CHAPTER 22

Excretion & Osmoregulation

INTRODUCTION

- **Excretion** is the elimination to waste products from the body.
- **Waste products** are unwanted and toxic by-products which are removed to maintain homeostasis and protect the body from their toxicity, e.g., jaundice in case of bile pigments, uremia in case of urea.
- Waste products (which do not accumulate in the body) are nitrogenous materials, CO_2, pigments, excess of water, inorganic salts, vitamins and hormones. Carbon dioxide and some water are excreted by lungs. Other waste materials are removed in the urine.
- The organs and tissues participating in the excretion of waste products constitute the excretory system. A major function of the **excretory system** is the excretion of nitrogenous waste. These include **ammonia**, **urea** and **uric acid**.
- Excretion also helps to maintain a constant body temperature by removing excess heat and maintain a constant internal environment in association with the other system of the body.
- **Defaecation** is elimination of undigested food residue from alimentary canal while **secretion** is the discharge of specially synthesised product, e.g., hormone by endocrine gland, saliva from salivary gland.
- **Osmoregulation** (term coined by Haber) is the regulation of osmotic concentration, that is, water contect and salt and cells.
- Both excretion and osmoregulation are helpful in maintaining homeostasis or constant favourable internal environment of the body. In vertebrates the two functions of excretion and osmoregulation are performed by kidneys and their associated structures in urinary system.
- The organs which form, store and void the urine constitute urinary system.
- Perspiration is another excretory process which removes salts and water although the primary purpose is cooling.

EXCRETORY PRODUCTS AND THEIR TYPES

- Excretory substances are produced during metabolism of nitrogeneous substances like amino acids and nucleic acids.
- Metabolism of carbohydrates and fats produces CO_2 and H_2O which are easy to remove. Their excretion is effected through lungs (expired air), skin (sweat) or kidneys (urine).
- Other excretory products are pigments, mostly formed by the breakdown of haemoglobin; drugs etc.
- Protein metabolism produces nitrogenous waste material such as ammonia, which is the basic nitrogenous catabolite of protein, formed by breakdown of amino acids. Removal of the amino group (NH_2) is known as **deamination** and it converts the amino acid into a keto acid. In vertebrates, deamination **takes place in the liver**. Ammonia thus produced is highly toxic and cannot be stored within the body. It needs to be eliminated immediately.

Table: Excretory organs of different animals.

No.	Animals	Excretory organ	Examples
1.	Protozoans	Plasmalemma	Amoeba
2.	Porifera	General body surface	Sycon
3.	Coelenterates	General body surface	Hydra
	In the above three, contractile vacuole is also there which is not really an excretory organ. It is specially for water balance & helps to get rid of extra water that diffuse into the cell.		
4.	Platyhelminthes	Flame cells (Solenocytes) Protonephridium	Taenia, Planaria Larva of platyhelminth miracidium, redia larva,
6.	Aschelminthes	Renette cell (excretory cell)	Ascaris
7.	Annelida	Nephridia Chloragogen cells	Earthworm Earthworm megascolex
8.	Arthropoda	Malpighian tubules, uricose gland, Urate cells Coxal gland Green gland	Cockroach Spider, Scorpion (arachnida) Prawn (crustacea)
	Special glands called rectal glands reabsorb water and ions and urine which are mixed with faeces. This is an adaptation of dry habitat.		
9.	Echinoderm	Tubefeet (podia) & dermal branchea (thin walls of gills)	Starfish
10.	Protochordates	Solenocytes Neural gland Glomerulus	Amphioxus Herdmania Balanoglossus

- Depending upon the form in which the ammonia or nitrogenous waste is excreted from the body, the organisms are grouped as under into **three categories**: **ammonotelic, uricotelic** and **ureotelic.**
- Besides these (ammonia, urea and uric acid) there are a few other types of minor nitrogenous excretory products, like—
  - **Trimethylamine oxide (TMAO):** Marine teleost fishes excrete a large proportion of their nitrogen as trimethylamine oxide (TMAO). Large amounts of this compound is also stored in their body for osmoregulation i.e. to minimize loss of water and entry of salts.
  - **Guanine:** Spiders excrete almost exclusively a chemical called guanine. It is even less soluble as compared to uric acid and hence requires no water for elimination. It is a metabolic waste of nucleotide metabolism. It is also found in penguins.
  - **Ornithuric acid:** It is excreted in small amount by birds and is formed by a combination of benzoic acid (formed during fat metabolism) in food with the amino acid ornithine.
  - **Hippuric acid:** It is formed when benzoic acid is combined with glycine. It is less toxic.
  - **Creatinine:** Mammals contain a small quantity of creatinine in their blood (1 mg/100 ml) which is a derivative of creatine. The excess is eliminated along with urine.
  - **Creatine:** Mammals also excrete creatine which is synthesized in the liver from three amino acids—arginine, glycine and methionine.

Ammonotelic

- Animals excreting their nitrogenous waste in the form of ammonia are known as ammonotelic. This phenomenon is known as ammonotelism.
- Ammonia is highly soluble in water with which it forms ammonium hydroxide (NH_4OH) which injures cells directly by alkaline caustic action. Hence excretion of ammonia requires large amounts of

water to be lost from the body. That is why such a mode is suitable for aquatic organisms which have a constant access to water.

- No energy is required to produce ammonia.
- E.g. all aquatic invertebrates, bony fishes and aquatic amphibians.
- Ammonia is the **first metabolic waste product** of protein metabolism.

> Aminotelism is the excretion of amino acids which cannot be metabolised due to their being in excess. The animals performing aminotelism are called aminotelic, e.g. some molluscs (Pila, Unio, Limnaea) and some echinoderms (starfish, Holothuria).

- In anurans (amphibians) the larval tadpoles excrete ammonia, while the adults produce urea.

Uricotelic

- Animals which excrete their nitrogenous waste mainly in the form of uric acid and urates are known as **uricotelic**. The phenomenon is known as **uricotelism**.
- All terrestrial animals like insects, reptiles, and birds excrete uric acid.
- Uric acid ($C_5H_4N_4O_3$) (which require more energy) is produced by degradation of purines (*e.g.* guanine) in liver and kidneys to some extent. In uricotelic animals, excess nitrogen is first used in synthesis of purines. A purine is changed to **xanthine** (from hypoxanthine or guanine) which is then **oxidised to uric acid**. Part of uric acid is **oxidised** further to form **allantoin** and **allantoic acid**. Teleost fish excrete allantoate or hydration product of allantoin. In most fishes and amphibians, allantoate is hydrolysed to urea and glyoxylate. Some marine invertebrates have gone a step further by hydrolysing urea to ammonia and carbon dioxide. Creatine is formed in liver from amino acids. Creatinine is produced from creatine.
- Conversion of ammonia to uric acid and its subsequent elimination requires lesser amount of water as it is comparatively less soluble in water and less toxic as compared to ammonia. Hence, it is observed in terrestrial animals that do not have constant access to water or rather have limited access to water.

Ureotelic

- Animals that excrete their nitrogenous waste mainly in the form of urea are known as ureotelic and the phenomenon is known as ureotelism.
- Urea can be stored in body for considerable periods of time, and is least toxic. It is eliminated in the form of urine.
- Ureotelism is exhibited by semi-terrestrial animals, e.g. some earthworms, adult amphibians, elasmobranch (cartilagineous fishes) and mammals.
- Frog like other amphibians is ammonotelic in tadpole state and ureotelic in mature state. Earthworm is similarly ammonotelic when sufficient water is available and ureotelic when water availability is reduced.

Check your **GRASP**

1. **A person has taken very high protein rich diet; his urine will eliminate more of**
   a. urea b. creatinine
   c. glucose d. glycogen
2. **Vertebrates kidney and contractile vacuole of protozoans resemble as both excrete**
   a. minerals b. water
   c. glucose d. nitrogenous wastes
3. **The passing out of almost solid excretory wastes in reptiles is an indication of**
   a. xeric habits b. excretion through skin
   c. excretion through alimentary canal
   d. reutilizing water of urine
4. **Most terrestrial insects get rid of bulk of their nitrogenous wastes as**
   a. amino acids b. urea
   c. uric acid d. ammonia
5. **The flame cell system of helminthes work**
   a. to remove ammonium ions and uric acids
   b. to remove uric acid
   c. to regulate pH
   d. for osmoregulation

6. Renal gland is the excretory organ of
a. annelida b. echinodermata
c. crustaceans d. molluscs

7. Deamination is first step in urea formation which means
a. reduction of ammonia
b. oxidation of ammonia
c. addition of amino group to organic molecule
d. removal of amino group from amino acid

8. Antennary glands are excretory organs of
a. spiders b. crustaceans
c. mollusca d. echinodermata

9. Protonephridia are present in platyhelminthes and metanephridia in
a. nematodes b. arthropoda
c. annelids d. platyhelminthes only

10. Excretory organs of protochordate Amphioxus are
a. malpighian tubules b. protonephridia
c. kidney d. none of these.

11. Major source of ammonia produced by kidney comes from
a. leucine b. glycine
c. glutamine d. alanine

12. Uric acid is the end product of metabolism of
a. proteins
b. glomerular acids
c. fats
d. lipids

13. Trimethylamine is excreted by
a. marine teleosts
b. mollusca
c. fresh water fish
d. amphibians

14. The kidneys resembles contractile vacuoles of protozoans in
a. expelling of excess water
b. expelling out salts
c. expelling out excess glucose
d. expelling out urea and uric acid

15. In one of the following groups the toxic substance benzoic acid after combining with amino acids glycine forms hippuric acid as material in
a. fish b. reptiles
c. amphibians d. mammals

16. Which is most toxic excretory product and require 600 ml of water for throwing one gm nitrogen ?
a. uric acid b. urea
c. ammonia d. hippuric acid

17. Which one of these animal excretes amino acid without deamination ?
a. rat b. earthworm
c. unio d. fly

18. Excess bile pigments in urine indicate
a. anaemia b. diabetes insipidus
c. jaundice d. all of these.

19. Ammonia is the end product of
a. glucose breakdown
b. fatty acid metabolism
c. protein metabolism
d. breakdown of biogenic amines

20. Pterydines are the excretory products of some
a. crustaceans b. molluscs
c. insects d. fish

21. The liver of which one of the following is richest source of arginase enzyme ?
a. bony fish b. cartilaginous fish
c. frog d. rabbit

22. Excretion is required for maintaining homeostasis of body fluids through regulation of their
a. volume, composition, pH and osmotic potential
b. volume
c. composition and pH
d. osmotic potential

23. Uric acid is excreted in
a. frog b. rabbit
c. man d. pigeon/crow

24. In human beings, gout is caused by
a. deficiency of iodine
b. excessive secretion of thyroid
c. excessive liberation of uric acid
d. deposition of uric acid

25. Deamination is the process in which
a. poisonous urea is removed from the blood and it occurs in kidneys
b. amino acids are absorbed from digested food, and it occurs in intestinal villi
c. amino acids are broken down to produce urea and it occurs in liver
d. amino acids are synthesised and it occurs in ribosomes

26. In aquatic organisms the waste end product of nitrogen metabolism is
a. urea b. nitrogen
c. ammonia d. allantois

27. Excretory products of mammalian embryo are eliminated by
a. placenta
b. amniotic fluid
c. allantois
d. ureters

28. The snakes living in deserts are mainly
a. ammonotelic b. aminotelic
c. ureotelic d. uricotelic

29. The excretory product of excess metabolism of creatine and guanine is
a. creatinine b. Urea
c. uric acid d. oxalic acid

30. In Rabbit and other terrestial mammals, the main nitrogenous waste material is
a. uric acid b. ammonia
c. urea d. urea and uric acid

31. Nitrogenous waste products are eliminated mainly as
a. urea in tadpole and ammonia in adult frog
b. ammonia in tadpole and urea in adult frog
c. urea in both tadpole and adult frog
d. urea in tadpole and uric acid in adult frog

32. In Prawn, excretion is carried out by
a. nephrons b. malpighian tubules
c. flame cells d. reptiles

33. Excretion is
a. removal of substances not required by body
b. removal of useless substances and substances present in excess
c. formation of substances having some role in body
d. all of the above

34. The animal which retain urea for hypertonicity is
a. man b. bird
c. elasmobranch d. amphibian

35. Aquatic animals are mostly ammonotelic because
a. ammonia helps in checking inflow of water into body
b. excretion of ammonia requires large amount of water which is available to these animals
c. water contains less nitrogen
d. these get less light

36. Excretion of nitrogenous waste product mainly as uric acid by birds is helpful in
a. conserving body heat
b. conserving water
c. eliminating excess water
d. eliminating excess body heat

37. Which one is the most soluble in water?
a. uric acid b. urea
c. fatty acids d. casein

38. Excretory product of birds and reptiles is
a. urea
b. uric acid
c. ammonia
d. TMO

39. Sea Gulls excrete salts through
a. liver b. lungs
c. urine d. nasal gland

40. In Amoeba, NH_3 is excreted through
a. food vacuole
b. plasma membrane
c. contractile vacuole
d. all of these.

41. Malphigian tubule are the excretory organs in
a. cockroach
b. platyhelminthes
c. Ascaris
d. Pila

42. Ammonia is changed to uric acid in the liver of
a. ammonotelic animals
b. uricotelic animals
c. ureotelic animals
d. ornithotelic animals

43. Which one is false?
a. nephrons perform excretion through filtration, reabsorption and secretion
b. nephridia are accessory excretory organs in Prawn
c. tapeworm have excretory flame cells
d. nephrons begin with Bowman's capsule having glomerulus

44. Which of the following is likely to accumulate in dangerous proportion in the blood of a person whose kidney is not working properly?
a. lysine b. urea
c. ammonia d. sodium chloride

45. Bony fishes are
a. ureotelic
b. uricotelic
c. aminotelic
d. ammonotelic

Answers

1. a.	2. a.	3. b.	4. c.	5. d.	6. d.	7. d.	8. b.	9. c.	10. b.
11. c.	12. b.	13. a.	14. a.	15. a.	16. c.	17. c.	18. c.	19. c.	20. c.
21. b.	22. a.	23. d.	24. d.	25. c.	26. c.	27. a.	28. d.	29. c.	30. b.
31.b.	32. d.	33. b.	34. c.	35. b.	36. b.	37. b.	38. b.	39. d.	40. a.
41.a.	42. b.	43. b.	44. b.	45. d.					

- Human beings are ureotelic i.e. excreting their nitrogenous waste as urea.

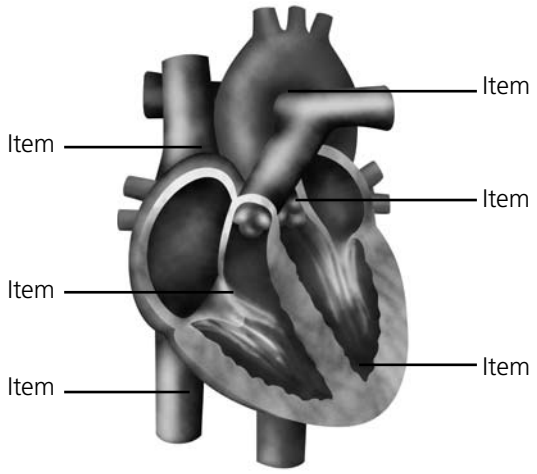


Fig. Excretory system.

Kidney

- Kidney are **mesodermal in origin** and developed from nephrostomes of early embryo.
- Kidney are **excretory** and **homeostatic organ**.
- Man possesses a pair of dark red, bean shaped, **metanephric** kidneys located in the peritoneal cavity outside the coelom (**retroperitoneal**).
- Kidney is covered by **peritoneum** on the ventral side.
- As the primary organs of excretion, the **kidneys perform two major functions**. They filter the blood, removing water, ions, and nitrogenous wastes and forming urine and in turn regulate the volume, osmotic pressure, and **pH of the blood and body fluids**.
- The body is very sensitive to its pH level. Outside the range of pH that is compatible with life, proteins are denatured and digested, enzymes lose their ability to function, and the body is unable to sustain itself.
- The kidneys maintain acid-base homeostasis by regulating the pH of the blood plasma. Gains and losses of acid and base must be balanced.
  - **Sources of acid gain**: carbon dioxide (since CO_2 and H_2O form H_2CO_3, carbonic acid, in the presence of carbonic anhydrase); production of nonvolatile acids from the metabolism of proteins and other organic molecules; and loss of bicarbonate in faeces or urine.
  - **Sources of acid loss**: use of hydrogen ions in the metabolism of various organic anions; and loss of acid in the vomitus or urine
- When **acid loss exceeds acid gain**, alkalosis occurs. When **gain exceeds** loss acidosis occurs. There are various renal responses to acidosis and alkalosis.
- **Responses to acidosis**:
  - Bicarbonate is added to the blood plasma by tubular cells.
    - Tubular cells reabsorb more bicarbonate from the tubular fluid.
    - Collecting duct cells secrete more hydrogen and generate more bicarbonate.
  - Ammoniagenesis leads to increased buffer formation (in the form of NH_3)
- **Responses to alkalosis**:
  - Excretion of bicarbonate in urine.
    - This is caused by lowered rate of hydrogen ion secretion from the tubular epithelial cells.
    - This is also caused by lowered rates of glutamine metabolism and ammonia excretion.
- Kidney also secretes hormones like – erythropoietin (which regulates red blood cell production in the bone marrow); renin (which is a key part of the renin-angiotensin-aldosterone system) and active form of vitamin D, calcitriol, and prostaglandins.
- The kidneys are situated below the diaphragm on the left and right sides, and are partially protected by the eleventh and twelfth pairs of ribs.
- **The right kidney is lower than the left** because the liver takes up much space on that side.
- Each kidney is surrounded by layers of fibrous connective tissue and a mass of adipose (fat) tissue which cushions it and holds it in place.
- The kidney consists of an **outer cortex** and an **inner medulla**. They both contains the uriniferous tubules or **nephrons** (the structural and functional unit of kidney).
- The **renal cortex** is granular in appearance because the tubules here are much convoluted (proximal and distal convoluted tubules) and contain malphigian corpuscles.
- The cortex overlies the bases of medullary pyramids and dips down between them. These displaced portions of cortex which invade the medullary territory are called the **renal columns of Bertini**.
- Cortex is sub-divided into alternating radial tracts known as rays and labyrinths. The rays are radially straight since they contain the straight parts of

Erythropoietin

The kidney cells that make EPO are specialized and are sensitive to low oxygen levels in the blood coming into the kidney. These cells release erythropoietin when the oxygen level is low in the kidney. Erythropoietin stimulates the bone marrow to produce more red blood cells which in turn increases the oxygen-carrying capacity of the blood.

Erythropoietin or EPO is a glycoprotein hormone that is a cytokine for erythrocyte (red blood cell) precursors in the bone marrow. Erythropoietin is available as a therapeutic agent produced by recombinant DNA technology in mammalian cell culture. It is used in treating anemia resulting from chronic renal failure or from cancer chemotherapy. Its use is also believed to be common as a blood doping agent in endurance sports such as bicycle racing, triathlons and marathon running.

EPO is produced not only in the kidney but also, to a lesser extent, in the liver. The EPO gene has been found on human chromosome 7 (in band 7q21). Different DNA sequences flanking the EPO gene act to control liver versus kidney production of EPO.

The measurement of EPO in the blood can indicate bone marrow disorders or kidney disease. Normal levels of EPO are 0 to 19 mU/ml (milliunits per millilitre). Elevated levels can be seen in polycythemia rubra vera, a disorder characterized by an excess of red blood cells. Lower than normal values of EPO are seen in chronic renal failure.

Using recombinant DNA technology, EPO has been synthetically produced for use in persons with certain types of anaemia: anemia due to kidney failure, anaemia secondary to AZT treatment of AIDS, and anaemia associated with cancer.

EPO has been much misused as a performance-enhancing drug in endurance athletes such as reportedly cyclists, long-distance runners, speed skaters, and Nordic (cross-country) skiers. When misused in such situations, EPO is thought to be especially dangerous (perhaps because dehydration can further increase the viscosity of the blood, increasing the risk for heart attacks and strokes. EPO has been banned by the Tour, the Olympics, and other sports organizations.

proximal tubules and the collecting ducts. They are continuous with striated medulla, hence called medullary rays. The labyrinths have a granular appearance because the convoluted tubules, which compose them, are cut irregularly.

- **Renal medulla** mainly contains loop of Henle, collecting tubules and ducts of Bellini.
- The medulla appears striated since the tubules run through it in a straight course radiating towards the pelvis.
- The medulla consists of 10 to 15 multilobular conical masses, the **renal pyramids**, whose bases are adjacent to the cortex and whose apices form the papillae. These papillae project into cup shaped channels called **calyces**.
- The spaces between calyces are part of the renal sinus and are filled with adipose tissue, vessels and nerves.
- The calyces join to form the **pelvis** which is the expanded beginning of the ureter.
- The medial concave border of a kidney contains a notch known as **hilus** through which the renal artery enters and the renal vein and ureter leave the kidney.
- The s**tructural and functional unit of a kidney is the nephron or the uriniferous tubule**.
- Nephrons are connected to collecting ducts which pass through the renal pyramids and open into the renal pelvis.
- Urine formed in the nephrons and collecting ducts empties into the renal pelvis and is carried away from the kidney by the ureter.

Types of Kidney

Archinephros

- It is the basic and ancestral form. Such kidney is found today in larvae of certain cyclostomes (Myxine), but do not occur in any adult vertebrate.
- Glomeruili are only present in some of the posterior tubules.

Pronephros

- Pronephros the **most primitive excretory organs** that develop in vertebrate, corresponding to the first stage of kidney development.
- The pronephros develops in the anterior nephrotomes of all vertebrates.
- It is a paired organ, consisting of a series of nephrons filtering urine from both the pericardium fluids via

openings called nephrostomes and blood from the glomerulus.

- The organ is active in adult forms of some primitive fish, like lampreys or hagfish. It is present at the embryo of more advanced fish and at the larval stage of amphibians.
- In human beings, it is rudimentary and replaced by mesonephros after 3.5 weeks.

Mesonephros

- The mesonephros (Latin for "**middle kidney**") serves as the **main excretory organ of aquatic vertebrates** and as a temporary kidney in higher vertebrates.
- The mesonephros is also called the Wolffian body after Caspar Friedrich Wolff who described it in 1759.
- The mesonephros is composed of the mesonephric duct (also called the Wolffian duct), mesonephric tubules, and associated capillary tufts. A single tubule and its associated capillary tuft is called a mesonephric excretory unit; these units are similar in structure and function to nephrons of the adult kidney.
- The mesonephros is derived from intermediate
- Mesoderm in the vertebrate embryo.
- In human males, the mesonephros gives rise to the efferent ductules of the testis, the epididymis, vas deferens, seminal vesicle, and vestigial structures such as the appendix testis, appendix epididymis, and paradidymis.
- The mesonephros largely regresses in human females, though vestigial structures such as Gartner's cysts, the epoophoron, and paroophoron are common.
- E.g. Fish and frog but in reptiles, birds and mammals it is functional in embryo.

Metanephric kidney

- Also called posterior kidney.
- Most advanced kidney in which loop of henle is present.
- E.g. Reptiles, birds & mammals.

Ureters, Urinary bladder and Urethra

- **Ureters** are thin muscular tubes emerge out from the hilum of kidneys. Urine enters the ureter from the renal pelvis and is conducted along the ureter by peristaltic waves on its walls.
- Ureter **develops in the region of calyces**.
- **Urinary bladder** is sac like structure which stores urine temporarily.
- Bladder has **three parts– apex, fundus** (or body) and neck.
- Body has triangular area called **trigone**. Neck regions possesses two sphincters– involuntary internal sphincter and voluntary external sphincter.
- **Ureters and urinary bladder are lined** by flexible **transitional epithelium**.
- **Urethra** is a membranous tube, which conduct urine to the exterior.
- The urethral sphincters keep the urethra closed except during voiding of urine.
- Urethra is concerned with the release of urine as well as semen (sperms + glandular secretion) through an aperture called urinogenital aperture at the tip of the penis.
- In the male, urethra has 4 parts–
  - **Urinary urethra** (preprostatic urethra). It is 1.0–1.5 cm long part which lies between urinary bladder and point of union with ejaculatory ducts.
  - **Prostatic urethra**. It is about 2.5 cm long and is surrounded by prostate gland.
  - **Membranous urethra**. It is about 2.5 cm long, without any covering.
  - **Penile urethra**. It is approximately 15cm long present inside the copulatory organ penis.

STRUCTURE OF NEPHRON OR URINIFEROUS TUBULE

- Nephrons or uriniferous tubule are **morphological and physiological unit of kidneys**.
  - Nephrons eliminate wastes from the body, regulate blood volume and pressure, control levels of electrolytes and metabolites, and regulate blood pH. Its **functions are vital to life and are regulated by the endocrine system by hormones** such as antidiuretic hormone, aldosterone, and parathyroid hormone.
- **Two types of nephrons** present in kidney are: **cortical** and **juxtamedullary nephrons**.
- **Cortical nephrons** (70–80%) close to kidney surface, have a shorter loop of Henle and peritubular capillary network.
- **Juxtamedullary nephrons** (20–30%) at the junction

of renal cortex and medulla, have a longer loop of Henle and vasa recta.

- A **nephron** consists of **two parts**– an initial filtering component (the renal corpuscle) and a long tubule (**renal tubule**) – both made of simple cuboidal epithelium.

Renal corpuscle

- The renal corpuscle **filters out large solutes from the blood, delivering water and small solutes to the renal tubule for modification**.
- The renal corpuscle (or Malphigian corpuscle) is **composed of a glomerulus and Bowman's capsule**. Where blood is filtered to begin the process of urine formation.
- The malpighian corpuscle named after **Marcello Malpighi** (1628 - 1694), an Italian physician and biologist.
- The nephron begins as a double-walled blind cup called **Bowman's capsule** (lined by squamous epithelium) which surrounds a network of capillaries known as **glomerulus**.
- **Glomerulus** is a capillary (fenestrated) tuft that **receives its blood supply from an afferent arteriole of the renal circulation**.
- Blood enters glomerular capillaries through **afferent arteriole** and leaves through **efferent arteriole**.
- The **diameter of afferent arteriole is much more than that of efferent arteriole**.
- Bowman's capsule is composed of **visceral (simple squamous epithelial cells) (inner) and parietal (simple squamous epithelial cells) (outer) layers**.
- Bowman's capsule is named after **Sir William Bowman** (1816–1892), a British surgeon and anatomest.
- The **visceral layer** lies just beneath the thickened glomerular basement membrane and is **made of podocytes** which send foot processes over the length of the glomerulus.
- **Foot processes** interdigitate with one another forming filtration slits that, in contrast to those in the glomeruluar endothelium, are spanned by diaphragms. The size of the filtration slits restricts the passage of large molecules (eg, albumin) and cells (e.g., red blood cells and platelets). As a result, the **filtrate** leaving the Bowman's capsule is very **similar to blood plasma** in composition as it passes into the proximal convoluted tubule.
- In addition, foot processes **have a negatively-charged coat (glycocalyx)** that limits the filtration of negatively-charged molecules, such as albumin.
- The parietal layer of Bowman's capsule is lined by a single layer of squamous epithelium.
- Between the visceral and parietal layers is Bowman's space, into which the filtrate enters after passing through the podocytes' filtration slits.
- Unlike the visceral layer, the parietal layer does not function in filtration. Rather, the filtration barrier is formed by three components: the diaphragms of the filtration slits, the thick glomerular basement membrane, and the glycocalyx secreted by podocytes.
- Podocytes are special, less flattened cells which line the concavity of Bowman's capsule.
- Podocytes prevents filteration of large macromolecules that might pass through basement membrane and endothelium.

Renal tubule

- Attached to each Bowman's capsule is a long, thin tubule (which functions as dialysis unit) with **three distinct regions– proximal convoluted tubule, loop of Henle and distal convoluted tubule**.
- The first region is called the **proximal convoluted tubule**. 'Proximal' means that it is near Bowman's capsule, and 'convoluted' describes its coiled and looped shape.
- **Proximal convoluted tubules (PCT) or pars convoluta** is about 14 mm long and lined by a single layer of cubical cells.
- Cells of the proximal convoluted tubule have numerous microvilli and mitochondria which provide surface area and energy and closeness of blood capillaries.
- The proximal convoluted tubule connects to the second region, the **loop of Henle**.
- The loop of Henle is a U-shaped or hair pin tube that dips deeply into the medulla within a renal pyramid and then loops back towards the cortex.
- Its **primary role** is to **concentrate the salt in the interstitium**; the tissue surrounding the loop.
- The loop of Henle is described as having a **descending limb** and an **ascending limb**. These limbs have different properties and play different roles in urine formation.

- **Descending limb** is permeable to water but completely impermeable to salt, and thus only indirectly contributes to the concentration of the interstitium. As the filtrate descends deeper into the hypertonic interstitium of the renal medulla, water flows freely out of the descending limb by osmosis until the tonicity of the filtrate and interstitium equilibrate.
- Longer descending limbs allow more time for water to flow out of the filtrate, so longer limbs make the filtrate more hypertonic than shorter limbs.
- Unlike the descending limb, the **ascending limb** of Henle's loop is **impermeable to water**, a critical feature of the counter-current exchange mechanism employed by the loop. The ascending limb **actively pumps sodium out of the filtrate, generating the hypertonic interstitium that drives counter-current exchange**. In passing through the ascending limb, the filtrate grows hypotonic since it has lost much of its sodium content. This hypotonic filtrate is passed to the distal convoluted tubule in the renal cortex.
- The thick ascending limb of the loop of Henle reaches the glomerulus of the nephron from which the tubule arises and passes close to its afferent arteriole and efferent arteriole.
- These limbs operates counter current mechanisms to made urine hypertonic.
- **Counter-current multiplier system** is an active process which is responsible for the production of concentrated urine in the collecting ducts of the nephrons. Sodium and chloride ions are actively pumped from the ascending limb of the loop but water is retained, since the ascending limb is impermeable to water. This creates a concentration gradient in the medulla in which the concentration of sodium and chloride is greatest in the region of the bend of the loop. Fluid passing from the loop of Henle to the distal tubule is less concentrated than that entering the loop, but because of the high osmotic pressure in the medulla water diffuses out of the collecting ducts, producing a concentrated urine.
- Peritubular capillaries called vasa rectae are present around loop of Henle. They help to retain reabsorbed ions and urea in the interstitial fluid, and help in maintaining high osmotic pressure in the medulla.
- The walls of the afferent arterioles contain the **renin-secreting juxtaglomerular cells**. At this point, the tubular epithelium is modified histologically to form the **macula densa**. The juxtaglomerular cells, the macula densa and the lacis cells (specialised glandular cells present at the vascular angle formed by the afferent and efferent arterioles whose significance at this location is unknown) are collectively known as the juxtaglomerular apparatus. **Juxtaglomerular apparatus** is one component of tubuloglomerular feedback mechanism that regulates renal blood flow and glomerular filteration rate.
- Juxtaglomerular cells are the **site of renin synthesis and secretion** and thus **plays a critical role in renin angiotensin system**.
- The third region of the nephron tubule is called the distal convoluted tubule. 'Distal' means that it is farther from Bowman's capsule than the other regions.
- The distal convoluted tubule is similar to the proximal convoluted tubule in structure and function. Cells lining the tubule have numerous mitochondria, enabling active transport to take place by the energy supplied by ATP.
- Distal convoluted tubules from many nephrons all connect to a common tube, the **collecting duct** which empties into the renal pelvis.
- **The collecting duct has important functions** in regulating the composition of urine, as water, ions, and nutrients are reabsorbed from the filtrate in the nephron tubules and collecting ducts.
- This reabsorption prevents the loss of useful nutrients, ions, and water, and provides an opportunity for tubule cells to regulate the composition of blood and the body fluids.
- The collecting duct system begins in the renal cortex and extends deep into the medulla. As the urine travels down the collecting duct system, it passes by the medullary interstitium which has a high sodium concentration as a result of the loop of Henle's counter-current multiplier system.
- Though the collecting duct is normally impermeable to water, it becomes permeable in the presence of antidiuretic hormone (ADH).
- The collecting ducts unite with each other in the medulla to form still larger ducts of Bellini. The **ducts of Bellini** open into renal pelvis.

Nephron's Blood Supply

- There is an intimate association between the blood vessels and the nephrons of the kidney. This

association permits both extensive filtration from the blood and selective reabsorption back into the blood.

- After entering each kidney, the **renal artery** branches repeatedly, forming smaller and smaller arteries, until tiny arterioles reach each of the 1 million nephrons.
- An **afferent arteriole** delivers blood to the glomerulus capillaries for filtration, an **efferent arterioles** drains filtered blood away from the same glomerulus.
- The efferent arteriole connects to a second network of capillaries, the **peritubular capillaries**, which are closely associated with the nephron tubule. It is into these peritubular capillaries that water, ions and nutrients are reabsorbed from the filtrate in the nephron tubule. After leaving the vicinity of the nephron, blood flows through progressively larger veins until reaches the **renal vein**, which leaves the kidney and returns blood to the inferior vena cava.

Process of Urine Formation

- The formation of urine is the result of the following process–
  - **ultra filtration or glomerular filteration** of the blood plasma by the glomeruli;
  - selective reabsorption by the tubules (useful substances such as sugar, salts, water are selectively reabsorbed from the glomerular filtrate to maintain the internal environment); and
  - **secretion by the tubules** (the tubules secrete certain substances like urea, uric acid, anions etc. from the blood into the tubular lumen for excretion into the urine).

Glomerular Filtration of Blood

- Glomerular filtration is the first of the three processes that form urine.
- Urine formation begins with filtration of blood through the epithelial walls of the glomerulus and Bowman's capsule.
- The fluid portion of the blood, which consists of water, urea, ions, nutrients and small proteins, is able to move across the capillary wall. Blood cells and larger proteins, however, cannot cross and are retained in the blood.
- The molecules that leave the blood and enter the glomerular capsule are called the **glomerular filtrate**. It is also termed as **primary urine**.
- Both kidneys produce glomerular filtrate at the rate of about 125 ml/min or 180 lt/day, equivalent to ten times the blood volume daily.
- Measuring the GFR (glomerular filtration rate) is a diagnostic test of kidney function. A decrease GFR may be a sign of renal failure.
- Water and dissolved substances are present in the filtrate at about the same concentrations as they are in the blood.
- If the glomerular filtrate were excreted from the body unchanged, persons would be in constant danger of both dehydration and starvation. Persons would need to spend most of their life drinking and eating to compensate for water and nutrient losses.
- Fortunately, humans do not excrete the glomerular filtrate. Water and other useful materials are reabsorbed from the filtrate, and only a small volume of concentrated urine is actually formed.
- Glomerular filtration occurs because the pressure of the blood flowing in the glomerular capillaries is higher than the pressure of the filtrate in Bowman's capsule. In other words, blood pressure drives glomerular filtration, and because the process takes advantage of a pressure gradient, glomerular filtration does not require the expenditure of energy by kidney cells.
- To prevent the rate of glomerular filtration from changing when blood pressure is altered as a result of exercise or other conditions in the body, a certain degree of self-regulation over filtration occurs in the kidney.
- Specialized cells in the nephron wall sense changes in blood pressure and rectrete chemicals that change the diameter of the arterioles connected to the glomerular capillaries. Changing the size of these vessels alters the amount of blood flowing through the glomerulus, maintaining a relatively stable rate of glomerular filtration and urine formation.
- GFR is auto-regulated by myogenic mechanism (increase in blood pressure tends to stretch the afferent arteriole which responds by contraction; reducing the diameter & hence blood flow) and juxtaglomerular apparatus (which responds to low blood pressure by secreting renin).
- Effective Filteration Pressure (EFP) is determined by 3 pressure -
  - GHP (Glomerular Hydrostatic Pressure) - It is blood pressure in a glomerular capillaries due

to narrower efferent arteriole and is the chief determinant of EFR. Its value is 75 mmHg.

- BCOP (Blood Colloid Osmotic Pressure) - It is osmotic pressure created in the blood of glomerular capillaries due to plasma proteins. Its value is 30 mmHg.
- CHP (Capsular Hydrostatic Pressure) - It is caused by fluid occupying the Bowman's capsule and resists filteration. Its value is 20 mmHg.

- Hence, EFP = GHP - (BCOP + CHP)
- = 75 - (30 + 20) = 25 mm Hg.
- About 1250 ml of blood circulates per minute through the two kidneys, and out of it 650-700 ml is plasma. This is called Renal Plasma Flow (RPF).
- Filtration Fraction (FF) is the fraction of the plasma.
- passing through kidneys which is filtered at the glomerulus, i.e., the ratio of GFR to renal plasma flow (RPF).
- Therefore FF = = = 0.17

Selective Tubular Reabsorption

- Tubular reabsorption is the second process in the formation of urine from filtrate. As a result of tubular reabsorption, much of the filtrate passes out of the nephron tubule and returns to the blood through the peritubular capillaries.
- As much as 99 per cent of the material in the filtrate is reabsorbed, preventing the loss of water, nutrients, and ions from the body. As a consequence of tubular reabsorption urine contains mostly waste materials and excess water.
- Reabsorption occurs within cell, three regions of the nephron and in the collecting duct, but most of it takes place within the proximal convoluted tubule.
- The epithelial cells of the proximal convoluted tubule have numerous microvilli which increase the surface area available for reabsorption.
- During reabsorption, molecules move out of the lumen of the tubule and enter the tubule's epithelial cells. They then pass out of the epithelial cells, cross into the peritubular capillaries, and enter the blood.
- Depending on the type of molecule being reabsorbed, movement into and out of epithelial cells occurs by passive transport or active transport.
- Water and urea, for example, are reabsorbed by passive transport, by which they move from regions of higher concentration to regions of lower concentration (water is reabsorbed by osmosis and urea by simple diffusion).
- Water is reabsorbed in all parts of the tubules except the ascending loop of Henle.
- Glucose and amino acids are reabsorbed by active transport.
- The reabsorption of Na+ occurs by both passive and active transport. Na+ moves passively by diffusion from the filtrate into tubule cells but is actively transported out of the tubule cells on its way to the peritubular capillaries.
- Renal threshold of a substance is its highest concentration in the blood upto which it is totally reabsorbed from the glomerular filtrate.
- High threshold substances are almost completely absorbed from nephric filtrate, e.g., glucose, amino acids, vitamin C, Na+, water. Glucose has a threshold value of 180 mg/100 ml.
- Low threshold substances (in which only very small reabsorption occurs) are urea, uric acid, xanthin, phosphate and non-threshold substances are not al all reabsorbed, e.g., creatinine, hippuric acid

Tubular Secretion

- Certain chemicals in the blood that are not removed by filtration from the glomerular capillaries are removed by a third process of urine formation called tubular secretion.
- These chemicals are removed from the blood in the
- peritubular capillaries to the nephron tubule by both passive and active transport.
- After entering the proximal or distal convoluted tubules, the chemicals are mixed with the glomerular filtrate and eliminated from the body with the urine.
- The chemicals moved by tubular secretion include those foreign body and the ions and molecules that are toxic at elevated levels.
- Ions removed from the blood by tubular secretion include potassium (K+), hydrogen (H+) and ammonium (NH4+).
- The secretion of H+ is an important way in which kidneys help control blood pH.
- In addition to ions, other molecules, such as food preservatives, medicines such as penicillin and metabolic by– products such as creatine, are removed from the blood by tubular secretion.

- The kidneys also rid the body of harmful drugs such as marijuana, cocaine and heroin by tubular secretion.

Route of urine flow

Role of hormones in urine formation

- Certain hormones and hormone like substances are intimately related to renal function.
- Hormones are important signalling molecules controlling the kidneys in the regulatory processes.
- Four major hormones help to maintain homeostasis by regulating the concentration and amount of urine excreted. They are: antidiuretichormone (ADH), aldosterone, angiotensin II, atrial natriuretic peptide (ANP).
- Water reabsorption is controlled by antidiuretic hormone (ADH) in negative feedback and aldosterone regulates the transfer of sodium from the nephron to the blood.

ADH

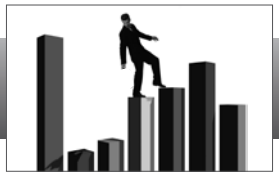
- ADH increases the reabsorption of water by the distal tubule and collecting duct.
- ADH or vasopressin (synthesized in hypothalamus and secreted by posterior pituitary gland) are produced outside the kidney and travel to the kidney via the blood as chemical messengers.
- ADH regulates water excretion by increasing the permeability of the collecting ducts to water and salt and by accelerating water and ion transfer in a direction determined by the osmotic gradient.
- The receptors at the base of the brain form part of the feedback mechanism that (1) stimulates ADH output if the osmotic concentration of extracellular fluid (ECF) is high, so as to concentrate the urine, and (2) reduces ADH output and so dilutes the urine if osmotic concentration of ECF (extra cellular fluid) and of plasma falls.
- Alcohol inhibits the release of ADH and caffeine interferes with ADH action and sodium reabsorption thus both artificially dilute urine to be produced.
- Drugs (called diuretics) increase the production of dilute urine and prevent the excessive water retention and tissue swelling (edema) that may accompany congestive heart failure, high blood pressure and other conditions.
- When water content in the body is low, the posterior pituitary secretes ADH, which makes the walls of DCT, collecting tubules and collecting ducts permeable to water. Water is reabsorbed in the surrounding tissue having hypertonic fluid and hypertonic urine is eliminated.
- Under the deficiency of ADH, a disease called diabetes insipidus is caused in which the output of urine may reach 3-–40 litre/day in place of normal 1.2–1.8 litre/day. Frequent urination (due to inadequately reabsorbed water from the collecting duct) and thrust is the symptoms of the disease.

Aldosterone

- Aldosterone is a hormone secreted by the outer layer of the adrenal gland (cortex part), a gland which sits like a cap above the kidney.
- Decreased blood volume and interstitial fluid level, resulting in decreased blood pressure, trigger aldosterone secretion.
- When aldosterone is present in the blood, all the Na+ in the filtrate is reabsorbed by the epithelial cells of the collecting duct.
- When aldosterone is absent, some Na+ remains in the filtrate and is excreted with the urine.
- The release of aldosterone is controlled by negative feedback.
- Retaining Na+, raises the osmotic pressure of the blood and reduces water loss from the body.

Angiotensin-II

- As blood pressure decreases, the cells of the juxtaglomerular apparatus release the enzyme renin and activate the renin-angiotensin-aldosterone pathway (RAAS). The juxtaglomerular apparatus is a small group of cells situated in the area where the renal tubule links up with the afferent and efferent arterioles. Renin converts angiotensinogen into angiotensin I. Angiotensin converting enzyme (ACE) then converts angiotensin I into angiotensin II, a peptide hormone that is the active form. Angiotensin II has the following effects:
  - Increases the synthesis and release of aldosterone
  - Raises blood pressure directly by constricting blood vessels
  - Stimulates sodium reabsorption by the proximal convoluted tubules



Test Your LEVEL

1. **Which of the following statements about metanephric kidneys is true?**
   a. they become functional at the end of the eighth week
   b. they are active throughout fetal development
   c. they are the third pair of kidneys to develop
   d. all of the above are true

2. **Which of the following statements about the renal pyramids is false?**
   a. they are located in the renal medulla
   b. they contain glomeruli
   c. they contain collecting ducts
   d. they empty urine into the calyces

3. **Sodium reabsorption from the distal tubule will be increased if there is an increase in**
   a. plasma potassium b. plasma volume
   c. urine flow rate d. plasma osmolality

4. **Antidiuretic hormone promotes the retention of water by stimulating**
   a. the active transport of water
   b. the active transport of chloride
   c. the active transport of sodium
   d. the permeability of the collecting duct to water

5. **Aldosterone stimulates sodium reabsorption and potassium secretion in**
   a. the proximal convoluted tubule
   b. the descending limb of the nephron loop
   c. the ascending limb of the nephron loop
   d. the cortical collecting duct

6. **Diuretic drugs that act in the nephron loop**
   a. inhibit active sodium transport and promote the excretion of salt and water
   b. cause an increased flow of filtrate to the distal convoluted tubule
   c. cause an increased secretion of potassium into the renal tubule
   d. all of the above

7. **Reabsorption of water through the tubules occurs by**
   a. osmosis b. active transport
   c. facilitated diffusion d. all of these

8. **The countercurrent exchange in the vasa recta**
   a. removes Na+ from the extracellular fluid
   b. maintains high concentrations of NaCl in the extracellular fluid
   c. raises the concentration of Na– in the blood leaving the kidneys
   d. all of the above

9. **Refer the figure and identify the marked alphabet which represents the sites at which tubular fluid osmolality exceeds that of plasma by greatest amount**

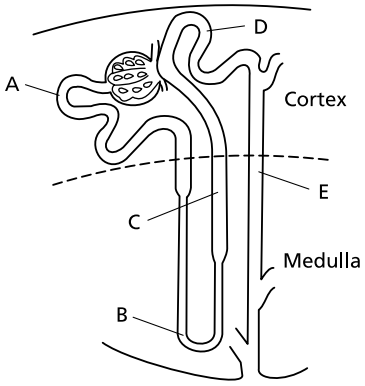


Fig. Juxtamedullary nephron.

   a. A b. B
   c. D d. C & E

10. **The kidneys help maintain acid-base balance by**
    a. the secretion of H– in the distal regions of the nephron
    b. the action of carbonic anhydrase within the apical cell membranes and the cytoplasm of the tubule cells
    c. the buffering action of phosphates and ammonia in the urine
    d. all of the above.

11. **The detrusor muscle is located in**
    a. the kidneys b. the ureters
    c. the urinary bladder d. the urethra

12. **Glucose reabsorption occurs in the**
    a. proximal tubule b. loop of Henle
    c. distal tubule d. medullary collecting duct

13. **Ammonia is an effective and important urinary buffer for which of the following reasons?**
    a. its production in the kidney decreases during chronic acidosis
    b. only the afferent arteriole is constricted
    c. only the efferent arteriole is constricted
    d. the efferent and afferent arterioles are both constricted

14. **Sodium reabsorption from the distal tubule will be increased if there is an increase in**
    a. plasma potassium b. plasma volume
    c. urine flow rate d. plasma osmolality

MCQ's From Competitive Exams

CBSE

1. If excess water passes out from the tissue without being restored by the kidneys, the cells would

a. burst open and die
b. take water from the plasma
c. not be affected at all
d. shriver and die

(Year 1994)

2. Which one of the four parts mentioned below does not constitute a part of single uriniferous tubule?

a. distal convoluted tubule b. collecting duct
c. Bowman's capsule
d. loop of Henle

(Year 1994)

3. Two examples in which the nitrogenous waste are excreted from body in the form of uric acid are

a. birds and lizards b. frogs and bony fishes
c. insects and bony fishes d. mammals and molluscs

(Year 1994, 2004)

4. The ornithine cycle removes two waste products from the blood in liver. These products are

a. CO_2 and ammonia b. ammonia and uric acid
c. CO_2 and urea d. ammonia and urea.

(Year 1996, 2005)

5. In ureotelic animals, urea is formed by

a. Kreb's cycle b. EM pathway
c. ornithine cycle d. Cori cycle.

(Year 1997)

6. The basic functional unit of human kidney is

a. nephridia b. Henle's loop
c. nephron d. pyramid.

(Year 1997)

7. A condition of failure of kidney to form urine is called

a. anuria b. deamination
c. entropy d. none of these.

(Year 1998)

8. Solenocytes are the main excretory structure in

a. echenodermalia b. platyhelminthes
c. annelids d. mollusc

AIIMS

17. Where the conversion of harmful prussic acid into potassium sulphocyanide takes place ?

a. bone marrow b. spleen
c. lymph glands d. liver

(Year 1996)

18. Assertion: The final reabsorption of water from urine into blood occurs through the collecting duct of a mammalian nephron, resulting in the production of hyperosmotic urine.

Reason: The loop of Henle is responsible for the formation of a sodium gradient across the depth of the cortical intersitium of a mammalian kidney.

a. If both Assertion and Reason are true and the Reason is a correct explanation of the Assertion.
b. If both Assertion and Reason are true but Reason is not a correct explanation of the Assertion.
c. If Assertion is true but the Reason is false.
d. If both Assertion and Reason are false.

(Year 1996)

19. Waste product of adenine and guanine metabolism are excreted by man as

a. uric acid b. urea
c. allantoin d. ammonia.

(Year 1997)

20. Assertion: In the descending limb of loops of Henle, the urine is hypertonic, while in ascending limb of loops of Henle, the urine is hypotonic.

Reason: Descending limb is impermeable to Na+, while ascending limb is impermeable to H_2O.

a. If both Assertion and Reason are true and the Reason is a correct explanation of the Assertion.
b. If both Assertion and Reason are true but Reason is not a correct explanation of the Assertion.
c. If Assertion is true but the Reason is false.
d. If both Assertion and Reason are false.

(Year 1997)

21. The cells named podocytes occur in

a. glomerulus of kidney b. wall of capillaries
c. neck region of nephrons
d. large intestine.

(Year 1998)

22. The function of renin is

a. stimulation of corpus luteum
b. vasodilation
c. to reduce blood pressure
d. degradation of angiotensinogen.

(Year 1999)

23. The end-product of ornithine cycle is

a. carbon dioxide b. uric acid
c. urea d. ammonia.

(Year 1999)