes separately. This regulation is complex and is accomplished by tubular reabsorption and secretion under the control of hypothalamic and adrenal hormones.

(E) Regulation of RBC-count in blood: In oxygen deficiency (hypoxia), kidneys secrete a hormone, erythropoietin into the blood. This hormone stimulates bone marrow to produce more RBCs.

(F) Regulation of renal blood flow: Through RAAS.

Test your Resonance with concept

1. Reabsorption of useful substances from glomerular filtrate occurs in
(1) Collecting tube (2) Loop of Henle
(3) Proximal convoluted tubule (PCT) (4) Distal convoluted tubule (DCT)

2. Brush border is characteristic of
(1) Neck of nephron (2) Collecting tube
(3) Proximal convoluted tubule (4) All of the above

3. If kidneys fail to reabsorb water the effect on tissue would
(1) Remain unaffected (2) Shrink and shrivel
(3) Absorb water from blood plasma (4) Take more O_2 from blood

4. A patient suffering from cholera is given saline drip because
(1) Cl^- ions are important component of blood plasma
(2) Na^+ ions help to retain water in the body
(3) Na^+ ions are important in transport of substances across membrane
(4) Cl^- ions help in the formation of HCl in stomach for digestion

5. A condition of failure of kidney to form urine is called
(1) Deamination (2) Entropy (3) Anuria (4) None of these

Answers

1. (3) **2.** (3) **3.** (2) **4.** (2) **5.** (3)

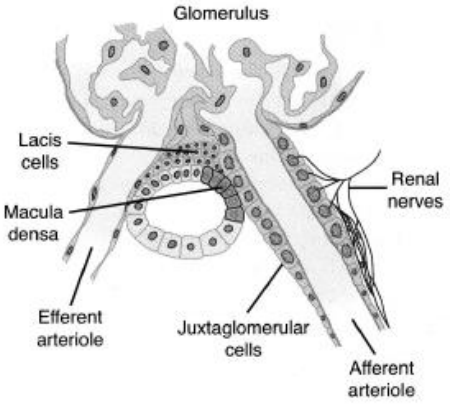
Regulation of kidney functions

The functioning of the kidneys is efficiently monitored and regulated by hormonal feedback mechanisms involving the hypothalamus, JGA and to a certain extent, the heart. Osmoreceptors in the body are activated by changes in blood volume, body fluid volume and ionic concentration.

(A) Control by antidiuretic hormone (ADH): ADH, produced in the hypothalamus of the brain and released into the blood stream from the pituitary gland, **enhances fluid retention** by making the kidneys reabsorb more water. The release of ADH is triggered when osmoreceptors in the hypothalamus detect an **increase in the osmolarity** of the blood above a set point of 300 mosm L^{-1}. In this situation, the osmoreceptor cells also promote thirst. Drinking reduces the osmolarity of the blood, which inhibits the secretion of ADH, thereby completing the feedback circuit.

(B) Control by juxtaglomerular apparatus (JGA) or RAAS mechanism:

(Low blood pressure triggers the renin-angiotension-aldosterone system [RAAS])



The JGA plays a complex regulatory role. A fall in glomerular blood flow/glomerular blood pressure/GFR can activate the JG cells to release **renin** which converts angiotensinogen in blood to angiotensin I and further to angiotensin II. Angiotensin II, being a powerful vasoconstrictor, increases the glomerular blood pressure and thereby GFR. Angiotensin II also activates the adrenal cortex to release Aldosterone. Aldosterone causes reabsorption of Na^+ and water from the distal parts of the tubule. This also leads to an increase in blood pressure and GFR. This complex mechanism is generally known as the Renin-Angiotensin Aldosterone pathway.

(C) Atrial natriuretic factor (ANF): An increase in blood flow to the atria of the heart can cause the release of Atrial Natriuretic Factor (ANF). ANF can cause vasodilation (dilation of blood vessels) and thereby decrease the blood pressure. ANF mechanism, therefore, acts as a check on the renin-angiotensin mechanism

(D) Parathormone: The hormone increases blood Ca^{++} (Hypercalcemia) and decreases PO_4^{3-} accordingly, it increases absorption of Ca^+, increases excretion of PO_4^{3-}.

(E) Thyrocalcitonin: It increases excretion of Ca^{++} in the kidney.

Accessory excretory organs

(A) Skin: Many aquatic animals, such as Hydra and starfish, excrete ammonia into the surrounding water by diffusion through the body wall. In land animals, the skin is often not permeable to water. This is an adaptation to prevent loss of body's water. Mammalian skin retains a minor excretory role by way of its sudoriferous, or sweat glands and sebaceous, or oil glands. **Primary function of sweat is to facilitate a cooling effect on the body surface.**

(B) Lungs: Carbon dioxide and water are the waste products formed in respiration. Lungs remove the large amount of CO_2 (200 ml/min) and significant quantities of water as vapour in the expired air. Lungs have access to abundant oxygen and oxidise foreign substances, thus causing detoxification and also regulate temperature.

(C) Liver: Liver is the largest gland in our body. Liver changes the decomposed haemoglobin of the worn-out red blood corpuscles into bile pigments, namely, bilirubin and biliverdin. These pigments pass into the alimentary canal with the bile for elimination in the faeces. The liver also excretes cholesterol, steroid hormones, certain vitamins and drugs *via* bile.

(D) Large intestine: Epithelial cells of the colon transfer some inorganic ions, such as calcium, magnesium and iron, from the blood into the cavity of the colon for removal with the faeces.

(E) Saliva: Heavy metals and drugs are excreted in the saliva.

(F) Gills: Gills remove CO_2 in aquatic animals. They also excrete salt in many bony fish.

Disorders of excretory system

(A) Uremia: Uraemia is the presence of an excessive amount of urea in the blood. It results from the decreased excretion of urea in the kidney tubules due to bacterial infection (nephritis) or some mechanical obstruction. Urea poisons the cells at high concentration.

(B) Kidney stone (Renal calculus): It is formed by precipitation of uric acid or oxalate. It blocks the kidney tubule. It causes severe pain (renal colic) in the back, spreading down to thighs. The stone may pass into the ureter or urinary bladder and may grow, and cause severe pain of blackade. When in bladder, the patient experiences frequent and painful urination and may pass blood in the urine. Surgery may be needed to remove stone and relieve pain.

(C) Glomerulonephritis: It is the inflammation of glomeruli. It is caused by injury to the kidney, bacterial toxins, drug reaction, *etc.* Proteins and R.B.Cs pass into the filtrate.

(D) Pyelonephritis: It is an inflammation of renal pelvis, calyces and interstitial tissue (*G.pyelos* = trough, tub; *nephros* = kidney; *itis* = inflammation). It is due to local bacterial infection. Bacteria reach here *via* urethra and ureter. Inflammation affects the counter current mechanism, and the victim fails to concentrate urine. Symptoms of the disease include pain in the back, and frequent and painful urination.

(E) Kidney (renal) failure (RF): Partial or total inability of kidneys to carry on excretory and salt-water regulatory functions is called renal or kidney failure. Kidney failure leads to (*i*) Uraemia, i.e., an excess of urea and other nitrogenous wastes in the blood (*G.ouron* = urine, *haima*-blood); (*ii*) Salt-water imbalance; and (*iii*) stoppage of erythropoietin secretion.

Causes Many factors can cause kidney failure. Among these are tubular injury, infection, bacterial toxins, glomerulonephritis (inflammation of glomeruli) arterial or venous obstruction, fluid and electrolyte depletion, intrarenal precipitation of calcium and urates, drug reaction, heammorrhage, etc.

(F) Cystitis: It is the inflammation of urinary bladder (*G.kystis* = bladder, *–itis* = inflammation). It is caused by bacterial infection. Patient has frequent, painful urination, often with burning sensation.

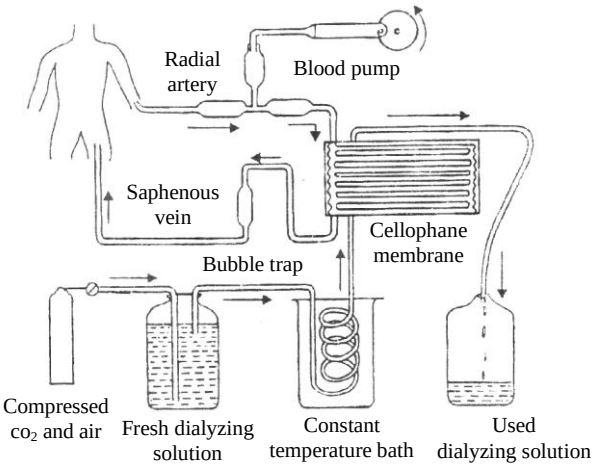
Artificial kidney

Artificial kidney, called haemodialyser, is a machine that is used to filter the blood of a person whose kidneys are damaged. The process is called haemodialysis. It may be defined as the separation of small molecules (crytalloids) from large molecules (colloids) in a solution by interposing a semipermeable membrane between the solution and water (dialyzing solution). It works on the principle of dialysis i.e. diffusion of small solute molecules through a semipermeable membrane (G. *dia* = through, *lyo* = separate).

Haemodialyser is a cellophane tube suspended in a salt-water solution of the same composition as the normal blood plasma except that no urea is present. Blood of the patient is pumped from one of the arteries into the cellophane tube after cooling it to $0^{o}C$ and mixing with an anticoagulant (heparin). Pores of the cellophane tube allow urea, uric acid, creatinine, excess salts and excess H^{+} ions to diffuse from the blood into the surrounding solution. The blood, thus purified, is warmed to body temperature, checked to ensure that it is isotonic to the patient's blood and is mixed with an antiheparin to restore its normal clotting power.

It is then pumped into a vein of the patient. Plasma proteins remain in the blood as the pores of cellophane are too small to permit the passage of their large molecules.

The use of artificial kidney involves a good deal of discomfort and a risk of the formation of blood clots. It may cause fever, anaphylaxis, cardiovascular problems and haemorrhage. Kidney transplant is an alternative treatment of chronic renal failure (CRF).



Flow of Blood through an artificial kidney for haemodialysis

Kidney transplantation

If the kidney failure cannot be otherwise treated, by drug or dialysis, the patients are advised for kidney **transplantation**. A donated kidney may come from an anonymous donor who has recentaly died, or from a living person, usually a relative. The kideny of donor must be a good match for recipient. The more the new tissue from the donor is like the recipient's tissue, the less likely the immune system of the recipient is to reject it. Immune system protects from disease by attacking anything that is not recognised as a normal part of the body. So, the immune system of the recipient will attack a kidney that appears too "foreign". Special drugs (Cyclosporin A, Cortisol) can help suppress the immune system of the recipient so it does not reject a transplanted kidney.

Test your Resonance with concept

1. There is no sugar in the urine. The blood entering the kidney has more sugar than the blood leaving the kidney because:
(1) sugar is absorbed by loop of Henle (2)sugar is used by kidney cells in metabolism
(3) sugar is absorbed by PCT (4) sugar is absorbed by urinary bladder

2. Ultratiltration occurs through:
(1) Basement membrane (2) Glomerular rnembrane
(3) Interpodocytic space (4) Capsular wall

3. Filtration fraction is the ratio of:
(1) GFR and RPF (2) Hb and HbO_2 (3) O_2 and CO_2 (4) HCO_3 and H_2CO_3

4. Total filtrate formed in 24 hours in human kidney is:
(1) 1.8 litre (2) 8.0 litre (3) 18 litre (4) 180 litre

5. Malpighian tubules remove excretory matter from the:
(1) oral cavity (2) alimentary canal (3) haemolymph (4) all of these

Answers
1. (2) **2.** (1) **3.** (1) **4.** (4) **5.** (3)

Additional information

1. SOME OTHER DISEASES RELATED TO EXCRETION

(i) **Anuria –** Failure of kidney to form urine.
(ii) **Oligouria –** Less urine output.
(iii) **Haematuria –** Presence of blood in urine.
(iv) **Aminoaciduria –** Urine with amino acids like cystine, glycine etc.
(v) **Dysuria –** Painful urination.
(vi) **Polyuria –** Increased urine volume as in Diabetes insipidus and mellitus.
(vii) **Nocturia –** Increased volume of urine at night.
(viii) **Diabetes mellitus –** Sugar appear in urine due to hyposecretion of insulin.
(ix) **Diabetes insipidus –** Tasteless more urine passing due to hyposecretion of A.D.H.
(x) **Cystitis –** Inflammation of urinary bladder.
(xi) **Gout –** Painful great toe (arthiritis) due to deposition of uric acid.
(xii) **Oedema –** Increased volume of interstitial fluid.
(xiii) **Polynephritis –** Inflammation of large number of nephrons.
(xiv) **Bright's disease –** Characterised by nephritis caused by streptococal infection.
(xv) **Ptosis –** Displacement of kidney.
(xvi) **Nephrotic syndrome –** Presence of massive amounts of proteins specially albumin auses oedema (accumulation of fluid in interstitial space) and hyperlipidemia (high level of cholesterol, phopholipids and triglycerides in blood).

2. ABNORMAL CONSTITUENTS OF URINE

(i) **Protein** – If protein is present in urine it may be due to infection or injury in kidney. (Mainly albumin is filtered)
(ii) **Blood** – Due to infection and injury of kidney blood may appear in urine.
(iii) **Sugar** – In diabetes mellitus sugar appear in urine.
(iv) **Bile or bile pigments** – In jaundice bile pigment appear in urine.
(v) **Ketone bodies** – They appear in cases of starvation and diabetes e.g. acetone, aceto acetate, β-hydroxybutyrate.

3. SOME OTHER FACTS RELATED WITH ULTRA FILTRATION

(i) **Net opposing filtration pressure:**
(NOFP) = BCOP+CHP = 50 mm Hg.

(ii) **Glomerular filtrate:** The plasma fluid that filters out from glomerular capillaries into Bowman's capsule of nephrons is called glomerular filtrate. It is a non-colloidal part and possess urea, water, glucose, amino acid, vitamins, fatty acid, uric acid, creatin, creatinine, toxins, salts etc. RBCs, WBCs, platelets and plasma proteins are the colloidal part of the blood and do not filtered out from glomerulus. Glomerular filtrate is isotonic to blood plasma.
Glomerular filtrate or Nephric filtrate = Blood – (Blood cells + Plasma protein)

(iii) **Glomerular filtration rate (GFR):** GFR is the amount of filtrate formed per minute in all nephrons of the paired kidney. In male the rate is 125 ml/min, in female it is 110 ml/min. GFR is affected by volume of circulating blood, neural activity, and stretch response to pressure of the wall of the arteriole. 180 litres of filtrate is formed per day, out of it, only 1.5 litre of urine is produced per day which is 0.8% of the total filtrate.

(iv) **Renal plasma flow:** About 1100-1200 ml (20% of cardiac output or total blood) blood circulates through kidneys each minute and of this blood, about 670 ml is the plasma. The latter is called the renal plasma flow (RPF).
RPF = 670 ml

(v) **Filtration fraction:** This is the ratio between GFR (glomerular filtration rate) and RPF (renal plasma flow).

$$\text{Filtration fraction} = \frac{GFR}{RPF} = \frac{125}{670} = 0.186$$

4. DEVELOPMENT OF KIDNEY

During embryonic development,fine tubules containg plate develops from mesoderm.Tubules are called nephros and plate is called as nephrotome plate those develope as nephrons and kidney respectively .Kidney can be developed from anterior , middle or posterior part of the nephrotome plate . On this basis, kidney are of 3 types.

(i) **Pronephric kidney:** It is developed from anterior part (Pronephros) of nephrotome plate.Similarly, nephros are not differentiated, so the nephrons are simple tubular e.g. cyclostomates & tadpole of frog and all anamniotes embryo.

(ii) **Mesonephric kidney or opisthonephros:** It is developed from middle part (Mesonephros of Nephrotome plate & remaining part of nephtotome is destroyed.Nephrons found in such kidney possess Bowman's capsule and simple tubular tract. e.g. most of the fishes & adult Amphibians, all amniotes.

(iii) **Metanephric kidney:** It is developed from posterior part (Metanephros) of nephrotome while remaining part is destroyed. Nephrons are well differentiated into Bowman's capsule PCT, DCT & loop of Henle e.g. reptiles, aves and mammals.

The hypothetical primitive kidney of ancestral vertebrate is called Archeonephros which is found in larva of myxine and some apodan amphibians.

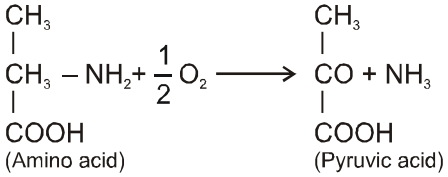
5. In frog, mesonephric duct is also known as **Bidder's canal** which carry sperm and urine both.

6. SYNTHESIS OF UREA IN LIVER:

Urea is formed in liver by two processes.

(i) Deamination **(ii)** Ornithine cycle

(i) **Deamination:** The amino acid is oxidised using oxygen. This results in removal of the amino group and leaves pyruvic acid. Pyruvic acid can enter the Krebs cycle and be used as a source of energy in cell respiration. The amino group is converted to ammonia during deamination. Deamination is also known as oxidative deamination.



(ii) Ornithine cycle or Urea Cycle (Kreb-Henseleit cycle):

In liver, one molecule of CO_2 is activated by biotin and combines with two molecules of NH_3 in the presence of carbamayl phosphate synthetase enzyme (CPS) and 2 ATP to form carbamoyl phosphate and one molecule of H_2O release. Carbamayl phosphate reacts with ornithine and form citrulline. Citrulline combines with another molecule of ammonia and form arginine. Arginine is broken into urea and ornithine in the presence of an enzyme **arginase** and water. Ornithine re-enters in the cycle. Liver cells, thus, continuously remove ammonia and some CO_2 from blood and release urea into the blood. Kidneys continuously remove urea from the blood to excrete it in urine.

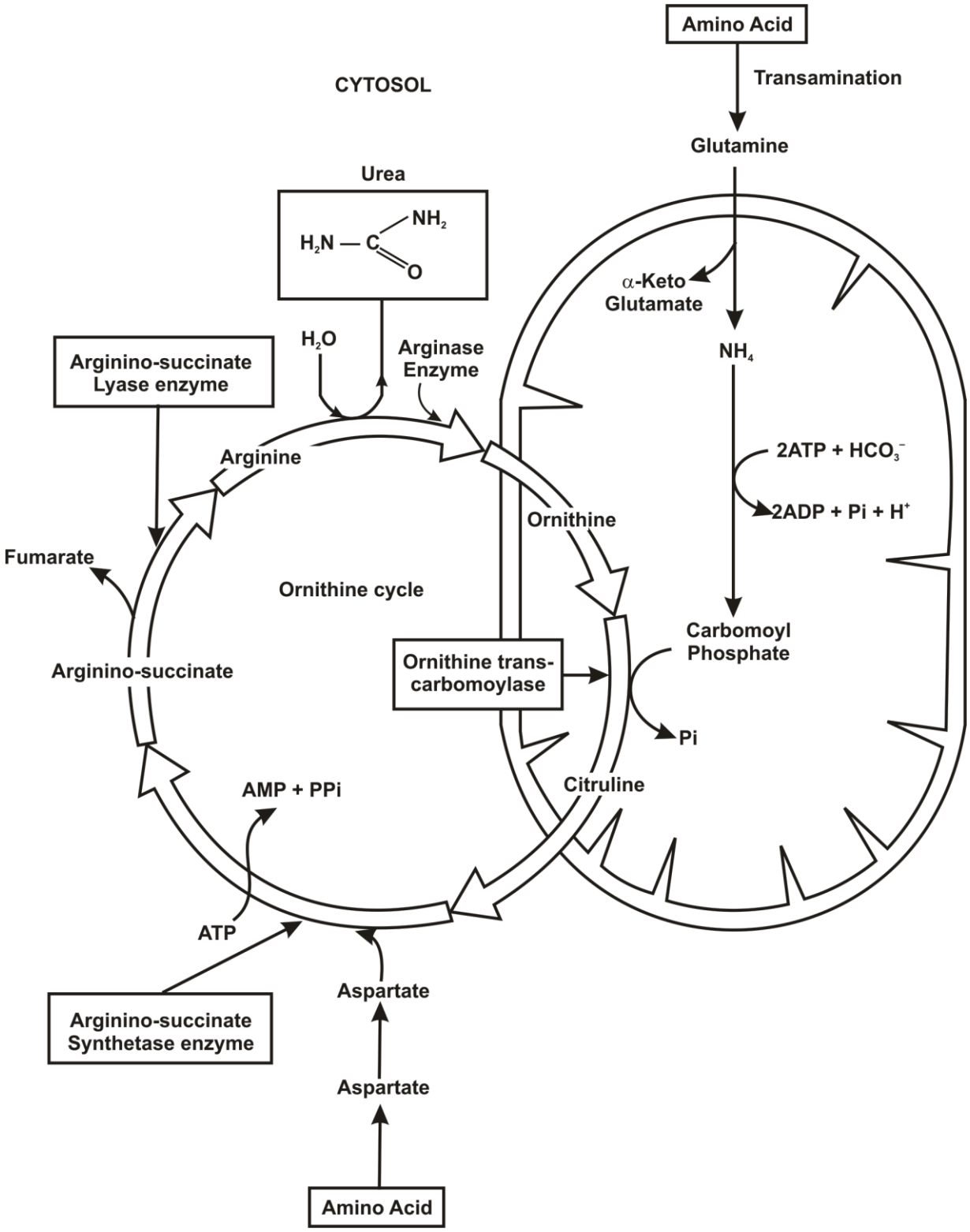


Figure - Urea cycle

7. THRESHOLD SUBSTANCES

(i) High threshold substances: Such substances are absorbed almost all. **e.g.** sugar, amino acids, vitamins, HCO_3^- and Na^+ etc.

(ii) Low threshold substances: They are absorbed in low concentration. **e.g.** urea, phosphate, uric acid, H^+, K^+.

(iii) Non threshold substances: They are not reabsorbed. **e.g.** creatinine and hippuric acid.

8. Allantoin and allantoic acid are nitrogenous excretory products formed during embryonic development of amniotes with shelled eggs which is stored in allantois foetal membrane.

9. Certain animals are both ammonotelic and ureotelic e.g. ascaris, earthworm, lung fish (African toad), etc.

10. Chordate with flame cells is *Branchiostoma* (also called *Amphioxus*).

11. The most frequent protozoan seen in urine is *Trichomonas vaginalis*, a cause of vaginitis in females and urethritis in males.

12. A starving person will also excrete more urea because during starvation proteins are broken down for energy production.

13. Xanthine excretory product in *Herdmania* (urochordata)

14. Nephrology is the specialized branch of medicine that deals with structure, functions and diseases of male and female urinary system and male reproductive system.

15. Urology is the branch of medicine related to male and female urinary system and male reproductive system.

16. Diuretics are the substances that increase the rate of urine flow. Naturally occurring diuretic include caffine in coffee, tea, and cola soda, which inhibit Na^+ reabsorption and alcohol in bear, wine and mixed drinks inhibits secretion of ADH.