(Natraj sir)

Chapter 48

Kidney

- INTRODUCTION
- FUNCTIONS OF KIDNEY
  - ROLE IN HOMEOSTASIS
  - HEMOPOIETIC FUNCTION
  - ENDOCRINE FUNCTION
  - REGULATION OF BLOOD PRESSURE
  - REGULATION OF BLOOD CALCIUM LEVEL
- FUNCTIONAL ANATOMY OF KIDNEY
  - DIFFERENT LAYERS OF KIDNEY
  - TUBULAR STRUCTURES OF KIDNEY

INTRODUCTION

Excretion is the process by which the unwanted substances and metabolic wastes are eliminated from the body.

A large amount of waste materials and carbon dioxide are produced in the tissues during metabolic process. In addition, residue of undigested food, heavy metals, drugs, toxic substances and pathogenic organisms like bacteria are also present in the body.

All these substances must be removed to keep the body in healthy condition. Various systems/organs in the body are involved in performing the excretory function, viz.

1. Digestive system excretes food residues in the form of feces. Some bacteria and toxic substances also are excreted through feces
2. Lungs remove carbon dioxide and water vapor
3. Skin excretes water, salts and some wastes. It also removes heat from the body
4. Liver excretes many substances like bile pigments, heavy metals, drugs, toxins, bacteria, etc. through bile.

Although various organs are involved in removal of wastes from the body, their excretory capacity is limited. But renal system or urinary system has maximum excretory capacity and so it plays a major role in homeostasis.

Renal system includes:

1. A pair of kidneys
2. Ureters
3. Urinary bladder
4. Urethra.

Kidneys produce the urine. Ureters transport the urine to urinary bladder. Urinary bladder stores the urine until it is voided (emptied). Urine is voided from bladder through urethra (Fig. 48.1).

FUNCTIONS OF KIDNEY

Kidneys perform several vital functions besides formation of urine. By excreting urine, kidneys play the principal role in homeostasis. Thus, the functions of kidney are:

1. ROLE IN HOMEOSTASIS

Primary function of kidneys is **homeostasis.** It is accomplished by the formation of urine. During the formation of urine, kidneys regulate various activities in the body, which are concerned with homeostasis such as:

I. *Excretion of Waste Products*

Kidneys excrete the unwanted waste products, which are formed during metabolic activities:

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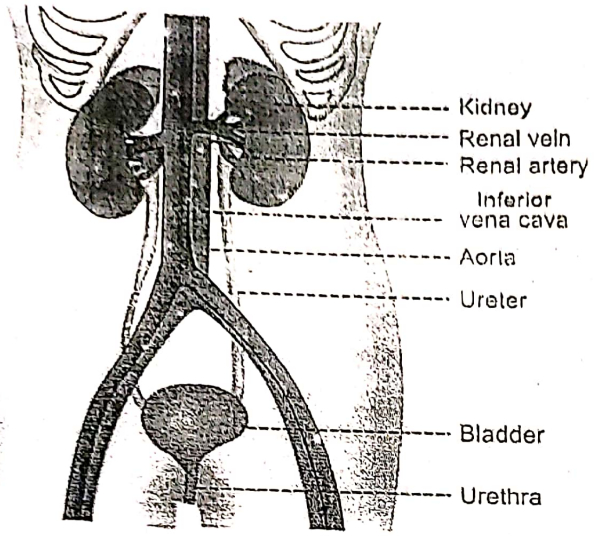

FIGURE 48.1: Urinary system

a. Urea (end product of amino acid metabolism)
b. Uric acid (end product of nucleic acid metabolism)
c. Creatinine (end product of metabolism in muscles)
d. Bilirubin (end product of hemoglobin degradation)
e. Products of metabolism of other substances.

Kidneys also excrete harmful foreign chemical substances such as toxins, drugs, heavy metals pesticides, etc.

ii. *Maintenance of Water Balance*

Kidneys maintain the water balance in the body by conserving water when it is decreased and excreting water when it is excess in the body. This is an important process for homeostasis (Refer Chapter 4 for details).

iii. *Maintenance of Electrolyte Balance*

Maintenance of electrolyte balance, especially sodium is in relation to water balance. Kidneys retain sodium if the osmolarity of body water decreases and eliminate sodium when osmolarity increases.

iv. *Maintenance of Acid–Base Balance*

The pH of the blood and body fluids should be maintained within narrow range for healthy living. It is achieved by the function of kidneys (Chapter 54). Body is under constant threat to develop **acidosis,** because of production of lot of acids during metabolic activities. However, it is prevented by kidneys, lungs and blood buffers, which eliminate these acids. Among these organs, kidneys play major role in preventing acidosis. In fact, kidneys are the only organs, which are capable of eliminating certain metabolic acids like sulfuric and phosphoric acids.

■ 2. HEMOPOIETIC FUNCTION

Kidneys stimulate the production of erythrocytes by secreting erythropoietin. Erythropoietin is the important stimulating factor for erythropoiesis (Chapter 10). Kidney also secretes another factor called thrombopoietin, which stimulates the production of thrombocytes (Chapter 18).

■ 3. ENDOCRINE FUNCTION

Kidneys secrete many hormonal substances in addition to erythropoietin and thrombopoietin (Chapter 72).

Hormones secreted by kidneys

i. Erythropoietin
ii. Thrombopoietin
iii. Renin
iv. 1,25-dihydroxycholecalciferol (calcitriol)
v. Prostaglandins.

■ 4. REGULATION OF BLOOD PRESSURE

Kidneys play an important role in the long-term regulation of arterial blood pressure (Chapter 103) by two ways:

i. By regulating the volume of extracellular fluid
ii. Through **renin-angiotensin** mechanism.

■ 5. REGULATION OF BLOOD CALCIUM LEVEL

Kidneys play a role in the regulation of blood calcium level by activating 1,25-dihydroxycholecalciferol into vitamin D. Vitamin D is necessary for the absorption of calcium from intestine (Chapter 68).

■ FUNCTIONAL ANATOMY OF KIDNEY

Kidney is a compound tubular gland covered by a connective tissue capsule. There is a depression on the medial border of kidney called hilum, through which renal artery, renal veins, nerves and ureter pass.

■ DIFFERENT LAYERS OF KIDNEY

Components of kidney are arranged in three layers (Fig. 48.2):

1. Outer cortex
2. Inner medulla
3. Renal sinus.

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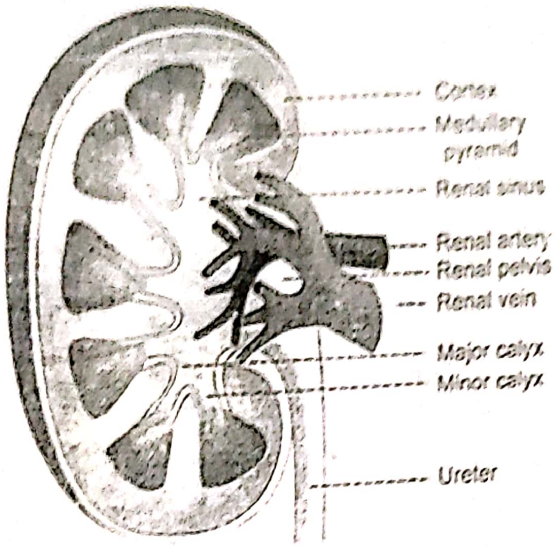

FIGURE 48.2: Longitudinal section of kidney

1. Outer Cortex

Cortex is dark and granular in appearance. It contains renal corpuscles and convoluted tubules. At intervals, cortical tissue penetrates medulla in the form of columns, which are called renal columns or columns of Bertini.

2. Inner Medulla

Medulla contains tubular and vascular structures arranged in parallel radial lines. Medullary mass is divided into 8 to 18 medullary or Malpighian pyramids. Broad base of each pyramid is in contact with cortex and the apex projects into minor calyx.

3. Renal Sinus

Renal sinus consists of the following structures

i. Upper expanded part of ureter called renal pelvis
ii. Subdivisions of pelvis: 2 or 3 major calyces and about 8 minor calyces
iii. Branches of nerves, arteries and tributaries of veins
iv. Loose connective tissues and fat

TUBULAR STRUCTURES OF KIDNEY

Kidney is made up of closely arranged tubular structures called **uriniferous tubules**. Blood vessels and interstitial connective tissues are interposed between these tubules.

Uriniferous tubules include:

1. Terminal or secretary tubules called nephrons, which are concerned with formation of urine
2. **Collecting ducts** or tubules, which are concerned with transport of urine from nephrons to pelvis of ureter.

Collecting ducts unite to form ducts of Bellini, which open into minor calyces through papilla. Other details are given in Chapter 49.

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Nephron

Chapter 49

- INTRODUCTION
- RENAL CORPUSCLE
  - SITUATION – TYPES OF NEPHRON
  - STRUCTURE
- TUBULAR PORTION OF NEPHRON
  - PROXIMAL CONVOLUTED TUBULE
  - LOOP OF HENLE
  - DISTAL CONVOLUTED TUBULE
- COLLECTING DUCT
- PASSAGE OF URINE

INTRODUCTION

Nephron is defined as the structural and functional unit of kidney. Each kidney consists of 1 to 1.3 millions of nephrons. The number of nephrons starts decreasing after about 45 to 50 years of age at the rate of 0.8% to 1% every year.

Each nephron is formed by two parts (Fig. 49.1):

1. A blind end called renal corpuscle or Malpighian **corpuscle**
2. A tubular portion called **renal tubule.**

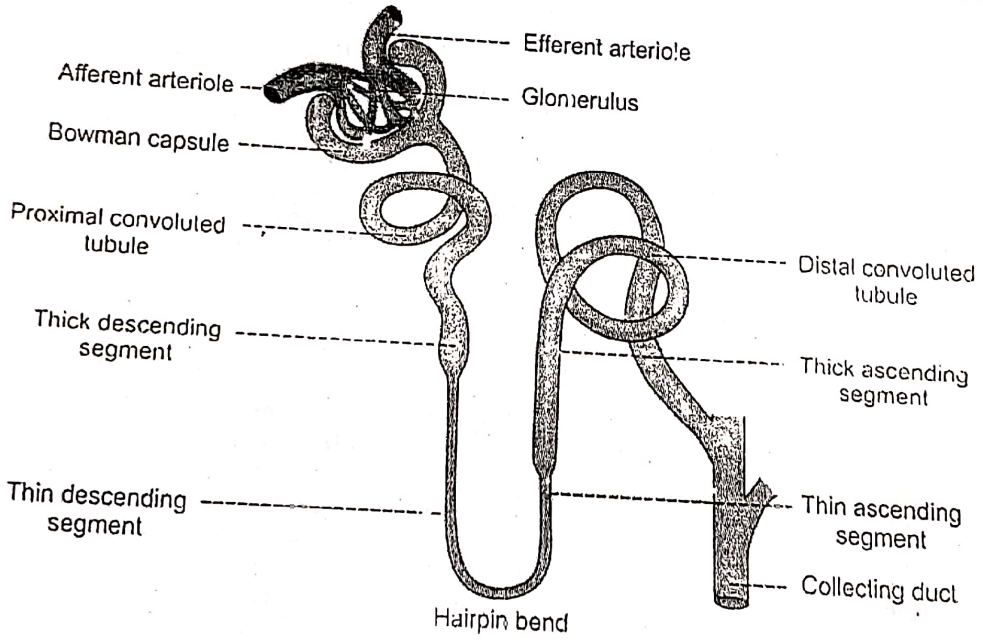

FIGURE 49.1: Structure of nephron

RENAL CORPUSCLE

Renal corpuscle or Malpighian corpuscle is a spheroidal and slightly flattened structure with a diameter of about 200 μ.

Function of the renal corpuscle is the filtration of blood which forms the first phase of urine formation.

SITUATION OF RENAL CORPUSCLE AND TYPES OF NEPHRON

Renal corpuscle is situated in the cortex of the kidney either near the periphery or near the medulla.

Classification of Nephrons

Based on the situation of renal corpuscle, the nephrons are classified into two types:

1. Cortical nephrons or superficial nephrons: Nephrons having the corpuscles in outer cortex of the kidney near the periphery (Fig. 49.2). In human kidneys, 85% nephrons are cortical nephrons.
2. Juxtamedullary nephrons: Nephrons having the corpuscles in inner cortex near medulla or corticomedullary junction.

Features of the two types of nephrons are given in Table 49.1.

STRUCTURE OF RENAL CORPUSCLE

Renal corpuscle is formed by two portions:

1. Glomerulus
2. Bowman capsule.

Glomerulus

Glomerulus is a tuft of capillaries enclosed by Bowman capsule. It consists of glomerular capillaries interposed between afferent arteriole on one end and efferent arteriole on the other end. Thus, the vascular system in the glomerulus is purely arterial (Fig. 49.3).

Glomerular capillaries arise from the afferent arteriole. After entering the Bowman capsule, the afferent

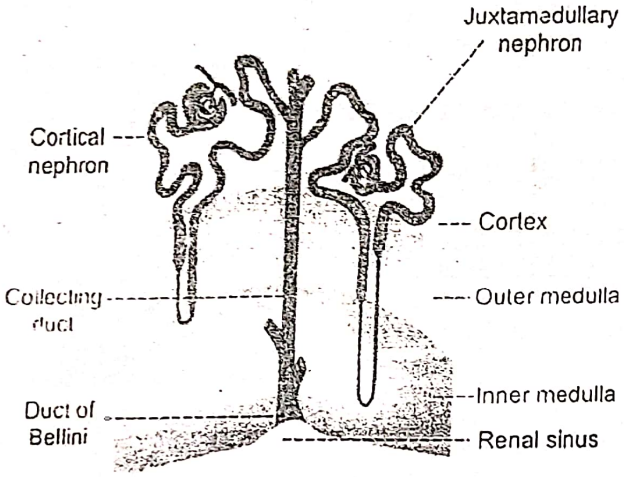

FIGURE 49.2: Types of nephron

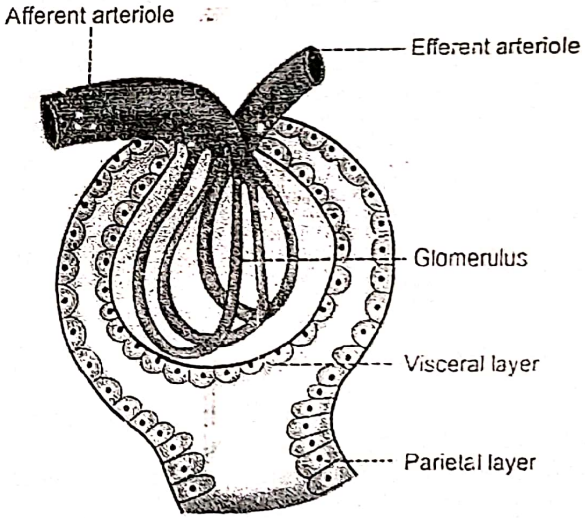

FIGURE 49.3: Renal corpuscle

TABLE 49.1: Features of two types of nephron

Features	Cortical nephron	Juxtamedullary nephron
Percentage	85%	15%
Situation of renal corpuscle	Outer cortex near the periphery	Inner cortex near medulla
Loop of Henle	Short Hairpin bend penetrates only up to outer zone of medulla	Long Hairpin bend penetrates up to the tip of papilla
Blood supply to tubule	Peritubular capillaries	Vasa recta
Function	Formation of urine	Mainly the concentration of urine and also formation of urine

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arteriole divides into 4 or 5 large capillaries. Each large capillary subdivides into many small capillaries. These small capillaries are arranged in irregular loops and form anastomosis. All the smaller capillaries finally reunite to form the efferent arteriole, which leaves the Bowman capsule.

Diameter of the efferent arteriole is less than that of afferent arteriole. This difference in diameter has got functional significance.

Functional histology

Glomerular capillaries are made up of single layer of endothelial cells, which are attached to a basement membrane. Endothelium has many pores called fenestrae or filtration pores. Diameter of each pore is 0.1 μ. Presence of the fenestra is the evidence of the filtration function of the glomerulus.

Bowman Capsule

Bowman capsule is a capsular structure, which encloses the glomerulus.

It is formed by two layers:

i. Inner visceral layer
ii. Outer parietal layer.

Visceral layer covers the glomerular capillaries. It is continued as the parietal layer at the visceral pole. Parietal layer is continued with the wall of the tubular portion of nephron. The cleft-like space between the visceral and parietal layers is continued as the lumen of the tubular portion.

Functional anatomy of Bowman capsule resembles a funnel with filter paper. Diameter of Bowman capsule is 200 μ.

Functional histology

Both the layers of Bowman capsule are composed of a single layer of flattened epithelial cells resting on a basement membrane. Basement membrane of the visceral layer fuses with the basement membrane of glomerular capillaries on which the capillary endothelial cells are arranged. Thus, the basement membranes, which are fused together, form the separation between the glomerular capillary endothelium and the epithelium of visceral layer of Bowman capsule.

Epithelial cells of the visceral layer fuse with the basement membrane but the fusion is not complete. Each cell is connected with basement membrane by cytoplasmic extensions of epithelial cells called **pedicles** or feet. These pedicles are arranged in an interdigitating manner leaving small cleft-like spaces in between. The cleft-like space is called **slit pore.** Epithelial cells with pedicles are called **podocytes** (Fig. 49.4).

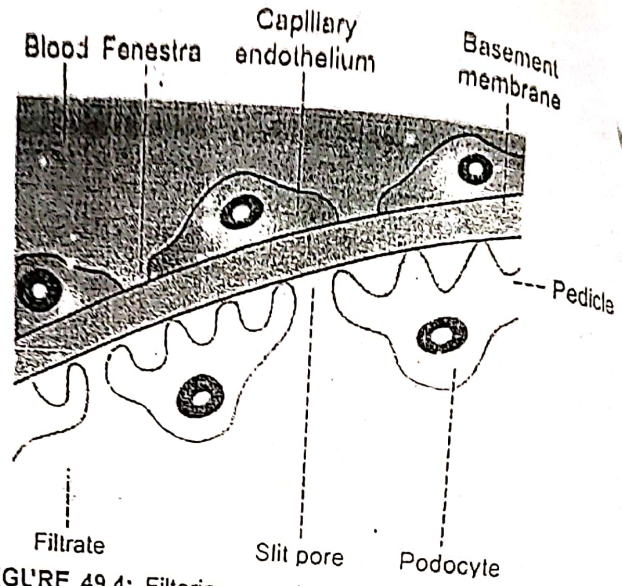

FIGURE 49.4: Filtering membrane in renal corpuscle. It is formed by capillary endothelium on one side (red) and visceral layer of Bowman capsule (yellow) on the other side.

■ TUBULAR PORTION OF NEPHRON

Tubular portion of nephron is the continuation of Bowman capsule.

It is made up of three parts:

1. Proximal convoluted tubule
2. Loop of Henle
3. Distal convoluted tubule.

■ PROXIMAL CONVOLUTED TUBULE

Proximal convoluted tubule is the coiled portion arising from Bowman capsule. It is situated in the cortex. It is continued as descending limb of loop of Henle. Length of proximal convoluted tubule is 14 mm and the diameter is 55 μ. Proximal convoluted tubule is continued as loop of Henle.

Functional histology

Proximal convoluted tubule is formed by single layer of cuboidal epithelial cells. Characteristic feature of these cells is the presence of hair-like projections directed towards the lumen of the tubule. Because of the presence of these projections, the epithelial cells are called **brush-bordered cells.**

■ LOOP OF HENLE

Loop of Henle consists of:

i. Descending limb
ii. Hairpin bend
iii. Ascending limb.

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i. Descending Limb

Descending limb of loop of Henle is made up of two segments:

a. Thick descending segment
b. Thin descending segment.

Thick descending segment

Thick descending segment is the direct continuation of the proximal convoluted tubule. It descends down into medulla. It has a length of 6 mm and a diameter of 55 µ. It is formed by brush-bordered cuboidal epithelial cells.

Thin descending segment

Thick descending segment is continued as thin descending segment (Fig. 49.5). It is formed by flattened epithelial cells without brush border and it is continued as hairpin bend of the loop.

ii. Hairpin Bend

Hairpin bend formed by flattened epithelial cells without brush border and it is continued as the ascending limb of loop of Henle.

iii. Ascending Limb

Ascending limb or segment of Henle loop has two parts:

a. Thin ascending segment
b. Thick ascending segment.

Thin ascending segment

Thin ascending segment is the continuation of hairpin bend. It is also lined by flattened epithelial cells without brush border.

Total length of thin descending segment, hairpin bend and thin ascending segment of Henle loop is 10 mm to 15 mm and the diameter is 15 µ.

Thin ascending segment is continued as thick ascending segment.

Thick ascending segment

Thick ascending segment is about 9 mm long with a diameter of 30 µ. Thick ascending segment is lined by cuboidal epithelial cells without brush border.

The terminal portion of thick ascending segment, which runs between the afferent and efferent arterioles of the same nephrons forms the macula densa. Macula densa is the part of juxtaglomerular apparatus (Chapter 50).

Thick ascending segment ascends to the cortex and continues as distal convoluted tubule.

Length and Extent of Loop of Henle

Length and the extent of the loop of Henle vary in different nephrons:

i. In cortical nephrons, it is short and the hairpin bend penetrates only up to outer medulla

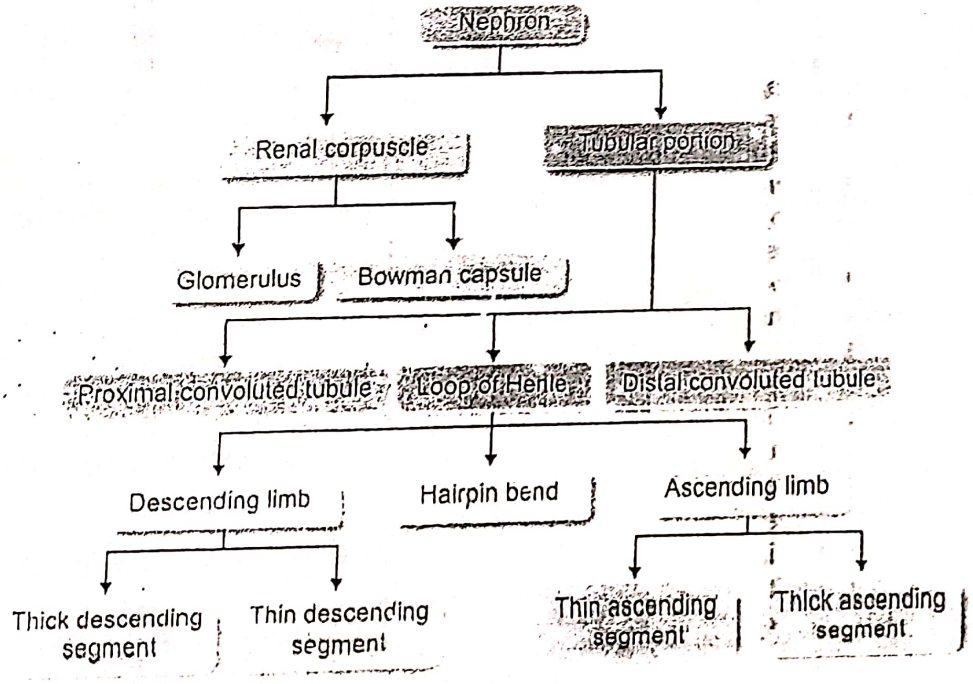

FIGURE 49.5: Parts of nephron

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TABLE 49.2: Size and cells of different parts of nephron and collecting duct

Segment	Epithelium	Length (mm)	Diameter (μ)
Bowman Capsule	Flattened epithelium	-	200
Proximal convoluted tubule	Cuboidal cells with brush border	14	55
Thick descending segment	Cuboidal cells with brush border	6	55
Thin descending segment, hairpin bend and thin ascending segment	Flattened epithelium	10 to 15	15
Thick ascending segment	Cuboidal epithelium without brush border	9	30
Distal convoluted tubule	Cuboidal epithelium without brush border	14.5 to 15	22 to 50
Collecting duct	Cuboidal epithelium without brush border	20 to 22	40 to 200

ii. In juxtamedullary nephrons, this is long and the hairpin bend extends deep into the inner medulla. In some nephrons it even runs up to the papilla.

DISTAL CONVOLUTED TUBULE

Distal convoluted tubule is the continuation of thick ascending segment and occupies the cortex of kidney. It is continued as collecting duct. The length of the distal convoluted tubule is 14.5 to 15 mm. It has a diameter of 22 to 50 μ (Table 49.2).

Functional histology

Distal convoluted tubule is lined by single layer of cuboidal epithelial cells without brush border. Epithelial cells in distal convoluted tubule are called intercalated cells (I cells).

COLLECTING DUCT

Distal convoluted tubule continues as the initial or arched collecting duct, which is in cortex. The lower part of the collecting duct lies in medulla. Seven to ten initial collecting ducts unite to form the straight collecting duct, which passes through medulla.

Length of the collecting duct is 20 to 22 mm and its diameter varies between 40 and 200 μ. Collecting duct is formed by cuboidal or columnar epithelial cells.

Functional histology

Collecting duct is formed by two types of epithelial cells:

1. Principal or P cells
2. Intercalated or I cells.

These two types of cells have some functional significance (Chapters 53 and 54).

PASSAGE OF URINE

At the inner zone of medulla, the straight collecting ducts from each medullary pyramid unite to form papillary ducts or ducts of Bellini, which open into a 'V' shaped area called papilla. Urine from each medullary pyramid is collected in the papilla. From here it is drained into a **minor calyx.** Three or four minor calyces unite to form one **major calyx.** Each kidney has got about 8 minor calyces and 2 to 3 major calyces.

From minor calyces urine passes through major calyces, which open into the **pelvis** of the **ureter.** Pelvis is the expanded portion of ureter present in the renal sinus.

From renal pelvis, urine passes through remaining portion of ureter and reaches urinary bladder.

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Juxtaglomerular Apparatus

Chapter 50

- DEFINITION
- STRUCTURE
  - MACULA DENSA
  - EXTRAGLOMERULAR MESANGIAL CELLS
  - JUXTAGLOMERULAR CELLS
- FUNCTIONS
  - SECRETION OF HORMONES
  - SECRETION OF OTHER SUBSTANCES
  - REGULATION OF GLOMERULAR BLOOD FLOW AND GLOMERULAR FILTRATION RATE

DEFINITION

Juxtaglomerular apparatus is a specialized organ situated near the glomerulus of each nephron (juxta = near).

STRUCTURE OF JUXTAGLOMERULAR APPARATUS

Juxtaglomerular apparatus is formed by three different structures (Fig. 50.1):

1. Macula densa
2. Extraglomerular mesangial cells
3. Juxtaglomerular cells.

MACULA DENSA

Macula densa is the end portion of thick ascending segment before it opens into distal convoluted tubule. It is situated between afferent and efferent arterioles of the same nephron. It is very close to afferent arteriole.

Macula densa is formed by tightly packed cuboidal epithelial cells.

EXTRAGLOMERULAR MESANGIAL CELLS

Extraglomerular mesangial cells are situated in the triangular region bound by afferent arteriole, efferent arteriole and macula densa. These cells are also called **agranular cells, lacis cells** or **Goormaghtigh cells.**

Glomerular Mesangial Cells

Besides extraglomerular mesangial cells there is another type of mesangial cells situated in between glomerular capillaries called **glomerular mesangial** or **intraglomerular mesangial cells.**

Glomerular mesangial cells support the glomerular capillary loops by surrounding the capillaries in the form of a cellular network.

These cells play an important role in regulating the glomerular filtration by their contractile property.

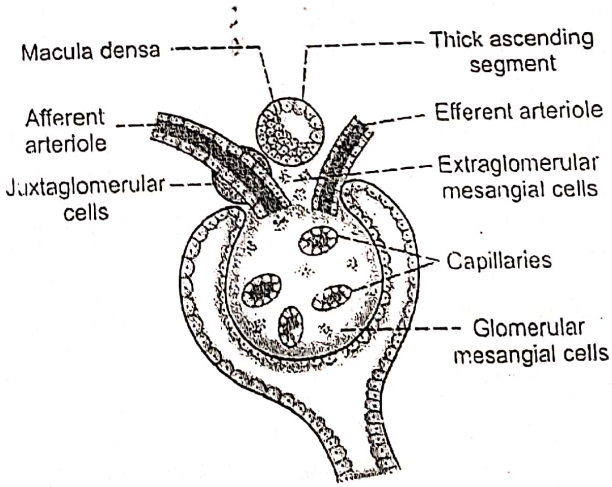

FIGURE 50.1: Juxtaglomerular apparatus

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Glomerular mesangial cells are phagocytic in nature. These cells also secrete glomerular interstitial matrix, prostaglandins and cytokines.

JUXTAGLOMERULAR CELLS

Juxtaglomerular cells are specialized smooth muscle cells situated in the wall of afferent arteriole just before it enters the Bowman capsule. These smooth muscle cells are mostly present in tunica media and tunica adventitia of the wall of the afferent arteriole.

Juxtaglomerular cells are also called **granular cells** because of the presence of secretary granules in their cytoplasm.

Polar Cushion or Polkissen

Juxtaglomerular cells form a thick cuff called polar cushion or polkissen around the afferent arteriole before it enters the Bowman capsule.

FUNCTIONS OF JUXTAGLOMERULAR APPARATUS

Primary function of juxtaglomerular apparatus is the secretion of hormones. It also regulates the glomerular blood flow and glomerular filtration rate.

SECRETION OF HORMONES

Juxtaglomerular apparatus secretes two hormones:

1. Renin
2. Prostaglandin.

1. *Renin*

Juxtaglomerular cells secrete renin. Renin is a peptide with 340 amino acids. Along with angiotensins, renin forms the renin-angiotensin system, which is a hormone system that plays an important role in the maintenance of blood pressure (Chapter 103).

Stimulants for renin secretion

Secretion of renin is stimulated by four factors:

i. Fall in arterial blood pressure
ii. Reduction in the ECF volume
iii. Increased sympathetic activity
iv. Decreased load of sodium and chloride in macula densa.

Renin-angiotensin system

When renin is released into the blood, it acts on a specific plasma protein called **angiotensinogen** or **renin substrate**. It is the α_2-globulin. By the activity of renin, the angiotensinogen is converted into a **decapeptide** called angiotensin I. Angiotensin I is converted into angiotensin II, which is an **octapeptide** by the activity of **angiotensin-converting enzyme** (ACE) secreted from lungs. Most of the conversion of angiotensin I into angiotensin II takes place in lungs.

Angiotensin II has a short half-life of about 1 to 2 minutes. Then it is rapidly degraded into a heptapeptide called angiotensin III by **angiotensinases**, which are present in RBCs and vascular beds in many tissues. Angiotensin III is converted into angiotensin IV, which is a **hexapeptide** (Fig. 50.2).

Actions of Angiotensins

Angiotensin I

Angiotensin I is physiologically inactive and serves only as the precursor of angiotensin II.

Angiotensin II

Angiotensin II is the most active form. Its actions are:

On blood vessels:

i. Angiotensin II increases arterial blood pressure by directly acting on the blood vessels and causing vasoconstriction. It is a potent constrictor of arterioles. Earlier, when its other actions were not found it was called **hypertensin.**
ii. It increases blood pressure indirectly by increasing the release of noradrenaline from postganglionic sympathetic fibers. Noradrenaline is a general vasoconstrictor (Chapter 71).

On adrenal cortex:

It stimulates zona glomerulosa of adrenal cortex to secrete aldosterone. Aldosterone acts on renal tubules and increases retention of sodium, which is also responsible for elevation of blood pressure.

On kidney:

i. Angiotensin II regulates glomerular filtration rate by two ways:
   a. It constricts the efferent arteriole, which causes decrease in filtration after an initial increase (Chapter 52)
   b. It contracts the glomerular mesangial cells leading to decrease in surface area of glomerular capillaries and filtration (see above)
ii. It increases sodium reabsorption from renal tubules. This action is more predominant on proximal tubules.

On brain:

i. Angiotensin II inhibits the baroreceptor reflex and thereby indirectly increases the blood pressure. Baroreceptor reflex is responsible for decreasing the blood pressure (Chapter 103)

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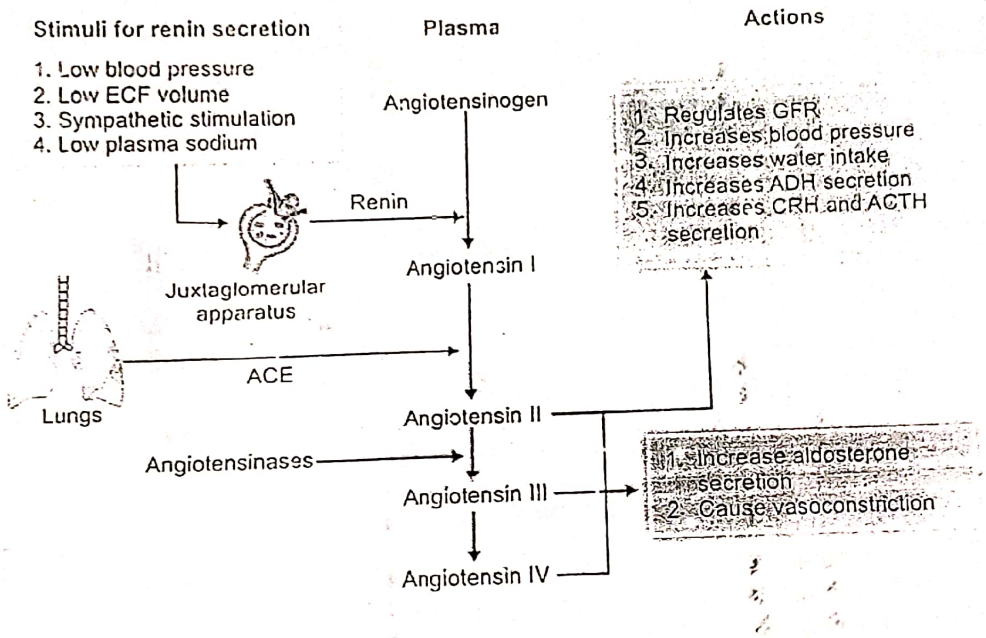

FIGURE 50.2: Renin-angiotensin system. ECF = extracellular fluid, ACE = Angiotensin-converting enzyme, GFR = Glomerular filtration rate, ADH = Antidiuretic hormone, CRH = Corticotropin-releasing hormone, ACTH = Adrenocorticotropic hormone.

ii. It increases water intake by stimulating the thirst center
iii. It increases the secretion of orticotropin-releasing hormone (CRH) from hypothalamus. CRH in turn increases secretion of adrenocorticotropic hormone (ACTH) from pituitary
iv. It increases secretion of antidiuretic hormone (ADH) from hypothalamus.

Other actions:

Angiotensin II acts as a growth factor in heart and it is thought to cause muscular hypertrophy and cardiac enlargement.

Angiotensin III

Angiotensin III increases the blood pressure and stimulates aldosterone secretion from adrenal cortex. It has 100% adrenocortical stimulating activity and 40% vasopressor activity of angiotensin II.

Angiotensin IV

It also has adrenocortical stimulating and vasopressor activities.

2. *Prostaglandin*

Extraglomerular mesangial cells of juxtaglomerular apparatus secrete prostaglandin. Prostaglandin is also secreted by interstitial cells of medulla called type I medullary interstitial cells. Refer Chapter 72 for details.

■ SECRETION OF OTHER SUBSTANCES

1. Extraglomerular mesangial cells of juxtaglomerular apparatus secrete cytokines like interleukin-2 and tumor necrosis factor (Chapter 17)
2. Macula densa secretes thromboxane A_2.

■ REGULATION OF GLOMERULAR BLOOD FLOW AND GLOMERULAR FILTRATION RATE

Macula densa of juxtaglomerular apparatus plays an important role in the feedback mechanism called **tubuloglomerular feedback** mechanism, which regulates the renal blood flow and glomerular filtration rate (Refer Chapter 52 for details).

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Urine Formation

Chapter 52

INTRODUCTION

Urine formation is a blood cleansing function. Normally, about 1,300 mL of blood (26% of cardiac output) enters the kidneys. Kidneys excrete the unwanted substances along with water from the blood as urine. Normal urinary output is 1 L/day to 1.5 L/day.

Processes of Urine Formation

When blood passes through glomerular capillaries, the plasma is filtered into the Bowman capsule. This process is called glomerular filtration.

Filtrate from Bowman capsule passes through the tubular portion of the nephron. While passing through the tubule, the filtrate undergoes various changes both in quality and in quantity. Many wanted substances like glucose, amino acids, water and electrolytes are reabsorbed from the tubules. This process is called tubular reabsorption.

And, some unwanted substances are secreted into the tubule from peritubular blood vessels. This process is called tubular secretion or excretion (Fig. 52.1).

Thus, the urine formation includes three processes:

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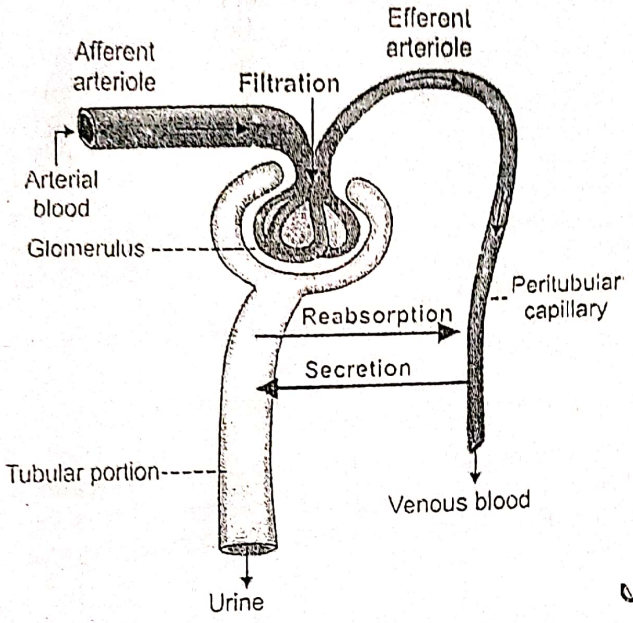

FIGURE 52.1: Events of urine formation

A. Glomerular filtration → glomerulus.
B. Tubular reabsorption } → tubular portion.
C. Tubular secretion

Among these three processes filtration is the function of the glomerulus. Reabsorption and secretion are the functions of tubular portion of the nephron.

GLOMERULAR FILTRATION

INTRODUCTION

Glomerular filtration is the process by which the blood is filtered while passing through the glomerular capillaries by filtration membrane. It is the first process of urine formation. The structure of filtration membrane is well suited for filtration.

Filtration Membrane

Filtration membrane is formed by three layers:

1. Glomerular capillary membrane
2. Basement membrane
3. Visceral layer of Bowman capsule.

1. *Glomerular capillary membrane*

Glomerular capillary membrane is formed by single layer of endothelial cells, which are attached to the basement membrane. The capillary membrane has many pores called **fenestrae** or **filtration pores** with a diameter of 0.1 μ.

2. *Basement membrane*

Basement membrane of glomerular capillaries and the basement membrane of visceral layer of Bowman capsule fuse together. The fused basement membrane separates the endothelium of glomerular capillary and the epithelium of visceral layer of Bowman capsule.

3. *Visceral layer of Bowman capsule*

This layer is formed by a single layer of flattened epithelial cells resting on a basement membrane. Each cell is connected with the basement membrane by cytoplasmic extensions called **pedicles** or **feet**. Epithelial cells with pedicles are called **podocytes** (Refer to Fig. 49.4). Pedicles interdigitate leaving small cleft-like spaces in between. The cleft-like space is called **slit pore** or **filtration slit**. Filtration takes place through these slit pores.

Process of Glomerular Filtration

When blood passes through glomerular capillaries, the plasma is filtered into the Bowman capsule. All the substances of plasma are filtered except the plasma proteins. The filtered fluid is called **glomerular filtrate**.

Ultrafiltration

Glomerular filtration is called ultrafiltration because even the minute particles are filtered. But, the plasma proteins are not filtered due to their large molecular size. The protein molecules are larger than the slit pores present in the endothelium of capillaries. Thus, the glomerular filtrate contains all the substances present in plasma except the plasma proteins.

METHOD OF COLLECTION OF GLOMERULAR FILTRATE

Glomerular filtrate is collected in experimental animals by micropuncture technique. This technique involves insertion of a micropipette into the Bowman capsule and aspiration of filtrate.

GLOMERULAR FILTRATION RATE

Glomerular filtration rate (GFR) is defined as the total quantity of filtrate formed in all the nephrons of both the kidneys in the given unit of time.

Normal GFR is 125 mL/minute or about 180 L/day.

FILTRATION FRACTION

Filtration fraction is the fraction (portion) of the renal plasma, which becomes the filtrate. It is the ratio

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between renal plasma flow and glomerular filtration rate. It is expressed in percentage.

$$\text{Filtration fraction} = \frac{\text{GFR}}{\text{Renal plasma flow}} \times 100$$

$$= \frac{125 \text{ mL/min}}{650 \text{ mL/min}} \times 100$$

$$= 19.2\%.$$

Normal filtration fraction varies from 15% to 20%.

PRESSURES DETERMINING FILTRATION

Pressures, which determine the GFR are:

1. Glomerular capillary pressure
2. Colloidal osmotic pressure in the glomeruli
3. Hydrostatic pressure in the Bowman capsule.

These pressures determine the GFR by either favoring or opposing the filtration.

1. *Glomerular Capillary Pressure*

Glomerular capillary pressure is the pressure exerted by the blood in glomerular capillaries. It is about 60 mm Hg and, varies between 45 and 70 mm Hg. Glomerular capillary pressure is the highest capillary pressure in the body. This pressure favors glomerular filtration.

2. *Colloidal Osmotic Pressure*

It is the pressure exerted by plasma proteins in the glomeruli. The plasma proteins are not filtered through the glomerular capillaries and remain in the glomerular capillaries. These proteins develop the colloidal osmotic pressure, which is about 25 mm Hg. It opposes glomerular filtration.

3. *Hydrostatic Pressure in Bowman Capsule*

It is the pressure exerted by the filtrate in Bowman capsule. It is also called **capsular pressure.** It is about 15 mm Hg. It also opposes glomerular filtration.

Net Filtration Pressure

Net filtration pressure is the balance between pressure favoring filtration and pressures opposing filtration. It is otherwise known as **effective filtration pressure** or **essential filtration pressure.**

Net filtration pressure =

$$\left\{\begin{array}{l}\text{Glomerular capillary pressure} \\ - \\ \text{Colloidal osmotic pressure} \\ + \\ \text{Hydrostatic pressure in Bowman capsule}\end{array}\right\}$$

$$= 60 - (25 + 15) = 20 \text{ mm Hg.}$$

Net filtration pressure is about 20 mm Hg and, it varies between 15 and 20 mm Hg.

Starling Hypothesis and Starling Forces

Determination of net filtration pressure is based on Starling hypothesis. Starling hypothesis states that the net filtration through capillary membrane is proportional to hydrostatic pressure difference across the membrane minus oncotic pressure difference. Hydrostatic pressure within the glomerular capillaries is the glomerular capillary pressure.

All the pressures involved in determination of filtration are called **Starling forces.**

FILTRATION COEFFICIENT

Filtration coefficient is the GFR in terms of net filtration pressure. It is the GFR per mm Hg of net filtration pressure. For example, when GFR is 125 mL/min and net filtration pressure is 20 mm Hg.

$$\text{Filtration coefficient} = \frac{125 \text{ mL}}{20 \text{ mm Hg}}$$

$$= 6.25 \text{ mL/mm Hg}$$

FACTORS REGULATING (AFFECTING) GFR

1. *Renal Blood Flow*

It is the most important factor that is necessary for glomerular filtration. GFR is directly proportional to renal blood flow. Normal blood flow to both the kidneys is 1,300 mL/minute. The renal blood flow itself is controlled by **autoregulation.** Refer previous chapter for details.

2. *Tubuloglomerular Feedback*

Tubuloglomerular feedback is the mechanism that regulates GFR through renal tubule and macula densa (Fig. 52.2). **Macula densa** of juxtaglomerular apparatus in the terminal portion of thick ascending limb is sensitive to the sodium chloride in the tubular fluid.

When the glomerular filtrate passes through the terminal portion of thick ascending segment, macula densa acts like a sensor. It detects the concentration of sodium chloride in the tubular fluid and accordingly alters the glomerular blood flow and GFR. Macula densa detects the sodium chloride concentration via Na^+-K^+-$2Cl^-$ cotransporter (NKCC2).

When the concentration of sodium chloride increases in the filtrate

When GFR increases, concentration of sodium chloride increases in the filtrate. Macula densa releases adenosine

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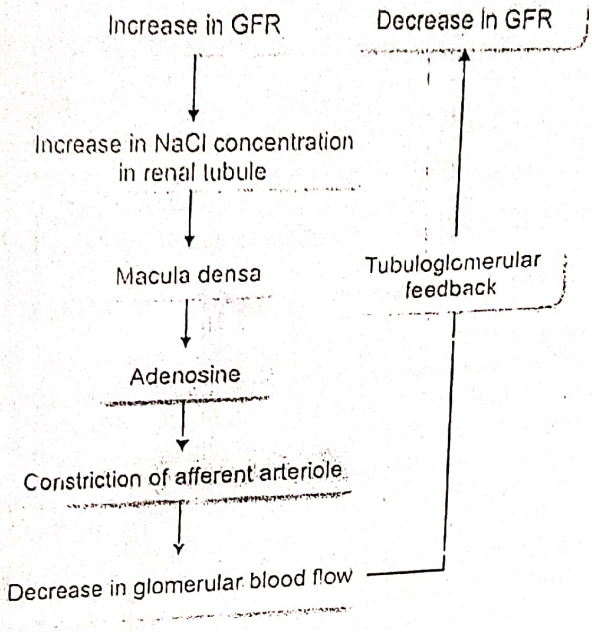

FIGURE 52.2: Tubuloglomerular feedback.
NaCl = Sodium chloride, GFR = Glomerular filtration rate.

from ATP. Adenosine causes constriction of afferent arteriole. So the blood flow through glomerulus decreases leading to decrease in GFR. Adenosine acts on afferent arteriole via adenosine A_1 receptors.

There are several other factors, which increase or decrease the sensitivity of tubuloglomerular feedback.

Factors increasing the sensitivity of tubuloglomerular feedback:

i. Adenosine
ii. Thromboxane
iii. Prostaglandin E_2
iv. Hydroxyeicosatetranoic acid.

Factors decreasing the sensitivity of tubuloglomerular feedback:

i. Atrial natriuretic peptide
ii. Prostaglandin I_2
iii. Cyclic AMP (cAMP)
iv. Nitrous oxide.

When the concentration of sodium chloride decreases in the filtrate

When GFR decreases, concentration of sodium chloride decreases in the filtrate. Macula densa secretes prostaglandin (PGE_2), bradykinin and renin.

PGE_2 and bradykinin cause dilatation of afferent arteriole. Renin induces the formation of angiotensin II, which causes constriction of efferent arteriole. The dilatation of afferent arteriole and constriction of efferent arteriole leads to increase in glomerular blood flow and GFR.

3. *Glomerular Capillary Pressure*

Glomerular filtration rate is directly proportional to glomerular capillary pressure. Normal glomerular capillary pressure is 60 mm Hg. When glomerular capillary pressure increases, the GFR also increases. Capillary pressure, in turn depends upon the renal blood flow and arterial blood pressure.

4. *Colloidal Osmotic Pressure*

Glomerular filtration rate is inversely proportional to colloidal osmotic pressure, which is exerted by plasma proteins in the glomerular capillary blood. Normal colloidal osmotic pressure is 25 mm Hg. When colloidal osmotic pressure increases as in the case of **dehydration** or increased plasma protein level GFR decreases. When colloidal osmotic pressure is low as in **hypoproteinemia**, GFR increases.

5. *Hydrostatic Pressure in Bowman Capsule*

GFR is inversely proportional to this. Normally, it is 15 mm Hg. When the hydrostatic pressure increases in the Bowman capsule, it decreases GFR. Hydrostatic pressure in Bowman capsule increases in conditions like obstruction of urethra and edema of kidney beneath renal capsule.

6. *Constriction of Afferent Arteriole*

Constriction of afferent arteriole reduces the blood flow to the glomerular capillaries, which in turn reduces GFR.

7. *Constriction of Efferent Arteriole*

If efferent arteriole is constricted, initially the GFR increases because of stagnation of blood in the capillaries. Later when all the substances are filtered from this blood, further filtration does not occur. It is because, the efferent arteriolar constriction prevents outflow of blood from glomerulus and no fresh blood enters the glomerulus for filtration.

8. *Systemic Arterial Pressure*

Renal blood flow and GFR are not affected as long as the mean arterial blood pressure is in between 60 and 180 mm Hg due to the autoregulatory mechanism (Chapter 51). Variation in pressure above 180 mm Hg or below 60 mm Hg affects the renal blood flow and GFR

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accordingly, because the autoregulatory mechanism falls beyond this range.

9. Sympathetic Stimulation

Afferent and efferent arterioles are supplied by sympathetic nerves. The mild or moderate stimulation of sympathetic nerves does not cause any significant change either in renal blood flow or GFR.

Strong sympathetic stimulation causes severe constriction of the blood vessels by releasing the neurotransmitter substance, noradrenaline. The effect is more severe on the efferent arterioles than on the afferent arterioles. So, initially there is increase in filtration but later it decreases. However, if the stimulation is continued for more than 30 minutes, there is recovery of both renal blood flow and GFR. It is because of reduction in sympathetic neurotransmitter.

10. Surface Area of Capillary Membrane

GFR is directly proportional to the surface area of the capillary membrane.

If the glomerular capillary membrane is affected as in the cases of some renal diseases, the surface area for filtration decreases. So there is reduction in GFR.

11. Permeability of Capillary Membrane

GFR is directly proportional to the permeability of glomerular capillary membrane. In many abnormal conditions like hypoxia, lack of blood supply, presence of toxic agents, etc. the permeability of the capillary membrane increases. In such conditions, even plasma proteins are filtered and excreted in urine.

12. Contraction of Glomerular Mesangial Cells

Glomerular mesangial cells are situated in between the glomerular capillaries. Contraction of these cells decreases surface area of capillaries resulting in reduction in GFR (refer Chapter 51 for details).

13. Hormonal and Other Factors

Many hormones and other secretory factors alter GFR by affecting the blood flow through glomerulus.

Factors increasing GFR by vasodilatation

i. Atrial natriuretic peptide
ii. Brain natriuretic peptide
iii. cAMP
iv. Dopamine
v. Endothelial-derived nitric oxide
vi. Prostaglandin (PGE_2).

Factors decreasing GFR by vasoconstriction

i. Angiotensin II
ii. Endothelins
iii. Noradrenaline
iv. Platelet-activating factor
v. Platelet-derived growth factor
vi. Prostaglandin (PGF_2).

TUBULAR REABSORPTION

INTRODUCTION

Tubular reabsorption is the process by which water and other substances are transported from renal tubules back to the blood. When the glomerular filtrate flows through the tubular portion of nephron, both quantitative and qualitative changes occur. Large quantity of water (more than 99%), electrolytes and other substances are reabsorbed by the tubular epithelial cells. The reabsorbed substances move into the interstitial fluid of renal medulla. And, from here, the substances move into the blood in peritubular capillaries.

Since the substances are taken back into the blood from the glomerular filtrate, the entire process is called tubular reabsorption.

METHOD OF COLLECTION OF TUBULAR FLUID

There are two methods to collect the tubular fluid for analysis.

1. Micropuncture Technique

A micropipette is inserted into the Bowman capsule and different parts of tubular portion in the nephrons of experimental animals, to collect the fluid. The fluid samples are analyzed and compared with each other to assess the changes in different parts of nephron.

2. Stop-flow Method

Ureter is obstructed so that the back pressure rises and stops the glomerular filtration. The obstruction is continued for 8 minutes. It causes some changes in the fluid present in different parts of the tubular portion.

Later, the obstruction is released and about 30 samples of 0.5 mL of urine are collected separately at regular intervals of 30 seconds. The first sample contains the fluid from collecting duct. Successive samples contain the fluid from distal convoluted tubule, loops of Henle and proximal convoluted tubule respectively. All the samples are analyzed.

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SELECTIVE REABSORPTION

Tubular reabsorption is known as selective reabsorption because the tubular cells reabsorb only the substances necessary for the body. Essential substances such as glucose, amino acids and vitamins are completely reabsorbed from renal tubule. Whereas the unwanted substances like metabolic waste products are not reabsorbed and excreted through urine.

MECHANISM OF REABSORPTION

Basic transport mechanisms involved in tubular reabsorption are of two types:

1. Active reabsorption
2. Passive reabsorption.

1. *Active Reabsorption*

Active reabsorption is the movement of molecules against the **electrochemical (uphill) gradient.** It needs liberation of energy, which is derived from ATP.

Substances reabsorbed actively

Substances reabsorbed actively from the renal tubule are sodium, calcium, potassium, phosphates, sulfates, bicarbonates, glucose, amino acids, ascorbic acid, uric acid and ketone bodies.

2. *Passive Reabsorption*

Passive reabsorption is the movement of molecules along the **electrochemical (downhill) gradient.** This process does not need energy.

Substances reabsorbed passively

Substances reabsorbed passively are chloride, urea and water.

ROUTES OF REABSORPTION

Reabsorption of substances from tubular lumen into the peritubular capillary occurs by two routes:

1. Trancelluar route
2. Paracellular route.

1. *Transcellular Route*

In this route the substances move through the cell.

It includes transport of substances from:

a. Tubular lumen into tubular cell through apical (luminal) surface of the cell membrane
b. Tubular cell into interstitial fluid
c. Interstitial fluid into capillary.

2. *Paracelluar Route*

In this route, the substances move through the intercellular space.

It includes transport of substances from:

i. Tubular lumen into interstitial fluid present in lateral intercellular space through the tight junction between the cells
ii. Interstitial fluid into capillary (Fig. 52.3).

SITE OF REABSORPTION

Reabsorption of the substances occurs in almost all the segments of tubular portion of nephron.

1. *Substances Reabsorbed from Proximal Convoluted Tubule*

About 7/8 of the filtrate (about 88%) is reabsorbed in proximal convoluted tubule. The brush border of epithelial cells in proximal convoluted tubule increases the surface area and facilitates the reabsorption.

Substances reabsorbed from proximal convoluted tubule are glucose, amino acids, sodium, potassium, calcium, bicarbonates, chlorides, phosphates, urea, uric acid and water.

2. *Substances Reabsorbed from Loop of Henle*

Substances reabsorbed from loop of Henle are sodium and chloride.

3. *Substances Reabsorbed from Distal Convoluted Tubule*

Sodium, calcium, bicarbonate and water are reabsorbed from distal convoluted tubule.

REGULATION OF TUBULAR REABSORPTION

Tubular reabsorption is regulated by three factors:

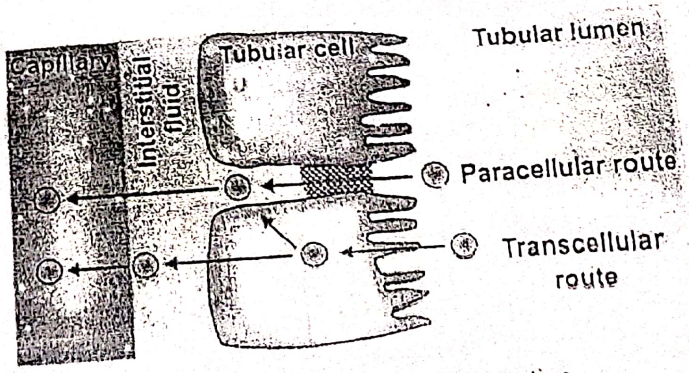

FIGURE 52.3: Routes of reabsorption

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1. Glomerulotubular balance
2. Hormonal factors
3. Nervous factors.

1. *Glomerulotubular Balance*

Glomerulotubular balance is the balance between the filtration and reabsorption of solutes and water in kidney. When GFR increases, the tubular load of solutes and water in the proximal convoluted tubule is increased. It is followed by increase in the reabsorption of solutes and water. This process helps in the constant reabsorption of solute particularly sodium and water from renal tubule.

Mechanism of glomerulotubular balance

Glomerulotubular balance occurs because of osmotic pressure in the peritubular capillaries. When GFR increases, more amount of plasma proteins accumulate in the glomerulus. Consequently, the osmotic pressure increases in the blood by the time it reaches efferent arteriole and peritubular capillaries. The elevated osmotic pressure in the peritubular capillaries increases reabsorption of sodium and water from the tubule into the capillary blood.

2. *Hormonal Factors*

Hormones, which regulate GFR are listed in Table 52.1.

3. *Nervous Factor*

Activation of sympathetic nervous system increases the tubular reabsorption (particularly of sodium) from renal tubules. It also increases the tubular reabsorption indirectly by stimulating secretion of renin from juxtaglomerular cells. Renin causes formation of angiotensin II, which increases the sodium reabsorption (Chapter 50).

THRESHOLD SUBSTANCES

Depending upon the degree of reabsorption, various substances are classified into three categories:

1. High-threshold substances
2. Low-threshold substances
3. Non-threshold substances.

1. *High-threshold Substances*

High-threshold substances are those substances, which do not appear in urine under normal conditions. The food substances like glucose, amino acids, acetoacetate ions and vitamins are completely reabsorbed from renal tubules and do not appear in urine under normal conditions. These substances can appear in urine, only if their concentration in plasma is abnormally high or in renal diseases when reabsorption is affected. So, these substances are called high-threshold substances.

2. *Low-threshold Substances*

Low-threshold substances are the substances, which appear in urine even under normal conditions. The substances such as urea, uric acid and phosphate are reabsorbed to a little extend. So, these substances appear in urine even under normal conditions.

3. *Non-threshold Substances*

Non-threshold substances are those substances, which are not at all reabsorbed and are excreted in urine irrespective of their plasma level. The metabolic end products such as creatinine are the non-threshold substances.

TRANSPORT MAXIMUM – Tm VALUE

Tubular transport maximum or Tm is the rate at which the maximum amount of a substance is reabsorbed from the renal tubule.

So, for every actively reabsorbed substance, there is a maximum rate at which it could be reabsorbed. For example, the transport maximum for glucose (TmG) is 375 mg/minute in adult males and about 300 mg/minute in adult females.

TABLE 52.1: Hormones regulating tubular reabsorption

Hormone	Action
Aldosterone	Increases sodium reabsorption in ascending limb, distal convoluted tubule and collecting duct
Angiotensin II	Increases sodium reabsorption in proximal tubule, thick ascending limb, distal tubule and collecting duct (mainly in proximal convoluted tubule)
Antidiuretic hormone	Increases water reabsorption in distal convoluted tubule and collecting duct
Atrial natriuretic factor	Decreases sodium reabsorption
Brain natriuretic factor	Decreases sodium reabsorption
Parathormone	Increases reabsorption of calcium, magnesium and hydrogen Decreases phosphate reabsorption
Calcitonin	Decreases calcium reabsorption

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Threshold Level in Plasma for Substances having Tm Value

Renal threshold is the plasma concentration at which a substance appears in urine. Every substance having Tm value has also a threshold level in plasma or blood. Below that threshold level, the substance is completely reabsorbed and does not appear in urine. When the concentration of that substance reaches the threshold, the excess amount is not reabsorbed and, so it appears in urine. This level is called the renal threshold of that substance.

For example, the renal threshold for glucose is 180 mg/dL. That is, glucose is completely reabsorbed from tubular fluid if its concentration in blood is below 180 mg/dL. So, the glucose does not appear in urine. When the blood level of glucose reaches 180 mg/dL it is not reabsorbed completely; hence it appears in urine.

REABSORPTION OF IMPORTANT SUBSTANCES

Reabsorption of Sodium

From the glomerular filtrate, 99% of sodium is reabsorbed. Two thirds of sodium is reabsorbed in proximal convoluted tubule and remaining one third in other segments (except descending limb) and collecting duct.

Sodium reabsorption occurs in three steps:

1. Transport from lumen of renal tubules into the tubular epithelial cells
2. Transport from tubular cells into the interstitial fluid
3. Transport from interstitial fluid to the blood.

1. *Transport from Lumen of Renal Tubules into the Tubular Epithelial Cells*

Active reabsorption of sodium ions from lumen into the tubular cells occurs by two ways:

i. In exchange for hydrogen ion by **antiport** (sodium counterport protein) – in proximal convoluted tubules
ii. Along with other substances like glucose and amino acids by **symport** (sodium co-transport protein) – in other segments and collecting duct.

It is believed that some amount of sodium diffuses along the electrochemical gradient from lumen into tubular cell across the luminar membrane. The electrochemical gradient is developed by sodium-potassium pump (see below).

2. *Transport from Tubular Cells into the Interstitial Fluid*

Sodium is pumped outside the cells by sodium-potassium pump. This pump moves three sodium ions from the cell into interstitium and two potassium ions from interstitium into the cell.

Tubular epithelial cells are connected with their neighboring cells by tight junctions at their apical luminal edges. But, beyond the tight junction, a small space is left between the adjoining cells along their lateral borders. This space is called **lateral intercellular space.** The interstitium extends into this space.

Most of the sodium ions are pumped into the lateral intercellular space by sodium-potassium pump. The rest of the sodium ions are pumped into the interstitium by the sodium-potassium pump situated at the basal part of the cell membrane.

(Transport of sodium out of the tubular cell by sodium-potassium pump, decreases the sodium concentration within the cell. This develops an electrochemical gradient between the lumen and tubular cell resulting in diffusion of sodium into the cell).

3. *Transport from Interstitial Fluid to the Blood*

From the interstitial fluid, sodium ions enter the peritubular capillaries by concentration gradient.

In the distal convoluted tubule, the sodium reabsorption is stimulated by the hormone aldosterone secreted by adrenal cortex.

Reabsorption of Water

Reabsorption of water occurs from proximal and distal convoluted tubules and in collecting duct.

Reabsorption of water from proximal convoluted tubule – obligatory water reabsorption

Obligatory reabsorption is the type of water reabsorption in proximal convoluted tubule, which is secondary (obligatory) to sodium reabsorption. When sodium is reabsorbed from the tubule, the osmotic pressure decreases. It causes osmosis of water from renal tubule.

Reabsorption of water from distal convoluted tubule and collecting duct – facultative water reabsorption

Facultative reabsorption is the type of water reabsorption in distal convoluted tubule and collecting duct that occurs by the activity of antidiuretic hormone (ADH). Normally, the distal convoluted tubule and the collecting duct are not permeable to water. But in the presence of ADH, these segments become permeable to water, so it is reabsorbed.

Mechanism of action of ADH – Aquaporins

Antidiuretic hormone increases water reabsorption in distal convoluted tubules and collecting ducts by

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stimulating the water channels called aquaporins. ADH combines with vasopressin (V2) receptors in the tubular epithelial membrane and activates adenyl cyclase, to form cyclic AMP. This cyclic AMP activates the aquaporins, which increase the water reabsorption.

Aquaporins (AQP) are the membrane proteins, which function as water channels. Though about 10 aquaporins are identified in mammals only 5 are found in humans. Aquaporin-1, 2 and 3 are present in renal tubules. Aquaporin-4 is present in brain and aquaporin-5 is found in salivary glands. Aquaporin-2 forms the water channels in renal tubules.

Reabsorption of Glucose

Glucose is completely reabsorbed in the proximal convoluted tubule. It is transported by secondary active transport (sodium cotransport) mechanism. Glucose and sodium bind to a common carrier protein in the luminal membrane of tubular epithelium and enter the cell. The carrier protein is called **sodium-dependant glucose cotransporter 2** (SGLT2). From tubular cell glucose is transported into medullary interstitium by another carrier protein called **glucose transporter 2** (GLUT2).

Tubular maximum for glucose (TmG)

In adult male, TmG is 375 mg/minute and in adult females it about 300 mg/minute.

Renal threshold for glucose

Renal threshold for glucose is 180 mg/dL in venous blood. When the blood level reaches 180 mg/dL glucose is not reabsorbed completely and appears in urine.

Splay

Splay means deviation. With normal GFR of 125 mL/minute and TmG of 375 mg/minute in an adult male the predicted (expected) renal threshold for glucose should be 300 mg/dL. But actually it is only 180 mg/dL.

When the renal threshold curves are drawn by using these values, the actual curve deviates from the 'should be' or predicted or ideal curve (Fig. 52.4). This type of deviation is called splay. Splay is because of the fact that all the nephrons do not have the same filtering and reabsorbing capacities.

Reabsorption of Amino Acids

Amino acids are also reabsorbed completely in proximal convoluted tubule. Amino acids are reabsorbed actively by the secondary active transport mechanism along with sodium.

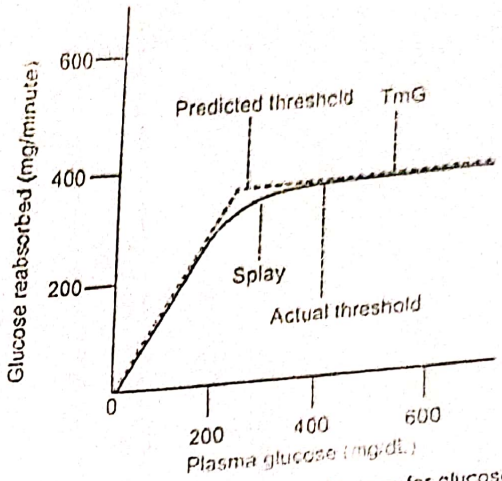

FIGURE 52.4: Splay in renal threshold curve for glucose

Reabsorption of Bicarbonates

Bicarbonate is reabsorbed actively, mostly in proximal tubule (Chapter 54). It is reabsorbed in the form of carbon dioxide.

Bicarbonate is mostly present as sodium bicarbonate in the filtrate. Sodium bicarbonate dissociates into sodium and bicarbonate ions in the tubular lumen. Sodium diffuses into tubular cell in exchange of hydrogen. Bicarbonate combines with hydrogen to form carbonic acid. Carbonic acid dissociates into carbon dioxide and water in the presence of carbonic anhydrase. Carbon dioxide and water enter the tubular cell.

In the tubular cells, carbon dioxide combines with water to form carbonic acid. It immediately dissociates into hydrogen and bicarbonate. Bicarbonate from the tubular cell enters the interstitium. There it combines with sodium to form sodium bicarbonate (Fig. 54.1).

TUBULAR SECRETION

INTRODUCTION

Tubular secretion is the process by which the substances are transported from blood into renal tubules. It is also called tubular excretion. In addition to reabsorption from renal tubules, some substances are also secreted into the lumen from the peritubular capillaries through the tubular epithelial cells.

Dye phenol red was the first substance found to be secreted in renal tubules in experimental conditions. Later many other substances were found to be secreted.

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Such substances are:

1. Para-aminohippuric acid (PAH)
2. Diodrast
3. 5-hydroxyindoleacetic acid (5-HIAA)
4. Amino derivatives
5. Penicillin.

SUBSTANCES SECRETED IN DIFFERENT SEGMENTS OF RENAL TUBULES

1. Potassium is secreted actively by sodium-potassium pump in proximal and distal convoluted tubules and collecting ducts
2. Ammonia is secreted in the proximal convoluted tubule
3. Hydrogen ions are secreted in the proximal and distal convoluted tubules. Maximum hydrogen ion secretion occurs in proximal tubule
4. Urea is secreted in loop of Henle.

Thus, urine is formed in nephron by the processes of glomerular filtration, selective reabsorption and tubular secretion.

SUMMARY OF URINE FORMATION

Urine formation takes place in three processes (Refer to Fig. 52.1).

1. *Glomerular filtration*

Plasma is filtered in glomeruli and the substances reach the renal tubules along with water as filtrate.

2. *Tubular Reabsorption*

The 99% of filtrate is reabsorbed in different segments of renal tubules.

3. *Tubular Secretion*

Some substances are transported from blood into the renal tubule.

With all these changes, the filtrate becomes urine.

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