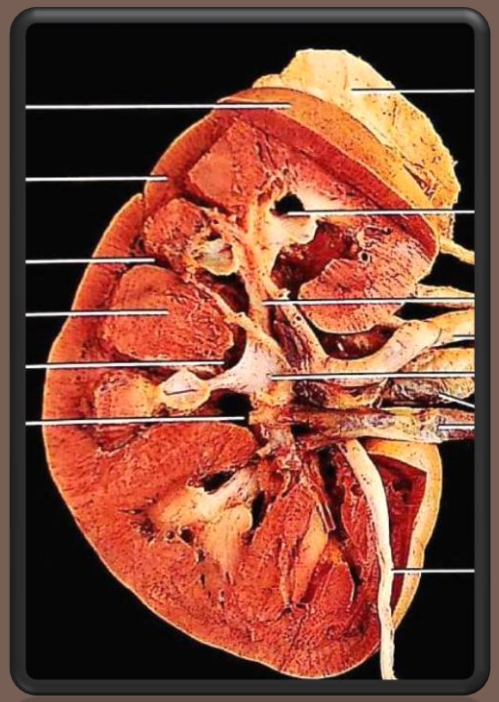
THE URINARY SYSTEM



BY

Dr. BHAGAT SINGH JAISWAL

ASSISTANT PROFESSOR

SCHOOL OF STUDIES IN PHARMACEUTICAL SCIENCES

JIWAJI UNIVERSITY GWALIOR

M.P., INDIA

The urinary system plays a vital part in maintaining homeostasis of water and electrolytes within the body. The kidneys produce urine that contains metabolic waste products, including the nitrogenous compounds urea and uric acid, excess ions and some drugs.

The urinary system is the main excretory system and consists of the following structures:

- **2 kidneys**, which secrete urine
- **2 ureters** that convey the urine from the kidneys to the urinary bladder
- **Urinary bladder**, which collects and stores urine the urethra through which urine leaves the body

The main functions of the kidneys are:

- ✓ **Formation of urine, maintaining water and electrolyte**
- ✓ **Regulating blood pH**
- ✓ **Excretion of waste products and foreign substances**
- ✓ **Production and secretion of Calcitriol (active form of Vitamin D) and**
- ✓ ***Erythropoietin, the* hormone that stimulates formation of RBC**
- ✓ **Production and secretion of *Renin, an important* enzyme in the control of blood pressure**
- ✓ **Maintaining blood osmolarity**
- ✓ **Regulating blood glucose level**
- ✓ **Regulating blood volume**

- **Urine is stored in the bladder and excreted by the process of *micturition*.**

KIDNEYS

The kidneys lie on the posterior abdominal wall, one on each side of the vertebral column, behind the peritoneum and below the diaphragm. They extend from the level of the 12th thoracic vertebra to the 3rd lumbar vertebra, receiving some protection from the lower rib cage.

- The right kidney is usually slightly lower than the left, probably because of the considerable space occupied by the liver.
- Kidneys are bean-shaped organs, about 11 cm long, 6 cm wide, 3 cm thick and weigh 150 g. They are embedded in, and held in position by, A mass of fat. A Sheath of Fibrous connective tissue, the *renal fascia*, *encloses the* kidney and the renal fat.

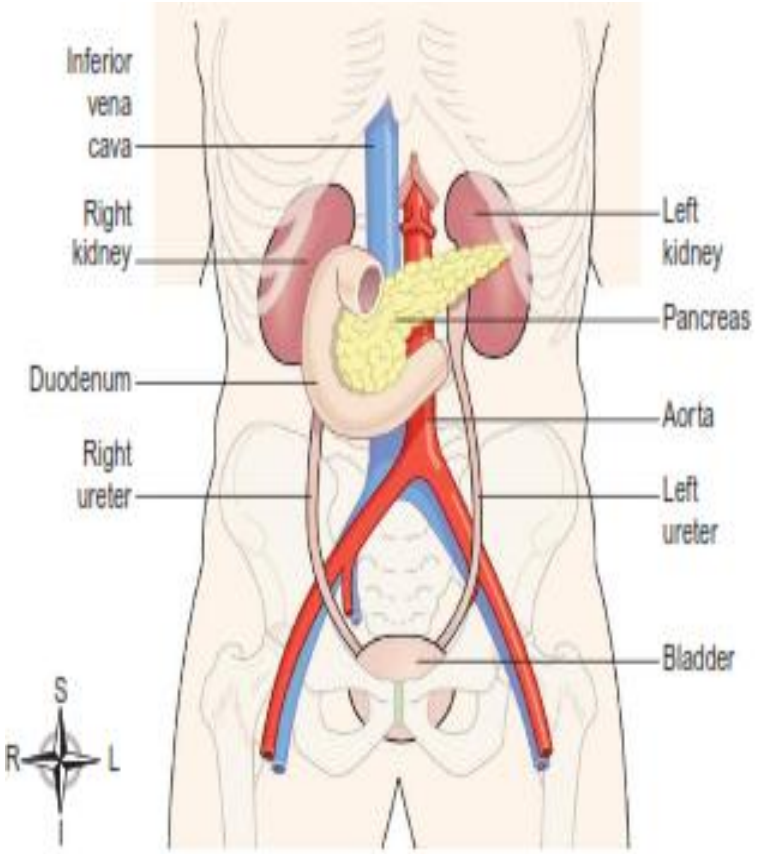


Fig 1: The parts of the urinary system (excluding the urethra) and some associated structures.

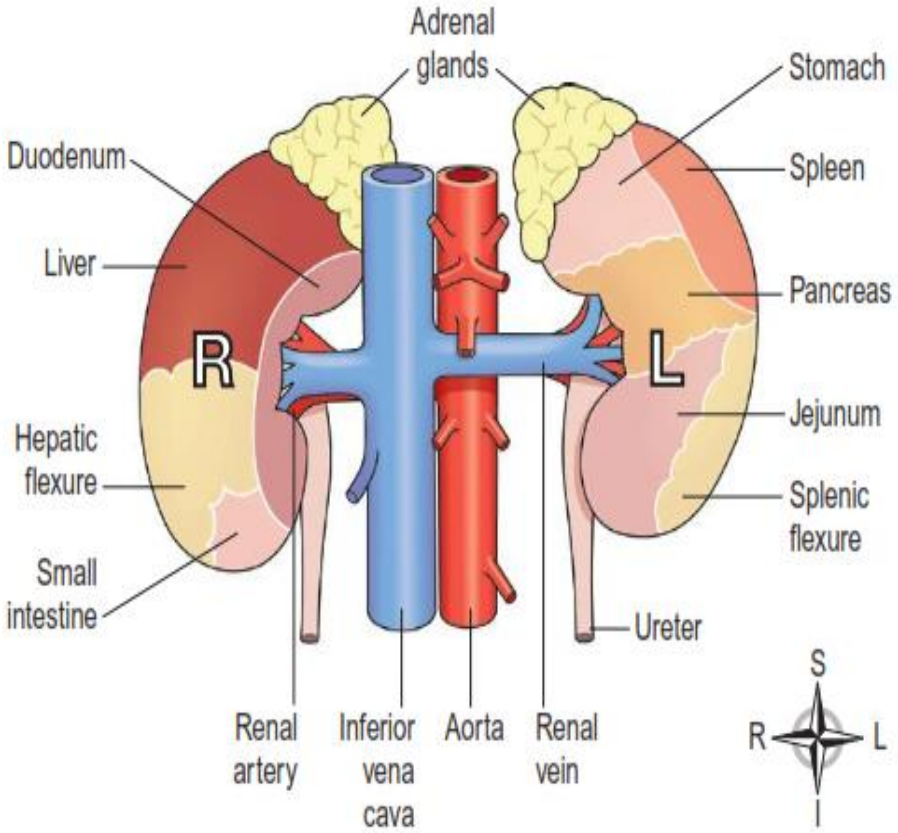


Fig 2: Anterior view of the kidneys showing the areas of contact with associated structures.

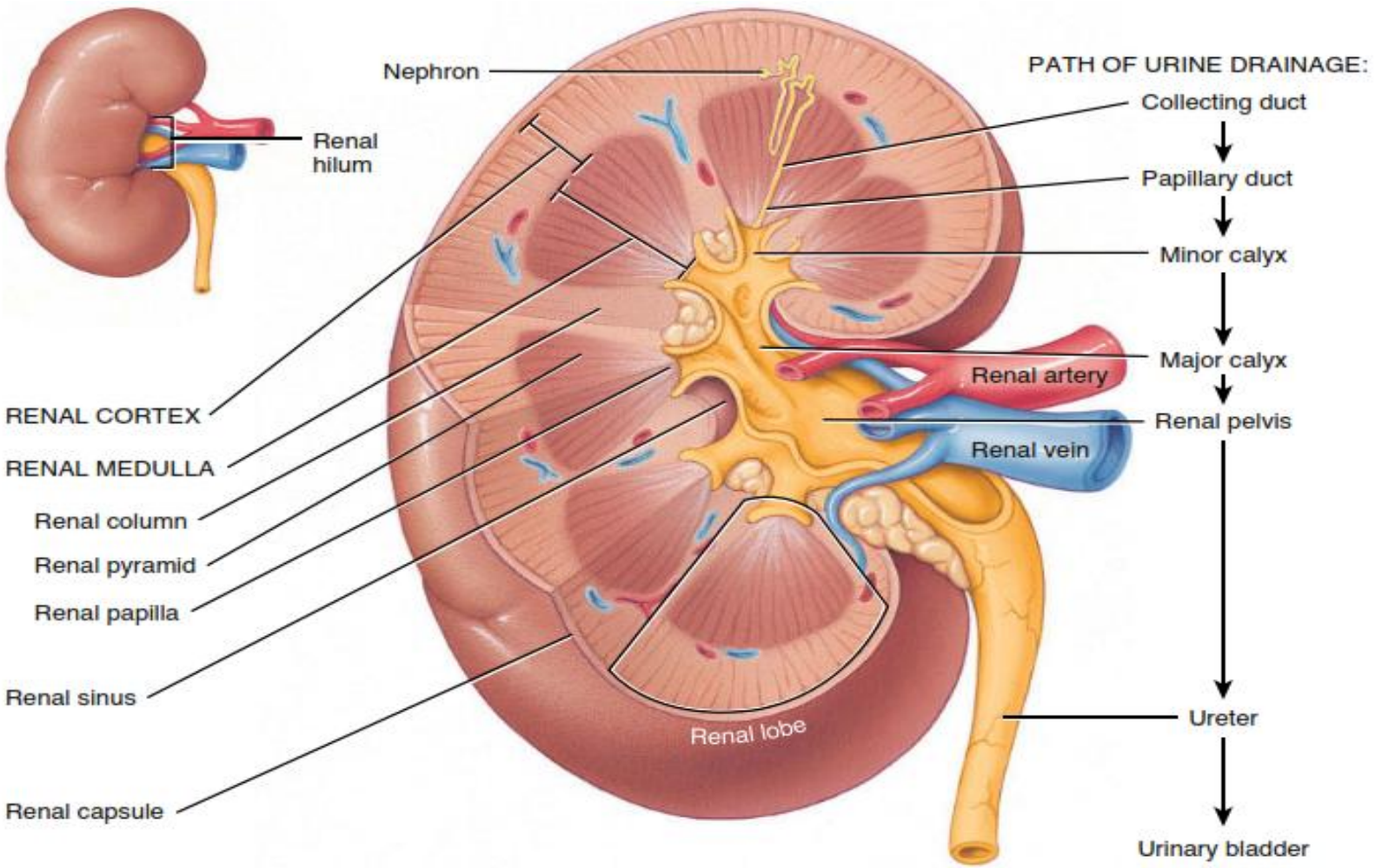


Fig 3: Anterior view of dissection of right kidney.

There are three areas of tissue that can be distinguished when a longitudinal section of the kidney is viewed with the naked eye:

- An outer fibrous *capsule*, *surrounding the kidney*
- *Cortex, a reddish-brown layer of tissue* immediately below the capsule and outside the *renal pyramids*
- *Medulla, the innermost layer, consisting of pale* conical-shaped striations, the renal pyramids.

Renal calyx – duct – like sections of renal medulla for collecting urine from nephrons and direct urine into renal pelvis. It consist the transitional epithelium and contain smooth muscle.

Renal pyramid – connective tissues in the renal medulla binding various structures together.

Renal pelvis – central urine collecting area of renal medulla.

Hilum – concave notch of kidneys where renal artery, renal vein, ureter, nerves, and lymphatic vessels converge.

Ureter – a tubule that transport urine (mainly by peristalsis) from the kidney to the urinary bladder.

Urinary bladder – a spherical storage organ that contains up to 400 ml of urine.

Urethra – a tubule that excretes urine out of the urinary bladder to the outside through the urethral orifice.

MICROSCOPIC STRUCTURE OF THE KIDNEY

- **Nephrons** (NEF-rons) are the **functional** units of the kidneys.
- The kidney contains about **1-2 million functional units, the *nephrons*.**
- They receive 20–25% of the resting cardiac output *via* the right and left **renal arteries**. In adults, **renal blood flow, the blood flow through** both kidneys, is about 1200 mL per minute.
- Each nephron consists of two parts: a **renal corpuscle (**tiny body), where blood plasma is filtered, and a **renal tubule** into which the filtered fluid (glomerular filtrate) passes. Closely associated with a nephron is its blood supply.
- The two components of a renal corpuscle are the **glomerulus** (capillary network) and the **glomerular capsule** or *Bowman's capsule*, a double-walled epithelial cup that surrounds the glomerular capillaries.

Note: **The number of nephrons is constant from birth. If nephrons are injured or become diseased, new ones do not form. Signs of kidney dysfunction usually do not become apparent until function declines to less than 25% of normal because the remaining functional nephrons adapt to handle a larger-than-normal load.**

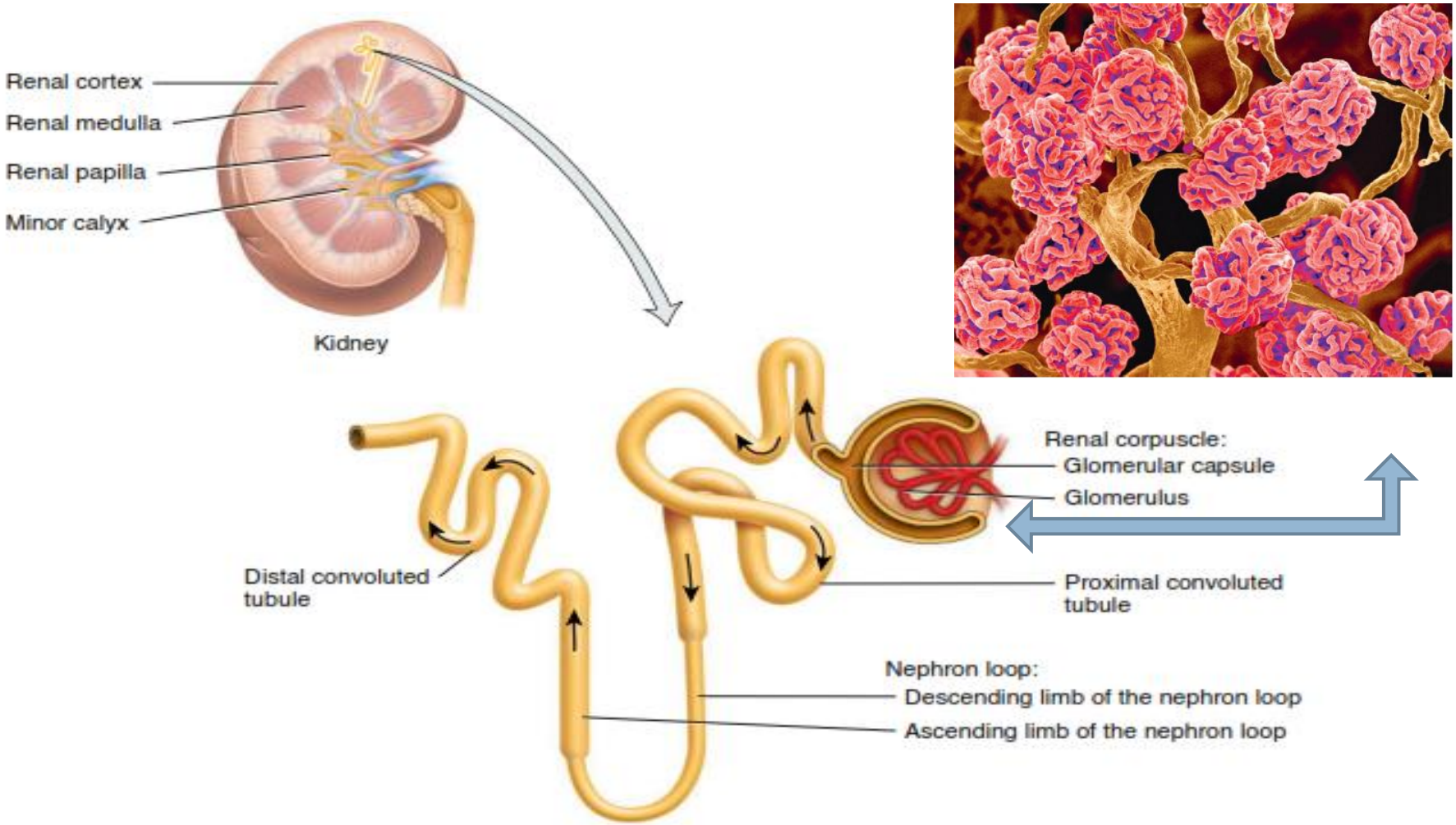


Fig 4: Components of nephron.

- The kidneys receive about 20% of the cardiac output. After entering the kidney at the hilum, the **renal artery** divides into smaller arteries and arterioles. In the cortex an arteriole, the **afferent arteriole, enters each glomerular capsule** and then subdivides into a cluster of tiny arterial capillaries, **forming the glomerulus**.

- Between these capillary loops are connective tissue **phagocytic mesangial cells**, which are part of the monocyte–macrophage defence system. The blood vessel leading away from the glomerulus is the **efferent arteriole**. The afferent arteriole has a larger diameter than the efferent arteriole, which increases pressure inside the glomerulus and drives filtration across the glomerular capillary walls.

- The **efferent arteriole** divides into a second **peritubular** (meaning ‘around tubules’) capillary network, which wraps around the remainder of the tubule, allowing exchange between the fluid in the tubule and the bloodstream. This maintains the local supply of oxygen and nutrients and removes waste products.

Blood plasma is filtered in the glomerular capsule, and then the filtered fluid passes into the renal tubule, which has three main sections. In the order that fluid passes through them, the renal tubule consists of ….

a) Proximal convoluted tubule (PCT)
b) Nephron loop (Loop of Henle)
c) Distal convoluted tubule (DCT)

The renal corpuscle and both convoluted tubules lie within the renal cortex; the nephron loop extends into the renal medulla, makes a hairpin turn, and then returns to the renal cortex.

The distal convoluted tubules of several nephrons empty into a single **collecting duct. Collecting ducts then unite and** converge into several hundred large papillary ducts, which drain into the minor calyces. The collecting ducts and papillary ducts extend from the renal cortex through the renal medulla to the renal pelvis. So one kidney has about 1 million nephrons, but a much smaller number of collecting ducts and even fewer papillary ducts.

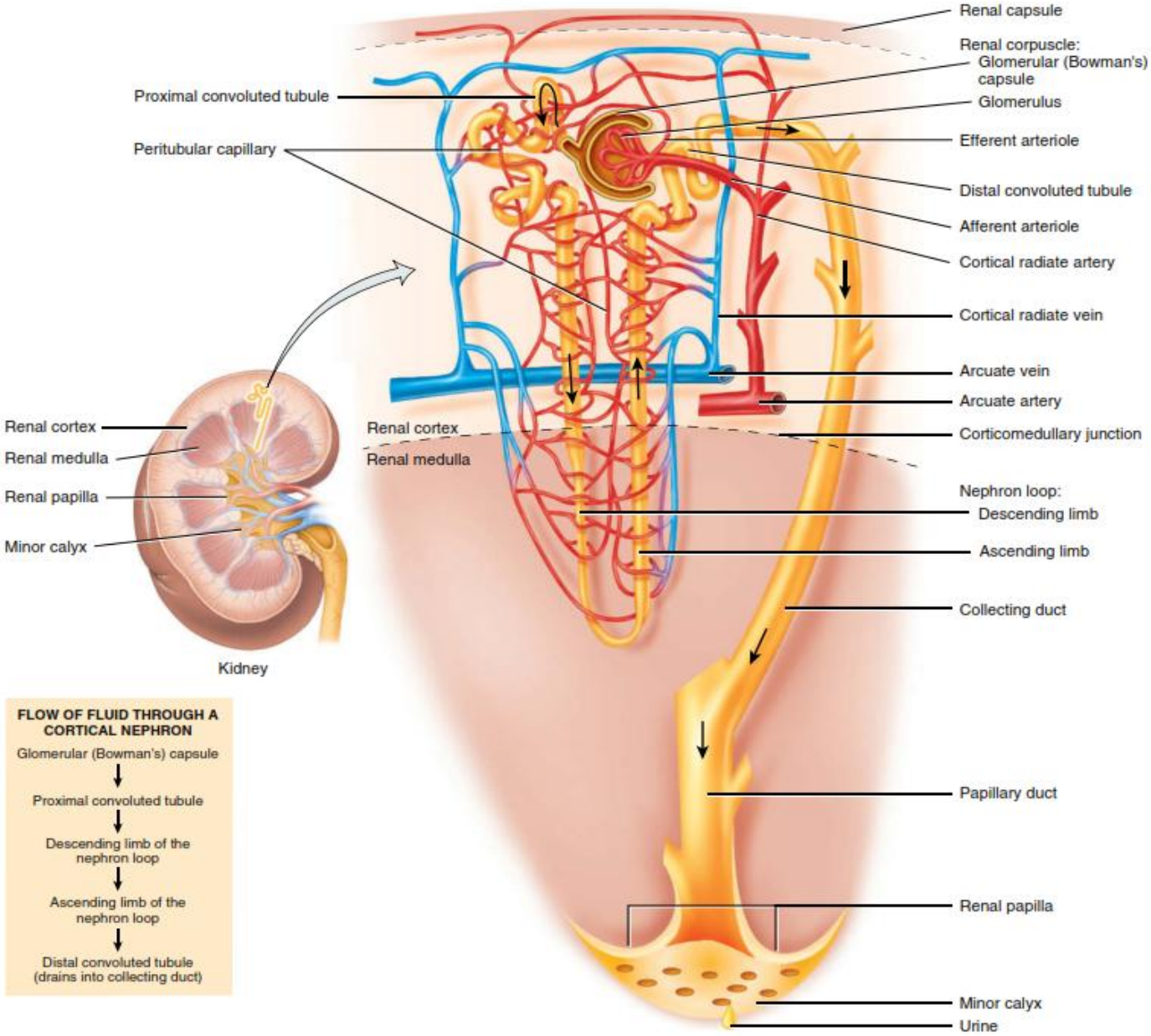


Fig 5: Cortical nephron and vascular supply.

HISTOLOGY OF THE NEPHRON AND COLLECTING DUCT

A single layer of epithelial cells forms the entire wall of the glomerular capsule, renal tubule, and ducts.

Glomerular Capsule

- **The glomerular (Bowman's) capsule** consists of visceral and parietal layers.
- The visceral layer consists of many foot like projections of cells (pedicels) called **Podocytes**.
- The parietal layer of the glomerular capsule consists of simple squamous epithelium and forms the outer wall of the capsule. Fluid filtered from the glomerular capillaries enters the **capsular space, the space between** the two layers of the glomerular capsule, which is the lumen of the urinary tube.

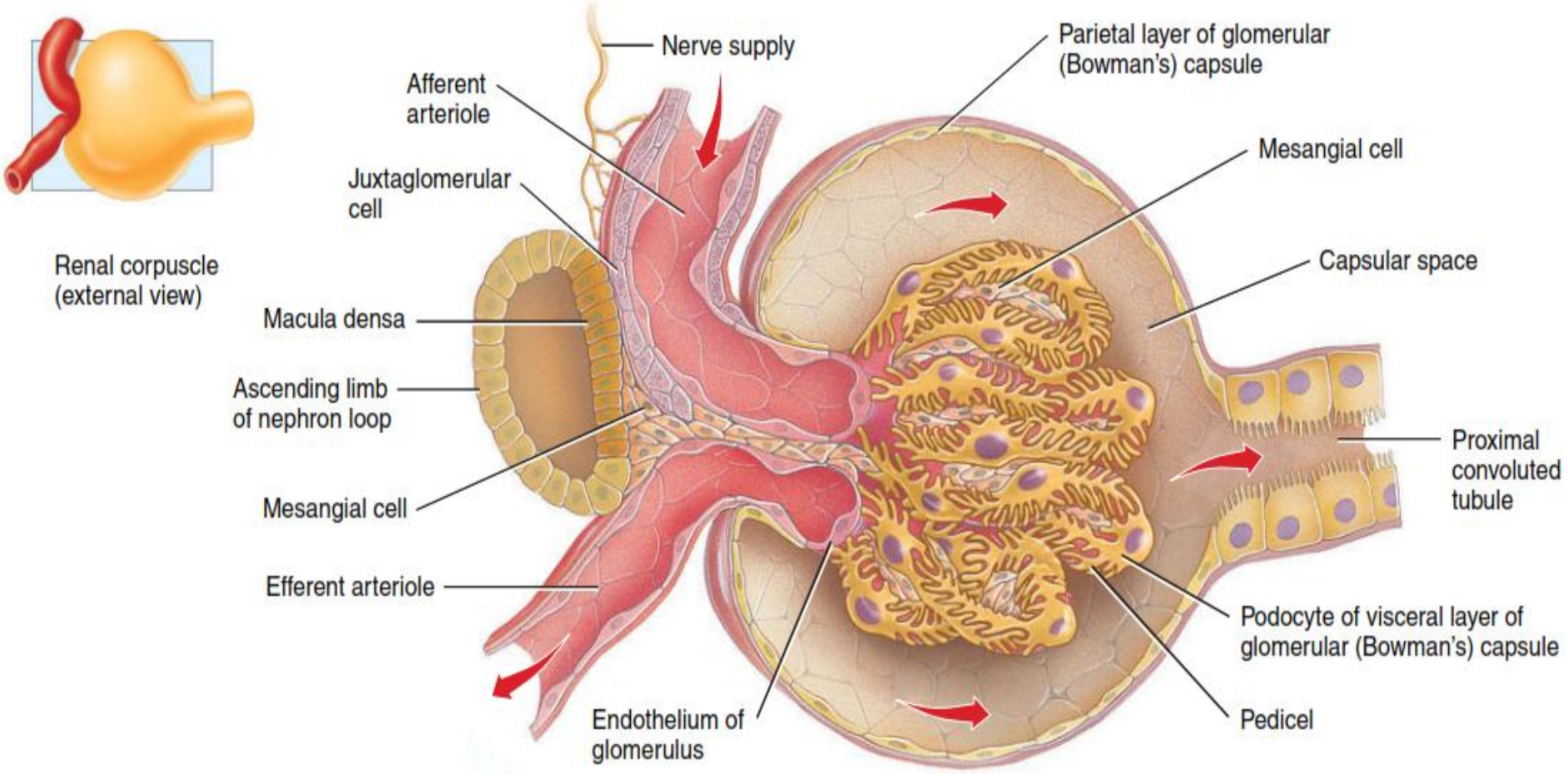


Fig 5: Renal corpuscle (internal view).

Renal Tubule and Collecting Duct

- The histology of the cells that form the renal tubule and collecting duct. In the PCT, the cells are simple cuboidal epithelial cells with a prominent brush border of microvilli on their apical surface.

Histological Features of the Renal Tubule and Collecting Duct

- These microvilli, like those of the small intestine, increase the surface area for reabsorption and secretion. The descending limb of the nephron loop and the first part of the ascending limb of the nephron loop (the thin ascending limb) are composed of simple squamous epithelium.
- The thick ascending limb of the nephron loop is composed of simple cuboidal to low columnar epithelium.
- In each nephron, the final part of the ascending limb of the nephron loop makes contact with the afferent arteriole serving that renal corpuscle.

- Because the columnar tubule cells in this region are crowded together, they are known as the **macula densa (macula -** spot**; densa -**dense).
- Alongside the macula densa, the wall of the afferent arteriole contains modified Smooth muscle fibers called **juxtaglomerular cells (JG).** Together with the macula densa, they Constitute the **juxtaglomerular apparatus (JGA). JGA play an important role to regulate the blood pressure.**
- When **blood volume and blood pressure decrease**, the walls of the afferent arterioles are stretched less, and the juxtaglomerular cells secrete the enzyme **Renin** into the blood. It affects renal physiology by 3 ways…….
- **It decreases the glomerular filtration rate by causing vasoconstriction of the afferent arterioles.**
- **It enhances reabsorption of Na^+, Cl^- and water in the PCT.**
- **It stimulates the adrenal cortex to release aldosterone which causes an increase in blood volume and blood pressure.**

- **DCT begins** a short distance past the **macula densa**. In the last part of the DCT and continuing into the collecting ducts, two different types of cells are present which have receptors for both antidiuretic hormone (ADH) and aldosterone, two hormones that regulate their functions.

Note: Surgical removal of one kidney, for example, stimulates hypertrophy (enlargement) of the remaining kidney, which eventually is able to filter blood at 80% of the rate of two normal kidneys.

FUNCTIONS OF THE KIDNEY

Formation of Urine

The kidneys form urine, which passes to the bladder for storage prior to excretion. The composition of urine reflects exchange of substances between the nephron and the blood in the renal capillaries. Waste products of protein metabolism are excreted, water and electrolyte levels are controlled and pH (acid–base balance) is maintained by excretion of hydrogen ions. There are three processes involved in the formation of urine:

1. **Glomerular filtration**
2. **Tubular reabsorption**
3. **Tubular secretion**

Glomerular filtration occurs in the renal corpuscle. Tubular reabsorption and tubular secretion occur all along the renal tubule and collecting duct.

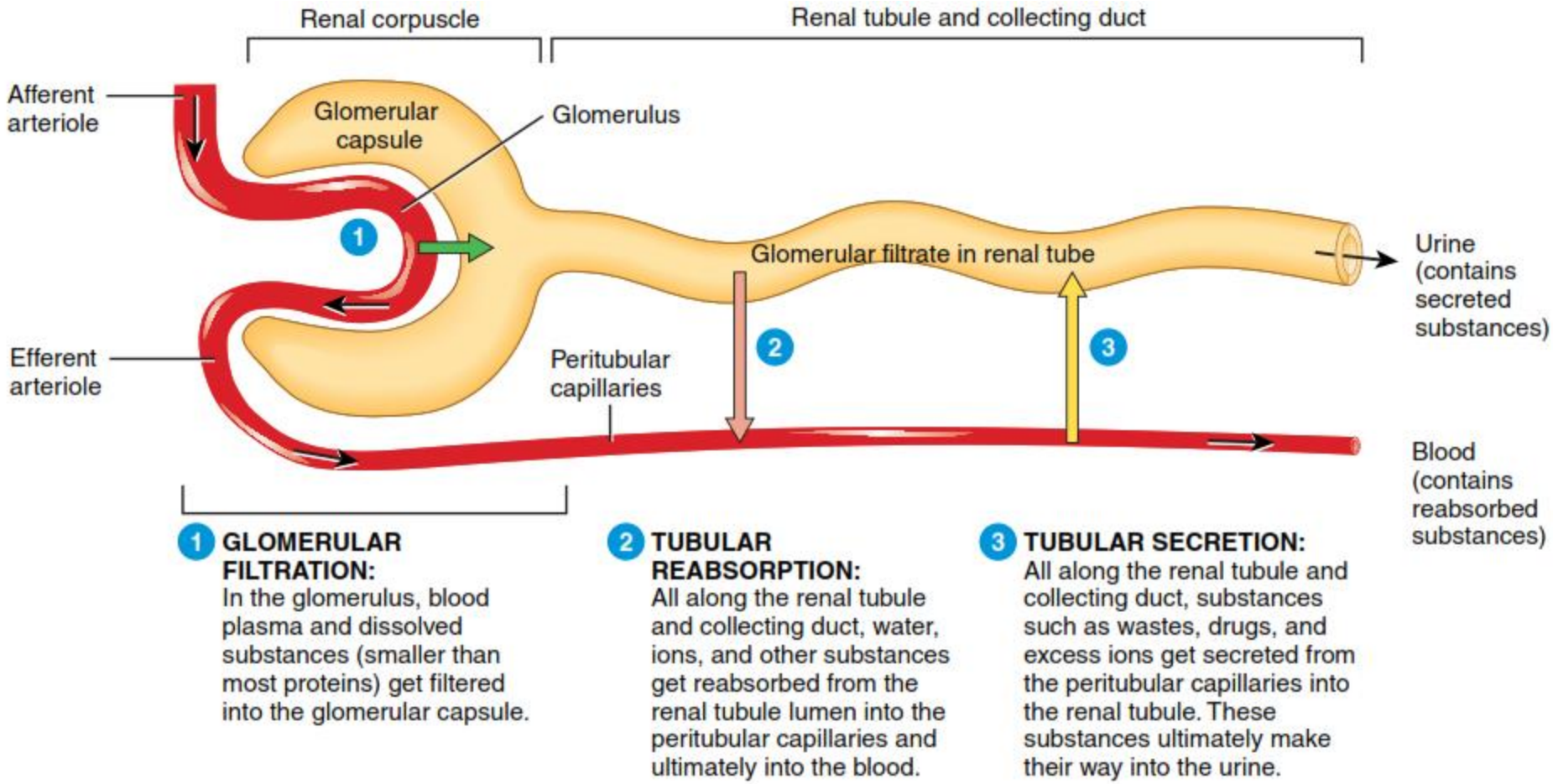


Fig 6: Relationship of a nephron's structure to its three basic functions: glomerular filtration, tubular reabsorption, and tubular secretion.

1. Glomerular filtration

- The fluid that enters the capsular space is called the **glomerular filtrate.**

- This takes place through the semipermeable walls of the glomerulus and glomerular capsule. Water and other small molecules readily pass through, although some are reabsorbed later.

- Blood cells, plasma proteins and other large molecules are too large to filter through and therefore remain in the capillaries. The filtrate in the glomerulus is very similar in composition to plasma with the important exceptions of plasma proteins and blood cells.

- **Note:** On average, the daily volume of glomerular filtrate in adults is 150 liters In females and 180 liters in males. More than 99% of the glomerular Filtrate returns to the bloodstream via tubular reabsorption, so only 1–2 liters is excreted as urine.

The Filtration Membrane

Together, the glomerular capillaries and the podocytes, which completely encircle the capillaries, form a leaky barrier known as the **Filtration membrane.** This sandwich like assembly permits filtration of water and small solutes but prevents filtration of most plasma proteins, blood cells, and platelets.
Substances filtered from the blood cross **three filtration barriers……..**

1. **Glomerular endothelial cells** are quite leaky because they have large **fenestrations** (pores) that measure 0.07–0.1 m in diameter. This size permits all solutes in blood plasma to exit glomerular capillaries but prevents filtration of blood cells and platelets.

2. **The basal lamina, a layer of acellular material between the** endothelium and the podocytes, consists of minute collagen fibers and proteoglycans in a glycoprotein matrix.

3. Extending from each podocyte are thousands of footlike processes termed **pedicels** (little feet) that wrap around glomerular capillaries. The spaces between pedicels are the **filtration slits.**

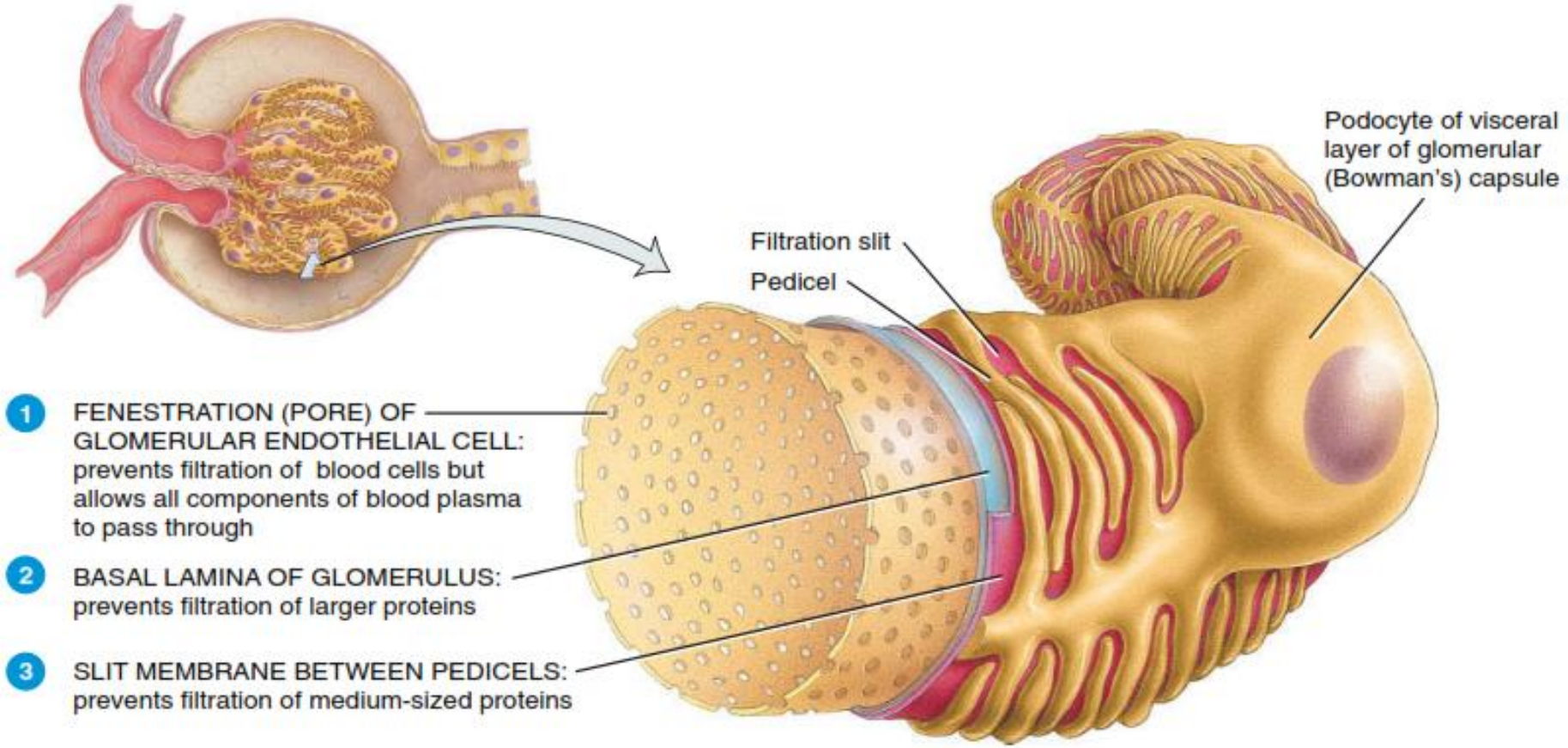


Fig 7: Details of filtration membrane.

Net Filtration Pressure

Filtration takes place because there is a difference between the blood pressure in the glomerulus and the pressure of the filtrate in the glomerular capsule. Because the efferent arteriole is narrower than the afferent arteriole.

Glomerular filtration depends on **three main pressures**.
One pressure promotes filtration and **two pressures oppose** filtration :

1. Glomerular blood hydrostatic pressure (GBHP) is the blood pressure in glomerular capillaries. Generally, GBHP is about 55 mmHg. It promotes filtration by forcing water and solutes in blood plasma through the filtration membrane.

2. Capsular hydrostatic pressure (CHP) is the hydrostatic pressure exerted against the filtration membrane by fluid already in the capsular space and renal tubule. CHP opposes filtration and represents a “back pressure” of about 15 mmHg.

3. Blood colloid osmotic pressure (BCOP), which is due to
the presence of proteins such as albumin, globulins, and fibrinogen in blood plasma, also opposes filtration. The average BCOP in glomerular capillaries is 30 mmHg.

Net filtration pressure (NFP), the total pressure that promotes filtration, is determined as follows:

NFP = GBHP - CHP - BCOP

By substituting the values just given, normal NFP may be calculated:

NFP = 55 mmHg - 15 mmHg - 30 mmHg
= **10 mmHg**

2. Selective Reabsorption

- Most reabsorption from the filtrate back into the blood takes place in the PCT, whose walls are lined with microvilli to increase surface area for absorption. Many substances are reabsorbed here, including some water, electrolytes and organic nutrients such as glucose. Some reabsorption is passive, but some substances e.g. glucose, are actively transported.
- Active transport takes place at carrier sites in the epithelial membrane, using chemical energy to transport substances against their concentration gradients
- Only 60-70% of filtrate reaches the medullary loop. Only 15–20% of the original filtrate reaches the DCT (quite dilute).
- Some ions, e.g. **sodium** and **chloride**, can be absorbed by both active and passive mechanisms depending on the site in the nephron.
- Some constituents of glomerular filtrate (e.g. **glucose, amino acids**) do not normally appear in urine because they are **completely reabsorbed** unless blood levels are excessive. Reabsorption of nitrogenous waste products, such as urea, uric acid and **creatinine** is very limited.

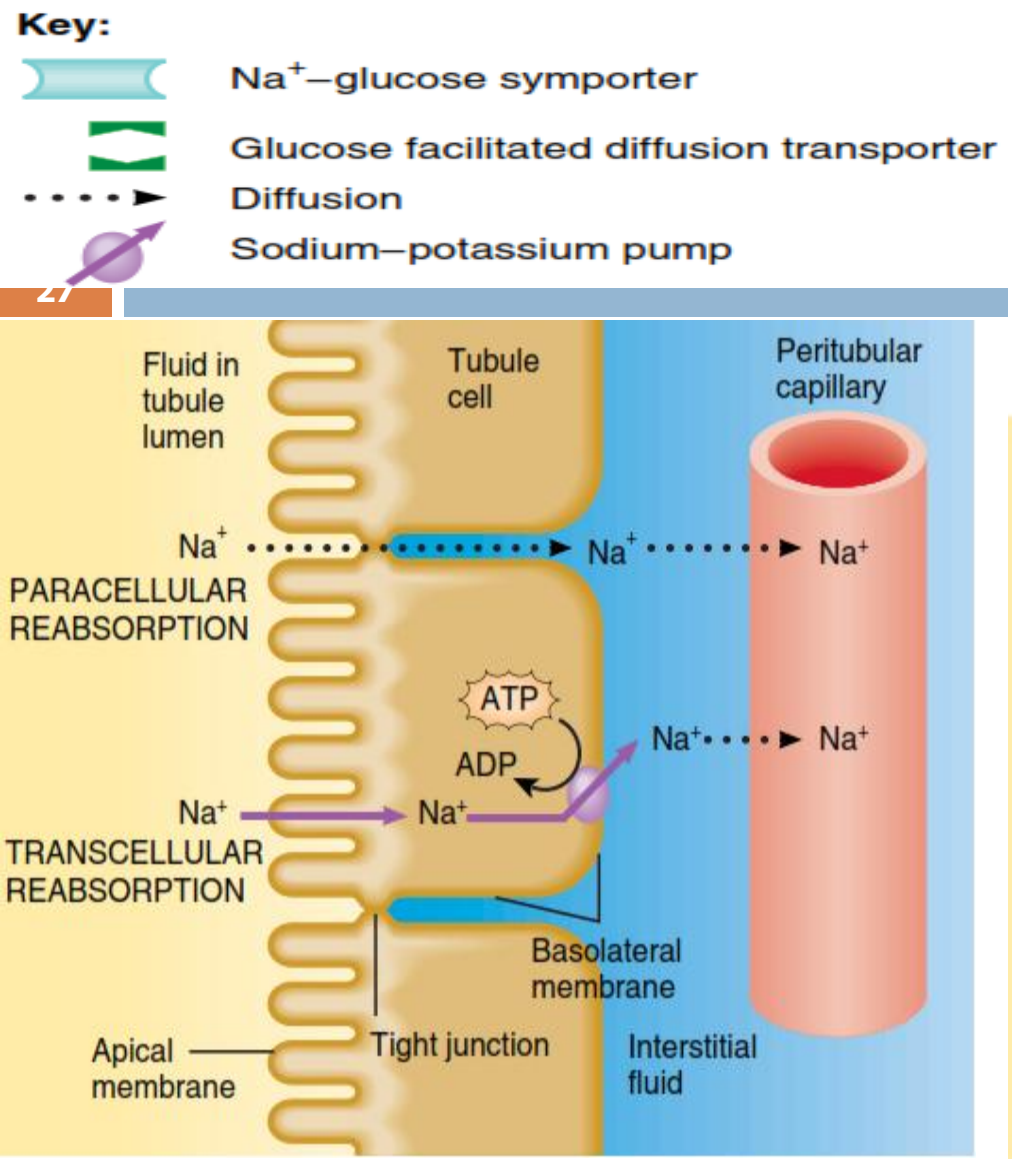


Fig 9: In paracellular reabsorption, water and solutes in tubular fluid return to the bloodstream by moving between tubule cells; in transcellular reabsorption, solutes and water in tubular fluid return to the bloodstream by passing through a tubule cell.

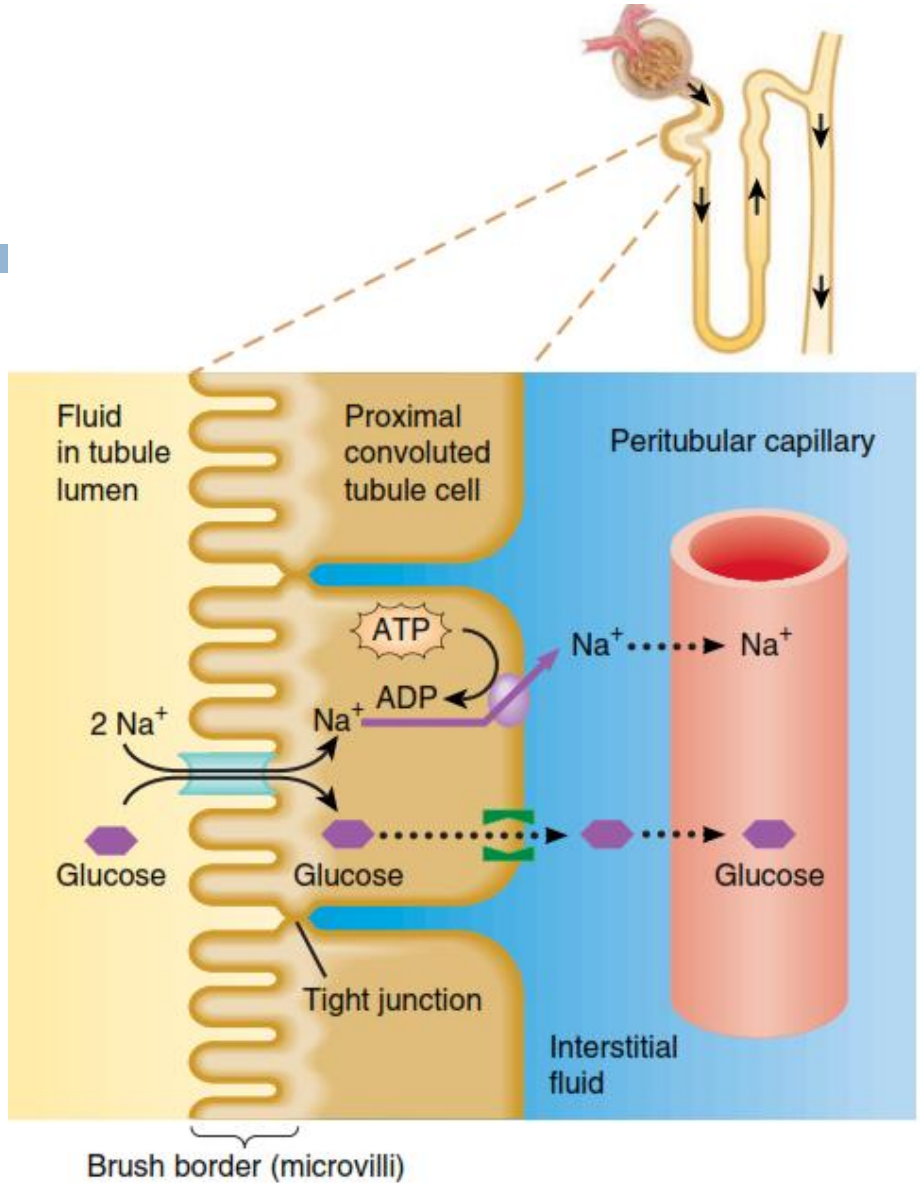


Fig 10: Reabsorption of glucose by Na-glucose symporters in cells of the proximal convoluted tubule (PCT).

Hormones That Influence Selective Reabsorption

Parathyroid hormone: This is secreted by the parathyroid glands and together with calcitonin from the thyroid gland regulates the reabsorption of calcium and phosphate from the DCT, so that normal blood levels are maintained. Parathyroid hormone increases the blood calcium level and calcitonin lowers it.

Antidiuretic hormone (ADH): This is secreted by the posterior pituitary. It increases the permeability of the distal convoluted tubules and collecting tubules, increasing water reabsorption. Secretion of ADH is controlled by a negative feedback system.

Aldosterone: Secreted by the adrenal cortex, this hormone increases the reabsorption of sodium and water, and the excretion of potassium. Secretion is regulated through a negative feedback system.

Atrial natriuretic peptide (ANP): This hormone is secreted by the atria of the heart in response to stretching of the atrial wall when blood volume is increased. It decreases reabsorption of sodium and water from the PCT and collecting ducts. Secretion of ANP is also regulated by a negative feedback system

3. Tubular Secretion

Filtration occurs as blood flows through the glomerulus. Substances not required and foreign materials, e.g. drugs including penicillin and aspirin, may not be entirely filtered out of the blood because of the short time it remains in the glomerulus. Such substances are cleared by secretion from the peritubular capillaries into the filtrate within the convoluted tubules. Tubular secretion of hydrogen ions (H^+) is important in maintaining normal blood pH.

Composition of urine

Urine is clear and amber in colour due to the presence of urobilin, a bile pigment altered in the intestine, reabsorbed then excreted by the kidneys. The specific gravity is between 1020 and 1030, and the pH is around 6 (normal range 4.5–8). A healthy adult passes from 1000 to 1500 mL per day. The volume of urine produced and the specific gravity vary according to fluid intake and the amount of solute excreted. The **constituents** of **urine** are:

Water 96% **Urea 2%** **Chlorides, Phosphates, Sulphates, Oxalates = 2%**
Uric acid, Creatinine, Ammonia, Sodium, Potassium = 2%

URETERS

- The ureters carry urine from the kidneys to the urinary bladder. They are about 25-30 cm long with a diameter of approximately 3 mm. The ureter is continuous With the funnel-shaped renal pelvis.

- It passes downwards through the abdominal cavity, behind the peritoneum in front of the psoas muscle into the pelvic cavity. Because of this arrangement, as urine accumulates and the pressure in the bladder rises, the ureters are compressed and the openings into the bladder are occluded. This prevents backflow of urine into the ureters (towards the kidneys) as the bladder fills and also during micturition, when pressure increases as the muscular bladder wall contracts.

Structure

The walls of the ureters consist of three layers of tissue…..

1. An outer covering of fibrous tissue, continuous with the fibrous capsule of the kidney.
2. A middle muscular layer consisting of interlacing smooth muscle fibres that form a functional unit round the ureter.
3. An inner layer of mucosa composed of transitional epithelium .

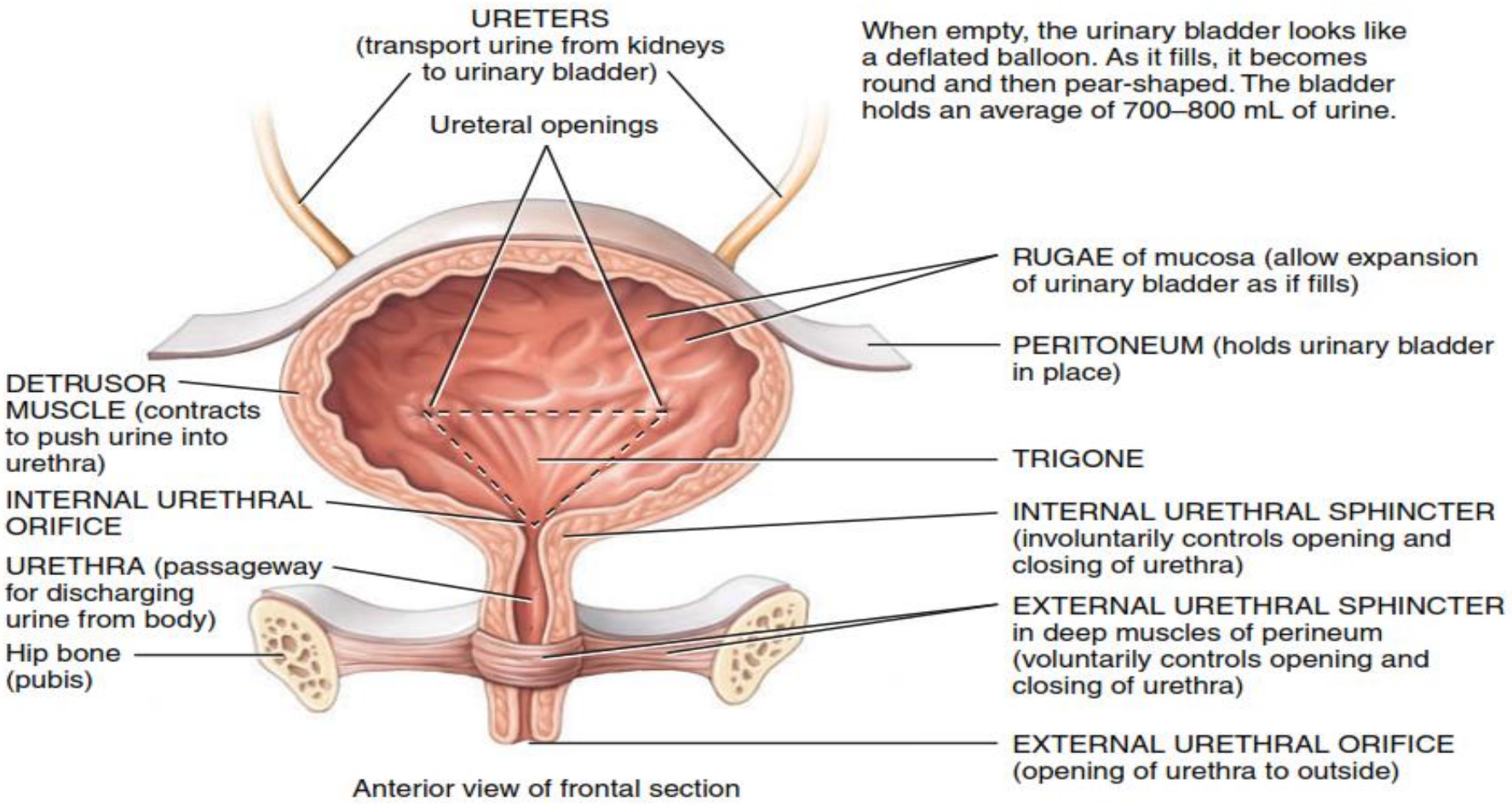


Fig 12: Ureters, urinary bladder, and urethra in a female.

Function of Ureters

- Peristalsis is an intrinsic property of the smooth muscle layer that propels urine along the ureter. Peristaltic waves occur several times per minute, increasing in frequency with the volume of urine produced, sending little spurts of urine along the ureter towards the bladder.

URINARY BLADDER

- The urinary bladder is a **reservoir for urine (capacity > 600 ml)**. It lies in the pelvic cavity and its size and position vary, depending on the volume of urine it contains. When distended, the bladder rises into the abdominal cavity.
- The bladder is roughly pear shaped, but becomes more balloon shaped as it fills with urine. The posterior surface is the base. The bladder opens into the urethra at its lowest point, the neck. **The bladder wall is composed of three layer…**

1. The outer layer of loose connective tissue
2. The middle layer consisting of interlacing smooth muscle fibres and elastic tissue : **Detrusor muscle**
3. The inner mucosa, composed of **transitional epithelium**

URETHRA

- **The urethra is a small tube leading from the internal urethral orifice in the floor of the urinary bladder to the exterior of the body**. In both males and females, the urethra is the terminal portion of the urinary system and the passageway for discharging urine from the body.
- In males, it discharges semen (fluid that contains sperm) as well.
- It is **longer** in the **male** than in the female. The male urethra is associated with both the urinary and reproductive systems. The female urethra is approximately 4 cm long and 6 mm in diameter.
- The external urethral orifice is guarded by the external urethral sphincter, which is under voluntary control.

THE MICTURITION REFLEX

- Discharge of urine from the urinary bladder, called **micturition**, is also known as urination or voiding.
- Micturition occurs via a combination of involuntary and voluntary muscle contractions. When the volume of urine in the urinary bladder exceeds 200-400 ml, pressure within the bladder increases considerably, and stretch receptors in its wall transmit nerve impulses into the spinal cord.
- These impulses propagate to the **micturition center** in sacral spinal cord segments S2 and S3 and trigger a spinal reflex called the **micturition reflex.**
- In this reflex arc, parasympathetic impulses from the micturition center propagate to the urinary bladder wall and internal urethral sphincter. The nerve impulses cause contraction of the detrusor muscle and relaxation of the internal urethral sphincter muscle. Simultaneously, the micturition center inhibits somatic motor neurons that innervate skeletal muscle in the external urethral sphincter.

- On contraction of the urinary bladder wall and relaxation of the sphincters, urination takes place. Urinary bladder filling causes a sensation of fullness that initiates a conscious desire to urinate before the micturition reflex actually occurs.
- In **infants**, accumulation of urine in the bladder activates **stretch receptors** in the bladder wall generating sensory (**afferent**) impulses that are transmitted to the spinal cord, where a **spinal reflex** is initiated. This stimulates involuntary contraction of the detrusor muscle and relaxation of the internal urethral sphincter, and expels urine from the bladder.
- The **cerebral cortex** can initiate micturition or delay its occurrence for a limited period.

Renin Angiotensin Aldosterone System (RAAS)

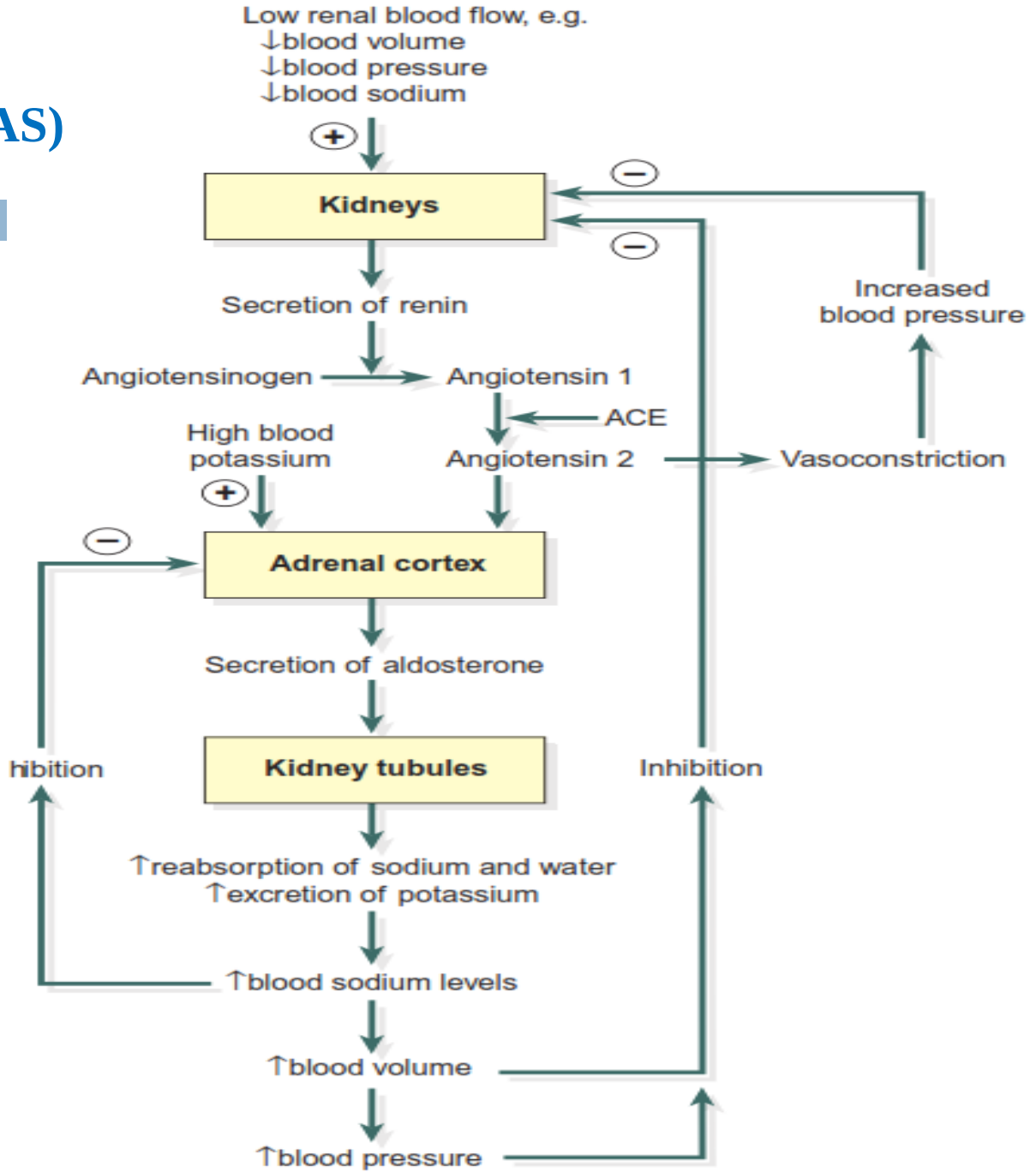


Fig 11: Negative feedback regulation of aldosterone secretion. ACE = angiotensin converting enzyme.

Diseases of the Kidneys

1. Glomerulonephritis (GN)

It is the **inflammatory** conditions of the **glomerulus.**

In many cases GN has an autoimmune component which leads to production of immune complexes that may lodge in the glomerular capillaries causing inflammation and impairment of Glomerular filtration.

Effects of GN

i. **Haematuria:** Usually **painless.** The **RBC** have **passed through** damaged glomeruli into the filtrate.
ii. **Asymptomatic proteinuria:** Damaged glomeruli may **allow protein to escape** from the blood into the filtrate.
iii. **Acute nephritis:** This is characterised by the **presence of:**
    oliguria (<400 mL urine/day in adults)
    hypertension
    haematuria
    uraemia

2. Nephrotic Syndrome

This is not a disease in itself but is an important feature of several kidney diseases. The main characteristics are:

- Marked proteinuria
- Hypoalbuminaemia
- Generalised oedema
- Hyperlipidaemia.

When glomeruli are damaged, the permeability of the glomerular membrane increases and plasma proteins pass through into the filtrate. Albumin is the main protein lost because it is the most common and is the smallest of the plasma proteins. When the daily loss exceeds the rate of production by the liver there is a significant fall in the total plasma protein level. The consequent low plasma osmotic pressure leads to widespread oedema and reduced plasma volume. This reduces the renal blood flow and stimulates the renin-angiotensin-aldosterone system, causing increased reabsorption of water and sodium from the renal tubules. The reabsorbed water further reduces the blood osmotic pressure and increases the oedema.

3. Diabetic Nephropathy

Diabetes causes damage to large and small blood vessels throughout the body In the kidney, these are known collectively as diabetic nephropathy or diabetic kidney and include:

- Progressive damage of glomeruli, proteinuria and
- Nephrotic syndrome
- Ascending infection leading to acute pyelonephritis
- Atheroma of the renal arteries and their branches leading to renal ischaemia and hypertension
- Chronic renal failure

4. Renal Calculi

Salts crystals present in urine occasionally precipitate and solidify into insoluble stones called renal calculi or kidney stones. They commonly contain crystals of calcium oxalate, uric acid, or calcium phosphate. Conditions leading to calculus formation include the ingestion of excessive calcium, low water intake, abnormally alkaline or acidic urine, and overactivity of the parathyroid glands.

5. Urinary Tract Infections

The term urinary tract infection (UTI) is used to describe either an infection of a part of the urinary system or the presence of large numbers of microbes in urine. UTIs are more common in females due to the shorter length of the urethra. Symptoms include painful or burning urination, urgent and frequent urination, low back pain, and bed-wetting. UTIs include *urethritis*, inflammation of the urethra; *cystitis*, inflammation of the urinary bladder; and *pyelonephritis*, inflammation of the kidneys.

6. Urinary Bladder Cancer

- It is three times more likely to develop in males than females.
- The disease is typically painless as it develops, but in most cases blood in the urine is a primary sign of the disease. Less often, people experience painful and/or frequent urination.
- It is frequently the result of a carcinogen. About half of cases are due to cigarettes smoking. The cancer also tends to develop in people those working in the leather, dye, rubber, aluminum industries and painters. Removal of bladder by surgery is the common and successful treatment strategy.

Thanks