Section VII

EXCRETORY SYSTEM

Introduction

Excretion means removal of waste products, *i.e.*, toxic and other unwanted materials from the body. Though the kidneys are the main organs for excretion, others, like the lungs, the skin, the GI system, etc., also have important roles in the process.

The kidneys while producing urine as the organs for excretion, perform many other functions (Table 7.1) and play a great role in the maintenance of **homoeostasis.** The kidneys are also instrumental in the production of important hormones like angiotensin II, 1,25-dihydroxycholecalciferol (calcitriol) and erythropoietin.

Table 7.1

Functions of Kidney
• Formation of urine.
• Fluid and electrolyte balance.
• Acid base balance.
• Preservation of nutrients.
• Excretion of waste products like urea, uric acid, creatinine.
• Secretion of renin, erythropoietin.
• Formation of prostaglandins, bradykinin and calcitriol.
• Detoxification and degradation of drugs, hormones, etc.
• Metabolic functions like gluconeogenesis.

1 CHAPTER — The Kidneys : Functional Anatomy and Blood Supply

The kidneys are situated on either side of the vertebral column in the posterior abdominal wall (Fig. 7.1). These are bean-shaped structures with a notch on the medial side, called **hilum.** The blood vessels, nerves and lymphatics pass into the kidneys through this hilum. The urine formed in the kidney is passed through a sac-like structure present in the hilum, called **renal pelvis.** The pelvis is continuous with the ureter. One ureter from each kidney drains into the **urinary bladder.** Urine is temporarily stored in the bladder to be voided from time to time through the **urethra.**

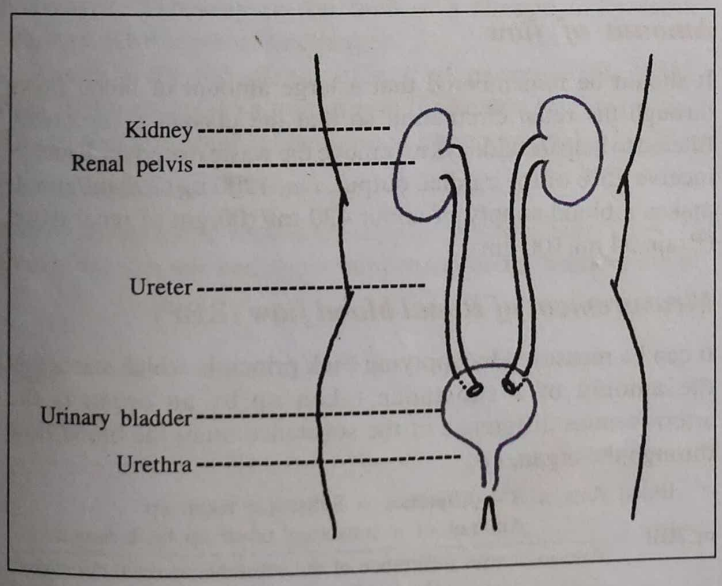


Fig. 7.1. *The excretory system.*

Structure

A coronal section (Fig. 7.2) of kidney shows two distinct zones, the outer cortex (red) and the central medulla (pale). The medullary tissue is arranged in the form of pyramids, called renal pyramids (8 to 18 in number) the apices of which are called renal papillae. In between the pyramids, the cortical structures, called renal columns of Bertin are present. The tip

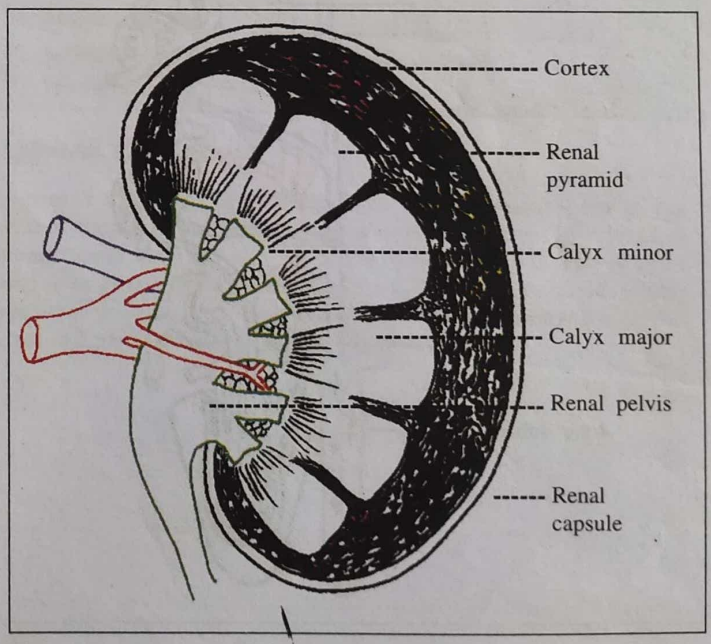


Fig. 7.2. *Macroscopic structure of kidney (coronal section).*

of a pyramid (papilla) abuts on a tubular structure called **calyx minor.** Minor calyces join to form **major calyces** and major calyces join to form the **renal pelvis.**

The urinary tract

The area from the minor calyces to the external opening of the urethra is called urinary tract. This part is lined by **urothelium** which is impervious, so, the urine once delivered to the urinary tract remains unchanged throughout.

Nerve supply

There is plenty of sympathetic supply to the renal blood vessels, particularly to the afferent and efferent arterioles. The juxtamedullary apparatus and the tubules are also supplied by sympathetic nerves. Sympathetic nerves by α_1 effect produce vasoconstriction and by β_1 effect increases renin secretion. Parasympathetic supply is also provided by the vagi, but their role is not clear. The afferent nerves carry pain sensation.

Blood supply

Each kidney gets one renal artery, a direct branch of the abdominal aorta. Before entering in the kidney, these arteries break into segmental arteries. Segmental arteries break into lobar arteries which, before entering the kidney substance, break into interlobar branches (Fig. 7.3) and then pass towards the cortex. The arcuate arteries arise from the interlober arteries and pass horizontally through the corticomedullary junction. From the arcuate arteries, interlobular arteries arise and pass vertically towards the surface. Afferent arterioles arise from these interlobular arteries and give rise to the glomerular capillaries. Afferent arterioles break up into 30 to 40 capillaries to form the glomerular tuft which in turn re-unite to form the efferent arterioles. The efferent arterioles are mostly narrower than the afferent arterioles. The effent arterioles end in the venous system through various ways :

(i) From the cortical nephrons, they form the peritubular capillary plexus around the renal tubules.

(ii) From the juxtamedullary nephrons they usually form vasa recta. The **vasa recta** are straight vessels which go down deep into the medulla and then turn back to the cortex forming loops.

(iii) Some afferent arterioles directly give rise to peritubular capillaries without forming glomerulus (a shunt pathway).

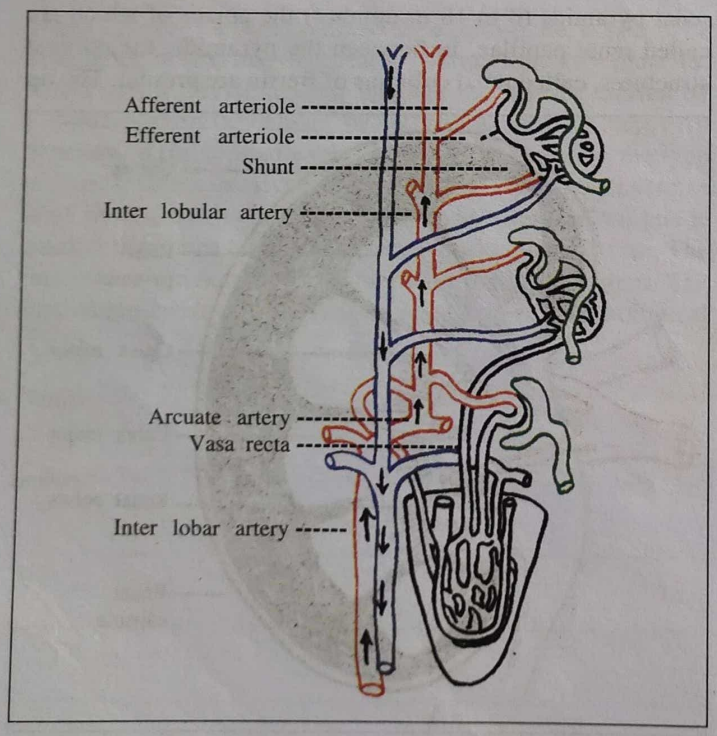


Fig. 7.3. *Blood vessels in the kidney.*

Venous Drainage

The peritubular capillary plexus drain into the venules. Both the cortical and medullary system of veins drain into the cortical venous system. Starting with interlobular veins, these unite to form ultimately the renal veins which drain into the inferior vena cava.

Peculiarities of renal circulation

(1) Renal arteries are direct and large branches of abdominal aorta. Its branches are also wider and shorter. The afferent arterioles are wider than the efferent arterioles. Hence, the pressure in the glomerular capillaries (G_c) is higher (45 mm of Hg) than in systemic capillaries (32 mm of Hg).

(2) Due to narrower efferent arterioles, the pressure in peritubular capillaries is very low (10 mm of Hg). This helps tubular reabsorption.

(3) Volume flow through renal circulation is high (25% of cardiac output).

(4) There are intrarenal shunts (of Ludwig, Trueta, etc.) which help to rearrange the blood flow within the kidney.

(5) Cortex receives more blood than the medulla. (In hypotension, blood supply through cortex decreases, juxtamedullary nephrons become active and concentrated urine is produced).

(6) Vasa recta act as counter current exchanger and help to maintain the medullary concentration gradient.

(7) It is a portal circulation having two sets of capillaries : glomerular and peritubular.

(8) Autoregulation is present.

(9) Pressure in the glomerular capillaries (G_c) can be adjusted nicely due to differential constriction and dilatation of afferent and efferent arterioles.

(10) Huge amount of filtration and reabsorption occurs in renal circulation.

Amount of flow

It should be remembered that a large amount of blood flows through the renal circulation so that the plasma is repeatedly filtered to help the kidneys to remove the waste materials. Kidneys receive 25% of the cardiac output, *i.e.,* 1200 to 1300 ml/min. It makes a blood supply of about 420 ml/100 gm of renal tissue (Brain 54 ml/100 gm).

Measurement of Renal blood flow (RBF)

It can be measured by applying Fick principle which states that the amount of a substance taken up by an organ is the arteriovenous difference of the substance times the blood flow through the organ, *i.e.,*

$$\text{Blood flow} \times \text{AV difference} = \text{Substance taken up}$$

$$\text{or, RBF} = \frac{\text{Amount of a substance taken up by kidney}}{\text{Arterio-venous difference of the substance in renal circulation.}}$$

(It is discussed in details in p. 274)

2 CHAPTER The Nephron

The nephrons are the structural and functional units of the kidneys and each kidney contains about 1.2 million nephrons. Functions of the kidneys means the sum of the functions of these nephrons. Urine is actually formed in these nephrons and is then delivered to the renal pelvis.

Parts of a Nephron

Each nephron is actually composed of a tuft of capillary, called **glomerulus** and a tube (3 cm × 20 to 60 μ), called renal tubule (Fig. 7.5A). The blind end of this tube is dilated, into which the capillary tuft is invaginated to form the **Malpighian corpuscle** (Fig. 7.5B); the other end is connected to the collecting system.

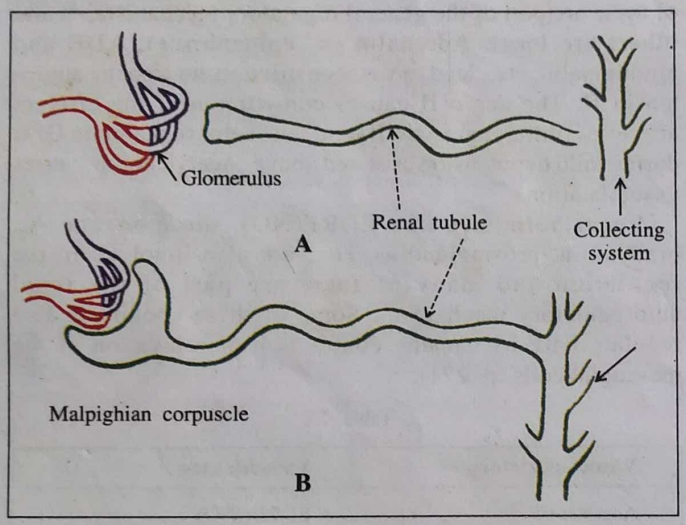
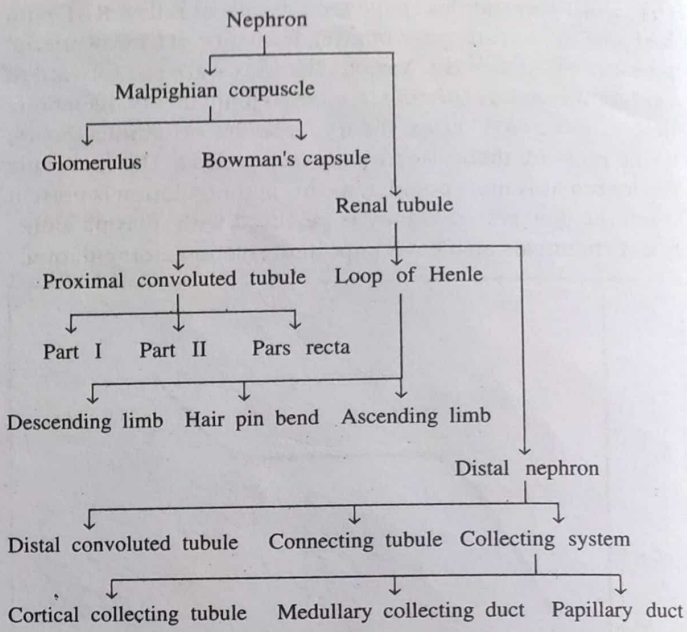


Fig. 7.5. *Genesis of nephron.*

The nephron is divided into various parts. The blind end of the tubule which invaginates the glomerular capillaries to form the Malpighian corpuscle is called **Bowman's capsule** (Fig. 7.6). The first part of the tubule is coiled and is called **proximal convoluted tubule** (PCT).

Then it takes the form of a hair pin and is called **loop of Henle.** Next portion is called **distal nephron** which includes another coiled portion called **distal convoluted tubule** (DCT) along with the connecting tubule and the collecting system. DCT is connected to the cortical collecting tubule by the **connecting tubule**. Each cortical collecting tubule receives many connecting tubules and continues as **medullary collecting duct** which is continuous with the **papillary collecting duct.** Several papillary collecting ducts join to form the **duct of Bellini** which drains into minor calyx through the tip of renal pyramids.

Therefore, the collecting system drains many nephrons together.



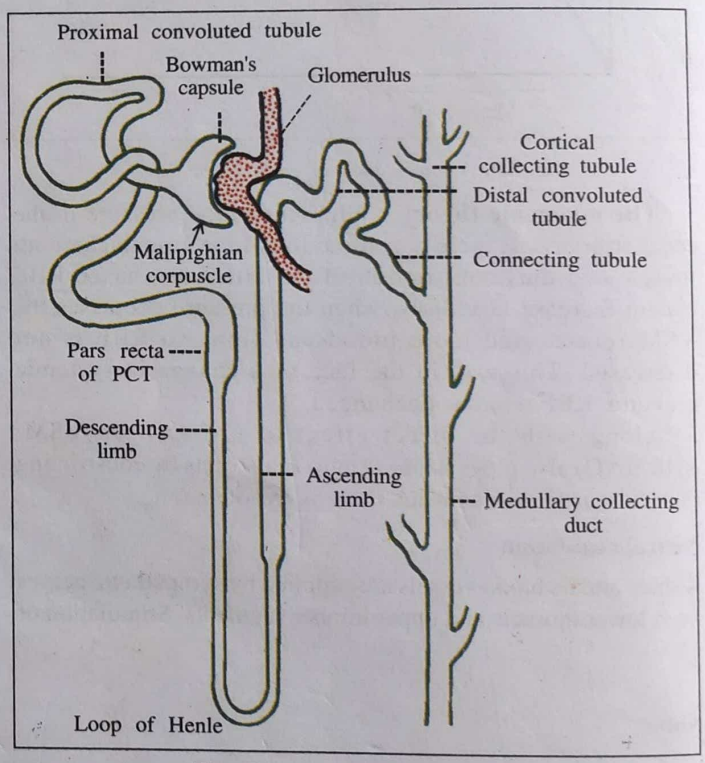


Fig. 7.6. *Nephron and its parts.*

Types of Nephrons

The nephrons are mainly of two types. The nephrons whose glomeruli are situated in the outer part of the cortex and the tips of the loops are in the outer medulla, are called cortical

nephrons (Fig. 7.7). These are more numerous (85%). The rest (15%) are called juxtamedullary nephrons whose glomeruli are in the inner cortex, and the loops are very long with the tips reaching upto the tips of the renal pyramids.

Note: There is also a third variety of nephron with intermediate characteristics.

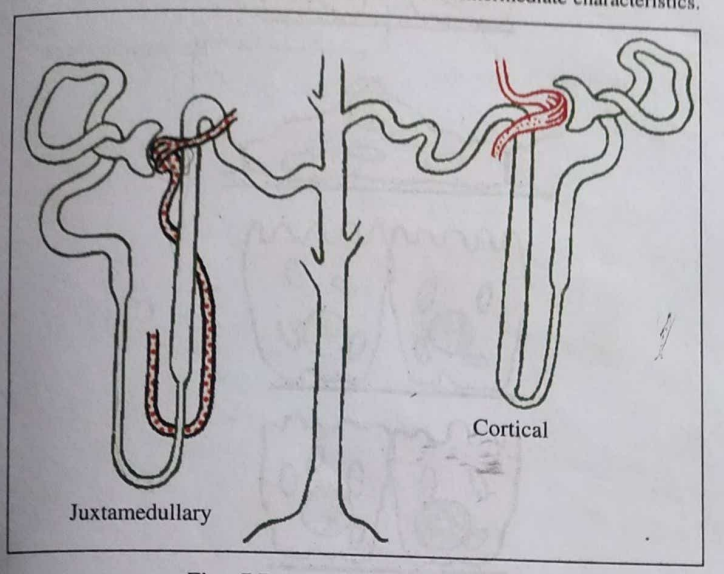


Fig. 7.7. *Two types of nephron.*

Table 7.3
The differences between the two types of nephrons

	Cortical nephron	Juxtamedullary nephron
• Number	More (85% of total)	Less (15% of total)
• Efferent arteriole	Narrower than afferent	Same as afferent
• Length of the loop of Henle	Shorter	Longer
• Ascending limb of the loop	Thick all along	To start with thin and then thick
• Concentration achieved	Low	High

Structure of Nephron

Renal Corpuscle (Malpighian corpuscle)

Glomerulus is the tuft of capillaries formed from the afferent arterioles (Fig. 7.8). These are surrounded very intimately by the visceral layer of the Bowman's capsule and each capillary is almost completely covered by the capsule. The parietal layer of the Bowman's capsule is continuous with the renal tubule; the space in between is called Bowman's space. Filtration occurs from the blood in the glomerular capillaries and the filtrate collects in the Bowman's space. The membrane through which filtration occurs (the filtering membrane) is composed of the capillary endothelium. the basement membrane and the podocytes (Fig. 7.8 inset).

The **podocytes** are the cells of the visceral layer of the Bowman's capsule and have foot processes towards the basement membrane. During filtration, the fluid passes down through the spaces in between these foot processes, called **slit pores** (Fig. 7.11).

The basement membrane is continuous with that in the rest of the renal tubule. There are pericyte like cells called **mesangial cells** on the surface of the glomerular capillaries. These cells have role in controlling GFR (p. 271), in phagocytosis of immune complexes and also are involved in causation of some renal diseases.

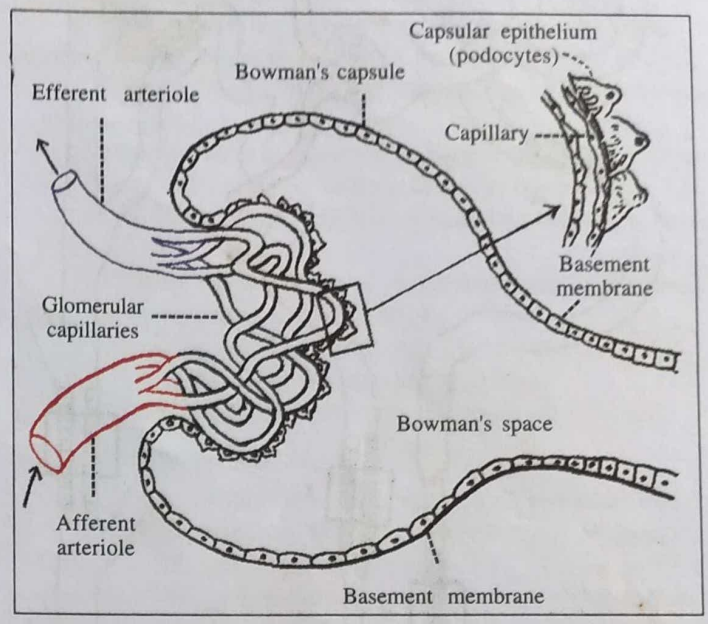


Fig. 7.8. *Structure of nephron (renal corpuscle).*

Proximal Convoluted tubule (PCT)

This is subdivided into early proximal convoluted tubule (PCT), late PCT (*i.e.*, part I and II) and the pars recta which is continuous with the descending limb of the Henle's loop. The PCT is lined by a single layer of cuboidal cells (Fig. 7.9A) situated on a basement membrane which is continuous with that of the Bowman's capsule.

The cells have luminal brush border which increases the surface area and there are cytoplasmic processes on the basal side. These cells are joined (side to side) by leaky tight junctions on the luminal side and are separated by basolateral spaces on the basal side. The cells are highly active as indicated by large number of organelles and the brush border in them. Most of the PCT except the pars recta, is situated in the cortex and is the most active part of the tubule. There is absorption of huge amount of solutes here and *this segment is freely permeable to water.*

Loop of Henle

It is formed of a descending and an ascending limb, which are respectively thin and thick in cortical nephrons. But in juxtamedullary nephrons, the early part of the ascending limb is also thin (upto the junction of the inner 2/3rd and outer 1/3rd of medulla). The thin segments are lined by flat cells (Fig. 7.9B) and may be 2 to 14 mm in length. Thick segments are lined by cuboidal cells (Fig. 7.9C) and is continuous with the DCT at **macula densa**. This part is lined by a row of closely packed cells and *always meets it's own glomerulus to form the JG complex* (see below). Basement membrane here shows gaps.

The descending limb is freely permeable to water but the ascending limb is impermeable to water. In the ascending limb, particularly in thick segment, a good amount of solutes are reabsorbed.

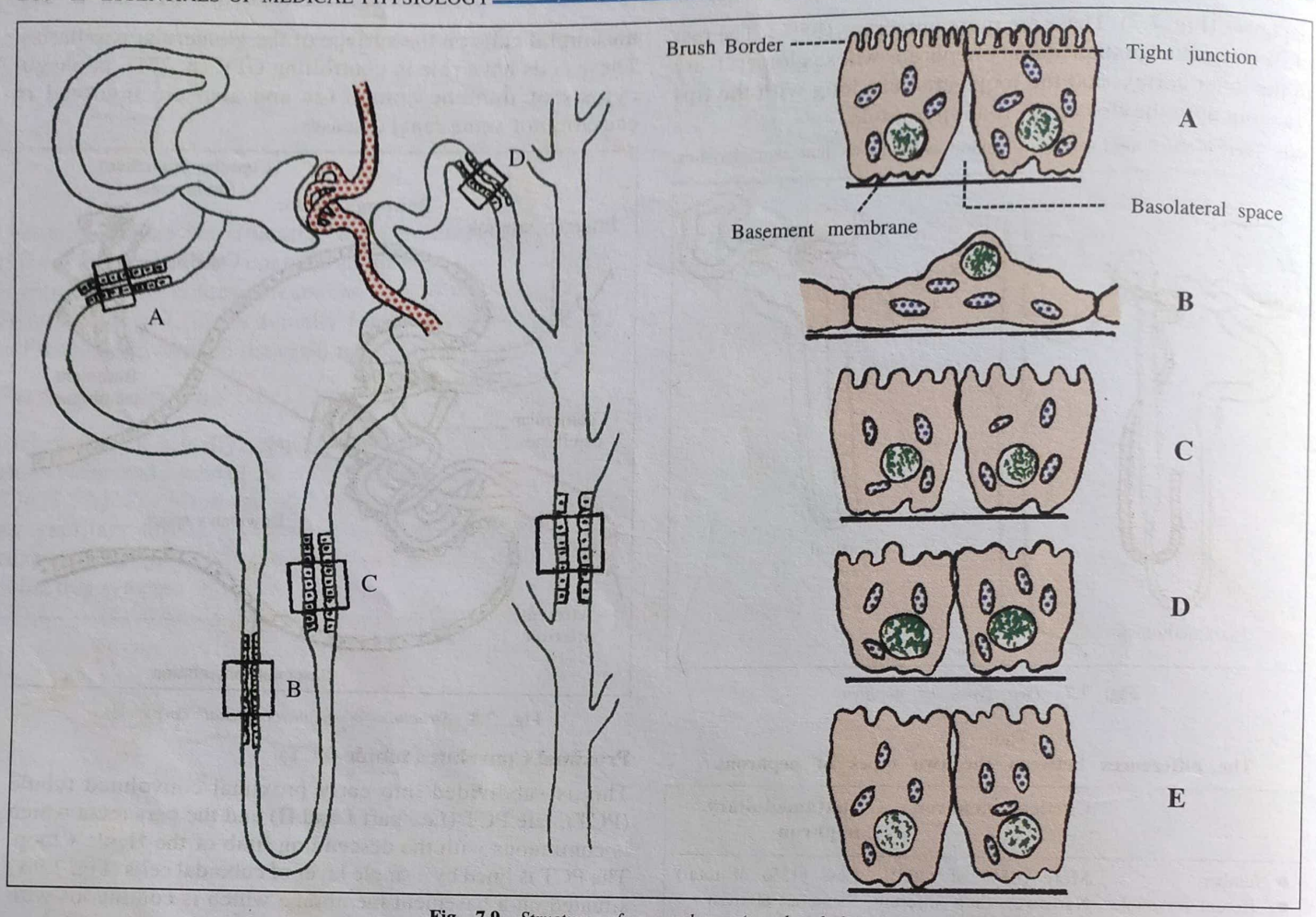


Fig. 7.9. *Structure of a nephron (renal tubule).*
A. Proximal tubule B. Thin segment C. Thick segment D. Distal tubule E. Collecting tubule.

Distal nephron

Distal convoluted tubule is about 3 mm long and is lined by cuboidal cells (Fig. 7.9D). **The connecting tubules** are lined by cells which are a bit taller than those in the DCT and several of these tubules join to a single collecting system. In the **collecting system** the lining cells are more tall and these cells become gradually taller (Fig. 7.9E) through **cortical collecting tubule → medullary collecting duct** and are columnar in the **papillary ducts.** The cells lining the collecting system are joined (side to side) in the luminal side by stronger **tight junctions.** This part is about 20 mm long. It has various types of cells, of them the **P cells** (principal cells) respond to vasopressin and the **I cells** (Intercalated cells) secrete acid. I- cells are also present in other parts of the tubule. There are also other varieties of cells serving specific purposes.

The distal nephron as a whole is *permeable to water only in presence of antidiuretic hormone.* There also occurs absorption of different solutes in this part of the nephron.

JUXTAGLOMERULAR APPARATUS (JGA)/ JG COMPLEX

Each ascending limb of loop of Henle always meets its own glomerulus and at this point a structure is formed, called juxtaglomerular apparatus (JGA) (Fig. 7.10). It is composed of

(a) Macula densa,
(b) Lacis cell, and
(c) JG cells.

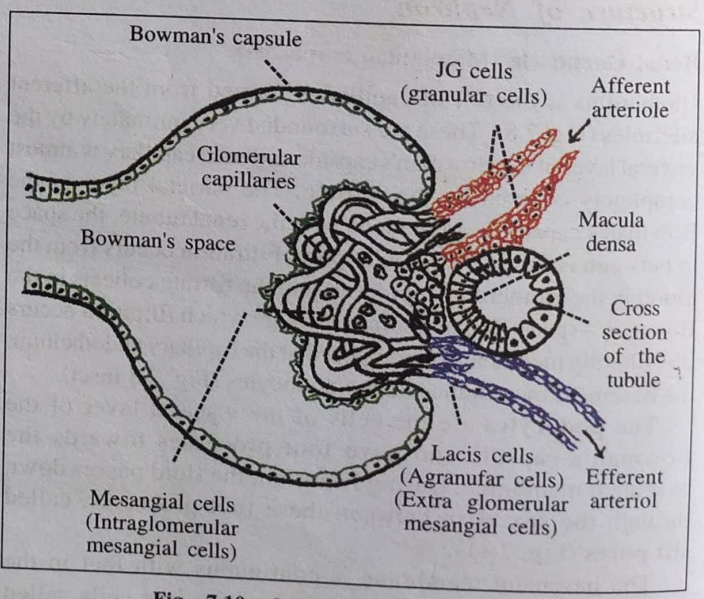


Fig. 7.10. *Juxtaglomerular apparatus.*

Macula Densa

It is a row of tightly packed cells lining the part of the renal tubule which is in contact with the efferent and afferent arterioles of its own glomerulus. In this part, there are gaps in the basement membrane and the macula densa cells are in good contact with the arterioles. Macula densa helps to regulate glomerular filtration. If there is more flow through macula densa, filtration is decreased and if flow decreases, filtration is increased. This is called tubuloglomerular feedback.

Lacis cells

These cells are found in the triangle formed by the afferent arteriole, efferent arteriole and the macula densa. These are also called agranular cells or extraglomerular mesangial cells by some authors. Some of these cells may be granulated and secrete renin.

Juxtaglomerular cells (JG cells)

These are also called **granular cells** or **Polkissen cells.** These cells are present in the tunica media of the afferent arteriole mainly and probably also in the efferent arterioles. These are modified smooth muscle cells and have granules which contain renin.

TUBULOGLOMERULAR FEEDBACK

The close proximity of the blood vessels with the macula densa leads to the speculation that they must have some functional relationship between them. In fact, the volume and the composition of the tubular fluid bathing the macula densa have role in regulation of blood flow through the glomerulus and thus in regulation of the rate of filtration. It is called **tubuloglomerular feedback.**

This is achieved by :

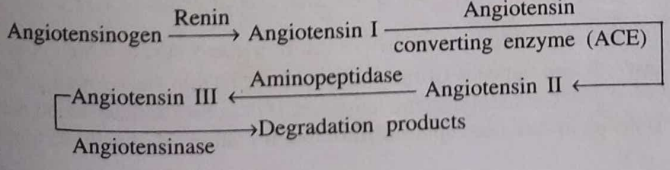
(i) Constriction or dilatation of the afferent arterioles by some local mechanisms *e.g.*, prostaglandins, adenosine, thromboxane A_2, etc.

(ii) Mesangial cell contraction leading to reduction of glomerular surface area may be another factor.

(iii) Macula densa is also involved in renin secretion from the JG cells (see below). The rate of transport of Na^+ and Cl^- by macula densa cells and also the amount of Na^+ and Cl^- delivered to this part of the tubule probably regulates the renin secretion. This renin helps to regulate filtration by local production of Angio II which constricts the efferent arterioles.

The Renin Angiotensin system

The physiologically active hormone of this system is angiotensin II (angio II) which is an octapeptide. It is produced by the action of renin (an enzyme secreted from the JG cells) on a plasma protein (α_2 globulin) called angiotensinogen as follows :



Angiotensin converting enzyme (**ACE**) is present in the endothelium of the pulmonary capillaries and also in other tissues. The angio II is degraded to angio III after its action is over. The angio III also shows some actions of angio II.

Stimulation of secretion of renin and thereby increased production of angio II is caused by :

(i) Low blood pressure (BP) in the afferent arterioles due to any reason.

(ii) Sympathetic stimulation and circulating epinephrine (via β_1 receptor). Change of posture from supine to upright.

(iii) Decreased Na^+ and Cl^- load to and through the macula densa.

Inhibition of secretion of renin and thereby decreased production of angio II is caused by :

(i) Increased Na^+ and Cl^- delivery to the macula densa.

(ii) Increased BP in the afferent arterioles.

(iii) Angiotensin II (feedback inhibition on JG cells).

Physiological actions

Angio II acts via angiotensin receptors (AT receptors) which are membrane proteins. There are several types of them *e.g.*, AT_1, AT_2, AT_3. AT_1 is of two types—AT_{1A} present in blood vessels and AT_{1B} present in adrenal cortex and in both the cases Ca^{2+} is used as 2nd messenger.

Angio II leads to :

(i) Vasoconstriction and increased arterial BP. *It is the most potent vasoconstrictor.* In kidney, it causes efferent arteriolar constriction to maintain GFR when there is systemic hypotension.

(ii) It has direct effect on Na^+ reabsorption in PCT.

(iii) Stimulates aldosterone secretion.

(iv) Increases thirst due to action on brain.

(v) Increases ADH secretion.

(vi) It has positive inotropic effect on heart.

(vii) It probably stimulates sympathetic nervous system.

Applied Physiology

Persistent rise of angio II activity leads to persistent rise of BP, called hypertension. This can be detected by estimating circulating angio II or plasma renin activity (PRA). The condition is treated in suitable cases by angiotensin converting enzyme (ACE) inhibitors or by removing the cause.

Sodium renin profile : It means estimation of renin in respect to body Na^+. This is necessary because renin activity depends on Na^+ intake and Na^+ level in plasma, so renin should be measured along with the Na^+ excretion while there is a fixed Na^+ intake.

Table 7.4

Hormones from kidney	Hormones acting on kidney
● Erythropoietin : It is a glyco-protein hormone which increases erythropoiesis. ● 1,25-DHCC : Kidney converts 25-(OH)CC into its active form 1,25-DHCC (calcitriol). ● Some local hormones like prostaglandins and bradykinin.	● Aldosterone ● Atrial natriuretic peptide ● Antidiuretic hormone ● Angiotensin II ● Parathormone, cortisol, etc.

Note : Renin from kidney helps to produce the hormone angio II.