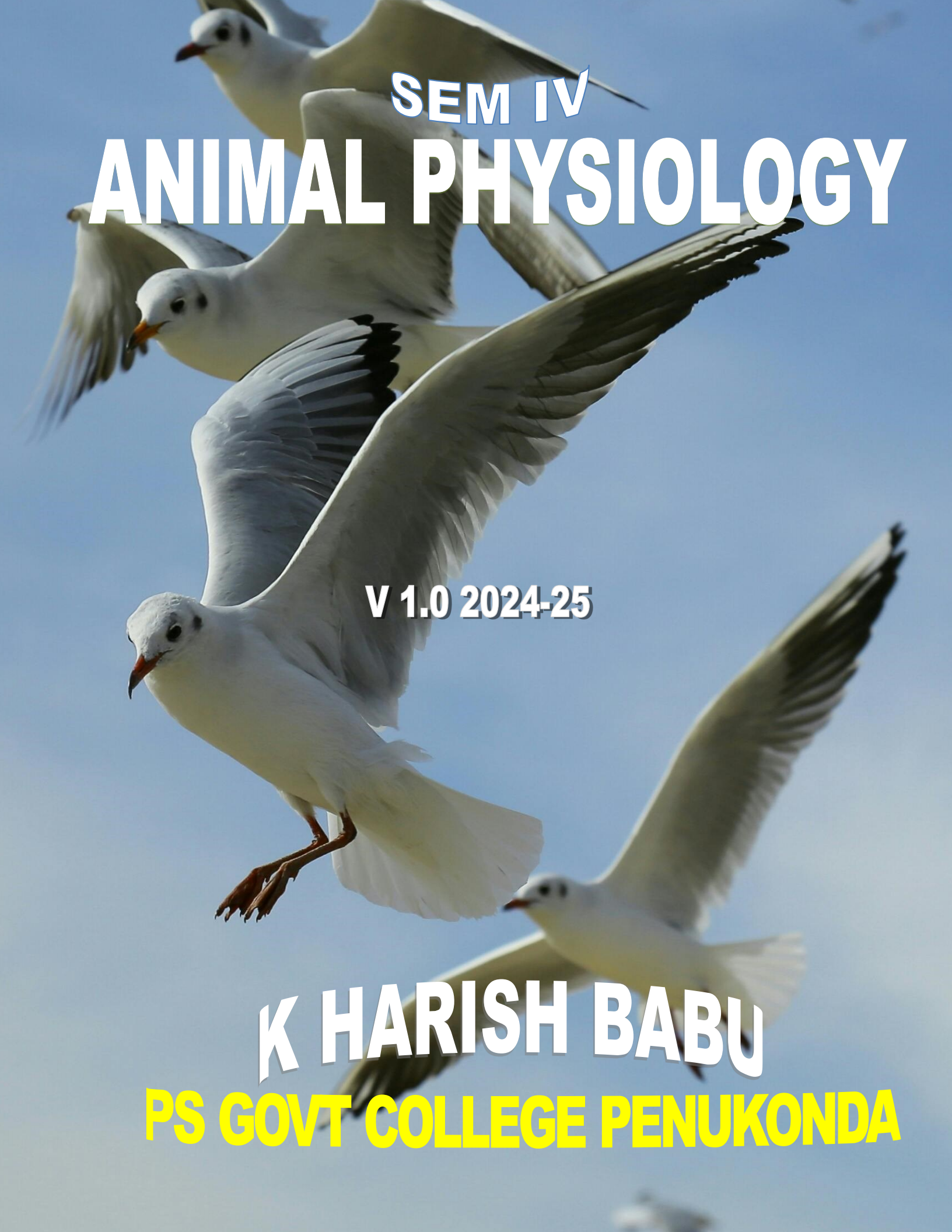

SEM IV

ANIMAL PHYSIOLOGY

V 1.0 2024-25

K HARISH BABU

PS GOVT COLLEGE PENUKONDA

SEMESTER-IV

COURSE 10: ANIMAL PHYSIOLOGY: LIFE SUSTAINING SYSTEMS

Theory Credits: 3 3 hrs/week

LEARNING OBJECTIVES

- To acquire knowledge of organ systems function.
- To develop the ability to integrate physiology from the cellular and molecular level to the organ system and organismic level of organization.
- To Effectively read, evaluate and communicate scientific information related to physiological processes in the body.
- To gain a deep knowledge of current topics in physiology.

LEARNING OUTCOMES

The overall course outcome is that the student shall develop deeper understanding of concepts of Physiology. This course will provide students with a deep knowledge in physiology by the completion of the course the graduate shall able to

- Understand the physiology of digestion and hormonal control of digestion
- Develop a comprehensive picture of respiratory physiology
- Acquire knowledge on the Renal physiology
- Understand the physiology of Nerve and muscle
- Understand the physiology of heart

SYLLABUS:

UNIT-I: Physiology of Digestion

1.1 Structural organization and functions of gastrointestinal tract and associated glands;

1.2 Vitamins & Mineral composition of food & Mechanical and chemical digestion of food;

1.3 Absorptions of carbohydrates, lipids, proteins, water, minerals and vitamins;

1.4 Hormonal control of secretion of enzymes in Gastrointestinal tract.

UNIT-II: Physiology of Respiration

2.1 Structural organization of Respiratory system, Mechanism of respiration, Control of respiration

2.2 Pulmonary ventilation; Respiratory volumes and capacities;

2.3 Transport of oxygen in blood and dissociation curves and the factors influencing it

2.4 Transport of Carbon dioxide in blood; dissociation curves and the factors influencing it, Carbon monoxide poisoning

UNIT-III: Renal Physiology

3.1 Structure of kidney and its functional unit

3.2 Mechanism of urine formation

3.3 Regulation of water balance

3.4 Regulation of acid-base balance

UNIT-IV: Physiology of exciting tissues

4.1 Neuron structure and types

4.2 Nerve impulse transmission- (Myelinated, Non-myelinated, synaptic)

4.3 Ultra structure of muscle

4.4 Molecular and chemical basis of muscle contraction

UNIT- V: Physiology of Heart

5.1 Structure of mammalian heart, Coronary circulation;

5.2 Structure and working of conducting myocardial fibers. Origin and conduction of cardiac impulses

5.3 Cardiac Cycle-Cardiac output and its regulation

5.4 Nervous and chemical regulation of heart rate. Blood pressure and its regulation

SEMESTER-IV

COURSE 10: ANIMAL PHYSIOLOGY: LIFE SUSTAINING SYSTEMS

Practical Credits: 1 2 hrs/week

LEARNING OBJECTIVES

- To acquire knowledge of anatomy of certain important organs.
- To develop the ability to test the biological sample like saliva and urine.
- To Effectively estimate the blood haemoglobin.
- To Acquire skill to use the sphygmomanometer in recording blood pressure.
- To observe the ECG

SYLLABUS:

1. Examination of sections of mammalian oesophagus, stomach, duodenum, ileum, rectum liver, trachea, lung, kidney
2. Study of activity of Salivary amylase under optimum condition
3. Qualitative tests for identification of Carbohydrates
4. Qualitative tests for identification of Proteins
5. Qualitative tests for identification of Fats
6. Urine test for sugar, albumin
7. Estimation of haemoglobin using Sahli's haemoglobinometer
8. Recording of blood pressure using a sphygmomanometer
9. Recording of frog's heart beat under in situ and perfused conditions
10. ECG observation- Spotting/identification of curves from the given ECG

RFERENCE WEB LINKS:

- https://www.vlab.co.in/participating-institute-amrita-vishwa-vidyapeetham
- https://library.csi.cuny.edu/oer/virtuallabs-simulations#anatomy
- https://www.labster.com/simulations?course-packages=animal-physiology
- http://www.zoologyresources.com/uploadfiles/books/dc64b77d8769325515d17c945e461b45.pdf
- https://physiology.elte.hu/gyakorlat/jegyzet/Physiology_Pactical_(2013).pdf

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1.1. Structural organization and functions of gastrointestinal tract and associated glands

The gastrointestinal (GI) tract and its associated glands have a complex structural organization and perform numerous functions essential for digestion, absorption, and overall homeostasis.

A. Structure of the GI Tract

1. Mouth: Includes the lips, teeth, tongue, and salivary glands. **Functions**: Ingestion, mechanical digestion (chewing), and chemical digestion (saliva containing amylase breaks down carbohydrates).

2. Pharynx and Esophagus: Muscular tubes connecting the mouth to the stomach. **Functions**: Transport food from the mouth to the stomach via peristalsis (coordinated muscle contractions).

3. Stomach: A muscular, J-shaped organ with four main regions: cardia, fundus, body, and pylorus. **Functions**: **Storage**: Temporarily stores ingested food; **Mechanical Digestion**: Churning and mixing food with gastric juices; **Chemical Digestion**: Secretes gastric acid (HCl) and enzymes (pepsin) to begin protein digestion; **Protection**: The acidic environment helps kill bacteria and pathogens.

4. Small Intestine: Composed of three sections: duodenum, jejunum, and ileum. Lined with villi and microvilli to increase surface area for absorption. **Functions**: **Digestion**: Continues the process of chemical digestion with enzymes from the pancreas and bile from the liver. **Absorption**: Major site for nutrient absorption into the bloodstream.

5. Large Intestine (Colon): Includes the cecum, ascending colon, transverse colon, descending colon, sigmoid colon, rectum, and anus. **Functions**: **Absorption**: Absorbs water, electrolytes, and vitamins produced by gut bacteria. **Formation of Feces**: Compacts and stores fecal matter before defecation.

B. Associated Glands

Salivary Glands: Major salivary glands include the parotid, submandibular, and sublingual glands. **Functions**: Produce saliva containing enzymes (amylase) for carbohydrate digestion, lubricate food, and aid in swallowing.

Liver: A large, lobed organ located in the upper right abdomen. **Functions**: **Bile Production**: Produces bile, which emulsifies fats to aid in their digestion; **Metabolism**: Processes nutrients absorbed from the small intestine; **Detoxification**: Detoxifies various metabolites and drugs; **Storage**: Stores glycogen, vitamins, and minerals.

Gallbladder: A small, pear-shaped sac located under the liver. **Functions**: Stores and concentrates bile produced by the liver, releasing it into the small intestine (duodenum) to aid in fat digestion.

Pancreas: A gland located behind the stomach with both endocrine and exocrine functions. **Functions**: **Exocrine**: Produces digestive enzymes (amylase, lipase, proteases) and bicarbonate, which are released into the duodenum to aid in digestion; **Endocrine**: Secretes hormones (insulin and glucagon) into the bloodstream to regulate blood glucose levels.

C. Functions of the GI Tract

1. **Ingestion**: Taking in food and liquids into the mouth.
2. **Secretion**: Release of digestive juices, enzymes, and mucus.
3. **Mixing and Propulsion**: Churning and moving food through the GI tract via peristalsis.
4. **Digestion**:
    - **Mechanical Digestion**: Physical breakdown of food (e.g., chewing, churning).
    - **Chemical Digestion**: Breakdown of food molecules into smaller molecules by enzymes.
5. **Absorption**: Transfer of nutrients from the lumen of the GI tract into the bloodstream or lymphatic system.
6. **Excretion**: Elimination of indigestible substances and waste products as feces.

1.2.1. Vitamins & Mineral composition of food

The vitamin and mineral composition of food varies widely depending on the type of food. Here is a summary of some common vitamins and minerals found in various food groups:

A. Vitamins

1. Vitamin A (Retinol, Beta-carotene):

Sources: Liver, fish oils, milk, eggs, leafy green vegetables, orange and yellow vegetables (e.g., carrots, sweet potatoes), and fruits (e.g., mangoes, apricots).

2. Vitamin D (Calciferol):

Sources: Fatty fish (e.g., salmon, mackerel, sardines), fish liver oils, fortified dairy products, and exposure to sunlight.

3. Vitamin E (Tocopherols and Tocotrienols):

Sources: Vegetable oils (e.g., sunflower, safflower), nuts, seeds, green leafy vegetables, and fortified cereals.

4. Vitamin K:

Sources: Green leafy vegetables (e.g., kale, spinach, broccoli), vegetable oils, and some fruits (e.g., blueberries, figs).

5. Vitamin C (Ascorbic Acid):

Sources: Citrus fruits (e.g., oranges, lemons), strawberries, kiwi, bell peppers, tomatoes, broccoli, and Brussels sprouts.

6. B Vitamins:

*** Thiamine (B1)**: Whole grains, pork, legumes, nuts, and seeds.

*** Riboflavin (B2)**: Milk, cheese, eggs, leafy green vegetables, lean meats, and fortified cereals.

*** Niacin (B3)**: Poultry, fish, beef, whole grains, and peanuts.

*** Pantothenic Acid (B5)**: Almost all foods, with high amounts in meat, whole grains, and broccoli.

*** Pyridoxine (B6)**: Poultry, fish, potatoes, chickpeas, bananas, and fortified cereals.

*** Biotin (B7)**: Eggs, almonds, spinach, and sweet potatoes.

*** Folate (B9)**: Leafy green vegetables, legumes, nuts, and fortified grains.

*** Cobalamin (B12)**: Meat, fish, poultry, eggs, and dairy products.

B. Minerals

Calcium: Sources: Dairy products (e.g., milk, cheese, yogurt), leafy green vegetables (e.g., kale, broccoli), fortified plant-based milks, and fish with edible bones (e.g., sardines, salmon).

Iron: Sources: Red meat, poultry, fish, lentils, beans, fortified cereals, and spinach.

Magnesium: Sources: Nuts (e.g., almonds, cashews), seeds (e.g., pumpkin, sunflower), whole grains, leafy green vegetables, and legumes.

Potassium: Sources: Bananas, oranges, potatoes, tomatoes, spinach, and beans.

Sodium: Sources: Table salt, processed foods, and naturally occurring in some vegetables and meats.

Zinc: Sources: Meat, shellfish, dairy products, legumes, nuts, and whole grains.

Phosphorus: Sources: Meat, poultry, fish, dairy products, nuts, and seeds.

Iodine: Sources: Iodized salt, seafood, dairy products, and eggs.

Selenium: Sources: Brazil nuts, seafood, meat, eggs, and whole grains.

1.2.2. Mechanical and chemical digestion of food

Digestion is the breakdown of food into particles/molecules small enough to pass into the blood.

Digestion in Mouth:

Mechanical breakdown begins in the mouth by chewing (teeth) and actions of the tongue.

Salivary glands secrete salivary amylase, an enzyme that begins the breakdown of starch into maltose. The action of amylase continues until the food reaches the stomach.

$$\textbf{Starch} \xrightarrow{\textbf{Salivary Amylase}} \boldsymbol{Maltose}$$

Saliva also contains an enzyme called lingual lipase, which breaks down fat in the stomach (acidic medium) but not in the mouth. Nearly 30% of fat in food is digested by this enzyme.

The Stomach: Food in the stomach mixes with gastric juice and becomes chyme.

i. Protein Digestion:

Hydrochloric acid activates pepsinogen and prorenin, converting them into pepsin and renin. Pepsin hydrolyzes proteins into peptides and polypeptides. In the presence of calcium, renin irreversibly changes the casein in milk into paracasein, which is then acted upon by pepsin.

$$\boldsymbol{Proteins} \xrightarrow{\boldsymbol{Pepsin}} \boldsymbol{Peptides}$$

Chyme, the acidic mixture of partially digested food and stomach acids, leaves the stomach and enters the small intestine.

ii. Fat Digestion:

Lipid (fat) digestion begins in the stomach with the aid of **lingual lipase** and **gastric lipase**. Due to the action of these enzymes, most short-chain fatty acids are digested and absorbed through the stomach wall into the portal vein.

Digestion in the Small Intestine:

The chyme from the stomach enters the small intestine and mixes with digestive secretions from the liver (bile), pancreas (pancreatic juice), and small intestine (intestinal juice). Bile and pancreatic juice neutralize the acidic chyme, converting it to an alkaline state.

i. Carbohydrates digestion

Pancreatic **amylase** and **α-glucosidase** digest carbohydrates into maltose, maltotriose and limit dextrins.

$$\boldsymbol{Polysaccharides}\ (\boldsymbol{Starch}) \xrightarrow{\boldsymbol{Amylase}} \boldsymbol{Disaccharides}$$

Small intestinal juice enzymes **Maltase, Dextrinase, Lactase, Sucrase** breaks down maltose, dextrins, lactose and sucrose respectively to form monosaccharides.

$$\boldsymbol{Maltose} + \boldsymbol{Maltotriose} \xrightarrow{\boldsymbol{Maltose}} \boldsymbol{Glucose} + \boldsymbol{Glucose}$$

$$\boldsymbol{Dextrins} \xrightarrow{\boldsymbol{\alpha-dextrinase}} \boldsymbol{Glucose}$$

$$\boldsymbol{Lactose} \xrightarrow{\boldsymbol{Lactase}} \boldsymbol{Glucose} + \boldsymbol{Galactose}$$

$$\boldsymbol{Sucrose} \xrightarrow{\boldsymbol{Sucrase}} \boldsymbol{Glucose} + \boldsymbol{Fructose}$$

At the end of carbohydrate digestion, glucose, fructose and/or galactose are formed.

ii. Protein digestion

The pancreatic juice contains inactive enzymes: **trypsinogen, chymotrypsinogen, procarboxy peptidases and nucleases**. Trypsinogen is activated by an enzyme, enterokinase, secreted by the intestinal mucosa into active trypsin, which in turn activates the other enzymes in the pancreatic juice.

Proteins, Proteoses and peptones (partially hydrolysed proteins) in the chyme reaching the intestine and are acted upon by the proteolytic enzymes of pancreatic juice as given below:

$$\boldsymbol{Proteins, Peptones, Proteoses} \xrightarrow[\boldsymbol{Carboxypeptidase}]{\boldsymbol{Trypsin/Chymotripsin}} \boldsymbol{Dipeptides}$$

Nucleases in the pancreatic juice, Nucleotidases and Nucleosidases of Intestinal juice acts on nucleic acids to form sugars and bases.

$$\boldsymbol{Nucleic\ acids} \xrightarrow{\boldsymbol{Nucleases}} \boldsymbol{Nucleotides} \xrightarrow{\boldsymbol{Nucleotidases}} \boldsymbol{Nucleosides} \xrightarrow{\boldsymbol{Nucleosidases}} \boldsymbol{Sugars} + \boldsymbol{Bases}$$

Dipeptidases of the intestinal juice acted on Dipeptides to form amino acids.

$$\boldsymbol{Dipeptides} \xrightarrow{\boldsymbol{Dipeptidases}} \boldsymbol{Amino\ acids}$$

iii. Fat digestion

The bile released into the duodenum contains bile pigments (bilirubin and biliverdin), bile salts, cholesterol, and phospholipids, but no enzymes. Bile aids in the emulsification of fats, breaking them down into very small micelles. Bile also activates lipases. Fats are broken down by lipases into di- and monoglycerides.

$$\boldsymbol{Fats} \xrightarrow{\boldsymbol{Lipases}} \boldsymbol{Diglycerides} \rightarrow \boldsymbol{Monoglycerides}$$

Intestinal Juice contains intestinal lipases which converts di and monoglycerides to fatty acids and glycerol.

$$\boldsymbol{Di} \ \& \ \boldsymbol{Monoglycerides} \xrightarrow{\boldsymbol{Lipases}} \boldsymbol{Fatty\ acids + Glycerol}$$

No significant digestive activity occurs in the large intestine. The functions of the large intestine include the absorption of some water, minerals, and certain drugs, as well as the secretion of mucus, which helps in adhering the waste (undigested) particles together and lubricating them for easy passage.

The undigested, unabsorbed substances, called feces, enter the cecum of the large intestine through the ileocecal valve, which prevents the backflow of fecal matter. Feces are temporarily stored in the rectum until defecation.

1.3 Absorptions of carbohydrates, lipids, proteins, water, minerals and vitamins

Absorption is the process by which the nutrients are circulated through the body by blood and lymph and supplied to all cells in the body according to their needs. Maximum absorption occurs in the small intestine. The inner surface of the intestine has circular folds called microvilli (brush boarder), that increases the surface area for absorption. Each villus has a capillary network supplied by a small arteriole. Absorbed substances pass through the brush border into the capillary via passive, active or facilitated transport mechanisms.

i. Absorption of monosaccharides and amino acids:

* Small amounts of monosaccharides like glucose, amino acids and some of electrolytes like chloride ions are generally absorbed by **simple diffusion**. The passage of these substances into the blood depends upon the concentration gradients.

* However, some of the substances like fructose and some amino acids are absorbed with the help of the carrier ions like Na^+. This mechanism is called the **facilitated transport**.

* Various nutrients like amino acids, monosaccharides like glucose, galactose, electrolytes (like Na^+) are absorbed into the blood by **active transport** which occurs against the concentration gradient and hence requires energy.

ii. Fat absorption:

Fat absorption in the intestine is a complex process that involves several steps. First, fats are emulsified and broken down into smaller droplets by bile salts and pancreatic enzymes. Then, the droplets are coated with a layer of protein and phospholipids to form **micelles**, which can be absorbed by the intestinal cells. Once inside the cells, the fats are reassembled into triglycerides and packaged into **chylomicrons**, which are transported into the lymph vessel (lacteals) in the villi, of the lymphatic system and then into the bloodstream. From there, the chylomicrons deliver the fats to various tissues throughout the body for energy or storage.

iii. Water and vitamin absorption:

Transport of water depends upon the osmotic gradient. **Fat-Soluble Vitamins (A, D, E, K)**: Absorbed along with dietary fats in the small intestine, incorporated into micelles, then into chylomicrons for transport via the lymphatic system. **Water-Soluble Vitamins (B-complex, C)** Absorbed via specific transport mechanisms in the small intestine. Vitamin B12 requires intrinsic factor (produced by the stomach) for absorption in the ileum.

iv. Minerals absorption:

Calcium absorbed in the small intestine via active transport regulated by vitamin D (active form: calcitriol) and passive diffusion. Iron absorbed in the duodenum. Heme iron (from animal sources) is absorbed more efficiently than non-heme iron (from plant sources). Non-heme iron absorption is enhanced by vitamin C and reduced by certain plant compounds (e.g., phytates, polyphenols). Sodium absorbed via various transport mechanisms including cotransport with glucose and amino acids. Potassium absorbed mainly via passive diffusion. Chloride absorbed through chloride-bicarbonate exchange and sodium cotransport.

1.4 Hormonal control of secretion of enzymes in Gastrointestinal tract.

The **hormonal control of enzyme secretion** in the gastrointestinal (GI) tract is a complex and highly regulated process involving several key hormones. These hormones are produced by the cells in the stomach, intestines, and other parts of the GI tract, and they work to ensure that digestive enzymes are secreted at the right time and in the right amounts to facilitate digestion. Here are the primary hormones involved in this process:

- **Gastrin** is produced in the stomach when it is stretched. It stimulates the release of gastric juice rich in pepsin and hydrochloric acid.
- **Enterogastrone:** It is secreted by the duodenal epithelium. It inhibits gastric secretion and motality. It slows gastric contraction.
- **Secretin:** It is secreted by the epithelium of duodenum. It releases bicarbonates in the pancreatic juice. It increases secretion of bile. It decreases gastric secretion and motality.
- **Cholecystokinin pancreozymin (CCK-PZ):** This hormone is secreted by the epithelium of entire small intestine. It stimulates the gall bladder to release bile and pancreas to secrete and release digestive enzymes in the pancreatic juice.
- **Duocrmin:** It is secreted by the duodenal epithelium and stimulates the Brunner's glands to release mucus and enzymes into the intestinal juice.
- **Enterocrinin:** It is secreted by the epithelium of entire small intestine. It stimulates the crypts of Lieberkuhn to release enzymes into the intestinal juice.
- **Pancreatic Polypeptide (PP):** It is secreted by the pancreatic polypeptide cells (also ailed PP cells or F-cells) of islets of Langerhans. It inhibits the release of pancreatic juice from the pancreas.

2.1.1. Structural organization of Respiratory system

The respiratory system is a complex network of organs and tissues responsible for the exchange of gases between the body and the environment. It consists of various structures, each with specific functions contributing to the process of respiration.

Upper Respiratory Tract

1. **Nose**:
    - Acts as the primary entrance for air into the respiratory system.
    - Contains nasal passages lined with mucous membranes and cilia, which help filter, warm, and humidify incoming air.
2. **Nasal Cavities**:
    - Located within the nose, these cavities are divided by the nasal septum and lined with mucous membranes and cilia.
    - The nasal conchae (turbinates) increase surface area for air conditioning and help redirect airflow.
3. **Pharynx**:
    - A muscular tube at the back of the throat that serves as a passageway for both air and food.
    - Divided into three parts: nasopharynx (above the soft palate), oropharynx (behind the mouth), and laryngopharynx (above the larynx).
4. **Larynx**:
    - Also known as the voice box, the larynx is located between the pharynx and the trachea.
    - Contains vocal cords that vibrate to produce sound during speech.

ii. Lower Respiratory Tract

5. **Trachea**:
    - A rigid tube composed of cartilage rings, extending from the larynx to the bronchi.
    - Lined with ciliated epithelium and mucus-producing cells to trap and remove debris from the airways.
6. **Bronchial Tree**:
    - Consists of the bronchi, bronchioles, and alveoli.
    - Bronchi branch off from the trachea and further divide into smaller bronchioles, eventually leading to the alveoli.
7. **Bronchi**:
    - Primary bronchi branch off from the trachea and enter each lung.
    - They divide into secondary bronchi, which further divide into tertiary bronchi and smaller bronchioles.

8. **Bronchioles**:
    - Small airway branches that lack cartilage and contain smooth muscle.
    - They regulate airflow and distribute air to the alveoli.
9. **Alveoli**:
    - Tiny air sacs located at the end of the bronchioles where gas exchange occurs.
    - Surrounded by capillaries, allowing for the diffusion of oxygen into the bloodstream and carbon dioxide out of the bloodstream.

iii. Pleural Cavity and Diaphragm

10. **Pleural Cavity**:
    - Surrounds each lung and is lined by the pleura, a thin membrane that reduces friction between the lungs and the chest wall during breathing.
11. **Diaphragm**:
    - A dome-shaped muscle located below the lungs that plays a crucial role in breathing.
    - Contraction and relaxation of the diaphragm alter the volume of the thoracic cavity, causing inhalation and exhalation.

iv. Functional Integration

The structural components of the respiratory system work together to facilitate the processes of ventilation (breathing), gas exchange, and regulation of blood pH. The upper respiratory tract filters, warms, and humidifies air, while the lower respiratory tract facilitates gas exchange in the alveoli. The diaphragm and other respiratory muscles control airflow and lung volume, enabling efficient breathing.

2.1.2. Mechanism of Respiration

The entire mechanism of respiration involves following steps:-

1. Breathing (Pulmonary ventilation):

The mechanism of breathing involves the **inspiration** and **expiration** of air with the movement of the diaphragm and intercostal muscles. During inhalation, external intercostal muscles contract. At the same time, the diaphragm contracts and flattens. These actions increase the volume of the thoracic (chest) cavity, and the air (oxygen) is forced into the lungs. On the contrary, exhalation occurs when the thoracic cavity is reduced, and the air (carbon dioxide) is expelled out.

2. External Respiration:

It involves the diffusion of oxygen and carbon dioxide between the alveoli and the pulmonary capillaries due to the partial pressure difference. The solubility of oxygen in the blood is not high, hence there is a big difference in the partial pressure of oxygen in the alveoli versus in the blood of the pulmonary capillaries. The partial pressure of oxygen in the alveoli is about 104mmHg, and it is about 40mmHg in the capillary blood. The

difference is about 64mmHg. This strong pressure gradient forces oxygen from the alveoli into the blood across the respiratory membrane.

The partial pressure of carbon dioxide between the alveolar air and the blood of the capillary is also different. However, the partial pressure difference is far less than that of oxygen, about 5mmHg. The partial pressure of carbon dioxide in the capillary blood is about 45mmHg and, in the alveoli, it is about 40mmHg. It is because the solubility of carbon dioxide in the blood is much greater than that of oxygen.

3. Internal Respiration:

The gaseous exchange process that takes place in the tissues is called internal respiration. The oxygen after dissociating from the haemoglobin reaches the tissues or cells. The oxygen causes the complete breakdown of the glucose molecules (food) into carbon, water, and energy. The energy remains stored in the form of ATP (Adenosine Triphosphate) and is further utilized to perform several living activities. This mechanism of internal respiration is also named **Cellular Respiration.**

4. Transport of Oxygen:

Oxygen is carried through the blood from the respiratory organs to the different tissues. Oxygen can be carried in two forms:

* **Through plasma**: Only about 3 per cent is dissolved in plasma.

* **Through RBCs**: Haemoglobin transports about 97 per cent of the oxygen in the form of oxyhemoglobin.

5. Transport of Carbon Dioxide:

Carbon dioxide is transported in the blood in the below-mentioned three ways:

a. In dissolved state: About 5−7% of carbon dioxide is transported, being dissolved in the plasma of blood.

b. In the form of bicarbonate (70%): 70% of the Carbon dioxide produced by the tissues diffuses passively into the blood and passes into the red blood corpuscles, where it reacts with water to form carbonic acid (H_2CO_3) and transported in the form of Bicarbonate form.

c. In carbaminohemoglobin form (23%):

Carbon dioxide reacts directly with the amine radicals (NH_2) of haemoglobin molecules and forms a carbaminonhemoglobin molecule. $CO_2 + NHbNH_2 \rightarrow HbNH.COOH$

2.1.3. Control of Respiration

Respiration is controlled by the **medulla oblongata** and the **pons**, which are parts of the brainstem. These areas contain specialized neurons that regulate the rate and depth of breathing by sending signals to the diaphragm and the intercostal muscles, prompting them to contract.

i. The medullary inspiratory center, located in the **medulla oblongata**, generates rhythmic nerve impulses that stimulate contraction of the inspiratory muscles (diaphragm and external intercostal muscles). Normally, expiration occurs when these muscles relax, but when breathing is rapid, the inspiratory center facilitates expiration by stimulating the expiratory muscles (internal intercostal muscles and abdominal muscles).

ii. The pheumotaxic area, located in the **pons**, **inhibits the inspiratory center**, limiting the contraction of the inspiratory muscles, and preventing the lungs from overinflating.

iii. The apneustic area, also located in the **pons**, **stimulates the inspiratory center**, prolonging the contraction of inspiratory muscles.

The respiratory centers are influenced by stimuli received from the following three groups of sensory neurons:

i. Central chemoreceptors (*nerves of the central nervous system*):

They are located in **the medulla oblongata**, monitor the chemistry of cerebrospinal fluid. When CO_2 from the plasma enters the cerebrospinal fluid, it forms HCO_3^- and H^+, and the pH of the fluid drops (becomes more acidic). In response to the decrease in pH, the central chemoreceptors stimulate the respiratory center to increase the inspiratory rate.

ii. Peripheral chemoreceptors (*nerves of the peripheral nervous system*):

They are located in aortic bodies in the **wall of the aortic arch** and in carotid bodies in the **walls of the carotid arteries**, monitor the chemistry of the blood. An increase in pH or pCO_2, or a decrease in pO_2, causes these receptors to stimulate the respiratory center.

iii. Stretch receptors:

These are located in the **walls of bronchi and bronchioles** are activated when the lungs expand to their physical limit. These receptors signal the respiratory center to discontinue stimulation of the inspiratory muscles, allowing expiration to begin. This response is called the **inflation (Hering-Breur) reflex.**

2.2.1 Pulmonary Ventilation

Pulmonary ventilation, commonly referred to as breathing, is the process of air moving into and out of the lungs. It's a vital function of the respiratory system, facilitating the exchange of gases (oxygen and carbon dioxide) between the lungs and the external environment.

Pulmonary ventilation consists of two main phases: inspiration (inhalation) and expiration (exhalation). Here's an overview of each phase:

1. Inspiration (Inhalation):

i. Mechanism: During inspiration, the diaphragm and external intercostal muscles contract.

*** Diaphragm Contraction**: The diaphragm, a dome-shaped muscle located at the base of the thoracic cavity, contracts and moves downward.

*** External Intercostal Muscle Contraction**: The external intercostal muscles, located between the ribs, contract, lifting the ribcage upward and outward.

ii. Thoracic Cavity Expansion: Contraction of the diaphragm and external intercostal muscles increases the volume of the thoracic cavity.

iii. Lung Expansion: The increase in thoracic cavity volume causes the lungs to expand passively due to their elastic properties.

iv. Decreased Intrapulmonary Pressure: As the lungs expand, the intrapulmonary pressure decreases, creating a pressure gradient between the atmosphere and the alveoli.

v. Airflow into the Lungs: Air flows from the higher-pressure environment outside the body into the lower-pressure environment inside the lungs until the pressure is equalized.

2. Expiration (Exhalation):

i. Mechanism: Expiration can be either passive (during resting conditions) or active (during forced breathing).

*** Passive Expiration**: In passive expiration, the diaphragm and external intercostal muscles relax.

*** Active Expiration**: During forced expiration, additional muscles such as the internal intercostal muscles and abdominal muscles contract to further decrease thoracic cavity volume.

ii. Thoracic Cavity Contraction: Relaxation of the diaphragm and external intercostal muscles decreases the volume of the thoracic cavity.

iii. Lung Recoil: The elastic recoil of the lungs, along with the inward pull of the chest wall, causes the lungs to passively recoil.

iv. Increased Intrapulmonary Pressure: As the thoracic cavity volume decreases, the intrapulmonary pressure increases.

v. Airflow Out of the Lungs: Air flows from the higher-pressure environment inside the lungs to the lower-pressure environment outside the body until pressure is equalized.

Pulmonary ventilation is essential for maintaining adequate gas exchange and oxygenating the blood to support cellular metabolism.

2.2.2. Respiratory Volumes and Capacities

Respiratory volumes and capacities are measurements used to describe different aspects of pulmonary ventilation. These measurements provide valuable information about lung function and are often assessed through pulmonary function tests. Here's an overview of some common respiratory volumes and capacities:

A. Respiratory Volumes:

1. Tidal Volume (TV): The volume of air inspired or expired during normal quiet breathing, typically around 500 milliliters (ml) in adults.

2. Inspiratory Reserve Volume (IRV): The maximum volume of air that can be forcibly inspired beyond the tidal volume, typically around 2,500-3,000 ml.

3. Expiratory Reserve Volume (ERV): The maximum volume of air that can be forcibly expired beyond the tidal volume, typically around 1,000-1,200 ml.

4. Residual Volume (RV): The volume of air remaining in the lungs after maximal expiration, serving to keep the alveoli inflated and prevent lung collapse, typically around 1,200 ml.

B. Respiratory Capacities:

1. Inspiratory Capacity (IC): The total volume of air that can be inspired after a normal expiration, calculated as the sum of tidal volume and inspiratory reserve volume: [IC = TV + IRV]

2. Functional Residual Capacity (FRC): The volume of air remaining in the lungs after a normal expiration, calculated as the sum of expiratory reserve volume and residual volume: [FRC = ERV + RV]

3. Vital Capacity (VC): The maximum volume of air that can be exhaled after maximal inspiration, representing the total capacity for gas exchange, calculated as the sum of inspiratory reserve volume, tidal volume, and expiratory reserve volume: [VC = IRV + TV + ERV]

4. Total Lung Capacity (TLC): The total volume of air contained in the lungs after maximal inspiration, calculated as the sum of inspiratory reserve volume, tidal volume, expiratory reserve volume, and residual volume: [TLC = IRV + TV + ERV + RV]

2.3. Transport of oxygen in blood and dissociation curves and the factors influencing it

2.3.1. Transport of oxygen

Oxygen is transported in the blood in two ways:

i. About **3%** of O_2 is carried through the **plasma** in a dissolved state.

ii. Almost **97%** of oxygen is bound to hemoglobin in red blood cells (RBCs) and transported to the tissues. Hemoglobin is composed of two alpha and two beta subunits. Each subunit surrounds a central heme group containing iron, which binds one oxygen molecule. Thus, each hemoglobin molecule can bind four oxygen molecules, forming oxyhemoglobin.

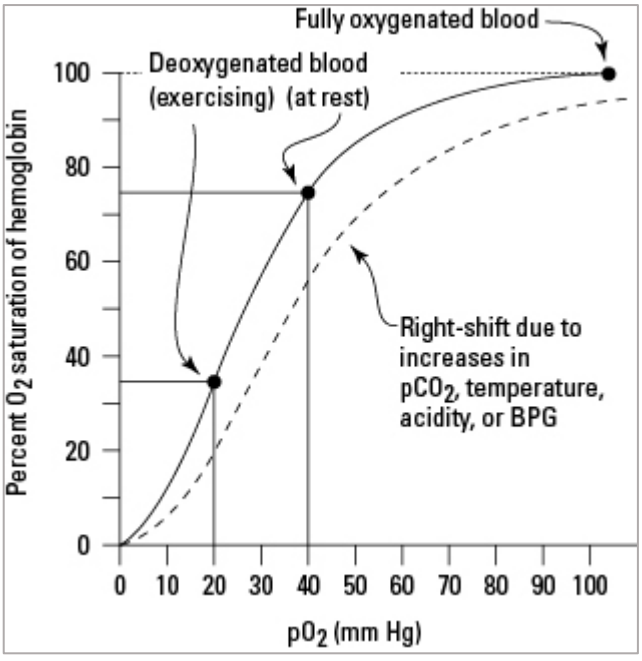
Hemoglobin undergoes a change in shape based on the number of oxygen molecules bound to it. This change in shape also affects its affinity for oxygen. As the number of oxygen molecules bound to hemoglobin increases, its affinity for oxygen also increases. This phenomenon is known as **cooperativity**. When no oxygen is bound, hemoglobin is in the **Tense State** (T-state), with a low affinity for oxygen. As oxygen binds to hemoglobin, it transitions to the **Relaxed State** (R-state), which has a higher affinity for oxygen.

In the **alveoli**, there is high **pO_2**, oxygen binds to Hb and forms oxyhemoglobin (HbO_2) (oxygen loading). **$Hb + O_2 \leftrightarrow Hb - O_2$**. When **oxyhaemoglobin** reaches a tissue with a low pO_2, it will dissociate into oxygen and haemoglobin (oxygen unloading).

2.3.2 The oxygen-hemoglobin dissociation curve:

The attachment of oxygen to hemoglobin is primarily determined by the partial pressure of oxygen (pO2). When the % saturation of hemoglobin with oxygen is plotted against the pO2, a sigmoid curve is formed. This curve is known as the oxygen dissociation curve.

Hemoglobin is considered 100% saturated when each hemoglobin molecule carries four oxygen molecules, forming oxyhemoglobin. It is said to be 50% saturated when, on average, each hemoglobin molecule carries two oxygen molecules.

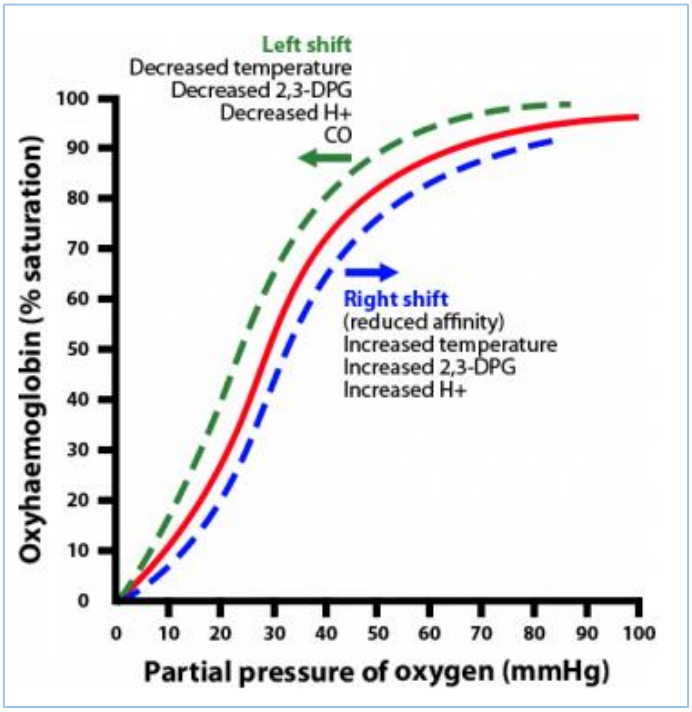


About 97% of hemoglobin is saturated in systemic arteries, where the pO_2 is approximately 95 mmHg. When the pO_2 decreases to 40 mmHg, the typical pO_2 of tissue cells at rest, hemoglobin saturation drops to around 75%. This means that approximately 22% of the oxygen transported by oxyhemoglobin is delivered to resting tissues, with the remaining oxygen held in reserve within the blood itself.

In inactive tissues such as skeletal muscles, where the pO_2 is much lower than 40 mmHg, there is a greater "unloading tension," leading to a significant release of oxygen from hemoglobin. For instance, at a pO_2 of 20 mmHg, the hemoglobin saturation percentage drops to only 35%. 50% haemoglobin is saturated at P50 (oxygen tension). The normal P50 is 26.7 mmHg.

2.3.3. Factors Affecting Oxygen dissociation curves

Various factors can affect the affinity of haemoglobin for oxygen:



i. pH / pCO_2:

When H^+ / pCO_2 increases and pH decreases, Hb enters the T state and its affinity for oxygen decreases. This is known as the **Bohr Effect**. Inversely, when H^+ / pCO_2 decreases and pH increases, the affinity of haemoglobin for oxygen increases.

ii. 2,3-diphosphoglycerate (2,3DPG):

2,3-DPG is produced in RBC during glycolysis. 2,3-DPG binds to the **beta** chains of haemoglobin. Increased levels of 2,3-DPG results in it binding to haemoglobin, **decreasing** the affinity of haemoglobin for oxygen. Conversely, when there are decreased 2,3-DPG levels, e.g states of decreased tissue metabolism, there are fewer 2,3-DPG molecules to bind to haemoglobin. This means there are more opportunities for it to bind and therefore it has a higher affinity for oxygen.

iii. Temperature

At increased temperatures, for example in active muscles, there is an increase in heat production which **decreases** the affinity of haemoglobin for oxygen. At decreased temperatures, e.g. decreased metabolic states, the reduced heat production means the affinity of haemoglobin for oxygen increases.

iv. Carbon Monoxide

Hemoglobin binds with carbon monoxide 240 times more readily than with oxygen, and therefore the presence of carbon monoxide can interfere with the hemoglobin's acquisition of oxygen. In addition to lowering the potential for hemoglobin to bind to oxygen, carbon monoxide also has the effect of shifting the curve to the left.

The affinity of haemoglobin for oxygen also results in a shift in the **oxygen-haemoglobin dissociation curve**. An **increase** in oxygen affinity results in the curve shifting to the **left**, whereas a **decrease** in oxygen affinity results in the curve shifting to the **right**.

2.4.1. Transport of Carbon dioxide in blood

Carbon dioxide is transported by three major mechanisms.

i. Dissolved form:

Carbon dioxide is more soluble in blood than oxygen. Hence a small amount of CO_2 (5-7%) is carried in the plasma as a dissolved gas.

ii. Carbaminohemoglobin form:

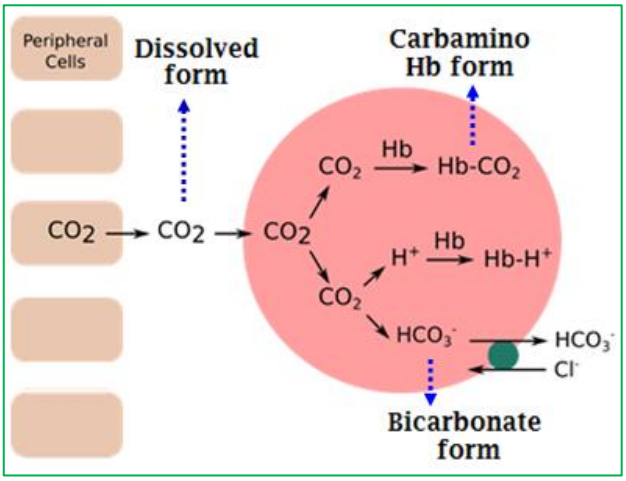
About 23% of carbon dioxide binds to plasma proteins or hemoglobin forming carbaminohemoglobin. This is a reversible reaction.

$$\mathbf{CO_2 + Hb \leftrightarrow HbCO_2}$$

Therefore, when it reaches the lungs, the carbon dioxide can freely dissociate from the hemoglobin and be expelled from the body.

iii. Bicarbonate from:

The majority of carbon dioxide molecules, around 70%, are transported as part of the bicarbonate buffer system. In this system, carbon dioxide diffuses into red blood cells (RBCs). Once inside the RBC, the enzyme carbonic anhydrase (CA) rapidly converts CO_2 into carbonic acid (H_2CO_3). Carbonic acid is an unstable molecule that quickly dissociates into bicarbonate ions (HCO_3^-) and hydrogen ions (H^+).



$$CO_2 + H_2O \leftrightarrow H_2CO_3 \text{ (carbonic acid)} \leftrightarrow HCO_3^- \text{ (bicarbonate)} + H^+$$

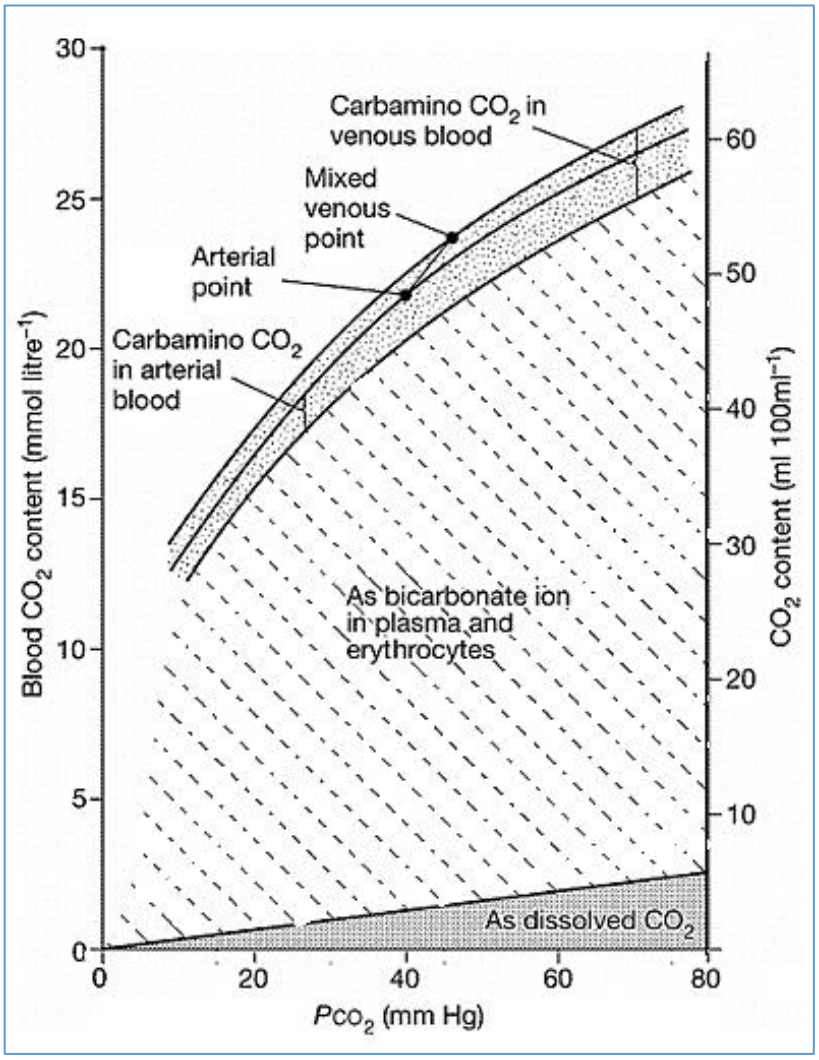
Bicarbonate tends to accumulate within the RBC, resulting in a higher concentration of bicarbonate inside the cell compared to the surrounding blood plasma. Consequently, some bicarbonate diffuses out of the RBC into the plasma, where it combines with sodium ions to form sodium bicarbonate ($NaHCO_3$). The loss of bicarbonate ions from the RBC leads to a net positive charge within the cell, which is balanced by the diffusion of chloride ions (Cl^-) from the plasma into the RBC. This exchange of Cl^- and HCO_3^- ions between the plasma and RBC is known as the chloride shift or Hamburger phenomenon. This process maintains the electrical neutrality of the cell and contributes to the production of H^+ ions. If an excessive amount of H^+ ions is generated, it can disrupt blood pH. However, hemoglobin binds to free H^+ ions, helping to stabilize pH levels.

When the blood reaches the lungs (at the pulmonary capillaries), much of the bicarbonate ions in the plasma are transported back into the red blood cells in exchange for chloride ions. The H+ ions dissociate from hemoglobin, allowing bicarbonate ions to combine with them to form carbonic acid. This carbonic acid is then converted back into carbon dioxide and water through the enzymatic action of carbonic anhydrase. The resulting carbon dioxide is expelled from the body through exhalation.

$$H_2O + CO_2 \longleftarrow H_2CO_3 \longleftarrow HCO_3^- + H^+$$

2.4.2. The Carbon dioxide Dissociation Curve and the factors influencing it

A. Carbon Dioxide Dissociation Curve:



i. The carbon dioxide dissociation curve illustrates the relationship between the partial pressure of carbon dioxide (pCO_2) in the blood and the amount of carbon dioxide carried in the blood.

ii. Linear relationship:

Unlike the oxygen dissociation curve, the carbon dioxide dissociation curve is linear.

iii. Forms of carbon dioxide transport:

It shows how much carbon dioxide is transported in the blood in the form of

*** Dissolved CO_2**: A small portion of the CO_2 is carried dissolved in the plasma.

*** Bicarbonate (HCO_3^-)**: The majority of CO_2 is transported as bicarbonate ions, which are formed when CO_2 reacts with water in the presence of the enzyme carbonic anhydrase.

*** Carbamino compounds**: A small amount of CO_2 binds to the amino groups of hemoglobin, forming carbamino compounds.

iv. An increase in pCO_2 leads to the formation of more carbonic acid, which dissociates into bicarbonate and hydrogen ions. This helps to buffer the blood and maintain pH balance.

v. There are two main points of interest along this curve:

* The arterial point corresponds to the CO_2 content of arterial blood: PCO_2 = 40 mmHg and the CO_2 content is 480 ml/L (or, 48ml/dL)

* The mixed venous point: CO_2 content of mixed venous blood: PCO_2 is 46 mmHg and the CO_2 content is 520 ml/L.

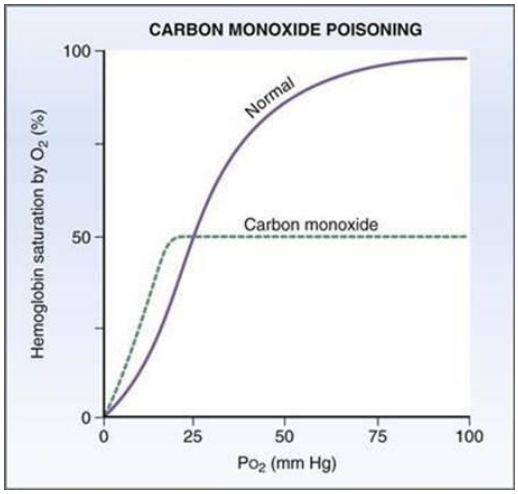
* Because of the Haldane effect, if this blood were to be "arterialised" by the addition of oxygen while the total CO_2 content remained the same, the extra CO_2 liberated by the oxygenation of haemoglobin would produce an increase in PCO_2 to something like 55 mmHg.

B. The carbon dioxide dissociation curve: The factors influenced by it

1. **pH:**
    - Increased pH (alkalosis) shifts the carbon dioxide dissociation curve to the left, meaning that at a given pCO_2, the blood will carry less CO_2.
    - Decreased pH (acidosis) shifts the curve to the right, meaning that at a given pCO_2, the blood will carry more CO_2.
2. **Temperature:**
    - Increased temperature shifts the carbon dioxide dissociation curve to the right, meaning that at a given pCO_2, the blood will carry more CO_2.
    - Decreased temperature shifts the curve to the left, meaning that at a given pCO_2, the blood will carry less CO_2.
3. **2,3-Diphosphoglycerate (2,3-DPG):**
    - Increased levels of 2,3-DPG, which is present in red blood cells, shift the carbon dioxide dissociation curve to the right, allowing for more CO_2 to be carried in the blood.
    - Decreased levels of 2,3-DPG shift the curve to the left, reducing the amount of CO_2 carried in the blood.
4. **Hemoglobin concentration:**
    - Increased hemoglobin concentration shifts the carbon dioxide dissociation curve to the right, allowing for more CO_2 to be carried in the blood.
    - Decreased hemoglobin concentration shifts the curve to the left, reducing the amount of CO_2 carried in the blood.
5. **Plasma bicarbonate concentration:**
    - Increased plasma bicarbonate concentration shifts the carbon dioxide dissociation curve to the right, allowing for more CO_2 to be carried in the blood.
    - Decreased plasma bicarbonate concentration shifts the curve to the left, reducing the amount of CO_2 carried in the blood.

These factors affect the carbon dioxide dissociation curve by influencing the equilibrium between dissolved CO_2, bicarbonate, and carbamino compounds in the blood, which determines the overall CO_2 carrying capacity of the blood.

2.4.3. Carbon monoxide Poisoning



Carbon monoxide (CO) poisoning occurs when an individual inhales excessive amounts of carbon monoxide gas. CO is colorless, odorless, and tasteless, and is therefore difficult to detect.

i. Mechanism of Toxicity:

1. Hemoglobin Affinity:

* CO has a high affinity for hemoglobin.

* Each of hemoglobin's four heme groups can also bind to carbon monoxide (CO), forming carboxyhemoglobin (COHb) more readily than oxygenhemoglobin. If this occurs, O_2 cannot bind and results in carbon monoxide poisoning.

* Carbon monoxide association with hemoglobin is directly related to the plasma partial pressure of CO (= pCO).

* At pCO = 0.4 mmHg, the hemoglobin is almost fully saturated with CO. This pressure is approximately 250 X less than the pO_2 needed to fully saturate hemoglobin with O_2. Therefore, if an individual breathes in a relatively small amount of CO, it will saturate the hemoglobin and prevent O_2 from binding. As a result, O_2 cannot be distributed as needed to the body's tissues.

2. Reduced Oxygen Delivery: When CO binds to hemoglobin, it displaces oxygen, reducing the blood's oxygen-carrying capacity. This results in tissue hypoxia, even in the presence of normal arterial oxygen levels.

3. Cellular Effects: CO also interferes with cellular respiration by disrupting mitochondrial function and inhibiting the utilization of oxygen by cells, further contributing to tissue hypoxia.

ii. Symptoms and Clinical Presentation:

a. **Headache**: One of the most common early symptoms of CO poisoning is a persistent headache.

b. **Dizziness and Nausea**: Individuals may experience dizziness, lightheadedness, and nausea, often mistaken for flu-like symptoms.

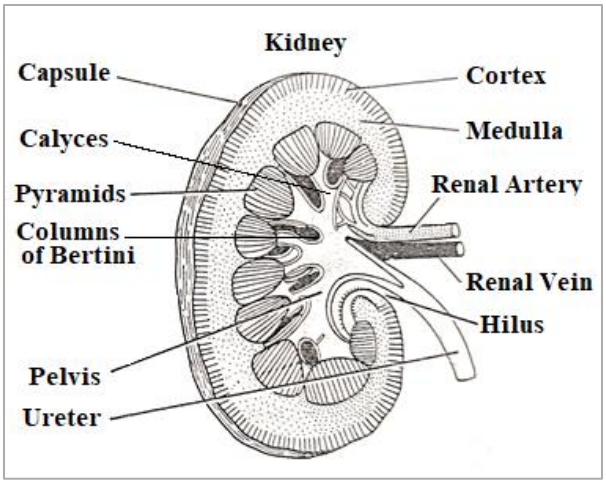
c. **Confusion and Impaired Judgment**: As CO levels increase, symptoms may progress to confusion, disorientation, and impaired judgment.

d. **Cardiovascular Effects**: Severe CO poisoning can lead to cardiovascular collapse, arrhythmias, and myocardial ischemia.

e. **Neurological Symptoms**: Prolonged exposure to high levels of CO can result in seizures, coma, and even death.

3.1. Structure of kidney and its functional unit

The kidneys are a pair of bean-shaped organs situated just below and posterior to the liver in the peritoneal cavity. Positioned at the back of the abdominal cavity, each kidney rests on either side of the spine. Typically, the right kidney is slightly smaller and lower than the left, accommodating the space needed for the liver. In terms of weight, each kidney ranges from 125–170 grams (g) in males and 115–155 g in females.



Externally, the kidneys are surrounded by three layers. The outermost layer, the **renal fascia**, is a tough connective tissue layer. Next is the **perirenal fat capsule**, which helps anchor the kidneys in place. The innermost layer is the **renal capsule**.

Internally, the kidney is divided into an **outer cortex** and an **inner medulla**. The cortex extends into the medulla, dividing it into triangular shapes known as **renal pyramids** (5-8). The apex of a renal pyramid is referred to as a **renal papilla**. Minor ducts arise from these pyramids, forming **minor calyces**. Several minor calyces merge to form a **major calyx**. Urine passes through the major calyces into the **renal pelvis**, a flattened and funnel-shaped structure. From there, urine drains into the **ureter**, which carries it to the bladder for storage.

The medial margin of each kidney is marked by a deep fissure, known as the **renal hilum**. This act as a gateway to the kidney – normally the **renal vessels** and **ureter enter/exit** the kidney via this structure.

Nephron: The Functional Unit of the Kidney

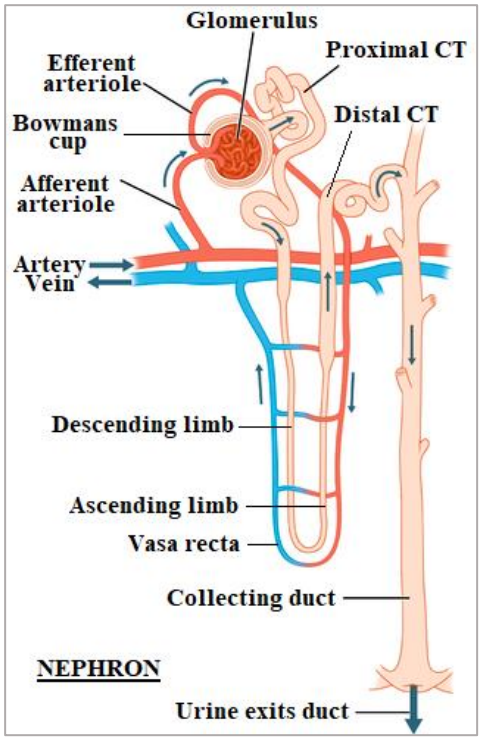
The nephron, the functional unit of the kidney, is responsible for removing waste from the body. There are over a million nephrons in each kidney. A nephron consists of three parts: a renal corpuscle, a renal tubule, and the associated capillary network, which originates from the cortical radiate arteries.

i. Renal Capsule:

The renal corpuscle, located in the renal cortex, is composed of two structures: **the glomerulus** and **Bowman's capsule**. The glomerulus is a cluster of capillary loops enclosed by cup-shaped Bowman's capsule. Bowman's capsule consists of two layers, a visceral layer of **podocytes**, which contacts the capillary epithelium of the glomerulus, and a **parietal layer** of simple squamous cells that contacts the epithelium of the PCT. Blood enters the renal corpuscle via **afferent arterioles** and then leaves via **efferent arterioles**.

ii. Renal Tubule:

The renal tubule is a long, convoluted structure that emerges from the glomerulus. It can be divided into three parts based on function. The first part is called the **proximal convoluted tubule** (PCT), due to its proximity to the glomerulus. The second part is known as the **loop of Henle**, or nephritic loop, as it forms a loop (with ascending and descending limbs) through the renal medulla. The third component of the renal tubule is the **distal convoluted tubule** (DCT), which is located in the renal cortex. Its initial segment lies adjacent to the glomerulus and forms the juxtaglomerular apparatus.



iii. Collecting Ducts:

This last part of the nephron connects with and empties its filtrate into **collecting ducts** that line the medullary pyramids. The collecting ducts amass contents from multiple nephrons, fusing together as they enter the **papillae** of the renal medulla.

Numerous collecting ducts merge into the **renal pelvis**, which then becomes **the ureter**. The ureter connects the kidney and the urinary bladder.

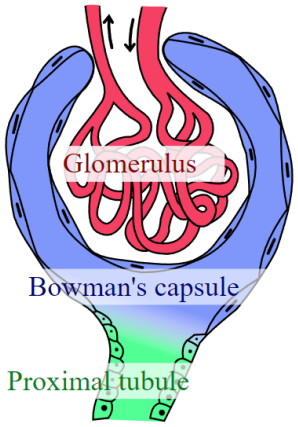
iv. Capillary network:

In cortical nephrons, the efferent arterioles flow into ***peritubular capillary beds*** that wrap around the tubules. In juxtamedullary nephrons, the efferent arterioles diverge into the **vasa recta**, long, straight vessels that run along the loop of Henle.

3.2 Urine Formation

There are three processes involved in the formation of urine: Glomerular filtration, Tubular Reabsorption, and Tubular Secretion.

i. Glomerular filtration (GF)



GF takes place through the semipermeable walls of the glomerular capillaries and Bowman's capsule. The afferent arterioles supplying blood to glomerular capsule. The diameter of efferent arterioles is narrower than afferent arterioles. Due to this difference in diameter of arteries, blood leaving the glomerulus creates the pressure known as hydrostatic pressure.

The **glomerular hydrostatic pressure** forces the blood to leaves the glomerulus resulting in filtration of blood. A capillary hydrostatic pressure of about **55 mmHg** builds up in the glomerulus. However this pressure is opposed by the **osmotic pressure** of the blood, provided mainly by plasma proteins, about **30 mmHg**, and by **filtrate hydrostatic pressure** of about **15 mmHg** in the glomerular capsule. The **net filtration pressure** is, therefore: **55-(30+15) = 10 mm Hg**. By the net filtration pressure (of 10 mmHg) gradient with in the glomerulus forces blood to move into the capsule space.

The filtrate containing large amount of water, glucose, amino acids, uric acid, urea, electrolytes etc., in the glomerular capsule is known as nephric filtrate of glomerular filtrate.

The volume of filtrate formed by both kidneys each minute is called the **glomerular filtration rate (GFR).** It is about 125 mL/min, or 180 litres of filtrate are formed each day.

ii. Selective reabsorption

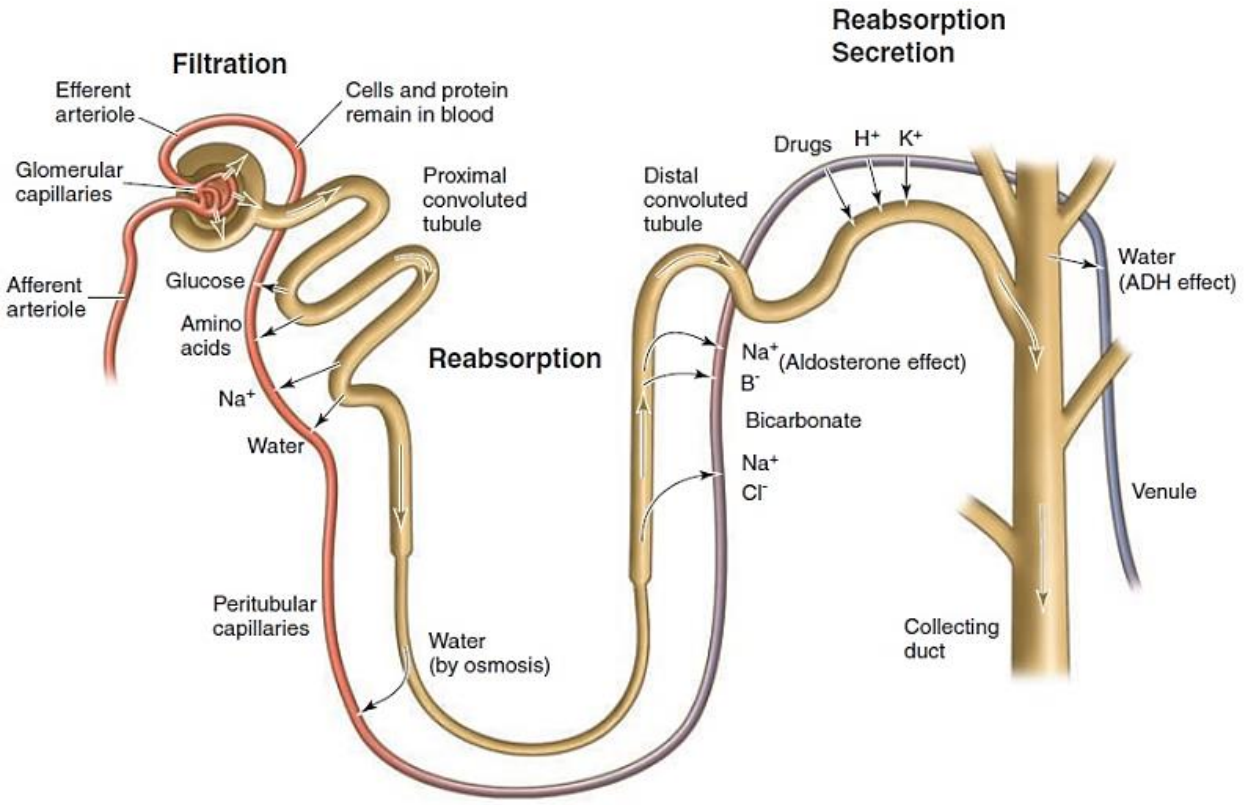
a. Proximal convoluted tubule (PCT):

As the filtrate passes to the renal tubules, useful substances including some water, electrolytes and organic nutrients such as glucose, amino acids, vitamins hormones etc., are selectively reabsorbed from the filtrate back into the blood in the PCT. Reabsorption of some substance is passive, while some substances are actively transported. Major portion of water is reabsorbed by Osmosis. Around 80% of the glomerular filtrate reabsorbed in this segment.

b. Loop of Henle:

The *descending* limb of the loop of Henle is thin and is permeable to **water** but almost impermeable to electrolytes. About 15 percent of the water found in the original filtrate is reabsorbed here. This concentrates the filtrate as it moves down.

The *ascending* limb of the loop of Henle is thick and is impermeable to water but allows transport of electrolytes (Na^+) actively or passively (absorbs about 25 % of the solutes). Therefore, as the concentrated filtrate pass upward, it gets diluted due to the passage of electrolytes to the medullary fluid.



c. Distal Convoluted Tubule (DCT) and Collecting Duct:

Conditional reabsorption of Na^+ and water takes place in this segment. DCT is also capable of reabsorption of HCO_3^- and selective secretion of hydrogen and potassium ions and NH_3 to maintain the pH and sodium-potassium balance in blood.

Distal convoluted tubule and collecting duct reabsorb about **7 % of solutes** (mainly Na^+ and Cl^-) and approximately **17 % water**. Their resorption is **affected by hormones** (e.g. ADH) – **facultative resorption**.

The distal part of the distal convoluted tubule and the collecting duct consist of two cell types: **Principal cells** responsible for the resorption of Na^+ ions and water (dependent on ADH) and secretion of K^+ ions. **Intercalated cells** containing carbonic anhydrase. They are involved in acid-base balance, because they can secrete both hydrogen and bicarbonate ions

iii. Tubular Secretion

Tubular secretion is the third step in urine formation and primarily occurs in the distal tubules and collecting ducts. Substances such as hydrogen ions (H^+), potassium ions (K^+), and certain drugs or toxins are actively secreted from the peritubular capillaries into the tubular fluid. Tubular secretion allows for the elimination of substances that were not filtered effectively or were reabsorbed back into the bloodstream during tubular reabsorption.

3.3. Regulation of water balance

Regulation of water balance in the human body is a complex process that involves multiple systems and mechanisms to maintain homeostasis. This balance is critical for normal physiological function and is primarily managed by the kidneys, with significant contributions from the hypothalamus, pituitary gland, adrenal glands, and cardiovascular system. Here's an overview of the key components and mechanisms involved:

1. Kidneys

- **Filtration and Reabsorption**: The kidneys filter blood, removing waste and excess substances while reabsorbing water and essential nutrients back into the bloodstream.
- **Renin-Angiotensin-Aldosterone System (RAAS)**: When blood volume or pressure drops, the kidneys release renin, which activates the RAAS. This leads to the production of angiotensin II, which constricts blood vessels and stimulates the release of aldosterone from the adrenal glands. Aldosterone promotes sodium and water reabsorption in the kidneys, increasing blood volume and pressure.

2. Hypothalamus and Pituitary Gland

- **Antidiuretic Hormone (ADH)**: The hypothalamus detects changes in blood osmolality (concentration of solutes). High osmolality triggers the release of ADH (also known as vasopressin) from the posterior pituitary gland. ADH increases the permeability of the kidney's collecting ducts, promoting water reabsorption back into the bloodstream and concentrating the urine.

3. Adrenal Glands

- **Aldosterone**: Produced by the adrenal cortex, aldosterone regulates sodium and potassium balance. By promoting sodium reabsorption and potassium excretion in the kidneys, it indirectly influences water retention and blood pressure.

4. Cardiovascular System

- **Atrial Natriuretic Peptide (ANP)**: When the atria of the heart are stretched due to increased blood volume, they release ANP. ANP promotes the excretion of sodium and water by the kidneys, reducing blood volume and pressure.

5. Thirst Mechanism

- **Osmoreceptors in the Hypothalamus**: Detect changes in blood osmolality. Increased osmolality stimulates thirst, prompting the individual to drink water, which helps restore normal osmolality and volume.

6. Electrolyte Balance

- Sodium, potassium, chloride, and other electrolytes play crucial roles in maintaining water balance. Sodium, in particular, is a major determinant of extracellular fluid volume. The kidneys adjust the excretion and reabsorption of these electrolytes to maintain balance.

7. Fluid Intake and Loss

- **Intake**: Water intake comes from drinking fluids and eating foods with high water content.
- **Loss**: Water is lost through urine, sweat, respiration, and feces. The body adjusts to varying levels of intake and loss to maintain balance.

Feedback Mechanisms

- **Negative Feedback Loops**: Most of the processes involved in water balance are regulated by negative feedback loops. For example, high blood osmolality triggers ADH release, which reduces osmolality by increasing water reabsorption.

Conditions Affecting Water Balance

- **Dehydration**: Results from insufficient water intake or excessive loss, leading to high blood osmolality and low blood volume. Symptoms include dry mouth, fatigue, and dizziness.
- **Overhydration**: Excessive water intake can dilute blood osmolality and overwhelm the kidneys' ability to excrete water, potentially leading to hyponatremia (low sodium levels).

Effective regulation of water balance ensures optimal functioning of cells and organs, highlighting its importance in overall health.

3.4. Regulation of Acid-base Balance

The regulation of acid-base balance is crucial for maintaining the pH of blood and other bodily fluids within a narrow range (7.35 to 7.45). This balance is essential for normal cellular functions and overall homeostasis. The body uses several mechanisms to regulate acid-base balance, primarily involving buffer systems, the respiratory system, and the renal system.

Regulation of acid - Base Balance

1. **Buffer Systems**

i. **Bicarbonate buffer**: The most important extracellular buffer produced by kidneys, has the largest buffering capacity (53%)

ii. **Hemoglobin buffer**: Main intracellular buffer of the blood (35%).

iii. **Protein buffer**: An extracellular buffer together with bicarbonate buffer, represented by plasma proteins (7%)

iv. **Phosphate buffer**: It takes part in hydrogen ions excretion in renal tubules, is not of great importance in blood (5%).

2. Cellular Buffering (*Intracellular Buffers)*

- **Components**: Proteins and phosphates within cells can act as buffers by absorbing or releasing H^+ as needed.
- **Ion Exchange**: Cells can exchange H^+ with other ions like potassium (K^+) to help balance pH.

3. Compensation Mechanisms

i. Respiratory mechanisms:

Lungs are responsible for volatile acid (carbon dioxide) emanation. CO_2 content in plasma depends on alveolar ventilation. Changes in pH lead to stimulation of chemoreceptor's in the brain stem, causing a compensatory mechanism; therefore changing the respiratory rate. In acidosis alveolar ventilation increases, pCO_2 decreases and pH tends to return to normal. These changes occur rapidly, but it takes 12 to 24 hours to stabilize acid-base status. Alkalosis causes hypoventilation and rise in pCO_2 that leads to fall in pit.

ii. Renal mechanisms:

Renal mechanisms are the most complex and effective. Renal compensation occurs by three main mechanisms:

1. Bicarbonate ions reabsorption in proximal tubules
2. Bicarbonate ions regeneration in distal tubules
3. Hydrogen ions excretion.

CO_2 reacts with water to produce carbonic acid into the renal tubular cells. Carbonic acid dissociates to yield H^+ and HCO_3^- reaction is catalyzed by carbonic anhydrase. Bicarbonate ion enter the systemic circulation, is secreted into the lumen. The secretion is coupled to the reabsorption of Na^+ and electro neutrality preserved. The secreted reacts with filtered bicarbonate to produce carbonic acid that dissociate into carbon dioxide and water. Hydrogen ions excretion begins at the second stage when the whole bicarbonate is reabsorbed. HPO_4 ion can't be reabsorbed from renal tubules because of charge, but it can bind secreted hydrogen ions. Produced H_2PO_4 - is excreted in urine, HCO_3 is reabsorbed into the blood.

After depletion of the latter mechanisms, the kidneys switch to ammonia buffer (NH_3/NH_4^+). The main source of ammonia is glutamine deamination. As NH_3 has no charge, it moves freely across the tubular cell membrane and appears in the urine, where it binds scatted proton to produce ammonium ions (NH_4^+). NH_4^+ can't be reabsorbed because of its charm. This process is termed as ammoniogenesis.

4.1. Neuron Structure and Types

The structure of neurons, also known as nerve cells, is highly specialized for transmitting electrical and chemical signals throughout the nervous system. Neurons come in various shapes and sizes, but they typically share common structural features. Additionally, neurons can be classified based on their structure, function, and location within the nervous system. Let's explore the structure and types of neurons:

i. Structure of Neurons:

1. **Cell Body (Soma)**:
    - The cell body contains the nucleus and most of the organelles necessary for cellular functions.
    - It integrates incoming signals from dendrites and generates outgoing signals along the axon.
2. **Dendrites**:
    - Dendrites are branched extensions of the cell body that receive signals (chemical or electrical) from other neurons or sensory receptors.
    - They contain receptors and synaptic terminals where neurotransmitters are released.
3. **Axon**:
    - The axon is a long, slender projection that carries electrical signals away from the cell body toward other neurons, muscles, or glands.
    - Some axons are encased in a myelin sheath, which speeds up the transmission of electrical impulses.
    - At the end of the axon are terminal branches called axon terminals or synaptic terminals, which form synapses with other neurons or target cells.
4. **Myelin Sheath**:
    - Myelin is a fatty substance formed by specialized glial cells (oligodendrocytes in the central nervous system and Schwann cells in the peripheral nervous system).
    - It wraps around the axon in segments, insulating it and increasing the speed of nerve impulse conduction.
5. **Nodes of Ranvier**:
    - Nodes of Ranvier are gaps in the myelin sheath along the axon.
    - They contain a high density of voltage-gated ion channels, facilitating the rapid propagation of action potentials.

ii. Types of Neurons:

1. Sensory Neurons:

* Sensory neurons, also called afferent neurons, transmit sensory information from sensory receptors (e.g., in the skin, eyes, ears) to the central nervous system (brain and spinal cord).

* They have specialized dendrites that detect specific stimuli, such as touch, temperature, pain, or light.

2. Motor Neurons:

* Motor neurons, also known as efferent neurons, transmit signals from the central nervous system to muscles or glands, eliciting a response.

* They have long axons that extend from the spinal cord or brain to target tissues, where they synapse with muscle fibers or glandular cells.

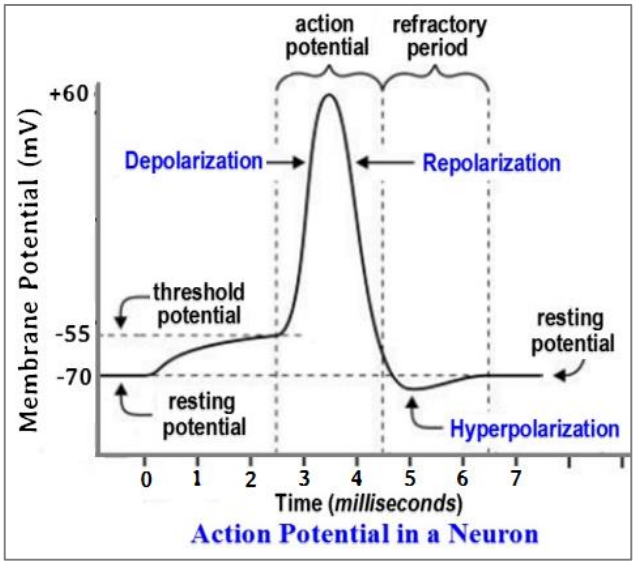
3. Interneurons:

* Interneurons, or association neurons, are located entirely within the central nervous system and facilitate communication between sensory and motor neurons.

* They integrate signals from multiple sources and play a crucial role in information processing, decision-making, and reflex arcs.

4.2.1 Neural Transmission in non-myelinated nerve fibers

Neural transmission in non-myelinated nerve fibers involves the propagation of action potentials along unmyelinated axons. This transmission of nerve impulse along nerve fibre can be summarized in three steps



i. Resting Membrane Potential

Neurons have a resting membrane potential, which is the electrical charge across the neuronal membrane when the cell is at rest. At this stage, the inside of the neuron is negatively charged compared to the outside, typically around -70 millivolts (mV). This polarization is maintained by the selective permeability of the neuronal membrane to ions, such as potassium (K+), sodium (Na+), and chloride (Cl-).

ii. Action potentials

Action potentials are the rapid changes in charge across the membrane that occur when a neuron fires. The characteristic phases of the action potential are caused by the opening and closing of voltage-gated Na^+, K^+ ion channels. An action potential occurs in the membrane of the axon of a neuron when depolarization reaches a certain level termed the threshold (-55mV). The phases of an action potential are as follows.

a. Depolarization phase: When the membrane potential at the axon hillock approaches the threshold potential, voltage-gated Na channels activate and begin to open rapidly. Na^+ begins to flow in. As more channels are opened, the Na^+ influx increases and the membrane further depolarizes and the membrane potential changes from -55mV to +60mV. However, shortly before the membrane reaches this point, the voltage-gated Na channels close, terminating the depolarization phase of the action potential. At the peak of the action potential, the inside of the membrane is more positive than the outside.

b. Repolarization Phase: A depolarization of the threshold level also opens voltage-gated K^+ channels in addition to voltage-gated Na^+ channels. The voltage-gated K^+ channels open more slowly, so their opening occurs at about the same time as the voltage-gated Na^+ channels close. K^+ channel opening accelerates the outflow of K^+. K^+ outflow changes the membrane potential from +60mV to -70mV making the intracellular side of the membrane more negative, and causing the repolarization phase of the action potential.

c. Hyperpolarizing phase: Following the repolarization phase, voltage-gated K^+ channels close slowly or remain open even after reaching the resting membrane potential (-70 mV). As a result, the membrane potential becomes even more negative than the resting membrane potential due to an excess efflux of K^+ ions from the axon (-90 mV; hyperpolarization). When the voltage-gated K^+ channels close, the membrane potential returns to -70 mV.

iii. Refractory Period

At the end of an action potential, some Na ions have entered the cell and some K ions have exited, leaving the cell in a slightly different state than before. During this period, the axon does not respond to new stimuli. The Na/K ATPase is crucial in the restoration of ion gradients. When these ions have been completely returned to their resting potential location, the neuron is ready for another stimulus.

4.2.2. Myelinated nerve impulse transmission

Myelinated neurons are covered by a myelin sheath. The Schwann cells form this sheath and they help in fast conduction of impulses across the nerve. Myelin is a fatty white substance, made mainly up of cholesterol, acts as an insulation around a wire. The nodes of Ranvier, are gaps in the myelin sheath along the axon. At the nodes, the axon membrane is exposed, containing a high density of voltage-gated ion channels. These unmyelinated spaces are about one micrometer long and contain voltage gated Na^+ and K+ channels. Flow of ions through these channels, particularly the Na^+ channels, regenerates the action potential over and over again along the axon.

Saltatory Conduction:

Action Potential Generation: At the initial segment of the axon, an action potential is initiated in response to a stimulus, such as a depolarizing current or neurotransmitter release. This depolarization opens voltage-gated sodium channels, allowing sodium ions to enter the axon and generate an action potential.

Propagation of Action Potential:

In myelinated axons, the action potential rapidly propagates along the myelinated segments of the axon through a process called saltatory conduction. Action potentials "jump" from one node of Ranvier to the next, bypassing the myelinated regions where the axon is insulated. This process significantly speeds up the transmission of nerve impulses compared to non-myelinated axons.

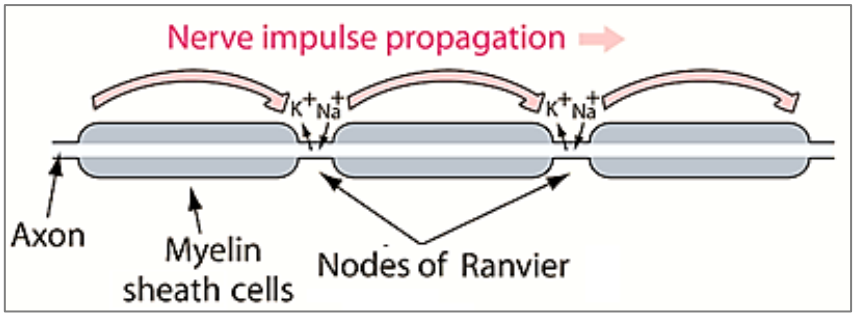
Regeneration of Action Potential:

At each node of Ranvier, the action potential is regenerated by the opening of voltage-gated ion channels. Sodium ions influx at the node, depolarizing the membrane and generating a new action potential.

Benefits of Myelinated Nerve Impulse Transmission:

Increased Speed: Saltatory conduction along myelinated axons allows for faster transmission of nerve impulses compared to non-myelinated axons. By skipping over the insulated segments, action potentials propagate more rapidly from one node to the next.

Conservation of Energy: Myelination reduces the energy required for action potential propagation by minimizing the movement of ions across the axonal membrane. This energy-efficient mechanism conserves metabolic resources and supports prolonged neuronal activity.

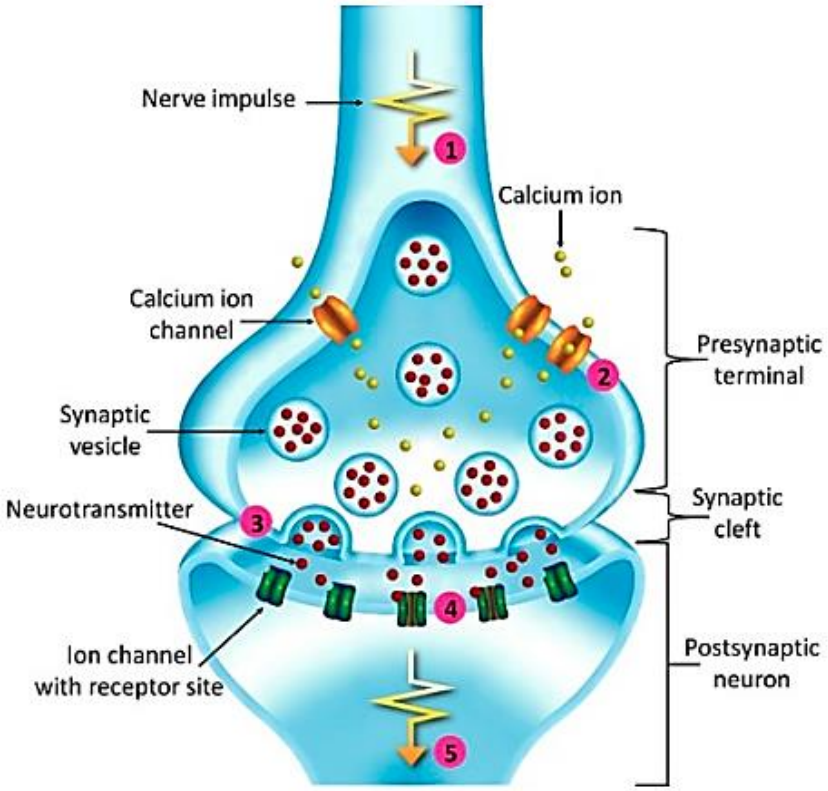


4.2.3 Synaptic transmission

Synaptic transmission is the process by which two neurons exchange information. An action potential can send information from a neuron's dendrites down the axon towards the axon terminal. Synaptic transmission is the process that takes place afterwards.
Synaptic transmission can be **chemical** or **electrical**.

i. Chemical synaptic Transmission

Majority in the nervous system, where information is transmitted from one neuron to another by means of chemical molecules called neurotransmitters. Stages of signal transmission at chemical synapses:



1. **Arrival of an Electrical Signal**

The triggering event is the arrival of an electrical signal (called an action potential) in the terminal buttons of the presynaptic neuron, i.e., the neuron that transmits the message.

2. Entry of Calcium (Ca^{2+}) in the Terminal Buttons

This electrical signal causes the opening of voltage-sensitive calcium channels located in the membrane of the terminal buttons. Their opening allows the rapid entry of Ca^{2+} into the terminal buttons of the presynaptic neuron.

3. Fusion of Synaptic Vesicles and Release of Neurotransmitters

Synaptic vesicles containing the neurotransmitters are synthesized by the neuron then stored in the terminal buttons. When the concentration of Ca^{2+} increases in the terminal buttons, a phenomenon of exocytosis occurs, i.e., the synaptic vesicles fuse with the membrane of the presynaptic neuron. This fusion results in the release of neurotransmitters into the synaptic cleft.

4. Binding of Neurotransmitters to Receptors and Opening of Postsynaptic Channels

Neurotransmitters diffuse into the synaptic cleft and bind to receptors in the membrane of the post-synaptic neuron, causes the opening or closing of channels located in the membrane of the post-synaptic neuron, depending on the type of neurotransmitter. There is a great diversity of neurotransmitters, in which some are excitatory and some are inhibitory. Dopamine, serotonin, norepinephrine, glutamate, GABA, acetylcholine and endocannabinoids are some examples of neurotransmitters.

5. Elimination or Degradation of Neurotransmitters and Recycling of Vesicles

The residual neurotransmitters are either destroyed or recaptured by the presynaptic neuron or by glial cells. After the neurotransmitters are released into the synaptic cleft, the synaptic vesicles that contained them are recycled for reuse.

It is important to mention that the same neuron can release different types of neurotransmitters. Moreover, since a single neuron can receive information from thousands of other neurons via its synapses, it is the sum of the conductance changes in the post-synaptic neuron that will determine whether or not this neuron will emit an electrical signal. This phenomenon is called the "summation of postsynaptic potentials".

ii. Electrical synaptic Transmission

* Electrical synapses are more common in squid or zebrafish but can also be found in humans. In humans these are abundant in the developing nervous system, but are less common than chemical synapses in the adult nervous system.

* Electrical synapses are found in several regions of the central nervous system, including the retina, olfactory bulbs, hypothalamus, cerebellum, and brainstem.

* Electric synapses occur when two neurons are not separated by a cleft but are joined by the **gap junction**, as they are very close together.

* Electrical synapses allow electrical signals to pass directly from one neuron to another, through gap junctions, which are specialized channels allowing direct contact between neurons.

* Electrical synapses do not require neurotransmitters because the information can travel electrically between neurons through the gap junction. The action potential is **not transformed** into chemical information.

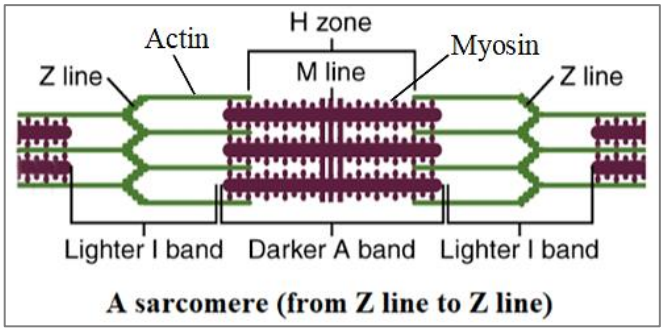
* Electric transmission is **faster** than chemical transmission (flow can occur almost instantaneously) and is **bidirectional** (this means that the ionic current flow can travel back and forth between the cells.)

* Electrical synapses have the advantage of allowing groups of neurons to have synchronized electrical activity, essential for rhythmic functions such as breathing, which is regulated by the brainstem.

3.3. Ultra structure of muscle

The ultrastructure of muscle refers to its microscopic anatomy, revealing the specialized structures and components that enable muscle contraction and function. Muscle tissue is composed of individual muscle fibers, which are long, cylindrical cells that are arranged in parallel bundles.

Within each muscle fiber, several key ultrastructural components can be observed. One of the primary features is the **myofibrils**, which are elongated structures that run along the length of the muscle fiber. Myofibrils are made up of repeating units called **sarcomeres**, which are responsible for muscle contraction.



A sarcomere (from Z line to Z line)

The sarcomeres are composed of thick filaments, primarily made of the protein **myosin**, and thin filaments, primarily made of the protein **actin**. The thick filaments are located in the center of the sarcomere, while the thin filaments extend from the ends of the sarcomere toward the center.

In addition to the myofibrils, other structures within the muscle fiber include the **sarcoplasmic reticulum (SR)** and the **T-tubules**. The SR is a specialized type of endoplasmic reticulum that surrounds the myofibrils, serving as a storage site for **calcium ions**. The T-tubules are invaginations of the muscle fiber membrane that penetrate deep into the interior of the muscle fiber, allowing for the rapid transmission of electrical impulses.

Furthermore, the muscle fiber is rich in **mitochondria**, which are responsible for producing ATP, the energy source required for muscle contraction.

The outer surface of the muscle fiber is surrounded by a connective tissue sheath called the **endomysium**. Several muscle fibers are bundled together by a coarser connective tissue called the **perimysium**, forming a fascicle. Multiple fascicles are then enveloped by the **epimysium**, forming the entire muscle structure.

3.4. Molecular and chemical basis of muscle contraction

The Contraction Cycle:

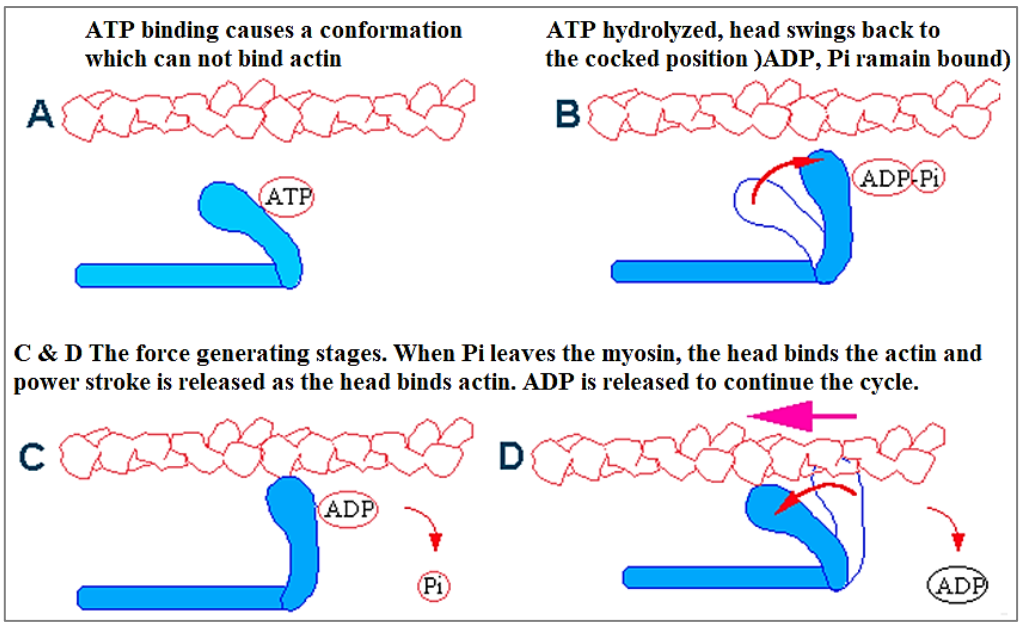
At the onset of contraction, the sarcoplasmic reticulum releases calcium ions (Ca^{+2}) into the sarcoplasm. There, they bind to troponin. Troponin then moves tropomyosin away from the myosin-binding sites on actin. Once the binding sites are "free," the contraction cycle-the repeating sequence of events that causes the filaments to slide begins. The contraction cycle consists of following steps:

1. ATP Binding:

The myosin head has an ATP-binding site. When ATP binds to this site, it is hydrolyzed by the enzyme activity of the myosin head (which functions as an ATPase). This hydrolysis reaction breaks down ATP into ADP and an inorganic phosphate (Pi).

2. Hydrolysis of ATP:

The energy released from the hydrolysis of ATP is stored in the myosin head. This stored energy "cocks" the myosin head into a high-energy state, similar to how a stretched spring stores energy. In this energized state, the myosin head is perpendicular to the thick (myosin) and thin (actin) filaments, ready to interact with actin. Notice that the products of ATP hydrolysis- ADP and a phosphate group are still attached to the myosin head.



3. Attachment of Myosin to Actin

The energized myosin head attaches to the myosin-binding site on actin and releases the previously hydrolyzed phosphate group. When a myosin head attaches to actin during the contraction cycle, the myosin head is referred to as a cross-bridge. Although a single myosin molecule has a double head, only one head binds to actin at a time.

4. Power Stroke

After a cross-bridge forms, the myosin head pivots, changing its position from a 90^0 angle to a 45° angle relative to the thick and thin filaments. As the myosin head changes to its new position, it pulls the thin filament past the thick filament toward the center of the sarcomere, generating tension (force) in the process. This event is known as the power stroke. Once the power stroke occurs, ADP is released from the myosin head.

5. Detachment of Myosin from Actin

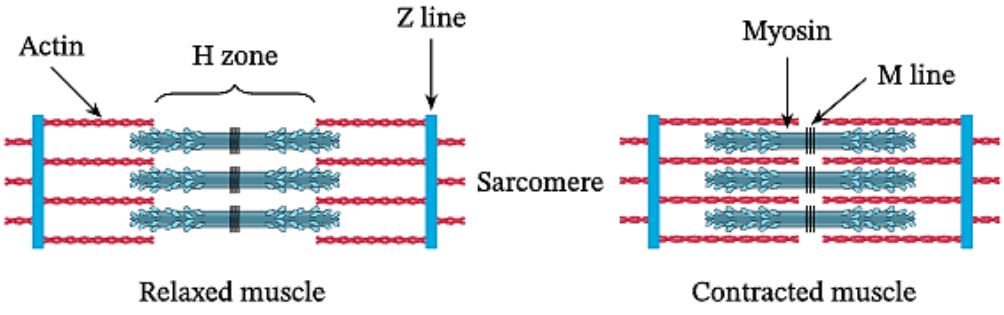
At the end of the power stroke, the cross-bridge remains firmly attached to actin until it binds another molecule of ATP. As ATP binds to the ATP binding site on the myosin head, the myosin head detaches from actin.

6. Contraction cycle repeats

The contraction cycle repeats as myosin ATPase hydrolyzes the newly bound ATP molecule, continuing as long as ATP is available and the Ca^{2+} level near the thin filament remains sufficiently high. The cross-bridges rotate back and forth with each power stroke, pulling the thin filaments toward the M line. In a thick filament, each of the 600 cross-bridges attaches and detaches about five times per second. At any given moment, some myosin heads are attached to actin, forming cross-bridges and generating force, while others are detached from actin, preparing to bind again.

7. Muscle fibre Shortens

As the contraction cycle continues, movement of cross-bridges applies the force that draws the Z discs toward each other, and the sarcomere shortens. During a maximal muscle contraction, the distance between two Z discs can decrease to half the resting length. The Z discs in turn pull on neighboring sarcomeres, and the whole muscle fiber shortens.



8. Movement of a part of the body

As the cells of a skeletal muscle begin to shorten, they initially pull on their connective tissue coverings and tendons. These coverings and tendons stretch and then become taut, transmitting the tension through the tendons to pull on the attached bones. This result in the movement of a part of the body.

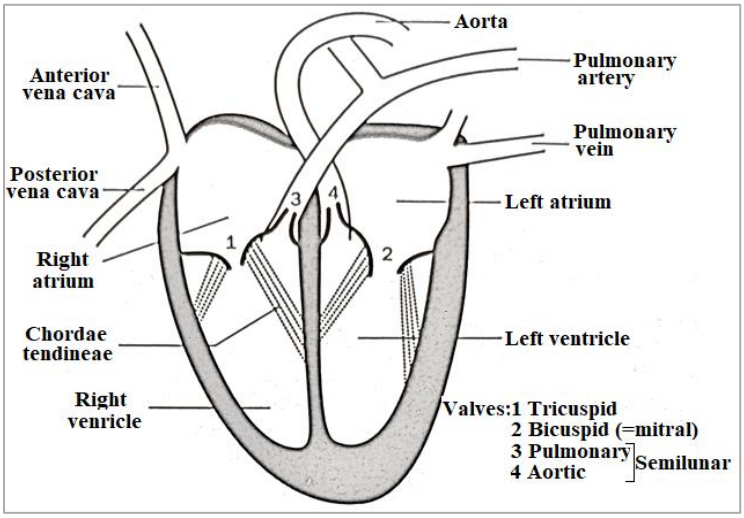
5.1.1. Structure of Mammalian Heart

The human heart is located slightly to the left within the thoracic cavity, positioned medially between the lungs in an area known as the mediastinum. Its shape resembles a pinecone, being broad at the superior surface and tapering down to the apex. A typical heart is approximately the size of a fist, measuring about 12 cm (5 in) in length, 8 cm (3.5 in) in width, and 6 cm (2.5 in) in thickness. The heart weighs around 250-350 grams.

i. External Structure of Heart

The pericardium, a double-layered, fluid-filled sac, surrounds and protects the heart. It consists of an outer tough fibrous layer, which safeguards the heart and maintains its position in the thorax, and an inner serous layer. The serous layer comprises two sub-layers: the parietal layer, lining the inside of the fibrous pericardium, and the visceral layer, or epicardium, which is the heart's outermost layer. A thin layer of pericardial fluid lies between the parietal and visceral layers of the serous pericardium, acting as a lubricant.

The walls of the heart consist of three layers: the **epicardium**, the **myocardium**, and the **endocardium**. The epicardium, the heart's outermost layer, acts as a protective covering. The myocardium, being the thickest layer, is crucial for the heart's mechanical function. The endocardium, the innermost layer, provides a smooth surface for blood flow within the heart.



ii. Internal Structure of Heart

The heart comprises four chambers: two upper chambers, known as the left atrium and right atrium, and two lower chambers called the left and right ventricles.

Atria:

The two upper chambers, known as atria, are thin-walled, less muscular, and smaller than the ventricles. They are separated by the interatrial septum. The right atrium receives deoxygenated blood from the veins and pumps it into the right ventricle. The left atrium receives oxygenated blood from the lungs and pumps it into the left ventricle.

Ventricles:

The ventricles, located in the lower portion of the heart, are larger and more muscular than the atria. They are separated by the interventricular septum. The right ventricle receives deoxygenated blood from the right atrium and pumps it to the lungs for oxygenation. The left ventricle, the strongest chamber, pumps oxygen-rich blood to the rest of the body. The powerful contractions of the left ventricle generate blood pressure.

The septum between the atria and ventricles is known as the **atrioventricular septum**. This septum features four openings that facilitate the flow of blood from the atria into the ventricles and from the ventricles into the pulmonary trunk and aorta. Each of these openings contains a valve, a specialized structure that ensures the one-way flow of blood. The valves between the atria and ventricles are generically known as atrioventricular valves, consisting of the **tricuspid valve** on the right and the **mitral valve** on the left. The valves located at the openings leading to the pulmonary trunk and aorta are generically known as **semilunar valves**.

5.1.2. Coronary circulation

Coronary circulation refers to the network of blood vessels that supply oxygenated blood to the heart muscle (myocardium) itself, ensuring its proper function. Here are some key points about coronary circulation:

1. Coronary Arteries:

* The coronary arteries originate from the aorta, just above the aortic valve. The two main coronary arteries are the left coronary artery (LCA) and the right coronary artery (RCA).

* The LCA divides into the left anterior descending artery (LAD) and the left circumflex artery (LCx), while the RCA supplies blood to the right atrium, right ventricle, and parts of the interventricular septum.

Function: Coronary circulation delivers oxygenated blood to the myocardium, providing the nutrients and oxygen necessary for cardiac muscle contraction. Adequate coronary blood flow is crucial for maintaining cardiac function and preventing ischemic damage to the heart muscle.

2. Coronary Venous System:

* Deoxygenated blood from the myocardium drains into the coronary sinus, located on the posterior surface of the heart.

* The coronary sinus empties into the right atrium, completing the cycle of coronary circulation.

3. Coronary Collateral Circulation:

* Collateral vessels are small arteries or arterioles that form connections between different parts of the coronary circulation.

* Collateral circulation can develop over time in response to chronic ischemia or occlusion of a coronary artery, providing an alternative route for blood flow to ischemic regions of the heart.

4. Regulation of Coronary Blood Flow:

* Coronary blood flow is regulated by several factors, including metabolic demands, autonomic nervous system activity, and local factors such as adenosine and nitric oxide.

* During periods of increased myocardial oxygen demand (e.g., exercise), coronary blood flow increases to meet the heart's needs.

Coronary circulation is essential for maintaining the vitality of the heart muscle by providing oxygenated blood and nutrients.

5.2. Structure and working of conducting myocardial fibers, Origin and conduction of cardiac impulses

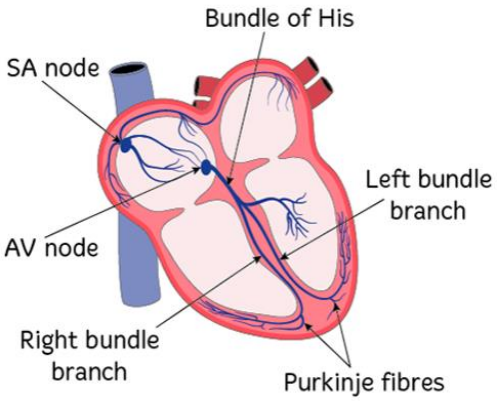
The heart's ability to pump blood efficiently relies on a specialized system of conducting myocardial fibers that ensure coordinated contraction. This system, composed of the sinoatrial (SA) node, atrioventricular (AV) node, bundle of His, bundle branches, and Purkinje fibers, initiates and propagates electrical impulses that regulate heartbeats. Understanding the structure and function of these fibers, as well as the origin and conduction of cardiac impulses, is crucial for comprehending how the heart maintains its rhythmic activity.

1. Structure of Conducting Myocardial Fibers

Conducting myocardial fibers are specialized cardiac muscle cells adapted for rapid transmission of electrical impulses. Unlike typical myocardial fibers, these cells have unique structural features:

a. Sinoatrial (SA) Node: Located in the right atrium near the entrance of the superior vena cava. It contains pacemaker cells with fewer myofibrils but abundant glycogen, specialized for automaticity.

b. Atrioventricular (AV) Node: Situated at the junction of the atria and ventricles in the interatrial septum. It composed of smaller cells with fewer gap junctions, which slow down impulse transmission to allow ventricular filling.



c. Bundle of His: It emerges from the AV node, traversing the interventricular septum. It divides into right and left bundle branches, which further branch into Purkinje fibers.

d. Purkinje Fibers: They spread throughout the ventricular myocardium. Larger and have fewer myofibrils, enabling rapid conduction of impulses to ensure synchronized ventricular contraction.

2. Origin and Conduction of Cardiac Impulses

The cardiac conduction system coordinates the heart's electrical activity through the following sequence:

i. Impulse Initiation at the SA Node:

* The SA node, the primary pacemaker, generates spontaneous action potentials due to its automaticity.

* Pacemaker cells exhibit a slow depolarization phase (phase 4) driven by inward sodium (Na+) and calcium (Ca2+) currents, reaching a threshold to trigger an action potential.

ii. Atrial Conduction:

* The action potential from the SA node spreads through the atrial myocardium via gap junctions, causing atrial contraction (atrial systole).

* This electrical wave reaches the AV node.

iii. Delay at the AV Node:

* The AV node introduces a crucial delay, slowing the impulse to allow the ventricles to complete filling before they contract.

* This delay is facilitated by the smaller diameter of AV nodal cells and fewer gap junctions.

iv. Conduction Through the Bundle of His and Bundle Branches:

* From the AV node, the impulse travels rapidly through the bundle of His.

* The bundle of His bifurcates into the right and left bundle branches, which conduct impulses toward the respective ventricles.

v. Ventricular Conduction via Purkinje Fibers:

* The bundle branches further divide into Purkinje fibers, which distribute the electrical impulse throughout the ventricular myocardium.

* Rapid conduction through Purkinje fibers ensures a coordinated and forceful contraction of both ventricles (ventricular systole).

3. Functional Significance

The coordinated conduction of electrical impulses is vital for the heart's functionality. The SA node's role as the primary pacemaker sets the heart rate, while the AV node's delay ensures proper ventricular filling. The rapid conduction through the bundle of His, bundle branches, and Purkinje fibers enables synchronized ventricular contractions, maximizing cardiac output.

5.3. Cardiac Cycle – Cardiac output and its regulation

5.3.1. Cardiac Cycle

The **cardiac cycle** comprises all of the physiological events associated with a single heartbeat, including electrical events, mechanical events (pressures and volumes), and heart sounds.

A healthy heart that beats 70-75 times a minute takes about 0.8 seconds to complete each cardiac cycle. The atria and ventricles alternately contract in each cardiac cycle. The pressures in the chambers change greatly over the course of the cardiac cycle.

The cardiac cycle is essentially split into two phases, **systole** (the contraction phase) and **diastole** (the relaxation phase). Each of these is then further divided into an atrial and ventricular component.

The cardiac cycle therefore proceeds in four stages:

1. **Atrial systole**: lasts about 0.1 seconds - both atria contract and force the blood from the atria into the ventricles.

2. **Ventricular systole**: lasts about 0.3 seconds - both ventricles contract, blood is forced to the lungs via the pulmonary trunk, and the rest of the body via the aorta.

3. **Atrial diastole**: lasting about 0.7 seconds - relaxation of the atria, during which the atria fill with blood from the large veins (the vena cavae).

4. **Ventricular diastole**: lasts about 0.5 seconds - begins before atrial systole, allowing the ventricles to fill passively with blood from the atria.

The 'lubb dubb' heart sounds heard through a stethoscope are the sounds of the **atrioventricular (AV)** valves and **semilunar (SL)** valves opening and closing.

Cardiac output: The volume of blood pumped by the heart each minute, calculated as heart rate (HR) X (times) stroke volume (SV). 72 X 70 = 5040 ml or 5 Lit per minute.

5.3.2. Cardiac Output and Its Regulation:

Cardiac output (CO) is defined as the volume of blood the heart ejects per minute, calculated by the product of heart rate (HR) and stroke volume (SV).

The formula is: Cardiac Output = Heart Rate (HR) **X** Stroke Volume (SV).

Stroke Volume (SV) is the volume of blood pumped by one ventricle in a single heartbeat. Heart Rate (HR) is the number of heart beats per minute. Cardiac output is regulated by several factors, including heart rate, stroke volume, and the intrinsic and extrinsic mechanisms controlling these parameters

1. Regulation of Heart Rate (HR):

i. Autonomic Nervous System (ANS):

- **Sympathetic Nervous System** (SNS): Increases heart rate via norepinephrine binding to beta-1 adrenergic receptors on the SA node, enhancing pacemaker activity.
- **Parasympathetic Nervous System** (PNS): Decreases heart rate through acetylcholine release, which binds to muscarinic receptors, slowing SA node activity.

ii. Hormonal Influence:

- **Epinephrine**: Released by the adrenal medulla during stress, it increases heart rate.
- **Thyroid Hormones**: Thyroxine and triiodothyronine elevate heart rate by boosting metabolic rate and enhancing SNS sensitivity.

2. Stroke Volume (SV) Regulation

i. Preload: The degree of ventricular stretch at the end of diastole.

According to the Frank-Starling law, increased preload (greater end-diastolic volume) enhances cardiac muscle contraction force, thereby increasing stroke volume. Venous return and atrial contraction are key determinants of preload.

ii. Afterload: The resistance the ventricles must overcome to eject blood.

Higher afterload, often due to increased arterial pressure, can reduce stroke volume by making it harder for the heart to pump blood.

iii. Contractility: The intrinsic ability of cardiac muscle to contract independently of preload and afterload.

Influences:

*** Sympathetic Activation**: Increases contractility through norepinephrine.
*** Positive Inotropic Agents**: Substances like digitalis increase contractility.
*** Calcium Ions**: Elevated intracellular calcium levels boost contractile strength.

3. Integrated Regulation Cardiac output: It is finely tuned through the interplay of these factors:

i. Neural Regulation:

*** Baroreceptor Reflex**: Detects blood pressure changes and adjusts HR and vessel tone accordingly.

*** Chemoreceptor Reflex**: Responds to blood gas levels, modulating HR and SV to maintain oxygen supply.

ii. Hormonal Regulation:

*** Catecholamines**: Epinephrine and norepinephrine from the adrenal medulla increase HR and contractility.

*** RAAS**: The renin-angiotensin-aldosterone system modulates blood volume and vascular resistance, affecting preload and afterload.

iii. Intrinsic Mechanisms:

*** Frank-Starling Law**: Adjusts stroke volume based on venous return.

*** Cardiac Conduction System**: Ensures coordinated contractions for efficient blood ejection.

Thus, precise regulation of cardiac output is essential for maintaining cardiovascular health and responding to physiological challenges.

5.4.1 Nervous and Chemical Regulation of Heart Rate

Regulation of heart rate is a complex process involving both nervous and chemical mechanisms. Here's an overview of how these systems work to control heart rate:

i. Nervous Regulation

The autonomic nervous system (ANS) plays a critical role in regulating heart rate through its two main branches:

1. **Sympathetic Nervous System (SNS)**:

Function: Increases heart rate and the force of heart contractions.

Mechanism: Sympathetic nerves release the neurotransmitter norepinephrine (noradrenaline), which binds to beta-1 adrenergic receptors on the heart's pacemaker cells (located in the sinoatrial (SA) node). This increases the rate of depolarization, leading to an increased heart rate (positive chronotropic effect).

Effect: Enhanced cardiac output during stress or physical activity, known as the "fight or flight" response.

2. Parasympathetic Nervous System (PNS):

Function: Decreases heart rate.

Mechanism: The vagus nerve releases the neurotransmitter acetylcholine, which binds to muscarinic receptors on the heart's pacemaker cells. This decreases the rate of depolarization, leading to a reduced heart rate (negative chronotropic effect).

Effect: Conserves energy and promotes "rest and digest" activities.

ii. Chemical Regulation

Several hormones and ions can influence heart rate and the strength of heart contractions.

1. Hormones:

a. Epinephrine (Adrenaline): Released from the adrenal medulla during stress, epinephrine binds to beta-adrenergic receptors on the heart, similar to norepinephrine, increasing heart rate and contractility.

b. Thyroid Hormones: Thyroxine (T4) and triiodothyronine (T3) increase the heart rate by enhancing the effects of the SNS and increasing the metabolic rate of the heart.

2. Ions:

a. Calcium (Ca^{2+}): Elevated levels of calcium ions can increase the strength of heart contractions (positive inotropic effect). However, extreme levels can lead to cardiac arrhythmias.

b. Potassium (K^{+}): Potassium levels influence the electrical activity of the heart. Hyperkalemia (high potassium) can decrease heart rate and lead to arrhythmias, while hypokalemia (low potassium) can also cause arrhythmias and potentially increase heart rate.

c. Sodium (Na^+): Sodium ions are crucial for the depolarization phase of the cardiac action potential. Imbalances can affect heart rate and rhythm.

iii. Integration of Nervous and Chemical Regulation

The heart rate is finely tuned by the interplay between the nervous and chemical regulatory mechanisms:

i. Baroreceptor Reflex: Baroreceptors in the aorta and carotid arteries sense changes in blood pressure and send signals to the brainstem, which adjusts the balance between SNS and PNS activity to maintain stable blood pressure and heart rate.

ii. Chemoreceptor Reflex: Chemoreceptors in the carotid and aortic bodies detect changes in blood oxygen, carbon dioxide, and pH levels. This information influences respiratory and cardiovascular centers in the brainstem to adjust heart rate accordingly.

Understanding the mechanisms behind nervous and chemical regulation of heart rate is essential for diagnosing and treating cardiovascular disorders.

5.4.2. Blood Pressure and its Regulation

Blood pressure is the measure of the pressure developed against the wall of the **arteries** by the circulating **blood**. It is the measure of the pressure of the blood in the major arteries during the systole and diastole stages of the cardiac cycle. It is also called the ***systemic arterial pressure***. The normal blood pressure of a human **is** 120/80 (systolic/diastolic) mm of Hg**.** The instrument used to measure human blood pressure is called a sphygmomanometer**.**

Blood pressure is regulated by various mechanisms, mainly by two major mechanisms viz. the baroreceptor reflex and the renin-angiotensin-aldosterone system (RAAS). Besides, there are several other minor mechanisms including low-pressure baroreceptor, antidiuretic hormone, atrial natriuretic peptide, fluid and electrolyte level, kidney function, etc.

1. Baroreceptor Reflex:

Baroreceptors are mechanoreceptors located inside our blood vessels. There are two major baroreceptors each located inside the **carotid sinus** and **aortic arch**.

The ***carotid baroreceptor*** responds to both increases and decreases in blood pressure and sends the signal to the medulla oblongata of the CNS via the glossopharyngeal nerve.

The ***aortic baroreceptor*** responds to an increment in blood pressure and sends the signal to the medulla oblongata via the vagus nerve.

Once receiving signals from these baroreceptors, the brain will adjust sympathetic and parasympathetic neural activity resulting in regulation of the blood pressure by changing heart rate, vessels diameter, and cardiac action potential.

2. Renin-Angiotensin-Aldosterone System (RAAS):

RAAS is a hormonal system for regulating blood pressure by changing blood volume and diameters of blood vessels.

*** Renin Release**: Reduced blood flow to the kidneys or decreased sodium chloride levels in the renal tubules stimulate the release of renin from the juxtaglomerular cells of the kidneys. Renin catalyzes the conversion of angiotensinogen (produced by the liver) to angiotensin I.

*** Angiotensin-Converting Enzyme (ACE)**: Angiotensin I is converted to angiotensin II by angiotensin-converting enzyme (ACE), primarily found in the lungs. Angiotensin II is a potent vasoconstrictor that increases peripheral vascular resistance, leading to elevated blood pressure.

*** Aldosterone Release**: Angiotensin II also stimulates the release of aldosterone from the adrenal cortex. Aldosterone acts on the kidneys to increase sodium and water reabsorption, leading to increased blood volume and blood pressure.

3. Autonomic Nervous System (ANS):

i. Sympathetic Nervous System (SNS): The SNS plays a crucial role in short-term regulation of blood pressure. Sympathetic nerve fibers release the neurotransmitter noradrenaline (norepinephrine), which acts on alpha-adrenergic receptors in peripheral arterioles. Activation of alpha-adrenergic receptors causes vasoconstriction, increasing peripheral vascular resistance and elevating blood pressure.

ii. Parasympathetic Nervous System (PNS): The PNS primarily affects blood pressure indirectly through its influence on heart rate. Parasympathetic nerve fibers release acetylcholine, which acts on muscarinic receptors in the heart, leading to a decrease in heart rate and cardiac output, thus lowering blood pressure.

4. Other Regulatory Mechanisms:

i. Atrial Natriuretic Peptide (ANP): ANP is released from the atria of the heart in response to atrial stretch caused by increased blood volume. ANP promotes vasodilation, increases urinary sodium excretion, and inhibits the renin-angiotensin-aldosterone system, thereby reducing blood pressure.

ii. Vasopressin (Antidiuretic Hormone, ADH): Vasopressin, also known as antidiuretic hormone (ADH), is released from the posterior pituitary gland in response to dehydration or increased plasma osmolality. It promotes water reabsorption in the kidneys, leading to increased blood volume and blood pressure.