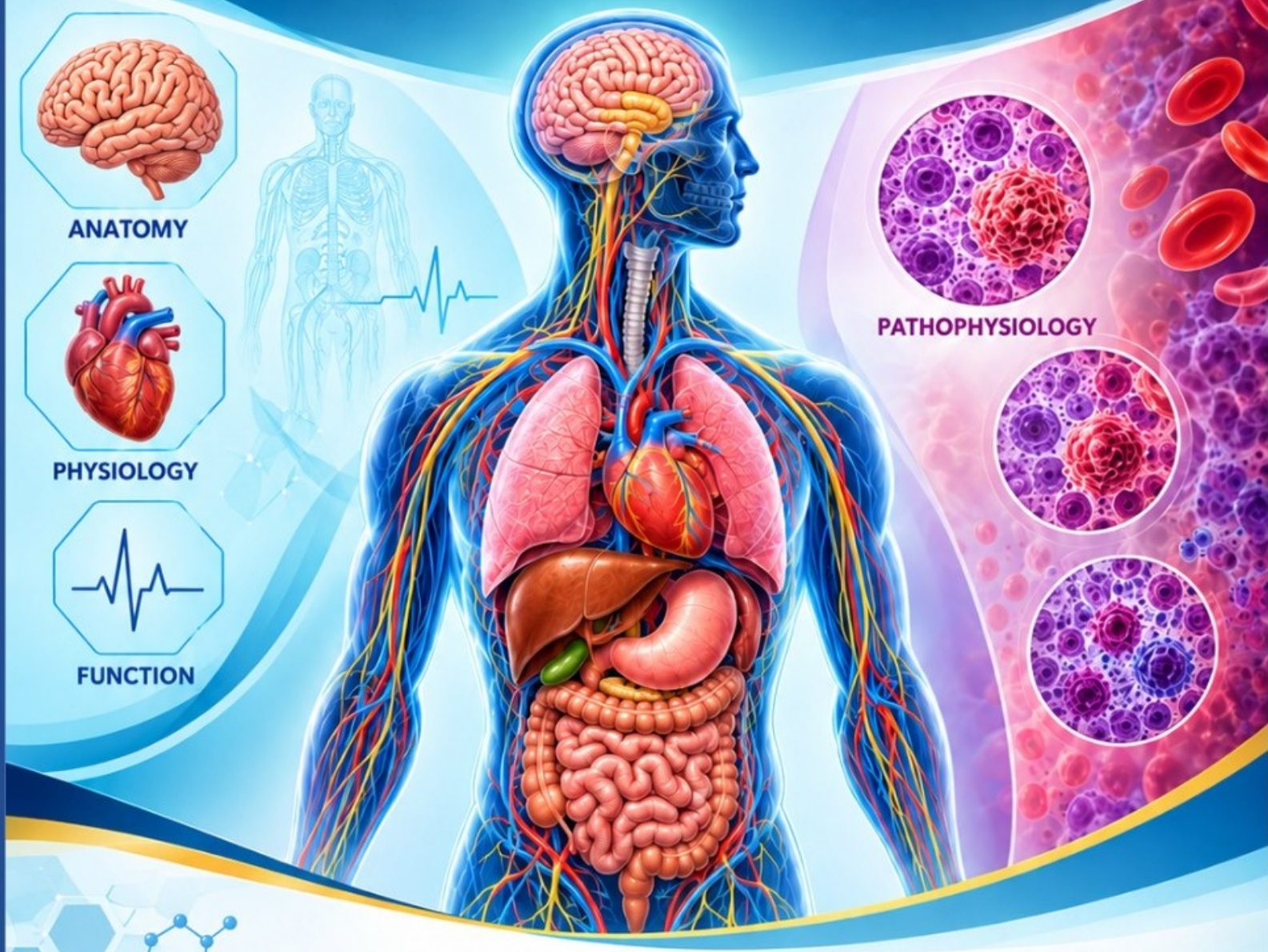
HUMAN ANATOMY, PHYSIOLOGY AND PATHOPHYSIOLOGY-II

EXCLUSIVELY DESIGNED AS PER NEP 2020 CURRICULUM, NEW SYLLABUS BY PCI NEW DELHI



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The completion of this book, *Human Anatomy, Physiology and Pathophysiology*, has been a fulfilling academic journey. **We** would like to express **our** sincere gratitude to all those who have contributed directly or indirectly to the successful completion of this work. First and foremost, we express our heartfelt gratitude to God Almighty for providing us with the strength, wisdom, and perseverance to complete this book. **We** sincerely thank **our** teachers, mentors, colleagues, and academic associates for their valuable guidance, encouragement, constructive suggestions, and continuous support. Their knowledge and expertise have been instrumental in shaping the content and presentation of this book. **We** are grateful to the authors, researchers, medical and pharmaceutical educators, and healthcare professionals whose textbooks, research publications, and scholarly contributions have provided valuable knowledge and references for the preparation of this work. **We** would also like to express **our** special appreciation to **our** students, whose curiosity, questions, and enthusiasm for learning have been a constant source of motivation. Their academic needs encouraged **us** to present complex concepts of anatomy, physiology, and pathophysiology in a clear, simple, systematic, and student-friendly manner. **Our** sincere thanks also go to **our** family members, friends, and well-wishers for their constant encouragement, patience, understanding, and moral support throughout the preparation of this book. Finally, **we** gratefully acknowledge everyone who has contributed in any way to the completion of *Human Anatomy, Physiology and Pathophysiology*. **We** sincerely hope that this book will serve as a valuable academic resource for students, teachers, researchers, and healthcare professionals and help readers develop a strong understanding of the structure, normal functioning, and disease processes of the human body.

Let me know if you would like me to adjust the text further, such as changing **"this book"** to **"these books"** if you are referring to a multi-volume series, or altering the overall **tone** of the acknowledgements.

The Authors

PREFACE

Human Anatomy, Physiology and Pathophysiology is an essential subject for understanding the structure, normal functioning, and disease processes of the human body. A sound knowledge of these fundamental concepts is important for students of pharmacy, medicine, nursing, and other healthcare disciplines.

This book has been prepared with the objective of presenting the subject in a simple, systematic, and student-friendly manner. It provides an integrated understanding of the major systems of the human body, beginning with their anatomical structure and normal physiological functions, followed by the mechanisms and manifestations of common pathological conditions.

The contents cover important topics related to the cell and tissues, skeletal and muscular systems, nervous system, cardiovascular system, respiratory system, digestive system, urinary system, reproductive system, endocrine system, and other major body systems, along with relevant concepts of pathophysiology.

Complex concepts have been explained in clear and concise language, with emphasis on their clinical and pharmaceutical significance. The book is primarily intended for B.Pharm and other healthcare students, and may also serve as a useful reference for teachers and professionals.

It is hoped that *Human Anatomy, Physiology and Pathophysiology* will help readers develop a strong conceptual foundation and understand the relationship between normal body functions and disease conditions, thereby supporting their further studies in pharmaceutical and health sciences.

The Authors

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Unit I...

NERVOUS SYSTEM

The nervous system is a crucial part of the human body that helps with communication and regulation. It aids the body's ability to detect both external and internal changes. It takes information from the senses, processes it, and then reacts correctly by sending the data to the right areas of the nervous system via specific receptors. By coordinating these processes, the nervous system aids the body in responding rapidly to different stimuli and maintaining a constant internal environment.

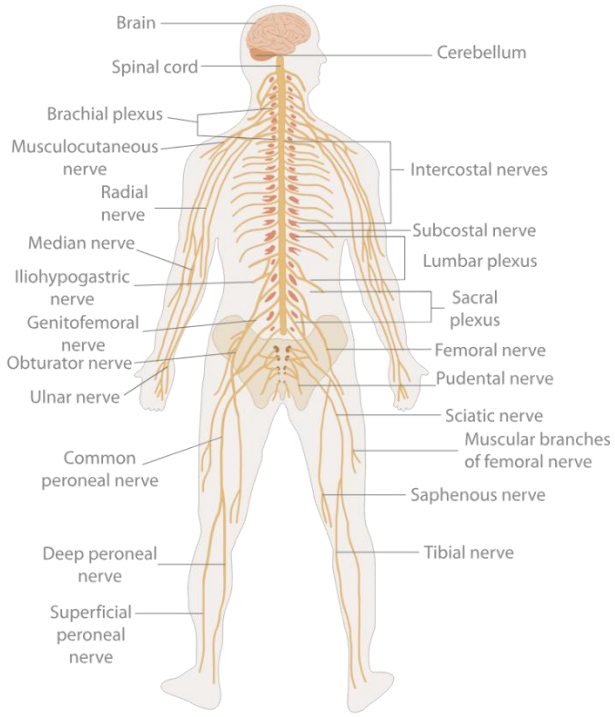


Figure 1.1: Nervous System

Source: (https://en.wikipedia.org/wiki/Nervous_system)

The nervous system regulates basic physiological functions in addition to being crucial for higher mental functions. The activity of nervous tissue is responsible for functions, such as learning, memory, intelligence, concentration, language, emotions, decision making and conscious awareness. It also controls and/or coordinates necessary functions such as maintaining posture, balance, muscle contraction, glandular secretion and some involuntary functions vital to life.

One half of the nervous system is located in the brain and the other half is in the rest of the body. Brain and spinal cord make up the central nervous system (CNS), the primary hub for processing and

integration. The peripheral nervous system (PNS) connects the various parts of the body to the central nervous system (CNS) via the nerves, nerve terminals, and ganglia located outside of the CNS. The proper transmission of sensory data to the central nervous system (CNS) and subsequent appropriate activation of muscles, glands, and other organs is guaranteed by this anatomical structure.

During normal neural activity, there is a constant flow of information between functional receptors, integrating centers, and effectors. Information about touch, pain, temperature, body posture, and internal organ activity is conveyed to the central nervous system (CNS) through the sensory or afferent component. Signals are transmitted to smooth muscles, cardiac muscle, and glands that are not voluntarily controlled by the motor/efferent division, which also conveys information from the central nervous system to an effector.

The nervous system is an integrated system that provides sensation, coordination, regulation, adaptation and response. It is well structured and has fast signaling pathways that enable the different organs and systems of the body to work together effectively to ensure normal physiological activities and overall homeostasis.

1.1 ORGANIZATION OF THE NERVOUS SYSTEM

In the neurological system, the most fundamental building blocks for receiving, processing, and transmitting information are the simplest structure-function units called neurones. Sensory neurones, motor neurones, and interneurons are the functional classifications of these, which are mainly made up of a cell body, dendrites, and axon. Structurally, they can be classed as unipolar, bipolar, multipolar, or pseudo unipolar. The astrocytes, oligodendrocytes, microglia, ependymal cells, Schwann cells, and satellite cells that make up neuroglia are responsible for sustaining, protecting, nourishing, insulating, and preserving the neurones' environment. Essential characteristics that allow for the efficient transmission of nerve impulses include excitability, conductivity, refractoriness, all-or-none response, and saltatory conduction. Nerve fibres can be either myelinated or unmyelinated.

1.1.1 Neurons

The building blocks of the nervous system, neurones also serve important functional and structural roles. A type of specialised cell that can take in data, process it, or integrate it with other signals, and then relay that data to other cells. Neurons transmit messages by way of electrical communications inside the cell, and chemical communications at the synapse. This communication allows for the coordination of the nervous system for sensory perception, movement, reflexes, and higher functions like learning and memory.

While neurons vary widely in size, shape and function, most have three major structural parts:

- **Cell body**
- **Dendrites**
- **Axon**

1. Cell Body

The cell body (soma, perikaryon) is where a neuron's metabolism and maintenance take place. Its nucleus and organelles enable it to conduct cellular activities such as energy production, protein synthesis, and other metabolic processes.

It contains:

- **Nucleus –** Keeps the DNA and RNA instructions for the cells under control.
- **Nucleolus –** primarily responsible for the production of the components of the ribosomes.
- **Mitochondria –** ATP production sites (mitochondria) for functioning of neurons.
- **Ribosomes** – involved in sites of protein synthesis.
- **Endoplasmic reticulum –** included in the process of protein expression and modification.
- **Golgi apparatus** – modifies, packages and moves around products of a cell.
- **Cytoplasm** – houses organelles and substances necessary for normal cellular functions.

The cytoplasm contains Nissl bodies, which are most commonly observed in neuronal cell bodies and dendrites. They are involved in the production of proteins vital to the upkeep and operation of the neurone; their principal components are the rough endoplasmic reticulum and ribosomes.

The cell body has a number of important functions such as:

- Maintaining the structural integrity of the neuron
- Synthesizing proteins and other cellular components
- Supplying energy for cellular processes
- Supporting growth and repair
- Receiving and integrating signals from dendrites and other neuronal regions

2. Dendrites

Dendrites are typically small processes that extend outward from the cell body. Their primary function is to receive signals sent by other cells, sensory receptors, or neighbouring neurones.

The branching architecture of dendrites provides a lot of room for synaptic development. Dendritic spines, which are tiny projections on some dendrites, can serve as potential sites of synapses. Dendrites receive signals from the outside world, which are processed by the neuronal membrane to alter its electrical characteristics. These changes are then sent to the cell body and the axon.

Therefore, dendrites are crucial in acquiring and synthesizing information from several sources.

3. Axon

Axons are specialised processes on the surface of each nerve cell that allow electrical impulses to be passed to other neurones or effector cells. It might be incredibly short or incredibly long; for example, axons can travel great distances throughout the body.

An axon hillock is the initial segment of an axon. These regions are crucial for the integration of incoming information and the threshold-dependent activation of action potentials.

Myelin is a protective sheath that most axons have; it speeds up and improves the efficiency of electrical signal transmission. At the points where myelin segments connect, holes called nodes of Ranvier are seen.

Axons can terminate in axon terminals or numerous branches at their distal ends. Neurotransmitters are stored in synaptic vesicles at the terminals. Neurotransmitters can be released into the synaptic gap and communicated to the next cell if the action potential reaches the terminal.

- ***Types of Neurons***

Structural classification is based on the number and arrangement of processes that extend from the cell body, while functional classification is based on the direction of information transmission, and both methods can be used to classify neurones.

A. Structural Classification

Unipolar Neurons

In a unipolar neuron there is only one process growing out of the cell body. The mature human nervous system contains very few truly unipolar neurons, but they are present in some invertebrates and at specific developmental stages of the nervous system.

Bipolar Neurons

Bipolar neurons has two processes from the cell body:

- One dendritic process
- One axonal process

They are related to specialized sensory function. For example, neurons found in the retina and parts of the olfactory system. They are arranged so as to convey information to higher centres from specialist receptors.

Multipolar Neurons

The axon and dendrites of a multipolar neurone are identical. These neurons have many dendritic processes that allow it to receive information from numerous other cells.

They are the most common type of neurons in the CNS and many of those involved in information processing and motor control are of this type.

Pseudounipolar Neurons

During development, bipolar neurones give rise to pseudounipolar neurones. The procedure splits in half as soon as it exits the cell body. The central nervous system (CNS) and the peripheral sensory receptor are both served by different branches.

Dorsal root ganglia and other sensory ganglia are characterised by their ability to transmit information from the sense of touch to the spinal cord.

B. Functional Classification

Sensory/Afferent Neurons

Sensory receptors send information to the central nervous system via afferent neurones. They let the neurological system detect changes in both the exterior and interior conditions of the organism.

They participate in sensing feelings like:

- Pain
- Temperature
- Touch
- Pressure
- Stretch
- Body position

These neurones transmit information about the senses to the central nervous system, which is essential for triggering the right responses.

Motor/Efferent Neurons

Messages are transmitted from the central nervous system to tissues known as effectors by motor or efferent neurones. The pathways that these neurones are a part of determine whether the responses are voluntary or involuntary.

Their targets include:

- **Skeletal muscles**
- **Smooth muscles**
- **Cardiac muscle**
- **Glands**

The nervous system can initiate movement and control a variety of physiological functions through these pathways.

Interneurons

The central nervous system is home to a specific type of neurone called an interneuron. They play a crucial role in the integration and processing of nervous system information because of the connections they form with other interneurons, including sensory, motor, and others.

They are important in determining reflexes, sensory interpretation, making decisions in neural circuits, and coordinating responding. Large numbers of interconnected interneurons can be found in complex neural pathways.

1.1.2 Neuroglia

Supporting neurones and keeping the nervous system in an optimal environment are two of the most important roles played by glial cells, which are specialised non-neuronal cells. While neurones are responsible for message transmission, glial cells are vital for the sustenance, protection, healing, and overall well-being of the nervous system.

Additionally, glial cells aid in chemical balance regulation and neuronal cell-to-cell communication. Cell division is possible in many types of glial cells but not in adult neurones.

There are several ways to group glial cells according to where they are located:

- **Glial cells of the CNS**
- **Glial cells of the PNS**

Glial Cells of the CNS

1. Astrocytes

Astrocytes are glial cells with a star shape that play a crucial role in supporting and constructing neurones. Neurones, blood arteries, and other glial cells are all contacted by their procedures.

Their functions include:

- Providing structural support to neural tissue
- Maintaining the appropriate extracellular ionic environment
- Regulating neurotransmitter concentrations
- Supporting neuronal metabolism
- Contributing to the blood-brain barrier
- Participating in tissue repair and scar formation following CNS injury

Astrocytes are therefore important for maintaining the stable environment required for normal neuronal activity.

2. Oligodendrocytes

Oligodendrocytes are specialised cells that provide the central nervous system (CNS) with the myelin coating. Myelin is an insulating layer that covers nerve fibres that enables electrical signals to pass through them more quickly and efficiently.

Unlike the PNS Schwann cells, a single oligodendrocyte is able to extend its process to myelinate more than one axon.

3. Microglia

The major immune and phagocytic cells of the CNS are the microglia. They are constantly present and activated by damage to the tissue or infection or inflammation.

They have the following primary roles:

- Engulfing cellular debris
- Removing damaged or dead cells
- Monitoring the local tissue environment
- Participating in inflammatory responses
- Contributing to defence against infection
- Assisting in tissue remodelling following injury

4. Ependymal Cells

The ependymal cells line the brain's ventricles and the spinal cord's central canal. Their primary function is the creation, transport, and control of cerebrospinal fluid (CSF).

The CSF protects and supports the CNS, and transports substances and removes metabolic waste from it.

Glial Cells of the PNS

1. Schwann Cells

The Schwann cells are the principal glial cells that myelinate the neurones at the periphery of the nervous system. In order to create the myelin sheath, which facilitates the efficient and rapid conduction of nerve impulses, they encase peripheral axons.

In a typical situation, myelin is produced when a single Schwann cell encases a portion of an axon. Additionally, Schwann cells play a crucial role in the regeneration and repair of peripheral nerve fibres.

2. Satellite Cells

The satellite cells are present around the neuronal cell body within the peripheral ganglia. They create a supportive layer around these neurons and regulate immediate external environment of these neurons.

They contribute to:

- Maintaining the chemical environment around neuronal cell bodies
- Providing structural support
- Regulating exchange of substances between neurons and surrounding tissues
- Supporting normal neuronal function

1.1.3 Classification and Properties of Nerve Fibres

A nerve fibre is usually considered as an axon, its coverings and supporting structures. Nerve fibres vary in structure and functional properties that affect their speed and efficiency of nerves impulse.

Nerve fibres can be categorised by:

- Presence or absence of myelin
- Diameter of the fibre
- Conduction velocity
- Functional role

Myelinated Nerve Fibres

Myelin encases the axon of a myelinated nerve fibre. Oligodendrocytes in the central nervous system and Schwann cells in the peripheral nervous system produce the sheath.

Myelin is a substance that is used to insulate an axon and prevent leakage of the electrical current across the axonal membrane. This allows an action potential to pass through the cell rapidly in a process known as saltatory conduction.

Myelinated fibres are especially vital in pathways that need quick information transfer, like pathways involved in moving, and some other sensory pathways.

Unmyelinated Nerve Fibres

Unlike myelinated fibres, unmyelinated nerve fibres are not surrounded by a multi layered myelin sheath. They conduct their action potential not in the saltatory fashion.

Therefore, they transmit impulses more slowly than similar myelinated fibres. They take part in multiple sensory and autonomic pathways.

❖ ***Important Properties of Nerve Fibres***

1. Excitability

A nerve fiber's excitability is its ability to alter its electrical characteristics in response to a specific stimulation. An action potential is produced when the stimulus exceeds the threshold, which causes alterations in the permeability of the neuronal membrane.

2. Conductivity

The conductivity is the capacity of a nerve fibre to conduct an electrical impulse from one part of the fibre to another. An action potential starts off and continues down an axon with a constant amplitude. Factors that affect the speed of conduction include axon diameter, myelination, and the properties of the axon membranes.

3. Refractoriness

The nerve fibre momentarily loses the ability to generate further action potentials once the first one has been triggered. The term used to describe this duration is the refractory period.

This is broken down into:

- There is typically no way to produce another action potential, no matter how strong the stimulation is, because of the **absolute refractory time**.
- An action potential may be generated by a stimulus that is stronger than usual, which is related to the **relative refractory period**.

Controlling the frequency of action potentials and ensuring that impulses travel just one way along an axon are both helped by refractoriness.

4. All-or-None Response

The membrane will not produce an action potential until it approaches threshold, according to the all-or-none principle. Once the threshold is crossed, the action potential's amplitude becomes relatively consistent. A single action potential's magnitude will not often be amplified in response to a stronger stimulation. Instead, changes in stimulus intensity are represented by variations in firing frequency and the recruitment of new nerve fibres.

5. Saltatory Conduction

Rapid impulse transmission, also known as saltatory conduction, occurs in myelinated axons. Since the myelin coating electrically insulates the majority of the axon membrane, the nodes of Ranvier are the primary sites of action potential regeneration along the axon. This causes the impulse to appear to “jump” between nodes. This mechanism can significantly enhance the conduction velocity, and also provide more energy-efficient signal transmission.

1.2 NEUROPHYSIOLOGY

The physiology of the functions, electrical properties, and mechanism of communication between neurons and between the nervous system. It describes how a neuron can produce an electrical signal, transmit information, receive sensory input, communicate via synapses and produce coordinated responses. These processes are the physiological underpinnings of sensations, actions, reflexes, thinking and regulation of bodily functions.



Figure 1.2: Neurophysiology

Source: (https://www.mcgill.ca/physiology/research/neurophysiology)

1.2.1 Electrophysiology

The study of the electrical activity generated by living cells, particularly neurones and muscle cells, is known as electrophysiology. Neurones produce electrical impulses by allowing charged ions to pass via specialised ion channels in the cell membrane. Neurones are able to receive, integrate, and transmit information through changes in electrical potential caused by ions flowing across the membrane.

A potential gradient exists between the intracellular and extracellular regions of a cell's membrane. This disparity is known as the membrane potential. The necessary movement of ions such as sodium (Na^+), potassium (K^+), chloride (Cl^-), and calcium (Ca^{2+}) allows for changes in membrane potential, which in turn mediates communication between neurones.

Resting Membrane Potential

Many neurones have a resting membrane potential of approximately -70 mV, which is the potential of a neurone when it is not generating an action potential. A negative number indicates that there is an electric charge on the inside of the neurone relative to the surrounding medium.

The resting potential is established and maintained by a number of interrelated processes:

- Ion distribution that is not uniform across the membrane
- Differential neuronal membrane permeability
- The movement of K^+ is facilitated by potassium leak channels, which follow its electrochemical gradient.
- The sodium-potassium pump is responsible for preserving the primary concentration gradients of sodium and potassium.

Active transport by the Na+/K+ ATPase is significant. To move, it draws energy from ATP:

- 3. The cell's sodium ions
- Two kelvins enter the cell

While the resting membrane potential is dependent on both the membrane's permeability to potassium and the pump, the latter is critical for sustaining the ionic gradients that are required for neuronal activity.

1.2.2 Action Potential

An excitable cell's membrane potential changes quickly and momentarily during an action potential. Neurones use it to send signals across vast distances with little degradation in signal strength.

To create an action potential, voltage-gated ion channels open and close in unison. Sodium and potassium ions are the ones that matter a lot.

Stages of an Action Potential

1. **Resting State:** Neurones approach their resting membrane potential just before action potentials begin. The ionic gradients are typically maintained by leak channels and ion pumps, while the sodium and potassium channels that are voltage-gated are closed.
2. **Threshold:** The point at which the membrane potential changes in response to an external stimulation. An action potential is initiated when the depolarisation reaches a certain threshold. The threshold usually ranges from approximately -55 mV, although it can differ among neurones and depend on their physiological condition. An important property of voltage-gated sodium channels is their threshold, which determines whether a given electrical shift is sufficient to open the channels regeneratively.
3. **Depolarization:** In response to a drop in intracellular potential, voltage-gated Na+ channels open rapidly. Sodium can enter the neurone via the electrochemical gradient. A temporary shift to a positive membrane potential is possible as a result of the increase in Na+ ions. In other words, this is a rapid depolarisation or increase in polarity.

4. Subsequently, following a short duration, the sodium entry (re-polarization) is decreased when voltage-gated sodium channels are rendered inactive. More voltage-gated K^+ channels open almost at the same time. The neurone releases K+, which removes the cell's positive charge. Repolarisation occurs as a consequence of this, as the membrane potential returns to a negative potential.
5. **Hyperpolarization:** During rest, the membrane does not immediately open potassium channels. The more time the channels stay open, the more potassium can leave the cell. For a short period, the membrane potential may be lower than the resting membrane potential. Hyperpolarisation or the after-hyperpolarization describes this stage.
6. **Return to Resting State:** Voltage-gated channels progressively go back to their resting states, while the Na+/K+ ATPase and leak channels keep the right ionic gradients.

After that, the neurone is prepared for additional electrical activity, and the membrane potential is returned to its resting state.

- **Refractory Periods:** The duration between action potentials during which neurones are less capable of generating more action potentials is called the refractory period.
  No further action potentials can be generated after the absolute refractory period, regardless of the strength of the stimulation. The key symptom is the deactivation of sodium channels that are controlled by voltage.
- **Relative refractory period:** It is possible to generate an additional action potential, but with more stimulation than usual. To a large extent, it resembles membrane hyperpolarisation.

To ensure that action potentials travel in an organised form, the refractory period helps to decrease the firing rate of neurones.

1.2.3 Nerve Impulse

Electrical activity travels along nerve fibres as a wave called a nerve impulse. It enables the transmission of information from one location within a neurone to another location, whether it be another neurone, a muscle, or a gland. In an unmyelinated axon, the action potential regenerates in a series of steps. The term for this phenomenon is continuous conduction. In a myelinated axon, the majority of the membrane is a myelin sheath, which serves as an electrical insulator. Saltatory conduction is the outcome of action potential regeneration mostly occurring at the nodes of Ranvier. In this manner, impulses can be transmitted more rapidly and effectively.

Factors Affecting Conduction Velocity

Several structural properties affect the speed of transmission of nerve impulses.

Conduction is generally faster when:

- Axon diameter is larger
- The axon is myelinated

An increase in the size of the axon will make less resistance to electrical current moving within the fibre and myelin will decrease the leakage of electrical current across the fibre. Thus, large myelinated fibres usually transmit impulses quickly and small unmyelinated fibres transmit them slowly.

1.2.4 Receptors

A sensory receptor is a special sensory cell or nerve ending or sensory structure which is specialized to detect a specific kind of stimulus and transduce it into an electrical signal that can be processed by the nervous system.

Each sensor has a specific function; one for detecting one type of energy or environmental alteration. This specialization enables the nervous system to make a distinction between different sensations.

❖ ***Types of Receptors***

1. Mechanoreceptors

Mechanoreceptors are those which are activated by mechanical distortion or external forces. They are involved in detecting:

- Touch
- Pressure
- Vibration
- Stretch
- Sound

They are found in skin, muscle, joints and specialized sensory organs.

2. Thermoreceptors

Thermoreceptors are receptors that detect changes in temperature. They are involved in sensing temperature differences in the environment and temperature changes within the body.

The information from these receptors affects temperature perception and thermoregulatory responses.

3. Chemoreceptors

Chemoreceptors are sensitive to certain chemicals. They participate in sensory functions such as:

- Taste
- Smell
- Detection of changes in blood chemistry

There are some internal chemoreceptors that assist in monitoring of variables like oxygen, carbon dioxide, and hydrogen ion concentration.

4. Photoreceptors

The specialized cells which respond to light are called photoreceptors. They can be found within the retina of the eye, and are primarily characterized by:

- **Rods** – specialized for vision under low-light conditions
- **Cones** – important for colour vision and detailed vision, particularly in brighter conditions

5. Nociceptors

Sensory receptors that respond to mechanical, chemical or thermal stimuli that could damage tissues are called nociceptors. Their activity helps to create the experience of pain and starts to trigger protective response to harmful conditions.

Proprioceptors

Specialised sensory receptors called proprioceptors detect changes in the body's position and motion. They have a special connection to the joints, muscles, and tendons.

They provide information concerning:

- Muscle length
- Muscle tension
- Joint position
- Body movement

This sensory information is vital to posture, balance, coordination and controlled movement.

1.2.5 Synapses

Information travels from neurones to other neurones or from neurones to effector cells across specialised functional junctions called synapses. Synaptic connections allow for the creation of elaborate networks of neurones, which are capable of processing and integrating vast amounts of data. Chemical and electrical synapses are the two main categories. There are two main types of synapses: chemical and electrical. The way signals pass the junction determines the kind of synapses.

- ***Types of Synapses***

Chemical Synapse

The vast majority of synapses in the human neurological system are chemical in nature. A little space, called the synaptic cleft, separates the two types of cells that communicate in this kind of synapse. The standard components of a chemical synapse are:

1. Presynaptic terminal
2. Synaptic cleft
3. Postsynaptic membrane

A series of processes culminates in the opening of voltage-gated calcium channels when an action potential is applied to the presynaptic terminal. The release of neurotransmitter into the synaptic cleft occurs when synaptic vesicles fuse with the membrane upon Ca^{2+} entrance.

After passing through the cleft, the neurotransmitter binds to specific receptors located on the postsynaptic membrane. A postsynaptic cell's excitatory or inhibitory response could result from this, depending on the neurotransmitter and receptor.

Electrical Synapse

Neighbouring cells can pass ions directly between each other by means of special structures called gap junctions in electrical synapses.

Communication is very fast since the electrical current flows directly from one cell to another. Electrical synapses are especially important in situations where groups of cells must activate simultaneously or synchronously.

Direction of Transmission

Most chemical synapses conduct messages in one direction only:

Presynaptic neuron → Postsynaptic cell

A directional organization enables the nervous system to channel information flow in specified neural pathways.

1.2.6 Neurotransmitters

Neurons release chemical messengers called neurotransmitters which send messages from one cell to another or target cells. They are released when the neurons are activated and bind to special receptors located on the post-synaptic cell.

Receptor structure is a major determinant of the effect of a neurotransmitter on its target cell. Thus, a single neurotransmitter may act in various ways in various tissues or pathways.

- ***Important Neurotransmitters***

Acetylcholine

Both the CNS and the periphery rely on the neurotransmitter acetylcholine (ACh).

It has significant functions in:

- Neuromuscular transmission

- Autonomic nervous system activity
- Attention, learning, and other CNS functions

Acetylcholine is a neurotransmitter that motor neurones can use to communicate with skeletal muscle fibres via the neuromuscular junction.

Dopamine

Dopamine plays a role in several different important neural pathways that are involved in:

- Movement
- Reward
- Motivation
- Cognitive functions

Alterations in dopaminergic signalling have been associated with a number of neurological and mental disorders. Reduced dopamine activity in specific motor pathways is a hallmark of Parkinson's disease.

Serotonin

A number of physiological and behavioural processes are regulated by 5-hydroxytryptamine (5-HT), often known as serotonin:

- Mood
- Sleep
- Appetite
- Pain processing

It further helps to manage the gastrointestinal and other functions of the body.

Noradrenaline

Significant roles are played by the neurotransmitter noradrenaline, which is also known as norepinephrine, in the following:

- Alertness
- Attention
- Arousal
- Stress responses
- Autonomic regulation

It aids the nervous system in regulating the body's function as the needs and demands of the environment and the body change.

Glutamate

The main excitatory neurotransmitter of the CNS is glutamate. It is especially important for communication between neurons and changes in the strength of the synapses.

It has significant contributions to the following:

- Learning
- Memory
- Synaptic plasticity
- Higher cognitive functions

However, under some pathological conditions excessive glutamate activity can be harmful to neurons.

- **GABA:** The brain's primary inhibitory neurotransmitter is gamma-aminobutyric acid (GABA). To keep nerve cells from becoming uncontrolled and too active, it reduces their activity, or excitability. The correct regulation of the excitation/inhibition balance in neuronal circuits is thus greatly influenced by GABAergic activity.
- **Glycine** is a key inhibitory neurotransmitter, especially in the brainstem and spinal cord. It regulates sensory and motor pathways and deactivates certain neurones. The correct balance of neuronal circuits is maintained by the combined action of excitatory and inhibitory neurotransmitters. Movement, feeling, thinking, autonomic nervous system regulation, and general nervous system function all depend on this balance.

1.3 CENTRAL NERVOUS SYSTEM

When it comes to processing and coordinating, the nervous system's central nervous system (CNS) is paramount. The central nervous system is comprised of the brain and spinal cord and is in charge of receiving information, coordinating reactions, and controlling the body's movements. Information from sensory pathways is continually transmitted to the CNS where it is used to produce motor, autonomic and behavioral responses that are appropriate.

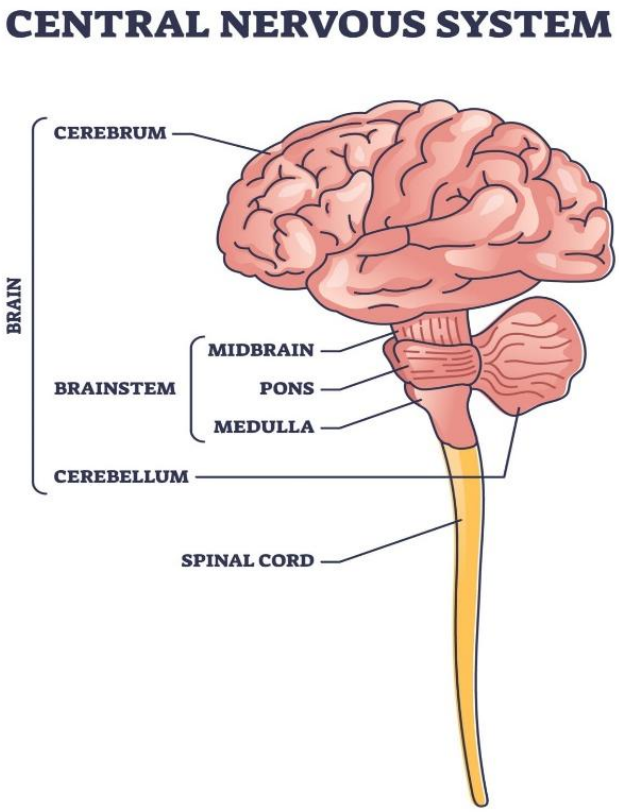


Figure 1.3: central nervous system (CNS)

Source: (https://www.simplypsychology.org/central-nervous-system.html)

The CNS is also the principal center for integration and/or higher neural activity. Each region has its own functions but they connect with each other without being separated as standalone structures. This organization makes it easy to coordinate sensory information, motor activity, autonomic regulation and cognitive processes efficiently.

1.3.1 Protective Structures

The brain and spinal cord are sensitive organs that must be properly protected as damage to the nervous tissue can cause a great deal of functional deficits. Skull and a vertebral column, meninges and cerebrospinal fluid provide protection, as well as special physiological barriers.

- ***Meninges***

The term "meninges" describes the three tiers of connective tissue that encase the central nervous system. The mechanical protection they provide includes supporting the blood vessels and helping to keep the environment surrounding the central nervous system (CNS) stable.

The meninges from outside to inside are:

1. Dura mater
2. Arachnoid mater
3. Pia mater

1. Dura Mater

The first meningeal layer is the thick, strong and relatively inelastic outer layer called dura mater. It gives good mechanical protection and helps to stabilize the CNS in the cranial cavity and the vertebral canal.

The dura mater in the skull is divided into two layers:

- **Periosteal layer –** very close to the inside of the skull.
- **Meningeal layer –** lies deeper and forms the principal meningeal covering.

In some areas the meningeal layer gives rise to dural folds between areas of the brain. These folds serve to provide structural support and to prevent too great a degree of movement of brain tissue.

2. Arachnoid Mater

In between the pia and dura maters is the thin and fragile arachnoid mater. Due to the thin strands of connective tissue that run from it toward the pia mater, it has a web-like appearance.

Underneath the arachnoid membrane lies the subarachnoid space. Vascularised CSF and the major blood arteries that supply the central nervous system populate this region. The subarachnoid space has a dual purpose: it carries fluids and provides a protected pathway for the vessels that supply the nervous system.

3. Pia Mater

The meninges' delicate pia mater lining is extremely thin and fragile. It has a tight fit with the brain and spinal cord, taking into account all of its ridges and valleys. It is closely related with superficial blood vessels of the CNS, and supports the underlying nervous tissue.

- ***Ventricles of the Brain***

The brain has a network of cavities that are interconnected, called the ventricular system. These cavities provide support and protection to and maintain CSF, which circulates through these cavities.

There are four major ventricles:

1. Right and left lateral ventricles
2. Third ventricle
3. Fourth ventricle

In comparison to the lateral ventricles located in the cerebral hemispheres, the third and fourth ventricles are located more centrally in the diencephalon and brainstem regions, respectively.

Flow of CSF

The CSF passes through the pathway of:

Lateral ventricles → Interventricular foramina → Third ventricle → Cerebral aqueduct → Fourth ventricle → Subarachnoid space

The cerebrospinal fluid (CSF) travels from the fourth ventricle into the subarachnoid region, which surrounds the central nervous system. The spinal cord's middle canal can also get a smaller amount. This continuous flow enables CSF to surround and regulate the CNS and to fulfil its protective functions.

- ***Cerebrospinal Fluid***

A transparent fluid called cerebrospinal fluid (CSF) envelops the brain and spinal cord and fills the ventricles. It shields the central nervous system from mechanical forces and maintains a specific fluid environment for the CNS.

Functions of CSF

1. **Protection from mechanical injury** – protects the brain and spinal cord from mechanical forces.
2. **Buoyancy –** decreases the weight of the brain, decreases pressure on supporting structures.
3. **Chemical stability –** keeps a proper chemical balance for neuronal activity.
4. **Waste removal –** to transport and eliminate metabolic waste.
5. **Substance exchange –** allows certain substances to be carried around the CNS.

The ventricular choroid plexuses are the principal organs responsible for cerebrospinal fluid production. The ventricular and subarachnoid spaces bring it into circulation, whereas arachnoid granulations mostly return it to the venous system.

1.3.2 Brain

The main integrating and coordinating organ is the brain of the CNS. It is responsible for taking in sensory information, making sense of it, having the right response(s) to it, and being involved in conscious awareness, thinking, feeling and controlling internal body functions.

There are the following major anatomical divisions:

- Cerebrum
- Diencephalon
- Brainstem
- Cerebellum

They have specialized roles but they do communicate a great deal with each other and the result is a coordinated nervous activity.

Cerebrum

As far as brain anatomy goes, the cerebrum is both the biggest and most advanced component. It consists of the two halves of the brain:

- Right cerebral hemisphere
- Left cerebral hemisphere

The corpus callosum is the most prominent of a vast network of nerve fibres that connects the two halves of the brain. The two hemispheres of the brain are able to communicate and work together thanks to these connections.

Cerebral Cortex

The cerebral cortex is a surface layer of the cerebrum that contains mainly grey matter. It has a large folding area to provide more space for neuronal processing.

The cerebral cortex is involved with:

- Conscious perception
- Voluntary movement
- Language
- Memory
- Reasoning
- Decision-making
- Learning

The different parts of the cortex are specialised to processes sensory, motor and association functions. Typically, however, the operation of complex behaviours requires communication between multiple areas of cortex and subcortical regions.

Major Lobes

- **Frontal Lobe**

A significant role is played by the frontal lobe in motor control and complex behavioural functions.

Its functions include:

- Voluntary motor control
- Planning and organization
- Decision-making
- Behaviour and personality
- Speech production

It also helps with attention, problem-solving and executive functioning.

- **Parietal Lobe**

Primarily concerned with processing and integrating data pertaining to bodily experience and spatial relationships, the parietal lobe.

Its functions include:

- Touch
- Pressure
- Pain
- Temperature
- Spatial awareness

It also plays a part in the brain's ability to understand the senses of body parts and how they relate to the external world.

- **Temporal Lobe**

The temporal lobe is related to several important functions of cognition and auditory processing.

Its functions include:

- Hearing
- Memory
- Language comprehension
- Emotional processing

It includes areas which assist in decoding sounds and comprehending speech.

- **Occipital Lobe**

Visual perception is mostly controlled by the occipital lobe. The visual regions of the occipital cortex receive the data from the retina and process it according to the image's characteristics, such as its shape, colour, motion, and spatial relationships.

Insula

Several sensory and affective processes are processed by the insula, which is located deep within the lateral sulcus.

It is involved in:

- Taste
- Visceral sensation
- Pain processing

- Emotional responses
- Autonomic functions

It contributes to the awareness of internal bodily states and their relationship to emotional experiences.

Brain Stem

An essential part of the neurological system, the brainstem acts as the principal connection between the cerebral cortex and the spinal cord. Along with serving as a conduit for information transmission, the brainstem has numerous crucial nuclei that control sensory, motor, and autonomic processes. All all, it has three major parts: the midbrain, the pons, and the medulla oblongata. Movement, feeling, reflexes, respiration, and regulation of the cardiovascular system are all made possible by the coordinated efforts of these structures.

The midbrain is located at the very top of the brainstem, halfway between the cerebral hemispheres and the pons. It plays a significant role in how our senses and muscles work together. The ability to swiftly respond to changes in light, motion, or sound is facilitated by visual and auditory reflexes, which are primarily controlled by the midbrain. Additionally, it aids in the regulation of muscular activity and eye movement. Important neural routes that facilitate communication between different parts of the nervous system, including the brain, brainstem, and spinal cord, are located in the midbrain.

Positioned halfway between the midbrain and the medulla oblongata, the pons is an essential component of the brain stem. As a hub for information transmission between various parts of the nervous system, it plays a crucial role. Furthermore, the pons is involved in breathing regulation and has pathways linked to sensory data and muscular control. Its links to the cerebellum, which controls and directs the smooth motions, make it significant.

At the bottom of the brainstem is the medulla oblongata which connects straight to the back bone. It is home to key centers that control multiple automatic and vital physiological processes. These include respiration and cardiovascular regulation which are required for life. The medulla also regulates or coordinates coughing, sneezing, vomiting and protective reflexes like swallowing. It controls a number of functions which are performed without conscious effort, so if the medulla is extensively damaged, the body functions may be seriously affected, and it could be life-threatening.

Cerebellum

A sizable region of the brain situated posterior to the brainstem is known as the cerebellum. It plays a crucial role in coordinating and refining motions, but not in initiating intentional motions. All the way from the brain and spinal cord to the vestibular system and sensory receptors, the cerebellum is

always taking in new information. It then compares the actual motion to the desired motion and takes this data into account when making changes.

The main role of the cerebellum is the control of movements. It promotes the movement to be smooth, accurate and controlled. It's also important to help maintain balance and posture by incorporating information about body position and balance. The cerebellum also plays a role in controlling muscle tone, ensuring that muscles have the right amount of tension when they are at rest and moving.

Learning motor skills, timing, and precision all include the cerebellum. It improves and polishes the previously acquired motor skills. Complex movements can be executed with ease and in unison because it regulates the timing and intensity of muscular contractions. So, while the cerebellum doesn't typically start voluntary movements on its own, it plays a significant role in making sure they're precise, coordinated, fluid, and synchronised.

A lesion to the cerebellum may affect normal coordination and balance. A common symptom is ataxia (lack of coordination with voluntary movement). Symptoms include poor coordination, stumbling and balance problems. Tremor can also occur when they are trying to carry out more precise motor functions, such as reaching for an object, and during purposeful movements.

Table 1.1: Structure and Functions of the Brain

Brain Region	**Major Functions**
Cerebrum	Consciousness, thinking, memory, sensation, voluntary movement
Frontal lobe	Planning, behaviour, voluntary movement, speech production
Parietal lobe	Somatic sensation and spatial processing
Temporal lobe	Hearing, memory, language comprehension
Occipital lobe	Visual processing
Brainstem	Vital functions, neural pathways, and reflexes
Cerebellum	Coordination, balance, posture, and motor learning
Hypothalamus	Homeostasis, autonomic regulation, and endocrine control
Thalamus	Major relay and processing centre for sensory information

1.3.3 Spinal Cord

A lengthy, slender structure that extends from the medulla oblongata via the vertebral canal is the spinal cord. It connects the central nervous system to the rest of the body's neurological systems.

The spinal cord's primary roles are:

- It acts as a 'highway' for the transmission of sensory and motor signals.
- It acts as an important integration centre for reflexes.

Connecting the central nervous system to various regions throughout the trunk and limbs, the spinal cord comprises 31 pairs of spinal nerves.

❖ ***Gross Structure of Spinal Cord***

The spinal cord has five distinct areas:

- Cervical region
- Thoracic region
- Lumbar region
- Sacral region
- Coccygeal region

The increase in diameter of two areas is due to the higher number of neurons and nerve fibres in the limbs.

❖ ***Cervical Enlargement***

The cervical enlargement is related to spinal nerves which innervate the upper limbs. The larger size is due to the extensive neural connections that are needed for the control and receipt of sensory information from the arms and hands.

❖ ***Lumbosacral Enlargement***

Lumbosacral enlargement is linked to nerves which innervate the lower limbs. It comprises circuits which control the sensation and movement of the legs.

The spinal cord is constricted and ends as the conus medullaris inferiorly. At this point, many nerve roots in the spine pass down into the vertebral canal. These nerve roots are part of what is called the “horse's tail” or cauda equina.

❖ ***Grey Matter and White Matter***

The structure of the spinal cord is different from the cerebrum.

In the spinal cord:

- **Grey matter** is located centrally.
- **White matter** surrounds the grey matter.

The central grey matter is butterfly or H-shaped, and includes both a number of neuronal cell bodies, dendrites, interneurons and supporting cells.

The grey matter includes:

- Posterior/dorsal horns
- Anterior/ventral horns
- Lateral horns in specific spinal cord regions

The posterior horns are mainly involved with sensory processing functions, while the anterior horns are housing motor neurons that provide skeletal muscle function. Lateral horns (if present) include neurons in autonomic functions.

Neighbouring white matter is composed of tracts of ascending and descending myelinated axons. These tracts connect the spinal cord with the higher areas of the brain.

❖ ***Functions of Afferent and Efferent Nerve Tracts***

Afferent/Ascending Tracts

Afferent or ascending pathways are the pathways that bring in sensory information from the body to higher centres in the CNS, specifically the brain.

They convey information about:

- Pain
- Temperature
- Touch
- Vibration
- Proprioception

The following ascending pathways are important:

- Dorsal column–medial lemniscus pathway
- Spinothalamic pathways
- Spinocerebellar pathways

These pathways have various pathways of sensory information they transmit and where they terminate in the brain. They work together to give the CNS the information it needs to detect conscious sensation, posture, coordination and protecting actions.

Efferent/Descending Tracts

Efferent or Descending pathways send motor commands from the higher centres of the brain down through the spinal cord to the motor neurons and other neural circuits.

Important pathways include:

- Corticospinal tract

- Vestibulospinal tracts
- Reticulospinal tracts

These pathways contribute to:

- Voluntary movement
- Postural control
- Muscle tone
- Balance
- Motor coordination

Descending pathways enable higher centres to modulate movements in the spinal motor circuits in response to sensory information and external stimuli.

Reflex Activity

A reflex is a rapid and relatively automatic response to a particular stimulus. The reflexes are also valuable protective mechanisms and play a role in maintaining posture and normal muscle activity.

A reflex arc is the nerve pathway involved in a reflex.

➢ Components of a Reflex Arc

Receptor → Sensory neuron → Integration centre → Motor neuron → Effector

The response can be generated in the spine and not reach the conscious brain for full processing, allowing the response to be made quickly without needing to wait for complete conscious processing in the brain.

Example: Withdrawal Reflex

When a person touches a hot object:

1. Pain and temperature receptors detect the harmful stimulus.
2. Sensory neurons transmit the information toward the spinal cord.
3. Interneurons integrate the incoming information.
4. Appropriate motor neurons are activated.
5. The relevant skeletal muscles contract.
6. The hand is rapidly withdrawn from the harmful stimulus.

Meanwhile, information from the senses is also conducted toward the brain so that a stimulus can be consciously perceived. So, a reflex response can offer protection quickly, which is followed by the brain's involvement with conscious awareness and additional behavioural responses.

1.4 PATHOPHYSIOLOGY OF NERVOUS SYSTEM DISORDERS

The study of disease and its effects on the body's structure and function is known as pathophysiology. Disruptions to normal brain circuit, neuronal, blood vascular, supporting cell, and communication pathway function can result from these alterations in neurological diseases. The disruption of essential bodily functioning, as well as sensory perception, motor control, cognition, and behaviour, can follow.

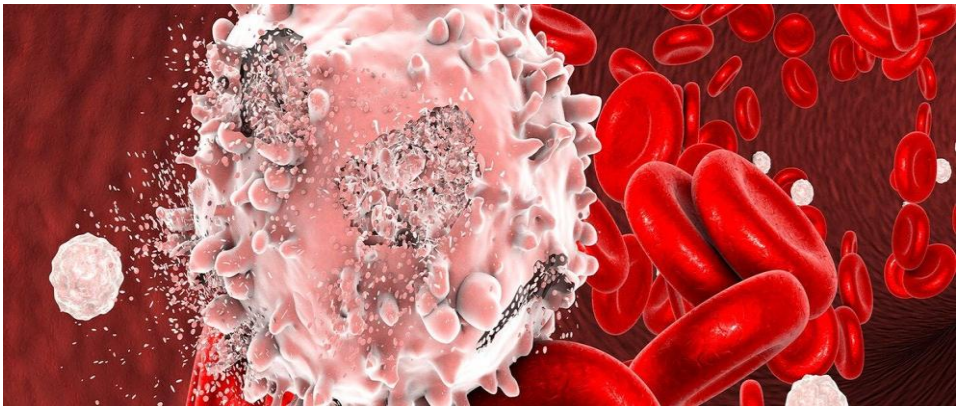


Figure 1.4: Pathophysiology

Source:(https://www.uclaextension.edu/sciences-math/sciences/course/introduction-pathophysiology-disease-states-human-body-physci-x-45910)

Nervous system problems can have many different origins, including as:

- Genetic abnormalities
- Vascular damage
- Infection
- Neurodegeneration
- Trauma
- Abnormal electrical activity
- Neurochemical imbalance
- Immune-mediated processes
- Tumours
- Metabolic abnormalities

These mechanisms can be independent or can interact with each other. Damage to the neurons, for instance, may change the activity of the neurons, impair the release of neurotransmitters, and, over time, impair the activity of larger neural networks. Likewise, damage to a given area of the brain may result in various symptoms because of the functions which the area normally performs.

The neurological disorders may result in sensory, motor, cognitive, emotional, behavioural and autonomic abnormalities since the nervous tissue coordinates and controls a wide range of body activities. The clinical signs vary with the location and size of the affected tissue, the cause of the problem and whether it is acute or chronic.

1.4.1 Epilepsy

Epilepsy is a disorder of the brain, a chronic predisposition to have recurrent unprovoked seizures. A seizure is a collection of neurons that starts abnormal, excessive electrical activity that is large enough or organized enough to disrupt normal brain function.

A seizure can affect some or all aspects of consciousness, movement, sensation, behaviour, or other neurological functions. Not all seizures are an indication of epilepsy; it is important to remember. Epilepsy is a chronic susceptibility towards spontaneous and recurrent seizures (which is the main diagnosis) and is supported by suitable neurological investigations.

❖ ***Pathophysiology***

Excitatory and inhibitory neuronal activity must be carefully balanced for normal brain function. Excitatory signals "activate" neurons while inhibitory signals "shut them down." During an episode of epilepsy, this balance could become disrupted so that some of the networks of neurons become too easily stimulated and more likely to fire together.

This abnormal excitability may be due to a number of mechanisms:

- **Altered ion channel function** – changes in the function of channels that transport ions across the surface of a neuron can change neuron excitability.
- **Neuron abnormalities –** altered levels of the neurotransmitter activity can lead to misaligned regulation of a neural circuit's activity.
- **Brain abnormalities –** abnormal or damaged areas of brain can form an area that can cause seizures.
- **Genetic predisposition –** inherited abnormalities can affect the ion channels, receptors or other parts of the process by which signals are passed between neurons.
- **Previous brain injury –** damage to neural tissue may result in long-term alterations in neuronal connectivity and excitability.
- **Some infections or metabolic disorders –** abnormal chemical or physiological changes in the brain can lead to abnormal electrical activity.

Seizures can be limited to a specific network of the brain or spread to other areas. The neurological effects of the seizure are dependent, in most part, on the location and pattern of the activity.

- **Types of Seizures**

Focal Seizures

Focal seizures start in a small area or network of one cerebral hemisphere. The symptoms are related to the affected functional area.

If a motor region is involved, for instance, then abnormal movements may occur; if a sensory region is involved, then unusual sensations may occur. Awareness can be preserved or may be impaired.

Generalized Seizures

In generalized seizures both cerebral hemispheres are engaged from the beginning. Consciousness is common (larger areas of the brain involved) and various motor manifestations may occur.

Clinical Manifestations

Symptoms can vary, depending on the abnormal electrical activity and its location, and include:

- Loss of consciousness
- Muscle jerking
- Muscle stiffening
- Abnormal sensory experiences
- Unusual behaviour
- Confusion
- Temporary loss of awareness

Some seizures may have a postictal state. In this period, normal brain activity slowly recovers and the person might be confused, fatigued, have a headache or experience brief neurological problems.

1.4.2 Parkinson's Disease

Parkinson's disease is a progressive neurological disorder which mainly targets the parts of the brain responsible for controlling and coordinating movement. As the disease advances, there can be non-motor deficits in addition to motor deficits.

- ***Pathophysiology***

One of the most important pathological alterations is the gradual loss of the neurons that produce the dopamine in the substantia nigra pars compacta. These normally release dopamine to the basal ganglia motor system structure, called the striatum.

Dopamine plays a role in the functioning of neural pathways that initiate and control movement. Individuals with low dopamine levels will have an imbalance of activity among basal ganglia circuits. This means that the movement may be slower and less automatic, and harder to get started. A second

characteristic pathological feature is the presence of abnormal intracellular protein aggregates which are related to Lewy bodies, and are generally labelled alpha-synuclein.

- **Major Symptoms**

The principal motor manifestations include:

- **Resting tremor**
- **Bradykinesia**
- **Rigidity**
- **Postural instability**

Other manifestations may include:

- Reduced facial expression
- Shuffling gait
- Speech changes
- Sleep disturbances
- Autonomic symptoms

The disease doesn't impact everyone equally. The non-motor features can precede, be concurrent with, or follow the major motor features and can be very mild or very severe.

1.4.3 Stroke

A stroke is a disruption of blood flow to an area of the brain, or a bleed into a blood vessel of the brain causing damage to brain tissue. Neurons need continuous and proper blood supply and disturbances of cerebral circulation can quickly affect the ability of the neurons to function.

Brain tissue always needs oxygen and glucose to produce energy to help maintain membrane potentials, ion gradients, and cellular functions. In the case of acute deficiency of this supply, cell energy deficiency results and damage can be inflicted on the neurons.

1. Ischemic Stroke

Ischemic stroke is a stroke caused by a blockage in the artery that feeds the brain. This slows the circulation to the damaged tissue and removes oxygen and nutrients that are needed by neurons.

Common mechanisms include:

- Thrombosis
- Embolism
- Arterial occlusion

When cerebral blood flow is decreased, there is a failure of cellular energy. As the deficiency progresses, normal membrane functioning is impaired, cell function ceases, and then cell injury continues. If the ischemia is too prolonged and severe, the brain tissue can be permanently damaged and the resulting infarction will be irreversible.

The damaged central area can be surrounded by impaired tissue which can be restored to function if blood flow is restored in time.

2. Hemorrhagic Stroke

In a haemorrhagic stroke, a blood vessel in the brain ruptures, causing blood to build up inside or on the brain.

The blood can cause mechanical damage, initiate inflammatory response and press on adjacent nerve structures. Blood can also build up and raise ICP, further impairing normal function of the brain.

- **Clinical Manifestations**

Symptoms of the disorder are related to the area and amount of brain damaged tissue. They may include:

- Sudden weakness or numbness
- Facial drooping
- Difficulty speaking
- Visual disturbances
- Loss of balance
- Severe headache, particularly in some hemorrhagic strokes
- Altered consciousness

Early recognition and treatment of stroke can limit neurological injury and improve the chances of recovery, so the immediate medical evaluation of stroke is necessary.

1.4.4 Migraine

Migraine is a chronic, neurological disorder with recurrent attacks of headache which can include sensory, gastrointestinal and neurological symptoms. The disease is not just vascular changes and is linked to changes in the activity of certain brain networks.

- ***Pathophysiology***

The trigeminal pain pathway is activated and aberrant functioning of related brain networks is associated with migraine. Neuropeptides like calcitonin gene-related peptide (CGRP) may be released upon activation of trigeminal fibres. CGRP changes the area around the blood arteries in the brain that are involved in migraines and also has a role in pain signals.

Cortical spreading depression has been linked to temporary neurological symptoms that occur before or during the headache in people who have an aura. This is a process of changing activity of the neurons and glia, which travels across regions of the cerebral cortex.

- **Symptoms**

A migraine attack may include:

- Moderate to severe headache
- Throbbing or pulsating pain
- Nausea

An aura can occur before or during the headache in some people. Aura may cause:

- Visual disturbances
- Sensory symptoms
- Speech disturbances

Migraine attacks can vary widely among individuals and even between different attacks for an individual.

1.4.5 Depression

Depression is a disorder that involves feelings, thinking, behaviour and physical function. It can disrupt significantly day to day functioning and social, academic, occupational and interpersonal functioning.

- ***Pathophysiology***

Depression is a polyetiology disease, not due to one single biological abnormality. It involves interplay between neural circuits, neurotransmitter systems, stress-response systems, genetic predispositions, environmental factors, and processes of neural plasticity.

Key neurotransmitter systems involved are:

- Serotonin
- Noradrenaline
- Dopamine

These systems are involved in the regulation of mood, motivation, reward, attention and other behaviour. But it is important not to think of depression as a problem with only one neurotransmitter. Disorder is also due to modifications in the communication between various areas of the brain, as well as changes in the control of neural networks.

- **Symptoms**

Common symptoms include:

- Persistent sadness
- Loss of interest or pleasure
- Fatigue
- Sleep disturbance

People with the disease have different symptoms. There may be noticeable physical or cognitive challenges, or greater emotional shifts.

1.4.6 Schizophrenia

Schizophrenia is a long-term mental health condition characterised by problems with thinking, perception, behaviour, emotions and learning. These changes may involve relationship issues, educational, work, and independent living problems.

- ***Pathophysiology***

Schizophrenia is characterized by abnormalities in multiple inter-related circuits in the brain, as well as in neurotransmitter systems. Signalling in the dopamine system plays a key role, and abnormalities of glutamatergic pathways and other systems also play a role.

The disorder involves several different neural pathways, which is why it gives rise to one or more clusters of symptoms: psychotic experiences, lack of motivation, emotional changes and cognitive difficulties.

- **Symptoms**

The symptoms are generally classified as positive, negative, and cognitive symptoms.

Positive Symptoms

These include experiences or behaviours that don't normally occur.

They include:

- Delusions
- Hallucinations
- Disorganized speech
- Disorganized behaviour

Hallucinations are false perceptions of an external stimulus that do not exist and delusions are fixed beliefs that are not supported by reality.

Negative Symptoms

Negative symptoms are a decrease in normal emotional or behavioral activities.

They include:

- Reduced emotional expression
- Social withdrawal
- Reduced motivation
- Reduced speech
- Loss of interest

These symptoms can significantly affect interpersonal relations and daily living.

Cognitive Symptoms

Cognitive changes may affect:

- Attention
- Memory
- Executive function
- Information processing

These challenges may disrupt planning, organizing, learning, and performing of complex daily activities. Often, individuals with schizophrenia need long-term clinical care, and therapy should aim at controlling symptoms, reducing the likelihood of a relapse, and promoting functioning.

1.4.7 Alzheimer's Disease

The neurodegenerative illness known as Alzheimer's is among the leading causes of dementia. Over time, it interferes with cognitive processes and, eventually, with how a person goes about their everyday life.

It primarily affects:

- Memory
- Thinking
- Learning
- Language
- Behaviour
- Ability to perform daily activities

Pathophysiology

Important pathological changes include:

1. Accumulation of amyloid-beta plaques
2. Abnormal tau protein forming neurofibrillary tangles
3. Synaptic dysfunction
4. Neuronal loss
5. Brain atrophy

Abnormal tau is found within neurons while amyloid-beta is found outside neurons. Abnormal tau disrupts the normal functioning and internal organization of the nerve cells.

Impaired communication between neurons is a critical aspect of synaptic dysfunction. As the damage to neurons continues, more neurons are lost until the areas of the brain that are damaged appear to shrink or the brain atrophies in those areas.

Structures involved in memory are typically the first and most commonly involved, such as the hippocampal formation. This is one reason why a loss of memory is a common early noticeable symptom.

- **Symptoms**

Early manifestations may include:

- Forgetfulness
- Difficulty learning new information
- Word-finding problems

With progression, individuals may develop:

- Severe memory impairment
- Disorientation
- Language impairment
- Behavioural changes
- Loss of independence

The disease typically runs a slow course, with how fast and how the cognitive decline happens being somewhat different from one person to another.

1.4.8 Meningitis

Meningitis is swelling of the membranes (meninges) that cover the brain and spinal cord. These protective membranes are in close proximity with the fluid and CNS, and inflammation can disrupt the normal functioning of the nervous system. Meningitis can happen due to:

Meningitis may result from:

- **Bacteria**
- **Viruses**
- **Fungi**
- Other infectious or non-infectious causes

Pathophysiology

One can develop infectious meningitis when a pathogen enters the CNS and triggers inflammation of the meninges and CSF. The inflammatory process may also involve the composition and movement of CSF and the adjacent blood vessels and nervous tissue.

The resulting inflammation may lead to:

- Increased intracranial pressure
- Cerebral dysfunction
- Altered CSF composition
- Damage to nervous tissue
- In severe cases, sepsis or neurological complications

The severity of the clinical disease depends on the type of organism, the level of inflammatory response and the rapidity of the appropriate treatment.

- **Common Symptoms**

Typical manifestations include:

- Fever
- Severe headache
- Neck stiffness
- Nausea and vomiting

Other complications may be seizures and neurologic deficits. Bacterial meningitis can develop quickly and is a medical emergency that must be treated quickly.

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Unit II…

GASTROINTESTINAL SYSTEM

The vast network of organs known as the gastrointestinal (GI) system, or digestive system, begins processing food the moment it enters the body and continues until the indigestible portions are eliminated. The transformation of nutrients into forms that may be absorbed by cells for energy production, development, tissue repair, and general function is made possible by these processes.

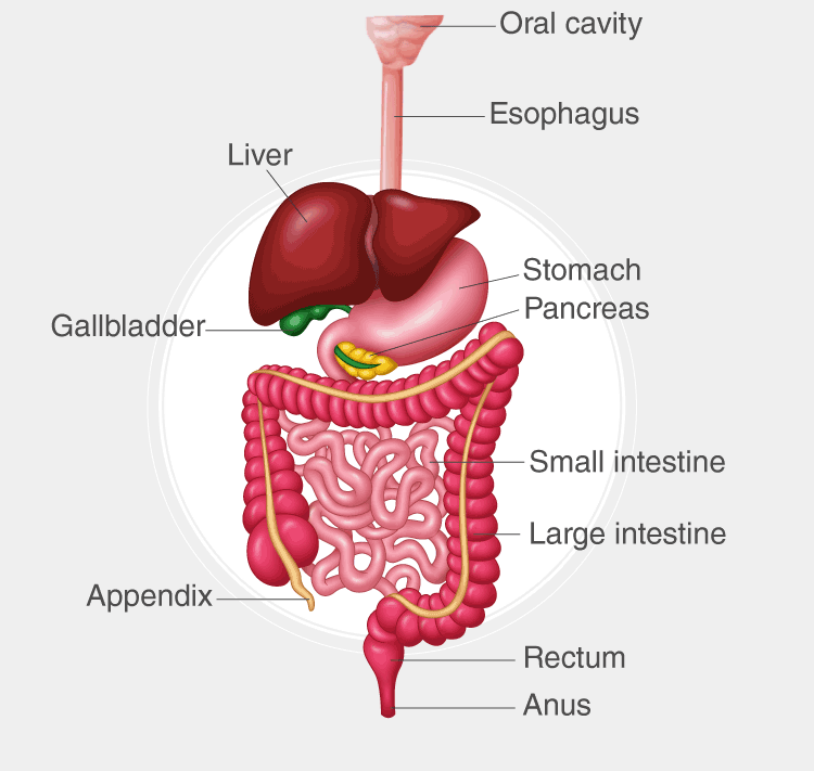


Figure 2.1: Gastrointestinal (GI) System

Source: (https://byjus.com/biology/gastrointestinal-tract/)

The digestive organs and the oesophagus, stomach, and small intestine make up what is called the gastrointestinal system. The oral cavity, pharynx, oesophagus, stomach, small intestine, large intestine, rectum, and anal canal make up the gastrointestinal tract, which is a continuous tube of muscles that starts at the mouth and ends at the anus. In order to aid in the digestion process, the pancreas, liver, gall bladder, and salivary glands secrete, store, or produce chemicals that are necessary for the disintegration and processing of food.

Ingesting food initiates a cascade of coordinated mechanical and chemical reactions that make up digestion. Chemical digestion makes use of digestive juices and enzymes to simplify nutritional

molecules, while mechanical digestion physically breaks food into tiny pieces. The gut wall acts as a conduit for the absorption and subsequent distribution of these products to different tissues. In the process of elimination, some of the food that isn't being broken down or absorbed is being forced farther and further down the digestive tract.

Ingesting, propelling, mechanical and chemical digestion, secretion, absorption, and faeces are the main activities of the gastrointestinal tract. Coordinating these processes involves a tight integration of the neurological systems, gastrointestinal hormones, local chemical signals, and smooth muscle action. For optimal digestion and absorption, it is best to arrange food in a specific way and at specific times.

In addition to digesting food, the gastrointestinal system also acts as a regulator and a barrier. Protecting the body against potentially dangerous foods and germs is a crucial function of the intestines and the immune tissues that line them. Specialised cells in the gastrointestinal tract play an important role in endocrine signalling, which regulates motility, food intake, digestion, and nutrient utilisation. The gastrointestinal system also controls the absorption and flow of water and dissolved chemicals, which serves to maintain the body's electrolyte and water balance.

2.1 ANATOMY OF THE GASTROINTESTINAL TRACT

The gastrointestinal tract (GI tract) is a muscular and membrane-lined tube that acts as a digestive system, taking in food, processing it, absorbing nutrients, and then passing the waste products out the back through the anus. Digestive organs such as the pancreas, liver, and small intestines are located inside this system, which also includes the mouth cavity, throat or pharynx, oesophagus, stomach, rectum, and small and large intestines. In most cases, it consists of mucosa, submucosa, muscularis externa, and serosa/adventitia; however, in certain organs, such as the intestines and stomach, it serves to store food, combine it with other substances, digest it, absorb nutrients, recover water and electrolytes, and produce and eliminate waste.

2.1.1 General Anatomy of the GI Tract

A lengthy muscular tube called the gastrointestinal (GI) tract or alimentary canal connects the anus to the oral cavity. It is the main function to receive food, to transport it, to mechanically and chemically break it down, to absorb nutrients and water and to remove the rest of the food which has not been digested. It is said to be a continuous tube, but structurally it is specialised to carry out specific functions in various regions.

The GI tract is aided by accessory digestive organs such as the liver, gall bladder and pancreas. These organs are not a continuous track through which food passes, but instead produce secretions that are necessary for the digestive system to function.

- **Major parts of the GI tract**

The digestive tract consists of:

1. Oral cavity
2. Pharynx
3. Oesophagus
4. Stomach
5. Small intestine
6. Large intestine
7. Rectum
8. Anal canal

These structures are the place where food passes by one after another. Every region alters the food before passing it on to the next part. Digestion starts in the mouth and the pharynx and the oesophagus are mainly involved in swallowing and transport. The stomach stores and mixes food, while the intestines are mostly digestion, absorption and faecal material making and elimination.

Coordinated smooth muscle activity, smooth muscle sphincter function, activity of the enteric nervous system and gastrointestinal hormones all regulate the transport of material through the GI tract. Sphincters are specialized muscle rings that open or close to pass contents from one area to another and to prevent contents from flowing backwards.

Basic wall structure of the GI tract

Most of the GI tract has four major layers:

1. Mucosa
2. Submucosa
3. Muscularis externa
4. Serosa or adventitia

Lumen surrounded by these layers concentrically. They are not uniform in thickness, cell content and in their special structures among regions depending on the specific functions of the segment.

1. Mucosa

As the innermost layer of the gastrointestinal tract, the mucosa comes into direct touch with lumen contents. It is consequently very specialized in its protective, secretive, digestive and absorptive functions.

The mucosa is consists of:

- Epithelium
- Lamina propria
- Muscularis mucosae

The epithelium is the surface lining and varies greatly throughout the GI tract. For instance, stratified squamous epithelium is found where there is a lot of mechanical friction, while simple columnar epithelium tends to line areas that are adapted for absorption and secretion.

The connective tissue layer under the epithelium is termed lamina propria. Containing miniature blood vessels, lymphatic vessels, immune cells, and, in certain areas, glands. The vascular supply is especially significant because many absorbed nutrients pass into the blood or lymphatic circulation through structures situated within this area.

The muscularis mucosae is thin smooth muscle layer which brings about local movements in the mucosa. The movements can enhance the mucosal surface-luminal contact and help secretions from some glands.

The mucosa has a number of important functions:

- Excessive secretion of mucus, enzymes and other substances.
- Nutrient, water and electrolyte absorption
- Protection from mechanical and chemical damage
- Immune defence against microorganisms and potentially harmful substances

Specialised cells are also found in the mucosa which can either produce hormones or detect sensory stimuli to enable the digestive tract to respond to the contents of the tube and the volume.

2. Submucosa

The submucosa is the supportive structure for the inner lining, or mucosa, and is adjacent to it.

It is formed of connective tissue which contains:

- Blood vessels
- Lymphatic vessels
- Nerves

- Glands in certain regions

Larger blood and lymphatic vessels that supply and drain the mucosa are located in this layer. Particularly in regions with high absorption rates, this is crucial. Additionally, Meissner's plexus, or the submucosal nerve plexus, is located in the submucosa. This segment of the enteric nervous system plays a critical role in regulating mucosal activity, local circulation, and gland secretion. In specific sections of the gastrointestinal tract, the submucosa allows the mucosa to slide and form folds due to its composition of flexible connective tissue. The extent to which the organ is swollen might cause these folds to alter.

3. Muscularis Externa

The primary layer of muscles responsible for propelling and combining gastric contents is the muscularis externa.

Typically, it includes:

- The inside of the quadriceps
- Longitudinal structure on the outside

A network of nerves known as the myenteric plexus or Auerbach's plexus connects two layers of muscle. Coordination of gastric propulsion relies on it.

The circular and longitudinal layers of muscle contract in different patterns, causing different types of movement. Coordinated waves of contraction, or peristalsis, advance the luminal contents. During segmentation, the intestines contract rhythmically, bringing their contents into closer proximity to the intestinal wall.

Muscularis externa activity is regulated by enteric nervous system activity, ANS, gastrointestinal hormones and local chemical stimuli. This makes it possible to regulate gastrointestinal movement based on the content and content volume of the gastrointestinal lumen. Muscle organization is different in special areas. For instance, the sphincters have a prominent circular muscle and help control the passage between different parts of the tract.

4. Serosa or Adventitia

Depending on the area, the lining of the gastrointestinal tract could be adventitia or serosa. Parts of the digestive system that dangle in the peritoneal space have an outside surface called the serosa. Mesothelium, a thin layer covering connective tissue, lines the inside. It provides a smooth surface that reduces friction between the organs of the abdomen.

The adventitia, however, contains primarily connective tissue and is the connection between an organ and other structures. Occurs where the GI tract is not lined by visceral peritoneum. The difference in

serosa versus adventitia is more related to the relationship of a given gastrointestinal segment to the peritoneal cavity and surrounding tissues.

2.1.2 Anatomy and Functions of the Stomach

The stomach is a muscular, expandable organ that mostly occupies the upper left quadrant of the abdominal cavity. The amount of food and the person's position determine the size and shape.

The stomach serves as an important transitional organ between the oesophagus and small intestine. It has a muscular wall which enables it to dilate following meals and produce strong contractions that help to mix food contents.

It connects:

Oesophagus → Stomach → Duodenum

The pyloric sphincter regulates the opening between the stomach and the intestines, while the gastro-oesophageal junction is responsible for the opening between the oesophagus and the stomach.

- **Major regions of the stomach**

The stomach is divided into:

1. Cardia
2. Fundus
3. Body
4. Pyloric part

Rugae are folds that are found in the inside of the stomach. The folds enable the stomach to expand quite a bit when food is taken. The stomach stretches and the rugae start to become flat.

1. Cardia

Cardia refers to the part around the opening where the oesophagus enters the stomach. It is rich in mucous glands which help to protect the gastric lining. The gastroesophageal junction is also a significant physiological barrier to reflux of acid stomach contents into the oesophagus.

The lower oesophageal sphincter is not so simple as an anatomical ring like the pyloric sphincter, but, like the other sphincters, it does play a role in the control of gastric reflux by increasing smooth muscle tone in the distal oesophagus.

2. Fundus

A person's fundus is the upper, dome-shaped portion of their stomach. Not only does it relax the stomach so that food may pass through, but it also has a specific function in the digestive process. Reason being, there's no proportional increase in intragastric pressure when the stomach is full.

The fundus is also an important site for temporary storage of swallowed food and air. The gastric secretory cells are found in the fundus throughout and help to secrete gastric fluid.

3. Body

Sitting between the fundus and the pyloric region, the stomach's biggest section is known as the body. It has a large number of gastric glands with specialised cells that make up parts of the gastric juice. The body is also heavily involved in mechanical mixing.

Contractions slowly grind up the food and mix it with the stomach's juices. This makes the relatively solid meal into a more homogeneous substance and allows to feed it gradually into the duodenum.

4. Pyloric part

The distal part of the stomach, the pyloric part, is composed primarily of:

- **Pyloric antrum**
- **Pyloric canal**

Pyloric antrum has strong muscular contraction which aids in grinding and mixing food particles with gastric secretion. The pyloric canal is a conduit to the duodenum, ending at the pyloric sphincter. The sphincter controls the amount of food which enters the small intestine. This helps to ensure that excess delivery of chyme is avoided and adequate time for intestinal digestion and neutralization.

- **Functions of the stomach**

The stomach is responsible for a number of vital processes:

- Temporary storage of food
- Mechanical mixing
- Secretion of gastric juice
- Initiation of protein digestion
- Formation of chyme
- Regulation of gastric emptying
- Secretion of intrinsic factor
- Limited absorption of certain substances

The stomach breaks down food that has been swallowed into a semi-liquid substance called chyme.

The stomach is not only a functional organ; it also serves as a protective barrier. Creates an acid environment that can inhibit or destroy many of the microorganisms that invade with food. Mucous layer and mucous secretions, bicarbonate secretion, integrity of the epithelial barrier and speedy cellular repair prevent the gastric mucosa from being degraded by its own secretions.

Another important function of the stomach is an endocrine function. Specific cells secrete hormones and signaling molecules that affect the secretion, motility, appetite and function of other digestive organs.

The specialised gastric parietal cells create the intrinsic factor, which is essential for the absorption of vitamin B_{12} in the terminal ileum. Hence, gastric function is crucial for vitamin B_{12} absorption, even though the stomach does not really absorb the vitamin.

2.1.3 Anatomy and Functions of the Small Intestine

Enzymatic digestion and nutrient absorption mostly occur in the small intestine, the longest and most specialised portion of the gastrointestinal system.

Its precise location is between the ileocecal junction and the pyloric sphincter. An increase in the area of interaction between the digested meal and the absorptive epithelial cells is caused by its length and highly specialised interior surface.

It has three parts:

1. Duodenum
2. Jejunum
3. Ileum

A huge network of blood and lymph vessels surrounds the small intestine. These are especially significant, as different kinds of digestive products are absorbed into different transport pathways.

1. Duodenum

In the small intestine, the duodenum is the first and least lengthy section. Transports food from the stomach to the small intestine after it has been partially digested.

It is given

- Stomach-derived chyme
- Liver and gallbladder waste
- Pancreatic bile and other secretions

Bile aids in the digestion and absorption of lipids and pancreatic secretions contain digestive enzymes and bicarbonate. Neutralisation of acid contents coming into the duodenum by the bicarbonate.

Digestive enzymes work best in an acidic environment, which is why the duodenal mucosa has its own unique glands that release an alkaline fluid to keep the intestinal mucosa in its protective barrier. Consequently, the duodenum plays a crucial role in the chemical breakdown of stomach contents prior to their passage in the intestines.

2. Jejunum

Nutrient absorption is the exclusive domain of the jejunum, a portion of the small intestine located in its central region. The folds, villi, and microvilli of the mucosal surface provide a wide surface area for absorption. The rapidly absorbed nutrients that are water-soluble are able to enter the circulation thanks to the abundant blood flow.

The jejunum plays a crucial role in the absorption of several nutrients, including water, electrolytes, vitamins, and lipid, carbohydrate, and protein waste products.

3. Ileum

The ileocecal junction connects the small intestine to the large intestine, and the last section of this tract is called the ileum.

Not only that, it's crucial for the absorption of many nutrients, including:

Vitamin B$_{12}$ combines with intrinsic factor:

- Complexes involving intrinsic factors and vitamin B_{12}
- Boiling salts

The ileal mucosa contains several lymphoid aggregates, the most notable of which are the Peyer's patches, which aid in the immunological monitoring of the intestines. In addition to regulating the flow of intestinal contents into the caecum, the ileocecal region also prevents the large intestine from having an over return flow.

❖ ***Intestinal villi and microvilli***

The inside of the small intestine is covered with villi, which resemble little fingers.

Miniature projections of the villi-lining epithelial cells are called microvilli. Intestinal epithelium contains a plethora of microvilli that form its brush boundary. By changing the structure in this way, we increase the surface area that can be used for digestion and absorption.

Inside each villus, you'll find blood capillaries and a central lacteal (lymphatic) vessel. While the majority of lipids are absorbed by the body and sent to the lymphatic system through the lacteals, the majority of water-soluble nutrients, including monosaccharides and several amino acids, reach the bloodstream through the capillaries.

The last stages of digestion might occur right adjacent to the absorptive surface because of enzymes located at the brush edges of the intestinal epithelial cells.

➢ **Functions of the small intestine**

The small intestine is responsible for:

- Completion of digestion

- Absorption of carbohydrates
- Absorption of amino acids
- Absorption of lipids
- Absorption of vitamins
- Absorption of minerals
- Absorption of water and electrolytes

Additionally, it plays a significant role in immune system function and endocrine system regulation. Hormones released by gut specialised cells regulate satiety, gastric emptying, gallbladder function, and pancreatic output.

2.1.4 Anatomy and Functions of the Large Intestine

The ileocecal junction to anus is the large intestine, the last and biggest part of the digestive tract. It is wider than the small intestine, but lacks the same villous surface area. It's internal structure, instead, is specialized to recover water and electrolytes, as well as process the increasingly drier intestinal content.

Its major parts are:

1. Caecum
2. Appendix
3. Colon
4. Rectum
5. Anal canal

The last part of the ileum empties into the caecum. The vermiform appendix is attached to it, which is a narrow tube with lymphoid tissue.

The colon is divided into:

- Ascending colon
- Transverse colon
- Descending colon
- Sigmoid colon

Food moves slowly from the intestines to the rectum through these regions. The colon's wall displays longitudinal bands of muscle known as teniae coli. Contractions of the colon's musculature mix, slow down, and generate mass movements that can push faecal material into the rectum, which in turn moves the contents of the colon.

❖ ***Functions of the large intestine***

The large intestine is involved in:

- Absorption of water
- Absorption of electrolytes
- Formation of faeces
- Storage of faecal material
- Elimination of faeces

Water and electrolytes are gradually absorbed from the intestine as it moves through the colon. This alters the relatively fluid material in the intestine into increasingly formed faecal matter. The large intestine is also home to a diverse population of gut bacteria. Some forms of dietary fibre are broken down by these microbes as they transit through the small intestine and are not digested.

Beneficial chemicals, such as short-chain fatty acids, can be utilised by colonic cells through the metabolic processes of microbes. Some vitamins, such vitamin K and B-group vitamins, are also produced or altered by the microbiota.

For the most part, the rectum is just a place to hold pee. When the rectum swells to an adequate level, sensors embedded in its walls can help set off the defecation reflex. To regulate the slow expulsion of waste, the final section, the anal canal, is equipped with internal and external sphincter devices. In contrast to the smooth muscle internal anal sphincter, which is not subject to voluntary control, the skeletal muscular external anal sphincter is.

Therefore, large bowel is more than a storage and elimination organ; however, it plays an important role in fluid balance, electrolytes conservation, microbial metabolism, immune activity and final processing of intestinal contents.

2.2 PHYSIOLOGY OF DIGESTION

Digestion, secretion, motility, and absorption are the four main physiological steps in the digestive process. The stomach's own acid and the enzyme pepsin initiate protein digestion in the stomach. Important digestive organs that secrete digestive fluids include the pancreas, the liver, and the salivary gland. Through the processes of peristalsis, segmentation, gastric mixing, and mass movements, the intestines transport, mix, and break down food into absorbable units as it passes through them. The body then receives the absorbed water, nutrients, vitamins, and minerals through the lymphatic or blood circulation after absorption in the small intestine.

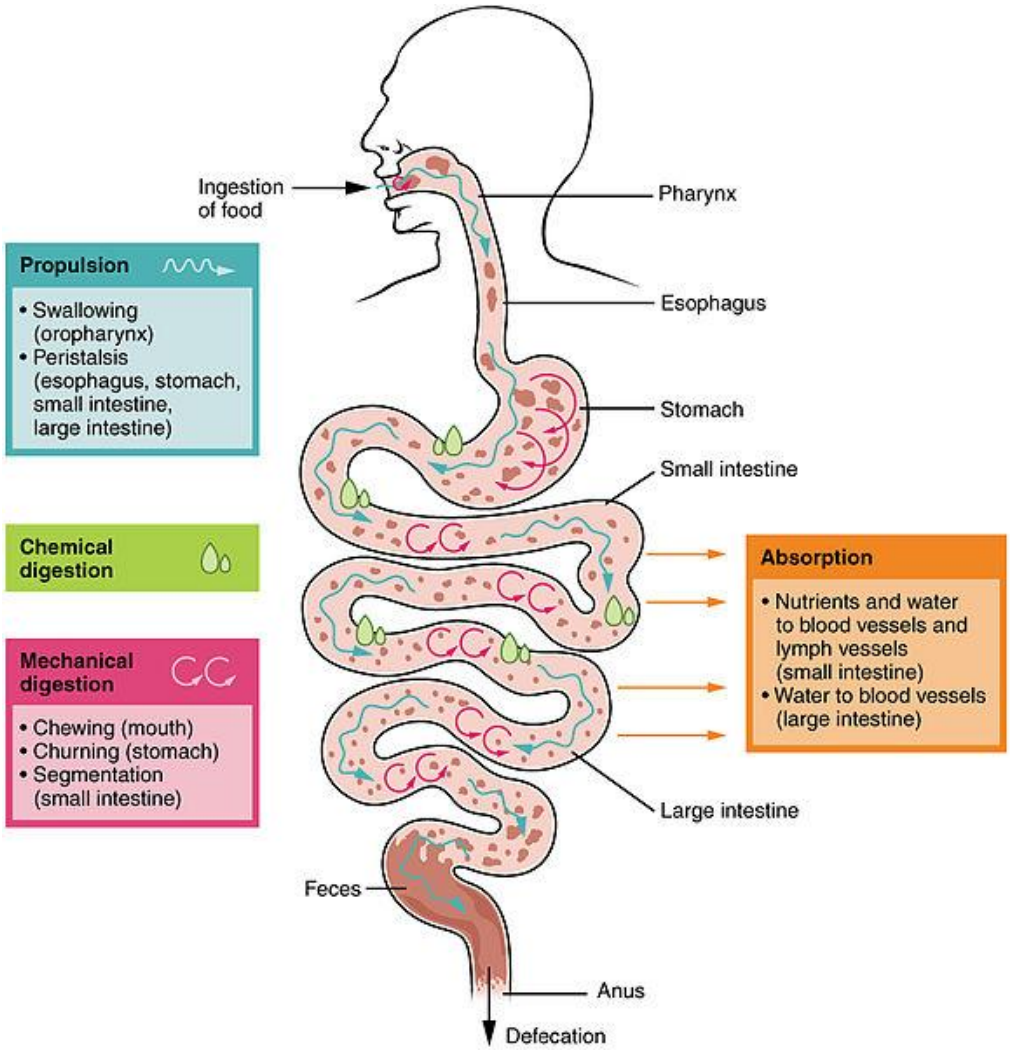


Figure 2.2: Physiology Of Digestion

Source: (https://wtcs.pressbooks.pub/medterm/chapter/12-5-physiology-of-the-digestive-system/)

2.2.1 Stomach

Interactions between gastric epithelial cells, the neurological system, and endocrine and paracrine mediators are crucial to the physiological regulation of stomach acid output. The oxyntic glands found in the stomach's mucosa and fundus are primarily responsible for the acid-producing capabilities of the stomach.

Due to its expansive intracellular canalicular system, the parietal cell is able to secrete from a wide surface area. Finally, the H+/K+-ATPase in the apical membrane is responsible for the last stage of hydrogen ion secretion into the stomach lumen. This mechanism relies on ATP and involves the transporter pumping hydrogen ions into the stomach lumen in return for potassium ions.

Clonidine also blocks chloride ion channels that allow chloride to enter the gastric lumen. This secretion contains hydrochloric acid and gives rise to the very low PH in the stomach necessary for the normal digestive activity of the stomach. One of the major effects of acid secretion is in the

parietal cell. As the hydrogen ions are formed, the bicarbonate that was produced will go into the blood stream. The increase in the blood bicarbonate following a meal is occasionally called the alkaline tide.

The stomach needs to create a strong protective mechanism as the stomach's acid can cause damage to the gastric epithelial cells. The mucus-bicarbonate barrier, intact epithelial junctions, adequate mucosal blood flow and continuous replacement and repair of surface epithelial cells provide protection.

- **Regulation of Acid Secretion Through the Parasympathetic Nervous System**

The vagus nerve is a crucial pathway for the brain to communicate with the stomach. Vagal activity has a direct effect on gastric glands and can also affect other cells that are engaged in acid secretion. Gastric secretion is tightly coupled to presentation and digestion of food. This will make sure that acid and digestive juices are produced when they can help and then lowered when foodstuff from the stomach starts to enter into the intestine.

1. **Cephalic phase**

Cephalic phase is the anticipatory part of gastric secretion. Neural signals start before significant amounts of food enter the stomach, and trigger the digestive system to be ready when food is about to arrive. Vagal stimulation stimulates activity of the gastric glands and aids gastric motility. This stage shows that digestion is stimulated by more than just the physical food; it is also stimulated by what is "sensed" and "thought" during the eating process.

2. **Gastric phase**

The gastric phase becomes more noticeable once food reaches the stomach. Distention of the stomach wall stimulates stretch receptors in the gastric wall, whereas chemical components of the meal excite receptor and endocrine cells in the gastric mucosa. Gastrin secretion and gastric secretory activity are stimulated by these signal pathways, which are located in the pyloric area and the major stomach body. Gastrin stimulates the stomach to secrete more acid and promotes the movement of the stomach. With the passage of digestion, other feedback mechanisms lessen the amount of acid by default.

3. **Intestinal phase**

Once chyme reaches the duodenum, the intestine starts to regulate gastric activity. The effects of small volumes of intestinal contents may, at first, be stimulatory; when the intestinal contents are strongly acid, concentrated or nutritious, the predominant effect is inhibitory. A physiologic significance is that the duodenum will need some time to neutralize the gastric acid and to neutralize

the nutrients that are introduced. The gastrointestinal system is then controlled by intestinal signals which coordinate the rate of gastric emptying to the small intestinal digestive capacity.

- **Major regulators of gastric acid secretion**

The three major stimulatory factors are:

Acetylcholine + Gastrin + Histamine

These mediators work via other receptors but come to the same result—increased activity of parietal cells.

- **Acetylcholine** is released from vagal and enteric nerve endings.
- **Gastrin** is released by G cells and promotes gastric secretory activity.
- **Histamine** is released primarily by enterochromaffin-like cells within the gastric mucosa.

When they act together, they cause a much greater secretory response than when they act individually. Secretory activity for acid is inhibited as well. Raising gastric acidity activates mechanisms that decrease additional acid secretion, which is a negative feedback loop to maintain an appropriate intragastric environment.

- **Role of Pepsin in Protein Digestion**

Pepsin is an endopeptidase in the stomach that begins the enzymatic digestion of dietary proteins. Pepsin is secreted as a zymogen (an inactive precursor) whereas many enzymes are secreted in an active form.

This inactive form is significant because it allows the enzyme to not break down the protein of the cells that make and store the enzyme. The pepsinogen is transformed in the gastric lumen (acidic pH) into active pepsin. When pepsin is formed, it can convert more pepsinogen to produce more pepsin, in an auto-catalytic reaction.

Pepsin is specific for the peptide bonds of certain amino acids and thus breaks proteins down into smaller peptides. When the food in the stomach becomes less acid, its activity drops significantly and when the enzyme reaches the more alkaline environment of the small intestine, it stops functioning. Most of protein digestion occurs then in the intestine with pancreatic proteolytic enzymes.

2.2.2 Accessory Digestive Organs

The accessory digestive organs provide secretions, enzymes or other substances needed to aid in digestion. Food itself is not normally conveyed by these organs, but products of these organs (such as bile) enter the GI tract at particular points and directly into digestive processes.

❖ ***Salivary Glands: Anatomy and Functions***

The exocrine salivary glands have a duct that leads into the mouth and releases saliva into the mouth. They produce water, electrolytes, mucus, enzymes and protective items.

1. **Parotid glands:** This is mainly serous glands and secretes a watery fluid rich in salivary amylase. Their ducts empty into the oral cavity in the vicinity of the upper molar teeth that enables the secretion to mingle with food during mastication.
2. **Submandibular glands:** The submandibular glands have a mixed secretion, both serous and mucous. They make up a significant portion of unstimulated and stimulated salivary secretion.
3. **Sublingual glands:** These glands are situated beneath the floor of the mouth's mucous membrane. They produce more mucus in their secretions, which is especially effective lubricating.

Functions of saliva

Saliva helps to regulate the chemical environment of the mouth as well as to help in the handling of the food. It has buffering ability which helps to buffer the pH changes in the oral cavity and antimicrobial properties which protect against microorganisms in the oral cavity. Saliva also plays a role in the maintenance of the health of the teeth and oral mucosa. Salivary flow also helps to wash away food particles and supplies minerals and protective factors to the oral tissues, which occurs continuously.

❖ **Salivary amylase**

The salivary glands have different serous and mucous cells, with serous cells producing salivary amylase. It breaks starch down into smaller carbohydrate molecules.

It starts activity in the oral cavity and, in some cases, may persist for a while after swallowing, as the enzyme is not affected by the rising acidity in the stomach.

❖ **Pancreas: Anatomy and Functions**

Positioned between the spleen and the duodenum, the pancreas is situated behind the stomach. The direct entry of pancreatic secretions into the initial segment of the small intestine highlights the significance of this anatomical relationship with the duodenum.

The gland is divided into:

- Head
- Neck
- Body
- Tail

The tail is near the spleen and the head is close to the duodenum.

Two distinct organ systems work together to make the pancreas tick. Intestinal secretions are supplied by the exocrine part, which is primarily made up of acinar and ductal cells. In the endocrine system, hormones are secreted into the blood by the pancreatic islets.

- **Exocrine function**

Digestive enzymes and bicarbonate rich fluid are secreted from the pancreas. The bicarbonate is of special significance for neutralising the acid that is coming from the stomach. When food enters the digestive tract, pancreatic enzymes are secreted as a response to neural and hormonal cues.

- **Pancreatic amylase:** Pancreatic amylase is responsible for further hydrolysis of starch and other carbohydrates that have not been fully digested in the oral cavity.
- **Pancreatic lipase:** Pancreatic lipase is one of the major enzymes that break down dietary triglycerides. The effect is more pronounced when lipids have been broken up into smaller droplets by bile salts.
- **Proteases:** A few pancreatic proteases are released in an inactive form. This offers an important protection mechanism, reducing premature digestion of the pancreas. The importance of trypsin lies in its ability to activate several pancreatic protease precursors in the intestinal lumen.
- **Nucleases:** Pancreatic nucleases are involved in the breakdown of dietary DNA and RNA to smaller nucleotide fragments that can be broken down further and absorbed.
- **Bicarbonate:** Increases the pH of the contents of the duodenum once the acidic gastric contents have passed into the intestine. This promotes the action of pancreatic enzymes and helps to keep the intestinal mucosa from becoming too acidic.

Liver: Anatomy and Functions

Located just below the diaphragm, the liver is a crucial metabolic organ. It receives nutrient-rich blood from the gastrointestinal tract and supplies it with blood from the hepatic artery and hepatic portal vein.

The liver is divided into small functional units, each comprising of hepatocytes, blood channels and bile canaliculi. This enables substances taken up from the intestine to be processed before entering the general circulation.

- **Major functions of the liver**

1. Bile production

The liver cells, known as hepatocytes, are constantly making bile. Digestive enzymes, electrolytes, phospholipids, cholesterol, and bile pigments are all components of bile. Bile salts aid in the digestion of lipids by dispersing dietary fats and forming micelles.

2. Metabolism

By storing, altering, synthesising, and dispersing nutrients, the liver manages the body's metabolic equilibrium. Glycogen is a storage form of glucose that the body can use in carbohydrate metabolism. Metabolic processes involving lipids, amino acids, and their metabolites also involve it.

3. Detoxification and biotransformation

The liver enzymes modify the chemical composition of several substances, making them more easily excreted. While this method does not always result in the complete removal of a drug, it has the potential to convert some compounds into metabolites that have different levels of biological activity.

4. Protein synthesis

The synthesis of plasma proteins by the liver is an important process for the maintenance of plasma oncotic pressure, transport functions and blood coagulation. For instance, albumin regulates fluid balance between blood and tissues, and carries various substances in the bloodstream.

5. Storage

The liver is important for the storage of nutrients and micronutrients. The ability to store glycogen enables the body to quickly mobilize glucose for energy needs. It also helps to store or participate in the storage and handling of several vitamins and minerals.

6. Bilirubin metabolism

Haem-containing compounds (especially old red blood cells) produce bilirubin. Bilirubin is absorbed by the liver, where it is chemically changed, and then excreted into bile. It then goes into the intestine, where derivatives are further metabolized by the microorganisms of the intestine.

7. Immune function

The Kupffer cells are hepatic sinusoidal macrophages that phagocytose microorganisms, damaged cells and particulate matter that enters the liver from the blood. The liver is thus a significant immunological barrier between the gut and circulation.

2.2.3 Gastrointestinal Functions

The movement of food through the gastrointestinal tract or gut is brought about primarily through the coordinated contraction of the gut's smooth muscles. These contractions are not random, but are

controlled by enteric nervous system, autonomic influences, gastrointestinal hormones and local conditions in the lumen.

Various portions of the tract have different patterns of movement as they function in storage, mixing, propulsion or elimination.

1. **Peristalsis**

Peristalsis is the result of the successive contraction and relaxation of the smooth muscle in the intestine. In a typical peristaltic wave, the contraction occurs behind the contents of the lumen, while the relaxation occurs in front of the contents. This generates a pressure gradient which propels the contents forward. Peristalsis plays a particular role in propelling food and digestive matter through the intestines and oesophagus.

2. **Segmentation**

The main effect of segmentation is not to generate fast forward. Rather, contraction movements alternate and break up the contents of the intestine into smaller chunks that are continually exposed to the intestinal wall. This enhances the interaction with digestive material and increases the absorption opportunities.

3. **Gastric mixing**

Stomach contractions start in the body and distal stomach and develop stronger as they approach the pyloric region. In addition to blending the food in the stomach, the contractions aid in chopping it into smaller bits. Additionally, powerful contractions close to the pylorus might hasten mechanical breakdown and, in certain cases, retropulsion (the forced backward movement of gastric contents) may occur.

4. **Mass movements**

Mass movements are a strong, relatively persistent contraction of the colon. They transport objects over a relatively long distance and can expel faecal matter into the rectum. They frequently occur in conjunction with the gastrocolic reflex, which indicates that the act of food entering the stomach triggers movement in the colon.

Digestion of Nutrients

1. Carbohydrate digestion

In general, carbohydrates need to be broken down into smaller absorbable molecules to cross the intestinal epithelium. They so digest in a progressive manner at various locations in the digestive tract.

- **Mouth:** It all starts when saliva mixes with chewed food. The salivary amylase begins hydrolysing starch molecules.
- The pancreatic enzyme amylase continues carbohydrate digestion in the **small intestine**. The intestinal brush border enzymes work their magic, reducing intermediate carbohydrate products to monosaccharides that the body can absorb.

Major absorbable monosaccharides are:

- Glucose
- Galactose
- Fructose

The chemicals are actively delivered into the bloodstream by means of the intestinal epithelial cells.

2. Protein Digestion

Progressive hydrolysis lowers the molecular weight of a protein, resulting in smaller peptides and, finally, amino acids that the body can absorb.

- **Stomach:** It creates an environment where pepsin can work by unfolding proteins. Pepsin is the enzyme that further hydrolyses proteins into smaller peptides.
- In the **small intestine**, protein digestion occurs extensively with the enzymes of the pancreatic and intestinal proteases.

Pancreatic proteases include:

- Trypsin
- Chymotrypsin
- Elastase
- Carboxypeptidases

These peptides are further broken down at the brush border of the intestine and in enterocytes to yield other peptides. The final products move through the intestinal epithelium and are mostly delivered to the portal circulation.

3. Fat Digestion

Fat digestion is more complex than the digestion of carbohydrates and proteins because fats are not very water soluble. Thus, physical dispersion of foodstuffs in addition to enzymatic hydrolysis is essential for good digestion.

Step 1: Emulsification

Bile salts decrease the tendency of fat droplets to coalesce and enable dispersion of dietary lipids in intestinal contents. This makes the area available to pancreatic lipase very large.

Step 2: Enzymatic digestion

Pancreatic lipase makes monoglycerides and fatty acids from triglycerides. These products bind to the bile salts and other lipid constituents present in the intestinal lumen.

Step 3: Micelle formation

Bile salts aggregate into small micelles that are able to transport the products of lipid digestion into the aqueous intestinal milieu to the epithelial surface. This makes it very easy to transport the lipid molecules to the absorptive membrane.

Step 4: Absorption

Once inside intestinal epithelial cells, the lipid is broken down and re-synthesized to triglycerides.

They are packaged with proteins and other lipids in chylomicrons. The chylomicrons are relatively large so they pass through the lacteals into the lymphatic circulation, not directly through to ordinary blood capillaries.

- ❖ **Absorption of Nutrients**

Absorption is the passage of the products of digestion, water, electrolytes, vitamins, and other beneficial substances into either the blood or the lymph from the gastrointestinal tract.

Carbohydrates

The principal absorbable carbohydrate products are:

- Glucose
- Galactose
- Fructose

They are absorbed by specific transport proteins in the intestinal epithelial cells. They are absorbed into the portal circulation then delivered to the liver for further metabolic processes.

Proteins

Protein-derived products include:

- Amino acids
- Small peptides

Small peptides can be absorbed into the interior of the cells of the intestinal wall epithelium, and then degraded to amino acids before being absorbed into the bloodstream.

Lipids

Lipid digestion products penetrate into the intestinal epithelial cells and are processed within the cells. Most long-chain dietary lipids are then carried by chylomicrons via the lymphatics. SHFAs can take several routes of entry and can enter the blood more directly.

Vitamins

There are different vitamin absorption requirements.

Vitamin A, D, E, K are **fat soluble vitamins**.

They are absorbed to a large extent with good digestion of the lipids and the presence of bile salts.

Fat soluble vitamins: A, D, E and K

These are typically taken up into the blood stream of the intestine via special transport or diffusion processes. An important exception is vitamin B_{12}, which is normally absorbed through binding with intrinsic factor and is mainly absorbed in the terminal ileum.

Minerals

The intestine controls the absorption of minerals as per physiological needs:

- Iron
- Calcium
- Magnesium
- Sodium
- Potassium

Factors affecting their absorption include: food composition, gut pH, hormones and mineral status.

Water

Solute absorption is essential for osmosis, the movement of water across the intestinal epithelium. Both the small intestine and the colon are responsible for reabsorption of water from the residual contents of the intestines. For proper faecal material production and fluid and electrolyte balance, this is critical.

2.3 PATHOPHYSIOLOGY OF GASTROINTESTINAL DISORDERS

GI disorders are caused by an upset of one or more digestive system processes. The effects are dependent upon the area of brain disturbance and the type and degree of the underlying abnormality. Any disturbance in the action of breakdown of nutrients, transport of intestinal contents, secretion of digestive substances, integrity of the intestinal mucosa, or metabolic function of accessory organs may interfere with nutrient metabolism.

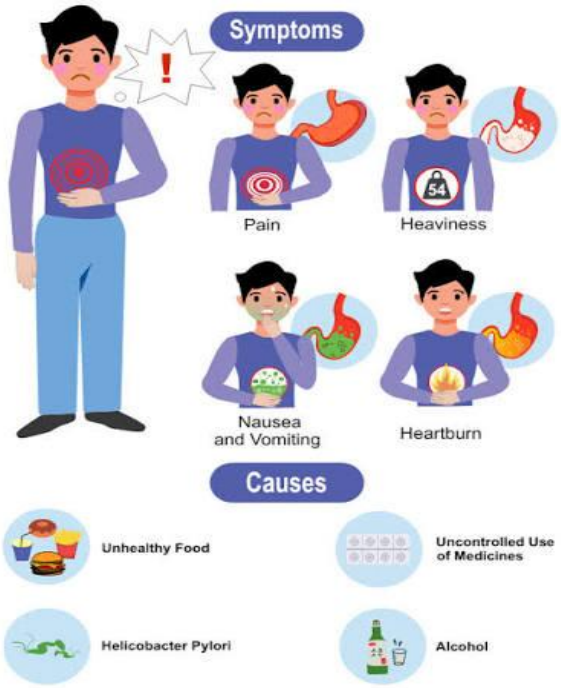


Figure 2.3: Gastrointestinal Diseases

Source: (https://pacificmedicaltraining.com/gastrointestinal-diseases)

Diseases in one area of the gastrointestinal system may have effects on other systems of the body, such as the immune, endocrine, nervous, and circulatory systems. For instance, long-term inflammation of the intestines can lead to poor nutrition, and long-term liver disease may lead to disturbances in blood coagulation, fluid balance and metabolism.

2.3.1 Inflammatory Bowel Diseases

A collection of long-term diseases characterised by chronic, uncontrolled inflammation of the gastrointestinal tract is known as inflammatory bowel disease (IBD). Inflammation can be rather high at times and quite low at other times.

The two most common types are:

1. Crohn's disease
2. Ulcerative colitis

Both diseases are characterized by ongoing inflammation of the intestine, but have different distribution, depth of involvement in the intestine, and typical patterns of intestinal injury.

- ***Crohn's Disease***

Inflammation can spread across the intestinal wall's thickness in Crohn's disease, a transmural inflammatory disorder. This deeper engagement is the reason for the occurrence of structural complications later on.

The disease is often segmental or patchy, where affected areas could be interspersed between relatively unaffected segments. The localized region of inflammation can cause swelling, ulceration, and thickening of the bowel wall. The chronic inflammatory process can slowly and continuously change the architecture of the intestine. Repeated inflammation and healing can result in fibrosis, narrowing the intestinal lumen.

Features

- Abdominal pain
- Chronic diarrhoea
- Weight loss
- Fatigue
- Reduced appetite

The clinical signs are in part related to the site and extent of inflammation. Small-intestinal involvement may cause malnutrition due to failure to absorb nutrients, and colonic disease may cause severe bowel-related symptoms.

Complications

The cause of strictures is chronic inflammation followed by thickening of the bowel wall and fibrosis. Constriction can obstruct the normal flow of the bowel, and can ultimately lead to obstructive symptoms.

Fistulas are abnormal connections that develop between the inflamed intestine and another organ or tissue surface. They are caused by inflammation that can spread up through the gut lining.

Abscesses can develop if infection and inflammation is contained in an area of tissue.

Nutritional problems can also be associated with longstanding disease, as inflammation, decreased appetite, increased physiological needs and decreased absorption can all occur at the same time.

- ***Ulcerative Colitis***

Ulcerative colitis is characterised by a primary infection of the mucosa and submucosa of the colon. Unlike other inflammatory bowel diseases, the inflammation in Crohn's begins in the rectum and spreads constantly rather than appearing in patches.

Ulceration can develop if the surface lining is damaged by chronic inflammation. The typical look and function of the intestinal mucosa is altered by frequent inflammation and repair.

Features

- Bloody diarrhoea
- Abdominal discomfort

- Urgency to defecate
- Rectal bleeding
- Fatigue

Inflammation of the lining of the colon leads to decreased absorptive and barrier function. If disease is severe, weakness and nutritional effects may be caused by bleeding and inflammatory exudate through the bowel.

❖ ***Pathophysiology of IBD***

There is no one cause of IBD. On the contrary, disease is a result of the interaction between genetic susceptibility, immune dysfunction, abnormalities of the intestinal barrier, microorganisms and environment.

For some people with a genetic predisposition, the immune system in the intestine reacts in an abnormal way to some substances in the intestinal environment. Rather than resolve accordingly, inflammatory signals can become chronic.

A dysfunctional epithelial barrier can lead to an increased exposure of immune cells to luminal antigens. Changes in the intestinal microbiota composition and activity could further impact immune responses.

The cycle that results from this can be summarized as:

Genetic susceptibility + barrier dysfunction + altered microbiota → inappropriate immune activation → chronic inflammation → mucosal injury → impaired intestinal function

Eventually, if the inflammation persists, it can lead to structural changes, nutritional disturbances and extra-intestinal manifestations.

2.3.2 Peptic Ulcer

Peptic ulcers are a disruption of the protective integrity of the upper gastrointestinal mucosa sufficiently to allow the formation of an inflammatory and tissue-destructive lesion.

The injury does not only affect the surface and may be deeper into the mucosa and underlying tissues.

➢ **Major causes**

Two major causes are:

1. **Helicobacter pylori infection**
2. **NSAID use**

Helicobacter pylori can survive within the gastric mucus layer and alter the local gastric environment. Its presence is associated with chronic gastritis and disruption of normal mucosal defenses.

It is related to chronic gastritis and disturbance of the normal mucosal defense. NSAIDs cause ulcers primarily by blocking the cyclooxygenase enzymes, thereby reducing the production of prostaglandins. Reduced prostaglandins decrease several protective mechanisms at one time: mucus and bicarbonate secretion, and mucosal blood flow.

- ***Pathophysiology***

In the normal GI mucosa, there is a balance of aggressive factors and protective mechanisms.

Gastric acid and pepsin, some drugs, infection and local tissue injury are all aggressive influences. Mucus production, bicarbonate secretion, sufficient circulation, epithelial restitution and prostaglandin mediated defense are protective mechanisms.

If the balance is tipped towards damage, the epithelium is damaged. Exposure of the gastric acid and pepsin may lead to deepening of the lesion.

The process may be represented as:

Mucosal defense impairment → epithelial injury → inflammation → deeper tissue damage → ulcer formation

Symptoms

- Burning or gnawing upper abdominal pain
- Indigestion
- Nausea
- Bloating

The pattern of pain can vary according to the location of the ulcer and its relationship to meals.

Complications

- If an ulcer erodes through into a blood vessel, then the patient has gastrointestinal bleeding. Depending on its severity, bleeding can result in anaemia or acute blood loss.
- When the ulcer goes all the way through the wall of the gastrointestinal tract, it is called perforation. This may permit the stomach or bowel contents to spill over into the peritoneum and cause severe inflammation.
- Chronic inflammation and scarring can lead to a narrowing of the route through which gastric contents usually leave the stomach, resulting in a gastric outlet obstruction.

2.3.3 Jaundice

A clinical sign seen when there is disruption in the metabolism, transport, conjugation or excretion of bilirubin causing blood bilirubin to rise and there is an increase in bilirubin in body tissues. Haemoglobin of ageing red blood cells is normally degraded to unconjugated bilirubin which is

carried to the liver in combination with albumin. Hepatocytes absorb bilirubin, convert it to a water-soluble state, and then release bile, which is expelled in the GI tract. Disruptions to this process can cause bilirubin to build up in tissues and the blood, which in turn causes the skin and sclera to become yellow.

- **Major types**

1. Prehepatic jaundice

Excessive haemoglobin oxidation is a common cause of pre hepatic jaundice, which occurs before bilirubin reaches the liver. The liver has to exert more effort to process the increased amounts of unconjugated bilirubin, which is a result of higher haemoglobin breakdown. The blood level of unconjugated bilirubin increases when the liver's bilirubin metabolism is sluggish compared to its production. This kind of jaundice occurs when there is an excess of bilirubin in the blood, even when the liver is structurally healthy.

2. Hepatic jaundice

Hepatic jaundice occurs if the hepatocytes are damaged or if their functions are impaired. Liver injury can disrupt the uptake, conjugation, and secretion of bilirubin into bile. This can lead to the rise of both conjugated and unconjugated bilirubin levels, depending on the kind and severity of liver disease. In a situation like hepatitis, cirrhosis and drug-induced liver injury, hepatic jaundice can develop if liver cells are damaged to the extent that one or more of the following normal metabolic and excretory functions is impaired.

3. Posthepatic/obstructive jaundice

Posthepatic or obstructive jaundice is a condition that develops when the bilirubin has been processed by the liver but the bile is not able to pass through the biliary system. This blockage causes bile to build up ahead of it, which allows conjugated bilirubin to get into the blood. Gallstones, biliary obstruction and tumours are common causes. Decreased output into the intestine also affects digestion and absorption of the fats in the diet.

Clinical features

The accumulation of bilirubin in tissues causes yellowing of the skin and eyes, which is the most noticeable sign of jaundice. If the conjugated bilirubin level is high or bile is blocked, other symptoms may include itching, dark urine, and light stools. Because it dissolves in water, conjugated bilirubin is expelled in the urine as black urine. Significant biliary obstruction can cause pale stools and itching is often linked to cholestasis and accumulation of substances that are excreted in bile.

2.3.4 Hepatitis

Damage to the liver tissue can lead to inflammation, which is known as hepatitis. It can be acute and reversible, or become chronic and progressive in nature causing structural damage. If the hepatocytes are damaged, enzymes and other substances can be found in the blood. Ongoing inflammation can cause a continual cycle of tissue damage and repair, which may lead to connective tissue building up and fibrosis forming. With ongoing progression, progressive fibrosis can lead to changes in the structure and function of the liver.

- **Causes**

There are multiple causes of hepatitis, such as viral infections, alcohol abuse, drugs and toxins, autoimmunity and metabolic disorders. These causes cause liver injury in different ways, but liver damage due to the inflammation may disrupt normal liver functions. Severity of hepatitis is dependent on the cause of the hepatitis, duration of the injury, amount of damage to the cells, and the body's reaction to the injury.

- **Viral hepatitis**

There are five major types of viral hepatitis: A, B, C, D, and E. These viruses have varying modes of transmission, clinical presentation, risk of chronic infection and chronic liver sequelae. Some are specifically linked to acute disease, while hepatitis B and C may cause a persistent infection in some people, leading to chronic disease. Over time, persistent infection can cause damage to the liver tissue, leading to fibrosis, cirrhosis and liver cancer.

- **Effects of hepatitis**

Inflammation and liver cell damage may affect critical liver functions like bilirubin processing, bile formation, protein synthesis, metabolism and detoxification. Ongoing trauma can disrupt the normal microscopic structure of liver tissue and prompt repair processes. If inflammation continues, an excessive amount of connective tissue may build leading to fibrosis. Eventually, progressive fibrosis can disrupt the liver's normal architecture, disrupt blood flow and result in multiple liver functions.

- **Symptoms**

Hepatitis symptoms might vary in intensity. Symptoms might range from being completely asymptomatic to more severe issues like jaundice, black urine, nausea, loss of appetite, abdominal discomfort, and extreme tiredness. Symptoms are usually more severe the more and the longer the inflammation of the liver. Chronic hepatitis can be asymptomatic and can slowly cause scarring and cirrhosis.

Chronic liver injury can be shown as:

Chronic inflammation → Fibrosis → Cirrhosis → Increased risk of liver cancer

With continued fibrosis, healthy liver cells are replaced by scar tissue. This alters vascular and cellular architecture of the liver and may lead to severe liver dysfunction.

2.3.5 Typhoid

Typhoid fever is a systemic bacterial infection characterised by the initial invasion of the gastrointestinal tract followed by invasion of deeper tissues and the blood stream. Salmonella Typhi enters into the small intestine and comes in contact with specialized regions of intestinal mucosa that are responsible for immune surveillance. It is capable of passing through the epithelial barrier and into the underlying lymphoid tissue and hence infecting beyond the gastrointestinal tract.

- **Pathophysiology**

Salmonella Typhi is capable of penetrating through the intestinal mucosa and residing within macrophages in the lymphoid tissue. The bacteria then spread through the reticuloendothelial system and bloodstream causing a systemic inflammatory response. Infection of the ILT may lead to inflammatory changes and enlargement of the lymphoid tissue, with severe or prolonged infection, ulceration may develop, especially in the terminal ileal region. Such intestinal alterations can result in severe gastrointestinal problems.

- **Clinical features**

Typhoid fever usually causes a prolonged, systemic illness with symptoms of fever, headache, weakness, abdominal discomfort, loss of appetite, nausea and changes in bowel habits – diarrhoea or constipation. The infection does not have to remain confined to the gi tract as it can spread through the blood stream. Symptoms may be more or less severe and may differ in distribution depending upon the level of dissemination of bacteria and the host's reaction to infection.

- **Complications**

Can be serious in severe or long-term infections. If the blood vessels are damaged in the intestinal wall by inflammatory ulceration, they can bleed. Sometimes an area of ulceration can be so weakened that it tears through the intestinal wall and lets contents of the intestines into the cavity of the abdomen, causing an intestinal perforation. This can also lead to encephalopathy, which is systemic infection and will cause neurological changes. Sepsis occurs when an infection and the body's inflammatory response spread throughout the body and cause organ dysfunction.

Maintaining safe drinking water, appropriate sanitation, good food hygiene and appropriate vaccination, in recommended settings, are important elements of prevention. These measures help to minimize exposure with contaminated food and water as well as spread of infection.

2.3.6 Alcoholic Fatty Liver Disease

The alcohol-associated liver disease (ALD) spectrum includes all liver injuries that are associated with chronic exposure to excessive amounts of alcohol. The very early stage is usually associated with triglyceride deposition in the hepatocytes, giving rise to fatty changes in the liver. Excessive alcohol intake could lead to inflammation, oxidative stress, hepatocyte damage, and subsequent fibrosis. Not all individuals will have liver disease and the progression of liver disease will differ depending on the rate.

- **Pathophysiology**

Alcohol is metabolized primarily in the liver and during metabolism the ratio of $NADH/NAD^+$ is changed, disrupting the normal lipid metabolism. This metabolic disturbance increases the possibility of triglycerides building up, favouring the process of lipids being produced, and diminishes the oxidation of fatty acids. Metabolism of alcohol can also produce reactive oxygen species that can lead to oxidative stress and injuries to cells. Chronic inflammatory signalling can lead to activation of immune responses and hepatic stellate cells and lead to increased collagen accumulation and ongoing fibrosis.

Disease can occur in the following steps:

Fat accumulation → Alcohol-associated hepatitis → Fibrosis/Cirrhosis

But this evolution is not so automatic. In some people, the condition may stay "fatty liver" and in others the inflammation, fibrosis and cirrhosis may progress.

- **Symptoms**

Early AAHL can be without symptoms or detected by chance. As the disease progresses, patients become tired, have abdominal pain and discomfort, jaundice, and enlarged liver. In the late stages of the disease, it can cause fluid build-up and other signs of chronic liver disease. As the liver function decreases, it can cause further complications due to the inability to make proteins, blood circulation in the liver change, and substances being trapped that are normally removed by the liver.

2.3.7 Non-Alcoholic Fatty Liver Disease

Metabolic dysfunction-associated steatotic liver disease (MASLD) is developing as a result of a connection between metabolic dysfunction and steatosis, or the buildup of fat in the liver. It is closely linked to the abnormalities in energy metabolism, insulin signalling and lipid handling. There are some individuals in whom fat accumulation does not increase greatly, however, others may have fat accumulation which is associated with inflammation and progressive fibrosis.

- **Major risk factors**

Obesity, insulin resistance, dyslipidaemia, metabolic syndrome, and type 2 diabetes are major risk factors. Fat buildup in the liver cells is a symptom of several conditions, which are linked to irregular glucose and lipid metabolism. The presence and the extent of these metabolic abnormalities may affect the risk of progression to more advanced liver disease.

- **Pathophysiology**

Insulin resistance disrupts glucose and lipid metabolism, and may lead to elevated fatty acid delivery to the liver. Lipid production is also increased and lipids are poorly metabolized, which also helps to lead to liver fat. While simple steatosis per se does not lead to significant liver damage, it can lead to lipotoxicity and oxidative stress, dysfunction of mitochondria and inflammatory signalling in vulnerable individuals. Hepatic stellate cells (HSC) can be activated by persistent inflammation and the deposition of extracellular matrix leads to progressive fibrosis:

Hepatic steatosis → Steatohepatitis → Fibrosis → Cirrhosis

Not all children will progress at the same rate and not all children will progress at all. Patients may develop chronic steatosis with little structural damage or chronic progressive inflammation and fibrosis.

- **Symptoms**

In its early stages, MASLD is characterised by a lack of obvious symptoms. When symptoms do appear, they may manifest as an enlarged liver, moderate stomach pain, and extreme lethargy. It can be detected by the evaluation of metabolic risk factors or abnormal liver-related laboratory tests, as it may not always manifest with symptoms.

Table 2.1: Alcohol-Associated Vs Metabolic Fatty Liver Disease

Feature	**Alcohol-associated fatty liver disease**	**Metabolic-associated fatty liver disease**
Primary underlying association	Chronic excessive alcohol exposure produces metabolic and cellular injury in the liver.	Hepatic steatosis occurs in association with metabolic dysfunction.
Major risk factors	Pattern and duration of alcohol exposure, together with individual susceptibility and other liver stressors.	Obesity, insulin resistance, diabetes, dyslipidaemia, and related metabolic abnormalities.

Initial hepatic change	Triglycerides accumulate within hepatocytes as alcohol metabolism disrupts lipid handling.	Altered fatty-acid delivery, synthesis, and disposal promotes lipid accumulation in hepatocytes.
Mechanism of progression	Continued alcohol exposure can promote oxidative stress, inflammation, hepatocyte injury, and fibrotic remodeling.	Metabolic stress may lead to lipotoxicity, oxidative injury, inflammation, and activation of fibrogenic pathways.
Potential progression	Fat accumulation → Alcohol-associated hepatitis → Fibrosis/Cirrhosis	Steatosis → Steatohepatitis → Fibrosis/Cirrhosis
Early clinical presentation	Often clinically silent or associated with nonspecific symptoms.	Frequently asymptomatic and may be identified during evaluation of metabolic abnormalities.
Principal management approach	Elimination of harmful alcohol exposure, nutritional support where appropriate, and management of established liver complications.	Reduction of metabolic risk through weight management, physical activity, dietary measures, control of diabetes and lipids, and management of liver disease.

Key pathological distinction

The most important distinction is the dominant underlying driver of hepatic fat accumulation and injury. In alcohol-associated disease, ethanol metabolism directly contributes to altered hepatic metabolism, oxidative stress, and inflammation. In MASLD, the central setting is metabolic dysfunction, particularly insulin resistance and associated cardiometabolic abnormalities.

Despite these different initiating factors, both conditions can ultimately converge on similar pathways of hepatocyte injury, inflammation, fibrosis, cirrhosis, and, in susceptible individuals, hepatocellular carcinoma.

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Unit III…

RESPIRATORY SYSTEM

The specialised network of organs in the respiratory system is in charge of taking gases from the air and transferring them to the rest of the body. One of its primary roles is to transport oxygen throughout the body, which cells need to produce energy. Another is to remove carbon dioxide, a byproduct of cellular metabolism.

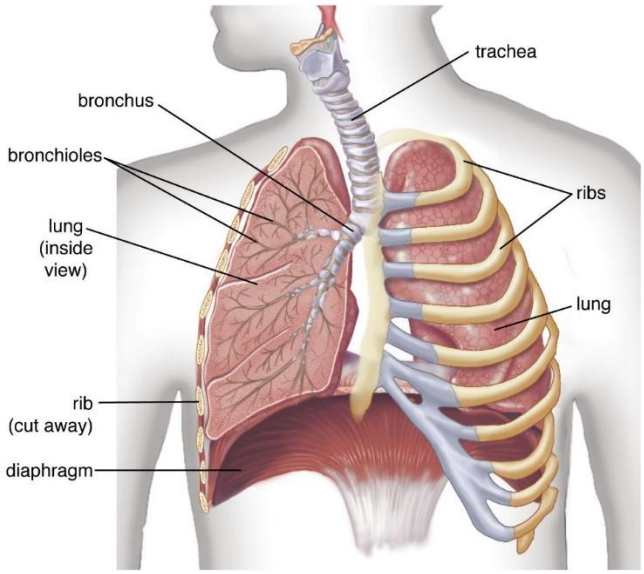


Figure 3.1: Respiratory System

Source: (https://www.britannica.com/science/human-respiratory-system)

A person's airways, lungs, and respiratory muscles are all part of their respiratory system. The lungs are the final destination for air that has entered the body via the nasal or oral cavity and passed via a network of capillaries. At last, air gets to the alveoli in the lungs, where it exchanges gases with blood, including oxygen and carbon dioxide.

Several interrelated processes are involved in respiration:

1. Ventilation, the process of air entering and leaving the lungs. When you inhale, air from the atmosphere enters your lungs, and when you exhale, air with a higher carbon dioxide concentration is expelled.
2. Secondly, there is gas exchange between the blood and the alveoli; specifically, oxygen goes into the pulmonary capillary blood from the alveoli and carbon dioxide goes out the other way. Diffusion across the airway mucosa is the principal mechanism here.

3. The movement of carbon dioxide and oxygen through the blood - Carbon dioxide is transported in several forms in the blood, with haemoglobin being the primary carrier within red blood cells. One of these forms is bicarbonate ion in the plasma.
4. Gas exchange between blood and tissues — At systemic tissues, oxygen is drawn out of the blood and taken up by cells for utilisation in metabolic activities. The process begins when cells release carbon dioxide into the bloodstream, which carries it to the lungs for exhalation.
5. Adapting breathing to meet metabolic demands — The body's oxygen, carbon dioxide, and hydrogen ion levels are constantly monitored and altered. Breathing rate and depth are controlled by sensory receptors and respiratory centers in the brainstem.
6. In addition to exchanging gases, the respiratory system helps with a number of other processes. Its regulation of carbon dioxide removal is a key function in preserving acid-base balance. Blood pH can thus be affected by changes in ventilation.

Another mechanism that enables the creation of voice and speech is the movement of air via the larynx and upper respiratory tracts. Nostril specialised receptors help in olfactory perception by picking up on volatile compounds in the air we breathe.

Significant defensive mechanisms against breathed particles and microbes are also provided by the respiratory tract. It is the job of the immune system, nasal hairs, mucus, cilia, coughing, sneezing, and the nasal passages themselves to keep dangerous chemicals out of the lungs.

3.1 ANATOMY OF THE RESPIRATORY SYSTEM

A person's respiratory system is in charge of breathing in oxygen and exhaling carbon dioxide. The lungs, airways for airflow, and respiratory tracts (both upper and lower) make up this system. The alveoli are tiny sacs in the lungs that take in air and release carbon dioxide and oxygen into the blood. In order to make breathing easier, the pleura covers the paired organs—the lungs—which have three lobes on each side. Alveoli, lymphatics, nerves, pulmonary blood arteries, and the bronchial tree all collaborate to make sure that gas exchange and ventilation are done well.

3.1.1 General Anatomy of the Respiratory System

The respiratory system is an intricate network of organs and tissues that maintains a constant gas exchange between the body and the surrounding environment. It mainly helps the body by removing carbon dioxide (CO2) from cells and supplying oxygen (O_2). In addition to exchanging gases, the respiratory system helps regulate blood gas levels, protects against microbes and particles in the air, and regulates vocalisation.

From a structural perspective, the lungs and airways form the respiratory system. In order to reach the respiratory parts of the lungs, where the blood exchanges carbon dioxide and oxygen, air must first travel via a series of increasingly narrow conducting passageways.

A. Upper Respiratory Tract

The respiratory pathway begins at the top with the upper respiratory tract. The primary function of its structures is to receive inspired air and prepare it for entry into the deeper airways.

1. **Nose:** The nasal passages serve as the exterior entrance to the respiratory system. Bone and cartilage provide stability, and it houses the external nares that allow air to enter and exit the body. Large particles are kept out of the respiratory tract by the nasal tissues. In addition to enhancing air contact with the mucosal surface, the configuration of the nasal passageways produces turbulence in the entering air. This helps to filter out moisture, heat, and airborne particles.
2. The **nasal cavity** is a long passageway that connects the nose to the back of the throat, where it opens into the nasopharynx. Its nasal conchae are creases in the wall that allow more surface area to come into touch with air that is inspired. Cells that secrete mucus and ciliated epithelial cells line the majority of the nasal canal; this lining is called respiratory mucosa. To remove debris from the lower airway, cilia transport mucus to the pharynx. Odour detection is carried out by olfactory receptors, which are located in a specific area of the nasal cavity located at the top.
3. The **paranasal sinuses** are hollow areas in the skull that are filled with air. The mucous membrane lining them allows them to communicate with the nasal cavity.

The major groups are:

- Frontal sinuses
- Maxillary sinuses
- Ethmoidal sinuses
- Sphenoidal sinuses

They have an effect on the voice's resonance and help condition the air that is inspired. Ciliary action often carries their mucosal secretions to the nasal cavity.

4. The first structure in the respiratory system is the **pharynx**, which is located below the mouth and nose and is a vital link between the airways. When you swallow, its muscular walls guide food and liquids into the right digestive tract passages.

B. Lower Respiratory Tract

Starting at the laryngeal area, the lower respiratory tract travels via progressively smaller airways to reach the parts of the lungs that exchange gas.

1. **Larynx:** The larynx is a structure in the neck that is held in place by a network of ligaments and muscles that link a framework of cartilages. The vocal folds, an integral feature of sound generation, are housed therein. The rima glottidis is formed by the gap between the vocal folds. The vocal folds' tension and position can alter the voice's qualities. An additional defensive function of the larynx is significant. Coordination of swallowing motions aids in keeping food and liquids out of the airway during the process.
2. **Trachea:** The trachea is located anterior to the oesophagus and extends inferiorly from the larynx. Its cartilage-supported wall allows for some pliability when breathing and neck movement while maintaining an open airway. Cilated pseudostratified columnar epithelium with mucus-producing goblet cells primarily lines the inside surface. Inhaled particles are helped toward the pharynx by this lining, which is part of the mucociliary clearing system. The trachea splits in two at its base, near the carina, to form the bronchi.
3. **Bronchi:** Air is directed into the lungs by the right and left major bronchi, respectively. The bronchi in each lung branch out multiple times to supply air to ever-tinier areas. When compared to its left counterpart, the right main bronchus is often narrower, shorter, and more perpendicular to the body's vertical plane. The right bronchial tree is more likely to receive aspirated foreign material due to its anatomical layout. The main bronchi branch off into smaller bronchi called lobar bronchi, which carry air to the various lung lobes. Then, these branch off into bronchi that serve individual bronchopulmonary segments, known as segmental bronchi.
4. **Bronchioles:** Without cartilage in their walls, bronchioles differ from bronchi and represent smaller conducting airways. The diameter is greatly affected by the relaxation and contraction of smooth muscles. As a result, the bronchioles are crucial for controlling airflow resistance. When these airways are constricted, airflow is reduced; when they are relaxed, their diameter increases, and airflow is facilitated. The conducting part ends with terminal bronchioles, which are the last branches.

Respiratory Zone

Structures that engage directly in gas exchange enter the airways beyond the terminal bronchioles.

Respiratory Bronchioles

A limited number of alveoli protrude from the inside of respiratory bronchioles. They link the gas-exchanging area to the conducting channels, thus representing a transition.

Alveolar Ducts

The walls of alveolar ducts have many holes that lead into alveoli and alveolar sacs. In addition to facilitating gas exchange, they draw air into the respiratory segment of the lungs.

Alveolar Sacs

A group of several alveoli that open into a shared chamber is called an alveolar sac. Because of their configuration, the alveoli in the lungs are able to house a vast respiratory surface area in a small space.

Alveoli

In order to facilitate effective gas exchange, the alveoli have evolved into specialised tiny structures. Rapid diffusion of oxygen and carbon dioxide is enabled by their enormous total surface area and intimate connection with pulmonary capillaries. Connected to the capillary network are the alveolar walls. A extremely thin diffusion barrier separates the air in the alveoli from the blood, reducing the amount of distance that gases have to travel.

- **Type I Pneumocytes:** The majority of the alveolar surface is covered by type I pneumocytes, which are incredibly thin cells. Respiratory gases have a shorter diffusion distance due to their flattened form.
- **Type II Pneumocytes:** The alveolar lining cells contain Type II pneumocytes, which are more spherical in shape. In order to lower the surface tension inside the alveoli, they produce and secrete surfactant. By reducing the effort needed to reinflate the alveoli during the following inspiration, surfactant plays a crucial role in preventing alveolar collapse, which is especially critical during expiration.

Alveolar Macrophages

In the respiratory zone, alveolar macrophages play a crucial defensive role. When airborne particles, bacteria, and cell debris reach the alveoli, they swallow them all.

Pulmonary Blood Supply

Gas exchange relies on the lungs' specialised blood supply. Blood that has been through the heart's right side and is relatively deoxygenated makes its way to the lungs via the pulmonary arteries. In the lungs, these arteries branch out along the airways and finally cluster into a web of capillaries that encircles the alveoli. Following gas exchange, the pulmonary veins collect the blood that is rich in

oxygen and send it back to the left side of the heart. To efficiently remove carbon dioxide and take in oxygen, the alveoli and pulmonary capillaries must be in close proximity to one another.

Pleura and Pleural Cavity

A serous membrane with two layers, the pleura, encircles each lung.

Here are the parts:

- The **visceral pleura** adheres snugly to the lung's outside.
- **Parietal pleura**—covers the inside of the chest cavity.

The pleural cavity, which holds a trace quantity of pleural fluid, is located between these layers. The smooth movement of the lungs within the thoracic cavity is made possible by this fluid, which lowers friction during respiratory motions.

Normal breathing relies on the pleural membranes' contribution to preserving the mechanical link between the thoracic wall and the lungs.

- **Functional Organization of the Respiratory System**

Two interrelated functional areas make up the respiratory system.

Conducting Zone

An airway and air conditioning system are the primary functions of the conducting zone. Several things happen at once when air passes through it:

- Removal of particulate matter
- Warming of inspired air
- Humidification
- Movement of mucus and trapped particles
- Regulation of airflow

Respiratory gas exchange does not typically take place primarily in the conducting channels.

Respiratory Zone

Pulmonary gas exchange is the exclusive function of the respiratory zone. Diffusion can occur efficiently because to its small size, large surface area, and abundant capillary supply. In a nutshell, the route is as follows:

Atmospheric air → Conducting airways → Respiratory bronchioles → Alveolar ducts → Alveoli → Pulmonary capillaries

Blood–Air Barrier

Air in the alveoli and blood in the pulmonary capillaries are separated by the blood-air barrier, a thin contact. For quick diffusion, its incredibly thin profile is a key adaption.

Most of the barrier is made up of:

1. Alveolar epithelium
2. Fused or closely associated basement membranes
3. Capillary endothelium

In addition to a thin barrier, other factors that contribute to efficient gas exchange include a wide alveolar surface area, sufficient pulmonary blood flow, and proper alveolar ventilation.

➢ Important Anatomical Features of the Lungs

On each side of the mediastinum lie the two paired lungs within the thoracic cavity.

Parts of the right lung are:

- Superior lobe
- Middle lobe
- Inferior lobe

The **left lung** is divided into:

- Superior lobe
- Inferior lobe

A smaller left lung is present due to the heart's occupation of a portion of the left side of the thoracic cavity. Additionally, it features the cardiac notch, an indentation on the heart.

There is a base of the lung that attaches to the diaphragm and an apex of the lung that juts upward toward the base of the neck.

Hilum, which is located on the medial surface of the lung, is the entry and exit point for bronchi, blood vessels, lymphatic vessels, and nerves. All of these parts come together to make the lung's base.

Clinical Significance

There are significant clinical implications of the respiratory tract's anatomy. The resistance to airflow can be significantly amplified if the bronchioles narrow, and regular ventilation can be disrupted by inflammation or secretion buildup.

When the alveolar walls are damaged, the surface area that can be used for gas exchange decreases. Thickening of the blood-air barrier can have a similar effect, increase the diffusion distance and making it harder for carbon dioxide and oxygen to be transferred.

Respiratory tract structural defences, including the alveolar macrophages and mucociliary system, offer persistent protection against inhaled particles and microbes. This means that the respiratory system's structure is directly tied to its capacity to exchange gases, protect the lungs, ventilate the alveoli, and conduct air.

3.1.2 Special Reference to the Anatomy of the Lungs

Located on either side of the chest cavity, the lungs are a pair of respiratory organs with a cone shape. Because of their unique adaptations, they take up the vast majority of room on either side of the mediastinum and facilitate the exchange of carbon dioxide and oxygen via a vast surface area.

A medial surface, lobes, apex, base, surfaces, borders, fissures, and a lung each allow vital tissues to flow through. The lung tissue is pliable, elastic, and somewhat spongy. Because of their elasticity, they can expand when we inhale and contract when we exhale.

Each lung's apex extends into the neck's base at a small elevation over the first rib level. The wide and concave base is supported by the diaphragm. With the liver positioned higher on the right side of the body, the diaphragm is also higher, which causes the right lung base to be slightly higher than the left.

External Features of the Lungs

There are three primary surfaces on each lung:

a) First, the **costal surface**, which is both flat and smooth. The ribs and the inside of the chest wall are its surfaces that it faces. The intercostal gaps and ribcage shapes determine its overall form.
b) **Mediastinal surface:** This surface is orientated toward the mediastinum. The hilum, which is a conduit for the bronchial, vascular, lymphatic, and neurological systems, is located within it. The surface also displays the marks left by nearby buildings. Left pulmonary hyperplasia stands out due to the cardiac impression.
c) Thirdly, the **diaphragmatic surface** is the foundation of each lung. It lies flat on the diaphragm and has a concave shape. A large portion of the variation in lung capacity during respiration is attributable to diaphragmatic movement.

Borders of the Lungs

The outward contour of each lung is defined by its own unique border.

- A narrow line runs down the front of the chest cavity, which is known as the **anterior border**. The cardiac notch, which houses a portion of the heart, interrupts it on the left side.

- Diaphragmatic surface, costal surface, and mediastinal surface are separated from one another by the **inferior border**. Because the lungs move in tandem with the diaphragm when we breathe, its posture varies as we breathe.
- **Posterior border:** Rounded and thicker in the back is the border. Along with the spinal column, it spans the space between the chest's upper and lower halves.

Right Lung

The right lung is:

- Generally shorter and broader
- Divided into three lobes

The lobes are:

1. Superior lobe
2. Middle lobe
3. Inferior lobe

They are separated by:

- Horizontal fissure
- Oblique fissure

The upper part of the right lung is occupied by the superior lobe. Situated between the oblique and horizontal fissures is the little middle lobe. Part of the lower half of the lung and a significant contributor to the diaphragmatic surface is the inferior lobe.

Because of how the fissures are arranged, the lobes can move independently during respiration to a certain degree. On its mediastinal surface, the right lung is also associated with structures including the right atrium, azygos vein, superior and inferior vena cava, and more.

Left Lung

The left lung has:

- Superior lobe
- Inferior lobe

The oblique fissure divides them.

The smaller left lung is a result of the heart's location on the left side of the thorax.

The upper part of the left lung is made up of the superior lobe, and the lower part and back of the left lung are occupied by the inferior lobe. One way to tell the left lung from the right is that there isn't a distinct center lobe.

Lingula

In relation to the right middle lobe, there is a projection on the left side of the brain called the lingula, which resembles a tongue.

The lingula begins in the inferior lobe and extends toward the cardiac notch. It is anatomically located on the front of the left lung and comes in two halves, the superior and inferior lingular segments.

- ***Internal Organization of the Lungs***

Lungs are more than just tissue masses. A series of internal branches known as the bronchial tree are responsible for distributing air throughout the pulmonary tissue. The trachea branches out into the primary bronchi on either side. After entering their respective lungs, the main bronchus branch out into lobar bronchi that serve the various lobes. After that, smaller and smaller bronchi and bronchioles branch out from these. The alveoli-containing respiratory regions of the lung are reached by the tiniest conducting airways. The bronchial tree is a popular term for this network of airways.

- ***Bronchopulmonary Segments***

The bronchopulmonary segments of each lung are physically and functionally separate. The pulmonary artery and a segmental bronchus work together to supply a segment. Because disease can sometimes stay localised to a certain segment, and because it is possible to remove some segments during surgery without removing the entire lobe, these segments hold great clinical significance.

- ***Alveoli***

In the last stages of the respiratory system, there are millions of tiny air sacs called alveoli.

Pulmonary capillaries round the alveoli, which have incredibly thin walls. Respiratory gases have a short diffusion pathway thanks to their thin nature.

The alveoli primarily perform the following functions:

- The process by which blood and alveolar air exchange oxygen
- Degassing the blood in the lungs
- Giving a lot of surface area for the lungs to breathe in
- Working in tandem with the pulmonary capillaries to keep gas exchange efficient

The thin gas-exchange surface, which lines the inner surface of the alveoli primarily with type I pneumocytes. The production of pulmonary surfactant by type II pneumocytes aids in the prevention of alveoli collapse by reducing surface tension.

- ***Blood Supply of the Lungs***

Both the pulmonary and bronchial circulations bring blood to the lungs, giving them a dual blood supply.

Pulmonary circulation

The pulmonary arteries transport the right ventricle's deoxygenated blood to the lungs. In the lungs, these arteries branch out into ever-tinier capillaries that round the alveoli. Following gas exchange, the heart's left atrium receives blood that has been oxygenated via the pulmonary veins.

Bronchial circulation

Lung tissues, including connective tissue, bronchi, and other supporting structures, receive oxygenated blood via the bronchial arteries. Instead of providing blood to the primary channel for gas exchange, this circulation mainly supplies nutrients to the lung tissue itself.

- ***Nerve Supply of the Lungs***

The pulmonary plexuses are the pathways via which autonomic nerve fibres enter the lungs.

- **Parasympathetic fibres:** The vagus nerves are the primary conduits for parasympathetic fibres. In most cases, they enhance glandular production and induce smooth-muscle contraction in the bronchi.
- **Sympathetic fibres:** Bronchodilation and decreased production by the bronchial glands are common effects of sympathetic fibres.

In addition to processing information about mechanical and chemical changes in the respiratory system, the lungs also have sensory fibres.

- ***Lymphatic Drainage***

A vast lymphatic network aids in the drainage of excess tissue fluid and offers a crucial route for immunological monitoring; it is located in the lungs. Lymph travels from the lungs to the rest of the body via the tracheobronchial lymph nodes via the pulmonary and bronchopulmonary lymph nodes.

Finally, lymph travels into the thorax's bigger lymphatic systems. When it comes to the progression and staging of lung infections and cancers, the lymphatic drainage pattern is clinically significant.

- ***Pleura***

A double-layered membrane known as the pleura encases each lung.

1. Visceral pleura

Wraps around the inside of the lungs.

2. Parietal pleura

Covers the inside of the chest cavity.

The pleural cavity sits between them and holds a tiny quantity of fluid that helps keep everything moving smoothly.

Functions of pleura

- Lessens air resistance when inhaling
- Assists in keeping the thoracic wall and lungs in close proximity to one another
- Helps create the atmospheric pressure necessary for lung expansion

The costal, mediastinal, diaphragmatic, and cervical sections of the parietal pleura are further subdivided based on the areas they cover. The part that covers the top of the lung is the cervical section, which reaches beyond the first rib.

Typically, there is just a thin layer of fluid in the pleural cavity. The smooth sliding of the two pleural layers over each other and the preservation of the mechanical link between the thoracic wall and the lungs are both made possible by this fluid.

Pleural Recesses

When you breathe quietly, your lung tissue does not fill up every inch of the pleural cavity. Pleural recesses are the medical terms for these openings.

Positioned between the costal and diaphragmatic pleura, the most significant is the Costo diaphragmatic recess. During deep inspiration, it gives the lungs more room to expand.

- **Hilum of the Lung**

Structures enter and exit the lung through the hilum, which is located on the medial surface of each lung.

These include:

- Main bronchus
- Pulmonary artery
- Pulmonary veins
- Bronchial vessels
- Lymphatic vessels
- Nerves

These structures, when joined, constitute the lung's root.

Connective tissue and pleura form a protective sheath around the root's constituent structures. Though their configuration varies between the two sets of lungs, the bronchus, pulmonary artery, and pulmonary veins all keep their vital connections. Blood is carried to the pulmonary capillary network by the pulmonary artery, and oxygenated blood is returned to the heart by the pulmonary veins. The major bronchus is the primary passageway for air to enter and exit the lungs.

➢ Clinical Importance of Lung Anatomy

To comprehend a number of respiratory diseases and therapeutic interventions, one must be well-versed on the anatomy of the lungs. Diagnostic imaging investigations, such as CT scans and radiography of the chest, are better understood when the pleura, lobes, fissures, bronchopulmonary segments, and hilar structures are located. In cases like pneumothorax (air entering the pleural space) and pleural effusion (extra fluid accumulating there), the pleural cavity becomes extremely significant. Radiological and clinical findings may be more localised when diseases impact certain bronchopulmonary segments or lobes.

Learning about the structure of the lungs lays the groundwork for learning about the processes of breathing, breathing in, breathing out, and respiratory gas exchange, which are covered in later parts.

3.2 PHYSIOLOGY OF RESPIRATION

A regulated physiological activity, respiration allows the body to take in oxygen for metabolic processes inside cells and exhale carbon dioxide from tissues. Although the term "breathing" is commonly used to describe the process of respiration, in reality, there are actually multiple layers of interrelated processes that occur during respiration.

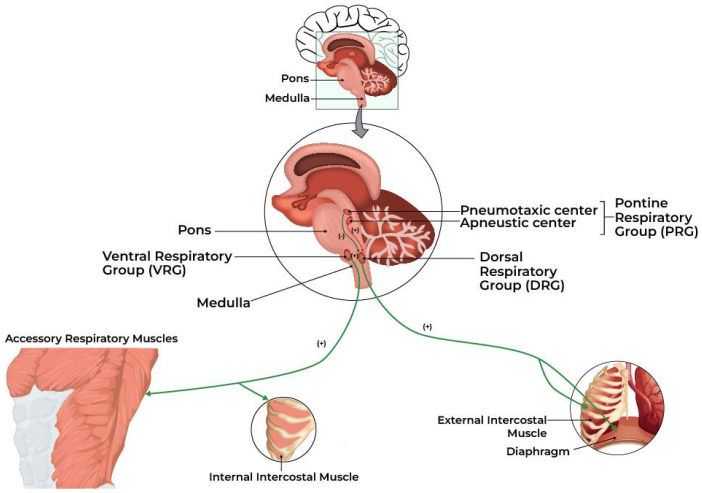


Figure 3.2: Regulation Of Respiration

Source: (https://www.geeksforgeeks.org/biology/regulation-of-respiration/)

The major processes include:

1. **Pulmonary ventilation** – movement of air between the atmosphere and lungs.
2. **External respiration** – exchange of oxygen and carbon dioxide between alveolar air and pulmonary blood.

3. **Transport of respiratory gases** – movement of oxygen and carbon dioxide through the circulation.
4. **Internal respiration** – exchange of gases between systemic blood and body tissues.
5. **Cellular respiration** – utilization of oxygen by cells for energy production, with carbon dioxide generated as a metabolic product.

Respiratory muscles, airways, alveoli, pulmonary circulation, blood, and regulatory processes all need to be in good working order for respiration to be efficient.

3.2.1 Mechanism of Respiration

Supplying and removing air from the lungs is called pulmonary ventilation.

It consists of:

1. Inspiration
2. Expiration

The main factors influencing ventilation are variations in thoracic cavity volume and the subsequent changes in lung pressure. As a result of their tight mechanical connection with the pleural membranes, the lungs do not actively draw air into the thorax but rather track the motion of the thoracic cage.

Pressure Changes During Breathing

Ventilation can be better understood by keeping in mind three pressure relationships:

- The force of the air pressured into a given area is known as the atmospheric pressure. When the air pressure inside the respiratory tract is different from that outside, air moves.
- The pressure inside the alveoli is known as intrapulmonary pressure. How it interacts with air pressure dictates the movement of air.
- Inhalation of air occurs when the pressure inside the lungs drops below that of the surrounding air. As it rises, air is expelled from the lungs.
- The pressure inside the pleural cavity, also known as intrapleural pressure. It stays below atmospheric pressure under typical circumstances.

By maintaining an internal pressure against the thoracic wall, this negative pressure aids in keeping the lungs inflated. A disruption in this pressure relationship could lead to partial or total collapse of the afflicted lung if air were to enter the pleural cavity.

Additional features of inspiration

The thoracic cage is enlarged when the external intercostal muscles are contracted, which raises the ribs. Chest size is increased by the diaphragm and ribs moving together.

The growth takes place in multiple planes, including the vertical, the anteroposterior, and the transverse. The result is that the lung capacity is enhanced.

The amount of inspiration might change based on what the body needs. Exercising, talking, coughing, or experiencing respiratory distress can cause a significant increase in the depth and frequency of breathing.

- ***Compliance of the Lungs***

When the pressure across the lungs changes, the lungs expand easily; this property is called lung compliance. Lungs that are more flexible can expand with less pressure, whereas those that are less flexible need more pressure to expand to the same extent. Lung tissue elastic characteristics, alveolar surface tension, pulmonary surfactant, and chest wall mechanical properties all contribute to compliance. The effort required to breathe is directly affected by changes in compliance. When respiratory diseases cause the lungs to stiffen and become less flexible, breathing becomes more of a challenge because more muscular effort is needed during inspiration.

- ***Airway Resistance***

Any obstruction that makes it harder for air to travel through the airways is called airway resistance. Restricting the airway causes a dramatic rise in airflow resistance, which is directly correlated with the airway's diameter or radius. The smooth muscle lining the bronchi can change the diameter of the airway in reaction to chemical and autonomic signals, which in turn changes the airflow. Airway inflammation, mucus buildup, or bronchoconstriction are all conditions that can cause the airways to constrict and heighten resistance. An important physiological basis for understanding illnesses linked with airflow blockage is increased airway resistance, which can make the movement of air more difficult, especially during expiration.

- ***Role of Surfactant***

Type II pneumocytes are responsible for producing pulmonary surfactant, a specialised material that is secreted onto the inner surface of the alveoli. Reducing surface tension at the air-fluid interface within the alveoli is its primary function. Surfactant lessens the muscular effort needed to breathe by lowering surface tension, which in turn minimises the likelihood of alveoli to collapse and promotes lung compliance. Particularly during expiration, when the volume of the alveoli diminishes, it aids in maintaining equilibrium across alveoli of varying sizes.

- ***Importance of surfactant***

The surfactant, which is mostly composed of lipids and some proteins, is distributed throughout the delicate fluid layer that encases the surface of the alveoli. The lungs are able to expand more freely during inspiration and assist prevent alveolar collapse during expiration by altering the forces

operating at this air-fluid interface. Hence, normal lung function cannot be sustained without an adequate surfactant. The synthesis of surfactant starts during foetal development and rises in the later stages of pregnancy. Premature infants may have respiratory distress due to insufficient production, which makes it more difficult to maintain their alveoli open.

Additional physiological importance

Surfactant stabilises alveoli of varying sizes, which is a crucial function. Otherwise, surface tension would cause smaller alveoli to undergo stronger collapse forces. By lowering these forces, surfactant aids in keeping alveoli open all the way through the breathing cycle. As a result, surfactant increases the mechanical efficiency of breathing and also makes it easier for the lungs to expand.

- **Pulmonary Gas Exchange**

Diffusion is the principal mechanism by which gases in the respiratory system migrate across the respiratory membrane in response to variations in their partial pressures; this allows for the exchange of gases in the lungs. As a result, the exchange of gases between the air in the alveoli and the blood in the pulmonary capillaries has a bidirectional flow of oxygen and carbon dioxide. The removal of carbon dioxide from cellular metabolism and the delivery of oxygen to tissues depend on how well this mechanism works.

- **Oxygen**

When blood enters the pulmonary capillaries, its partial pressure of oxygen is typically lower than that of the alveolar air. This causes the alveoli to release oxygen into the bloodstream via diffusion across the respiratory membrane.

O_2: Alveoli → Blood

After that, the oxygen can be delivered to the tissues of the body by means of the circulatory system.

- **Carbon dioxide**

Blood entering the pulmonary capillaries has a higher partial pressure of carbon dioxide compared to alveolar air. So, carbon dioxide goes in the other way, diffusing into the alveoli from the blood.

CO_2: Blood → Alveoli

The carbon dioxide that reaches the alveoli is subsequently removed from the body during expiration.

- **Respiratory Membrane**

The respiratory membrane, which is incredibly thin, allows gas exchange to occur between the air in the alveoli and the blood in the pulmonary capillaries. Alveolar epithelial cells, basement membranes that support them, and endothelial cells that line capillaries make up the bulk of it. Rapid exchange

of oxygen and carbon dioxide occurs between the alveoli and the pulmonary circulation due to the short diffusion distance provided by the thin structure of this barrier.

Factors affecting gas diffusion

There are a number of variables that affect how well gases diffuse into the lungs, including as the amount of surface area accessible for gas exchange, the thickness of the respiratory membrane, the partial-pressure gradient, the gas characteristics, and the connection between breathing and blood flow in the lungs. When the respiratory membrane is thin and has a big surface area, gas exchange is efficient. When the membrane is thick and has a small surface area, oxygen transmission is hindered. For exchange to work, there must be sufficient pressure gradients and the airflow must be properly matched with the blood flow.

Ventilation–Perfusion Relationship

Airflow to the alveoli (ventilation) and blood flow via the pulmonary capillaries (perfusion) are described by the ventilation-perfusion (V/Q) relationship. Finding the sweet spot between the two is essential for gas exchange efficiency. Even with enough airflow, an alveolus with low blood flow cannot effectively transport oxygen into the bloodstream, and vice versa: blood travelling through an alveolus with inadequate ventilation cannot be oxygenated to an adequate level.

Thus, to keep good gas exchange and oxygen absorption, it is critical to synchronise alveolar ventilation with pulmonary perfusion. Arterial oxygenation is affected by disturbances in this connection, which can decrease the efficiency of gas exchange in the lungs.

3.2.2 Regulation of Respiration

Neuronal and endocrine systems mainly control breathing by constantly adjusting breathing in response to metabolic demands. The brainstem, and more specifically the medulla and pons, house the majority of the respiratory control system. Automatically increasing ventilation at times of high metabolic demand (like exercise) and decreasing it during periods of low metabolic demand (like sleep) are functions of these centers. While most of the brain controls breathing automatically, it can briefly alter respiration for tasks including speaking, singing, swallowing, and holding one's breath voluntarily. But eventually, changes in chemical variables, like as carbon dioxide levels, can overcome intentional control and trigger breathing.

- ***Medulla***

An essential network of neurones that both creates and controls the respiratory cycle is located in the medulla oblongata. Consciously or unconsciously, the rhythmic pattern of breathing is produced by the coordinated contraction and relaxation of the inspiratory and expiratory muscles by means of these respiratory centers. Over the course of a continuous period, the medulla combines signals

produced in the brainstem with data received from sensory receptors. The ability to adapt respiratory activity to variations in blood gas levels, airway patency, and pulmonary mechanics is facilitated by this. As a result, the medulla is an important hub for regulating the fundamental automatic pattern of breathing.

- ***Pons***

Modifying and directing the medulla-generated respiratory pattern is a key function of the pons. The timing, depth, and transition between inspiration and expiration are regulated by pontine respiratory centers through interactions with medullary networks. Instead of sudden spikes and dips in respiratory activity, this interaction helps create a regular rhythm of controlled breathing. The pons has an impact on the overall coordination of respiratory motions and on the ability of respiration to adapt to various physiological circumstances.

- ***Chemoreceptors***

Specialised sensory receptors called chemosensors relay information about chemical changes in the internal environment to the respiratory centers. Particularly, they react to variations in the concentrations of carbon dioxide (CO_2), hydrogen ions (H^+), and oxygen (O_2). Ventilation is controlled by the information received from these receptors, which ensures that blood gas levels and acid-base balance stay within normal physiological limits. Chemoreceptor activation enhances or alters respiratory activity in response to major changes, enabling the lungs to fine-tune carbon dioxide clearance and oxygen absorption.

- ***Central Chemoreceptors***

Situated in the brainstem, central chemoreceptors are especially attuned to fluctuations in the concentration of carbon dioxide and hydrogen ions in the cerebrospinal fluid. The quantity of hydrogen ions in cerebral fluid is increased when carbon dioxide, which can pass the blood-brain barrier, takes part in chemical reactions. The central chemoreceptors and respiratory control centers are both stimulated by this shift. In order to restore carbon dioxide levels and maintain acid-base equilibrium, increasing ventilation causes the lungs to eliminate more carbon dioxide.

- ***Mechanism***

The mechanism can be summarized as:

CO_2 increases → H^+ increases in cerebrospinal fluid → central chemoreceptor stimulation → respiratory drive increases → ventilation increases → CO_2 removal increases

This mechanism provides an important means of maintaining relatively stable carbon dioxide levels and controlling the acid–base status of the body.

❖ ***Peripheral Chemoreceptors***

The carotid and aortic bodies are the primary sites of peripheral chemoreceptors. In particular, they react to variations in arterial blood oxygen levels, carbon dioxide levels, and acidity. A rise in respiratory activity is brought about via the transmission of signals to the brainstem's respiratory centers through these receptors. For the detection of severe drops in arterial oxygen, the carotid bodies play a crucial role. The vagus nerve carries information from the aortic bodies to the brainstem, while the glossopharyngeal nerve is the principal conduit for sensory input. Peripheral chemoreceptors quickly report changes in the arterial blood's chemical composition in this manner.

Role of Carbon Dioxide

An essential chemical regulator of respiration is carbon dioxide. Boosting the concentration of hydrogen ions in the blood causes carbon dioxide levels to rise, which in turn activates the respiratory control system. Exhalation removes more carbon dioxide as a result of the subsequent increase in ventilation.

The basic feedback mechanism can be represented as:

$$\mathbf{CO_2 \uparrow \rightarrow H^+ \uparrow \rightarrow \text{Respiratory drive} \uparrow \rightarrow \text{Ventilation} \uparrow \rightarrow CO_2 \downarrow}$$

In the blood, carbon dioxide is bound firmly to the bicarbonate buffering mechanism. The concentration of hydrogen ions and the pH of the blood are both affected by changes in CO_2 levels. Hence, keeping the acid-base balance is intimately related to controlling respiration. An essential short-term method for managing blood pH is respiratory regulation, which is made possible by the lungs' relatively rapid ability to change carbon dioxide levels.

Relationship with blood pH

The body's acid-base balance is directly affected by changes in carbon dioxide levels. Carbon dioxide tends to build up as ventilation drops, which raises the concentration of hydrogen ions and decreases pH. Increased ventilation, on the other hand, tends to lower hydrogen ion concentration while removing more carbon dioxide. Consequently, chemical buffering systems and respiratory regulation act in tandem to keep the interior environment at a suitable level.

Other Factors Influencing Respiration

Chemical regulation is the backbone of respiratory control, but mechanical sensors, irritant receptors, and higher brain centers also play a role. The respiratory system is able to adapt to changes in lung expansion, airway circumstances, behavioural or emotional states, and more with the aid of these systems.

- Lung and airway stretch receptors detect changes in lung expansion and release endogenous endogenous stretch signals. The sensory signals are sent to the system that regulates

breathing, allowing them to alter the rate of breathing. By modulating the respiratory pattern when lung expansion becomes large, these receptors assist regulate respiratory motions and protect the lungs from excessive inflation.

- Irritant receptors: These receptors in the airways react to potentially dangerous chemicals and physical or chemical stimuli. These receptors can be activated by exposure to smoke, inhaled particles, chemical irritants, and other hazardous substances. When activated, they can trigger defence mechanisms including coughing and alterations in airway calibre, which can help clear the respiratory tract of harmful particles.
- The cerebral cortex and other higher-level brain regions have the ability to momentarily affect breathing. When engaging in tasks like speaking, singing, swallowing, or holding one's breath, the ability to control one's respiration is essential. Additionally, messages from higher brain areas can affect breathing patterns in response to emotional moods. Voluntary control has its limits, though, due to the fact that the brainstem respiratory centers are still stimulated by variations in blood carbon dioxide and other chemical variables, guaranteeing that necessary breathing is eventually maintained.

3.2.3 Lung Volumes and Capacities

Vital metrics used to characterise lung air content and air movement during respiration include lung capacity and volume. Lung capacities are the sum of two or more lung volumes, whereas lung volumes are the amounts of air used in individual respiratory motions. You may learn a lot about the respiratory system's mechanical qualities and current functioning state from these measurements. Age, sex, height, body mass index, level of physical fitness, posture, and the prevalence of respiratory illnesses are some of the variables that influence the values of lung capacities and volumes in different persons.

❖ **Lung Volumes**

The lung capacity to take in and expel air at rest and at maximum effort is a measure of its volume. Respiratory reserve volume, tidal volume, inspiratory reserve volume, and residual volume are the four main lung volumes that are recognised. When taken as a whole, these volumes shed light on the respiratory system's ability to handle air.

1. Tidal Volume (TV)

The amount of air that is taken in or expelled during a typical, calm breath is called tidal volume (TV). Body size, age, level of physical activity, and other physiological variables affect the actual value of tidal volume, which in a normal healthy adult is around 500 mL. In most cases, this volume is more than enough to fulfilll the normal respiratory needs of a resting body when breathing quietly.

No amount of tidal volume reaches the alveoli. Even though most people don't generally exchange much gas while breathing, some of the air that is inspired stays in the conducting airways such the nose, pharynx, larynx, trachea, and bronchi. Anatomical dead space is the name given to this section. This means that, relative to the total tidal volume, less fresh air reaches the alveoli. The amount of air that reaches the alveolar areas, as opposed to just the overall volume of air moved during breathing, determines effective gas exchange, so this difference is significant.

2. Inspiratory Reserve Volume (IRV)

The additional amount of air that can be forcefully breathed following a regular inhalation is called inspiratory reserve volume (IRV). It is not common practice to let the lungs expand to their full capacity when breathing quietly. On the other hand, the inspiratory reserve allows the respiratory system to enhance the depth of inspiration at times of increased oxygen demand, like during physical exercise.

Thus, inspiratory reserve volume gives the lungs more ventory capacity, enabling them to take in more air as needed. Several factors impact its value, including but not limited to: physical condition, size, lung compliance, chest-wall movement, respiratory muscle strength, and the existence of respiratory disorders.

3. Expiratory Reserve Volume (ERV)

A person's expiratory reserve volume (ERV) is the amount of extra air that can be forcedly expelled following a typical, peaceful expiration. Conventional breathing typically terminates before the lungs reach their maximal capacity to empty. A greater amount of air can be evacuated by contracting the expiratory muscles with greater force.

Expiratory reserve is influenced by the mechanical characteristics of the lungs and chest wall, the activity of the respiratory muscles, and the body's position. Different respiratory disorders may also cause changes to ERV. When there is an obstruction to lung expansion or chest-wall movement, ERV can be reduced.

4. Residual Volume (RV)

The amount of air that stays in the lungs following a maximal forceful expiration is called residual volume (RV). No matter how hard one breathes out, their lungs will never be totally empty. The remaining volume is the air that is referred to as residual volume.

There are significant physiological roles for residual volume. By doing so, it aids in avoiding total pulmonary collapse and maintains the patency of minor airways and alveoli. Between breaths, the leftover air serves as a reservoir and contributes to the generally constant composition of alveolar

gas. Consequently, carbon dioxide and oxygen concentrations in the alveoli do not undergo a dramatic shift with each respiratory cycle.

Voluntary expulsion of all residual volume is not possible, and direct measurement of residual volume by spirometry alone is not possible. If the residual volume needs to be measured precisely, specialised pulmonary function testing procedures are what you need.

❖ Lung Capacities

Lung capacities are combinations of two or more individual lung volumes. They provide a broader assessment of the functional ability of the respiratory system and indicate the amount of air that can be inhaled, exhaled, or retained within the lungs under different conditions. The major lung capacities are inspiratory capacity, functional residual capacity, vital capacity, and total lung capacity.

1. Inspiratory Capacity (IC)

Inspiratory capacity (IC) is the maximum amount of air that can be inhaled following a normal expiration. It is composed of the tidal volume and inspiratory reserve volume.

IC = Tidal Volume + Inspiratory Reserve Volume

Inspiratory capacity represents the ability of the respiratory system to increase lung volume from the normal end-expiratory position to the maximum inspiratory position. It is influenced by the mechanical properties of the lungs and chest wall as well as the strength and function of the respiratory muscles.

An adequate inspiratory capacity is important when the body requires increased ventilation. During exercise or other situations in which metabolic activity increases, the respiratory system can increase ventilation by increasing both the depth and frequency of breathing.

2. Functional Residual Capacity (FRC)

Functional residual capacity (FRC) is the amount of air remaining in the lungs after a normal, quiet expiration. It consists of the expiratory reserve volume and residual volume.

FRC = Expiratory Reserve Volume + Residual Volume

FRC represents an important resting volume of the respiratory system. At the end of normal expiration, the inward elastic recoil of the lungs is balanced by the outward tendency of the chest wall. This balance establishes the resting volume of air remaining in the lungs.

FRC also serves as an important reservoir of air between breaths. It helps maintain relatively stable oxygen and carbon dioxide concentrations in the alveoli and allows gas exchange to continue between individual breaths.

FRC is affected by body position, lung mechanics, chest-wall mechanics, and abdominal pressure. It generally changes when a person moves between standing, sitting, and lying positions. Conditions that restrict lung expansion or alter the mechanics of the chest wall may also reduce FRC.

3. Vital Capacity (VC)

Vital capacity (VC) is the maximum volume of air that can be exhaled following a maximal inspiration. It represents the total amount of air that can be voluntarily moved between the maximum inspiratory and maximum expiratory positions.

VC = Inspiratory Reserve Volume + Tidal Volume + Expiratory Reserve Volume

Vital capacity reflects the combined ability of the respiratory system to expand and empty the lungs. It is influenced by body size, age, lung and chest-wall mechanics, respiratory muscle strength, and physical conditioning.

A reduction in vital capacity may occur when the lungs are unable to expand adequately, when the chest wall restricts movement, or when the respiratory muscles are unable to generate sufficient force. Therefore, VC is an important parameter in the assessment of pulmonary function.

4. Total Lung Capacity (TLC)

Total lung capacity (TLC) is the total amount of air contained in the lungs after a maximal inspiration. It represents the maximum volume to which the respiratory system can expand.

TLC = Vital Capacity + Residual Volume

Total lung capacity includes all four primary lung volumes: tidal volume, inspiratory reserve volume, expiratory reserve volume, and residual volume. It is determined by the combined effects of lung elasticity, chest-wall mechanics, respiratory muscle function, and other factors affecting thoracic expansion.

TLC is clinically useful in evaluating respiratory disorders. In **obstructive respiratory disorders**, increased airway resistance can make expiration difficult and may cause air trapping, whereas in **restrictive respiratory disorders**, expansion of the lungs or thoracic system is limited, generally resulting in reduced lung volumes.

Clinical Significance of Lung Volumes and Capacities

An integral part of pulmonary function testing is the measurement of lung capacities and volumes. By taking these readings, one can learn more about the degree to which respiratory dysfunction is present and how well the respiratory system is working mechanically.

Enhanced resistance to airflow, especially during expiration, is the primary issue with obstructive diseases. If the airways are narrowed or blocked, the lungs may not be able to clear completely,

leading to air trapping and an increase in residual air. This pattern of ventilation may be observed in patients with asthma and chronic obstructive lung disease.

Restrictive diseases are characterised by a diminished capacity for thoracic or lung expansion. As a result, this limits the total amount of air that the lungs can hold. The respiratory muscles, the chest wall, or the lungs can all be affected by anomalies that generate restrictive patterns.

Therefore, measuring lung capacities and volumes is important for tracking pulmonary health and distinguishing between various forms of respiratory dysfunction.

- **Minute Ventilation**

Minute ventilation is the total volume of air moved into or out of the respiratory system in one minute. It depends on both the tidal volume and the respiratory rate.

Minute Ventilation = Tidal Volume × Respiratory Rate

For example, if a person has a tidal volume of 500 mL and a respiratory rate of 12 breaths per minute, the minute ventilation is approximately 6,000 mL/min or 6 L/min.

Minute ventilation provides an overall indication of the amount of air being moved by the respiratory system each minute. However, it does not indicate how much of this air actually participates in gas exchange because a portion of each breath remains in the conducting airways as dead-space air.

- **Alveolar Ventilation**

Alveolar ventilation refers to the volume of fresh air that reaches the alveoli and is available for gas exchange per minute. It is therefore more directly related to the effective exchange of oxygen and carbon dioxide than total minute ventilation.

The relationship can be expressed as:

Alveolar Ventilation = (Tidal Volume − Dead Space Volume) × Respiratory Rate

As we look at various breathing patterns, the significance of alveolar ventilation becomes apparent. Effective alveolar ventilation may not rise in direct correlation with respiratory rate. Breathing quickly and shallowly causes a significant amount of air to stay in the airways that conduct the breath. There may be a little increase in the quantity of fresh air reaching the alveoli, despite a possible rise in total minute ventilation.

Because the dead-space volume is a smaller proportion of each breath when breathing deeply, more fresh air is delivered to the alveoli. Therefore, the depth of each breath, in addition to the frequency of breaths, determines effective ventilation.

Relationship Between Lung Volumes, Capacities, and Ventilation

Comparing lung volumes with lung capacities paints a more complete picture of pulmonary function, as the former describe the distinct components of respiratory movement while the latter combine them. Minute and alveolar ventilation are both affected by tidal volume, whereas residual volume is the amount of air that stays in the lungs following maximal expiration.

One can have a general idea of how the respiratory system works by adding up lung capacity, minute ventilation, alveolar ventilation, and lung volume. Indicators of airflow capacity, air retention in the lungs, and airflow to the alveoli for gas exchange. In order to comprehend normal respiratory physiology and to detect and assess respiratory system disorders, several measures are crucial.

3.2.4 Transport of Respiratory Gases

It is mostly via the circulatory system that oxygen and carbon dioxide are carried from the lungs to the various tissues of the body. Pulmonary gas exchange and cellular metabolism are linked through the circulatory system, which is vital. After entering the alveoli, oxygen from the air diffuses over the alveolar-capillary membrane and is then carried to the tissues by the blood. Oxygen is transported to cells at the tissue level so that they can participate in metabolic processes. As a byproduct of metabolism, carbon dioxide is constantly released into the bloodstream from tissues. It then makes its way back to the lungs, where it is expelled during expiration after being released into the alveoli.

The circulatory system, haemoglobin, plasma, and red blood cell characteristics are the primary determinants of the effective transport of these breathing gases. There is a huge difference between the transportation of oxygen and carbon dioxide. Carbon dioxide is mostly transported as bicarbonate ions, while oxygen is mostly transported in conjunction with haemoglobin.

- **Transport of Oxygen**

Both attached to haemoglobin and dissolved in plasma are the two main types of oxygen delivery in the blood. These two kinds provide very different amounts. While a tiny amount of oxygen is physically dissolved in plasma, the great majority is carried by haemoglobin within red blood cells.

1. Oxygen Bound to Haemoglobin

Haemoglobin, an iron-containing respiratory pigment found in red blood cells, is reversibly attached to the majority of the oxygen delivered in blood. "Oxyhaemoglobin" is the result of haemoglobin and oxygen binding together. Because this bond is reversible, haemoglobin can store oxygen in the blood and then release it when it reaches tissues that need it.

Blood has a far greater capacity to carry oxygen than plasma alone due to haemoglobin's ability to transport oxygen. Because of the high partial pressure of oxygen in the pulmonary capillaries, haemoglobin is able to bind oxygen with relative ease. The tissues receive the oxygenated blood via

the systemic circulation. When metabolic activity is high and the oxygen partial pressure is low, haemoglobin releases oxygen and lets it diffuse into cells.

2. Oxygen Dissolved in Plasma

The plasma physically dissolves a tiny bit of oxygen before transporting it. Although it only makes up a small fraction of blood oxygen levels, the physiological significance of dissolved oxygen lies in the fact that its partial pressure dictates the diffusion gradient that propels oxygen transport from the lungs to the blood and tissues.

The partial pressure of oxygen and its solubility in blood are the primary factors that determine the amount of oxygen dissolved in plasma. A carrier protein is not necessary for oxygen in solution, in contrast to oxygen bound to haemoglobin. Unfortunately, the body's typical oxygen needs cannot be satisfied by this form alone due to oxygen's comparatively poor solubility in plasma. So, the main way that enough oxygen can be transported is through haemoglobin.

- **Oxygen–Haemoglobin Relationship**

For oxygen to reach tissues efficiently, the connection between haemoglobin and oxygen is crucial. In the lung, where the partial pressure of oxygen is high, haemoglobin has a comparatively high affinity for oxygen. When this happens, haemoglobin turns into oxyhaemoglobin because it is so saturated with oxygen.

Oxygenated blood's partial pressure drops when it flows into tissues from the systemic circulation. Because of this, haemoglobin is able to release more oxygen. After leaving the circulation, the oxygen diffuses into the interstitial fluid and, finally, into the cells.

If you plot the oxygen-haemoglobin dissociation curve against the partial pressure of oxygen, you can see the link between the two variables. Because haemoglobin shows cooperative binding, the curve has a distinctive sigmoidal or S-shaped look. When haemoglobin binds to an oxygen molecule, it alters its structure and becomes more capable of binding to more oxygen molecules. On the other side, subsequent oxygen unloading is made easier by releasing just one oxygen molecule.

- **Factors Promoting Oxygen Unloading**

When tissues are metabolically active, oxygen unloading from haemoglobin rises. Increased carbon dioxide and heat production, as well as an acidic environment, are hallmarks of active tissues. Because of these factors, haemoglobin is able to release more oxygen because its affinity for it decreases.

Rising temperatures, acidity, or hydrogen ion concentrations, as well as metabolic activity, are important variables that encourage oxygen unloading. During exercise, when oxygen consumption and metabolic waste are both increased, these alterations take on added significance.

Therefore, haemoglobin is not a passive transporter of oxygen. Because of its oxygen-binding capabilities, oxygen supply can be fine-tuned to meet the metabolic demands of various tissues.

Bohr Effect

The Bohr effect describes how the concentration of CO_2 and H+ ions affects haemoglobin's oxygen affinity. Cellular metabolism in tissues with an active metabolic rate results in the production of carbon dioxide. Acidity is increased when carbon dioxide combines with water, which helps to generate hydrogen ions.

A decrease in haemoglobin's affinity for oxygen occurs due to the elevated concentration of carbon dioxide and hydrogen ions. Hence, haemoglobin delivers more oxygen to the tissues. Areas with high metabolic activity and oxygen demand can be more easily delivered oxygen by doing this.

In order to ensure that oxygen delivery is proportional to tissue metabolic needs, the Bohr effect offers a crucial mechanism. It becomes much more crucial when tissue metabolism is elevated, as it does during exercise.

Transport of Carbon Dioxide

Transporting carbon dioxide from tissues to the lungs for excretion is an essential process in cellular metabolism. Carbon dioxide can be carried in multiple chemical forms, in contrast to oxygen. A little quantity is transferred as carbamino compounds and physically dissolved carbon dioxide, while the majority is conveyed as bicarbonate ions.

In order for the blood to maintain an adequate acid-base balance, carbon dioxide must first be converted into various transport forms. This process permits the blood to carry relatively large amounts of carbon dioxide.

7. Transport as Bicarbonate Ions

In the blood, bicarbonate ions (HCO_3^+) carry most of the carbon dioxide. Carbon dioxide diffuses into red blood cells after entering the bloodstream from metabolically active tissues. When carbon dioxide and water are mixed within red blood cells, the result is carbonic acid.

The reaction can be represented as:

$$\mathbf{CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-}$$

The red blood cell enzyme carbonic anhydrase significantly speeds up this process. The ionisation of carbonic acid by bicarbonate and hydrogen occurs at a quick rate. Afterward, the bicarbonate enters the plasma and is primarily responsible for transporting carbon dioxide throughout the bloodstream.

Since the carbon dioxide-bicarbonate system functions as a crucial physiological buffer, it is essential for regulating the blood's acid-base balance.

8. Transport as Carbamino Compounds

Reversible binding to blood proteins reduces the amount of carbon dioxide transferred. In this process, haemoglobin plays a crucial role. Haemoglobin and other proteins have amino groups that can be bound to by carbon dioxide to create carbamino compounds.

A molecule called carbaminohaemoglobin is formed when haemoglobin binds to carbon dioxide. Because carbon dioxide binds to separate locations on the haemoglobin molecule, this method of transport is unique from oxygen binding to haemoglobin.

An important factor in the effective removal of carbon dioxide from tissues, the quantity of carbon dioxide transported in this form is affected by the oxygenation status of haemoglobin.

9. Transport as Dissolved Carbon Dioxide

Plasma physically dissolves a lesser amount of carbon dioxide before transmission. Being far more soluble in blood than oxygen, carbon dioxide is able to stay dissolved in plasma to a higher extent.

Dissolved carbon dioxide is just a small part of the overall carbon dioxide transit, but it's a crucial aspect because it determines the partial pressure of CO_2 in blood. Carbon dioxide can diffuse from tissues to blood and alveolar air thanks in part to this partial pressure and the diffusion gradient.

Chloride Shift

Moving chloride ions across red blood cell membranes is related to bicarbonate production and transport. The term for this phenomena is the chloride shift, however it is sometimes called the Hamburger effect.

Red blood cells undergo a process that transforms carbon dioxide into bicarbonate and hydrogen ions upon entry. Once bicarbonate has been generated, it is expelled from the red blood cell and into the plasma. Chloride ions are transported into red blood cells from the plasma in order to keep the electrical potential across their membranes neutral.

By allowing large amounts of carbon dioxide to be carried in the blood, the chloride shift facilitates the ongoing conversion of carbon dioxide into bicarbonate. The process is turned around when blood reaches the lungs; bicarbonate goes into the red blood cells and chloride ions return to the plasma. This makes it easier for bicarbonate to be converted back into carbon dioxide.

Carbon Dioxide Release in the Lungs

The processes involved in the transfer of carbon dioxide are basically turned upside down when blood rich in carbon dioxide enters the capillaries surrounding the alveoli in the lungs. Re-entering the red blood cells, bicarbonate ions mix with hydrogen ions to produce carbonic acid. Subsequently, carbon dioxide and water are produced from carbonic acid.

After being created by red blood cells, carbon dioxide diffuses into plasma, which it then passes via the alveolar-capillary membrane to reach the alveoli. Alveolar air and blood have a different partial pressure and concentration gradient, which allows for this movement.

During expiration, the carbon dioxide that has built up in the alveoli is expelled from the body. This ongoing mechanism prevents the buildup of excess carbon dioxide in the body, which is a byproduct of cellular activity.

Haldane Effect

The effect of oxygenation on the transport of carbon dioxide and hydrogen ions by haemoglobin is known as the Haldane effect. When compared to oxygenated haemoglobin, deoxygenated haemoglobin is better at binding hydrogen and carbon dioxide ions.

Because it releases oxygen, haemoglobin becomes relatively deoxygenated in systemic tissues. This makes it easier for the blood to absorb hydrogen and carbon dioxide ions. Since the blood returning from the tissues is deoxygenated, carbon dioxide can be readily transported to the lungs.

Oxygen attaches to haemoglobin as blood enters the pulmonary circulation. The capacity of haemoglobin to transport hydrogen and carbon dioxide ions is diminished during oxygenation, leading to an increase in their release. After that, the alveoli receive the transformed CO2 and exhale it during expiration.

As a result, the Haldane effect makes it easier for tissues to absorb CO2 and for the lungs to exhale CO2.

Relationship Between the Bohr Effect and Haldane Effect

In order to coordinate the movement of respiratory gases, the Bohr effect and the Haldane effect collaborate. Where there is an increase in acidity and carbon dioxide content, the Bohr effect helps oxygen to be unloaded from haemoglobin. In comparison, the Haldane effect makes it easier for tissues to absorb carbon dioxide from blood that has lost some oxygen and for the lungs to exhale carbon dioxide when haemoglobin is oxygenated.

Haemoglobin is able to carry the two respiratory gases in opposite directions efficiently because of these supplementary mechanisms. Lungs take in oxygen and exhale it to tissues, while tissues give up carbon dioxide to the lungs.

Integration of Respiration

Respiration is a continuous and coordinated process involving several sequential stages:

Ventilation → Alveolar gas exchange → Blood transport → Tissue gas exchange → Cellular utilization

Afterward, oxygen is drawn into the pulmonary capillary blood via diffusion from the alveolar air, and carbon dioxide is drawn out of the blood and back into the alveoli in the opposite direction.

When oxygen enters the bloodstream, haemoglobin is the main molecule responsible for delivering it to the tissues throughout the body. When it reaches the tissues, haemoglobin releases oxygen, which then diffuses into cells and is used for metabolic processes. One of the main byproducts of this metabolic process is carbon dioxide.

Subsequently, CO2 is released into the bloodstream through cellular diffusion. While carbamino compounds and dissolved carbon dioxide carry smaller amounts, bicarbonate ions account for the majority of its transport. This CO_2 is recycled via the veins and arteries to the lungs, where it is re-gasified and expelled via the alveoli. During expiration, it is finally expelled from the body.

As a result, the respiratory system, the heart, the lungs, the alveoli, the pulmonary circulation, the haemoglobin, the red blood cells, the cardiovascular system, and the chemical and neurological regulating systems must all work together for respiration to be effective. Damage to any one of these parts can prevent oxygen from reaching cells or carbon dioxide from being expelled, both of which are essential for optimal cellular activity.

3.3 ARTIFICIAL RESPIRATION AND RESUSCITATION

When the body's natural respiratory or circulatory systems fail or become insufficient, life-saving measures such as artificial breathing and resuscitation are essential. Because of the constant need for oxygen by the brain and other critical organs, they play a key role.



Figure 3.3: Artificial Respiration

Source: (https://www.researchgate.net/figure/Artificial-respiration-mouth-to-mouth-technique-with-help-of-the-pocket-mask-and-Ambu_fig5_350118033)

Hypoxaemia, unconsciousness, cardiac arrest, and permanent organ damage can quickly result from ineffective breathing. In a similar vein, tissues no longer receive the oxygen they need when circulation stops. So, until the root cause can be addressed and the patient regains spontaneous breathing and circulation, the goal of resuscitation is to provide temporary support to vital physiological functions.

The availability of skilled staff and necessary equipment, as well as the individual's age, condition, and the reason for their decline, determine the method that is taken.

3.3.1 Artificial Respiration

Artificial respiration refers to methods used to provide or assist ventilation when a person is not breathing adequately.

The purpose is to:

- Provide oxygen to the lungs
- Remove carbon dioxide
- Maintain oxygenation of vital organs

Historically, artificial respiration included various manual techniques. Modern emergency care primarily uses rescue breathing and positive-pressure ventilation, when indicated.

Physiological Basis of Artificial Respiration

Normal spontaneous breathing depends on the coordinated activity of the respiratory centres, respiratory muscles, airways, lungs, and chest wall. When this system fails, air may no longer move adequately between the atmosphere and alveoli.

Artificial ventilation compensates for the loss or inadequacy of spontaneous ventilation by creating airflow into and out of the lungs.

When positive pressure is applied to the airway, air is pushed into the lungs. During removal of the applied pressure, elastic recoil of the respiratory system can assist expiration.

The effectiveness of artificial ventilation depends on:

- Adequate airway patency
- Appropriate ventilation technique
- Sufficient chest expansion
- Proper positioning
- Prevention of excessive ventilation

Airway and Ventilation

An open airway is essential for effective artificial respiration. Obstruction by the tongue, secretions, vomitus, foreign material, or swelling can prevent air from reaching the lungs.

In an unconscious person, loss of normal muscle tone may allow the tongue and surrounding soft tissues to obstruct the upper airway.

Therefore, emergency airway management focuses on maintaining a clear passage between the mouth or nose and the lower respiratory tract.

For trained rescuers, basic airway-opening techniques may include:

- Head-tilt and chin-lift
- Jaw-thrust manoeuvre in selected situations where spinal injury is suspected

The appropriate technique depends on the circumstances and the rescuer's level of training.

❖ *Methods of Artificial Ventilation*

When a person's natural breathing mechanisms are inadequate, there are a number of artificial ventilation techniques that can help them breathe. What tools are at hand, how bad the patient's breathing is, and how competent the rescuer or medical worker is all play a role in deciding which approach to use. In order to remove carbon dioxide and bring oxygen to the alveoli, artificial ventilation mainly involves pumping air into and out of the lungs. Mechanical ventilation, bag-valve-mask ventilation, and mouth-to-mouth ventilation are common ways.

Mouth-to-Mouth Ventilation

When someone isn't breathing properly, a rescuer can use their own exhaled air to help them breathe again by doing mouth-to-mouth ventilation. Until the patient is able to breathe on their own or more sophisticated respiratory assistance is available, a rescuer can help with ventilation by breathing into the patient's airway. With proper execution, this method can aid in the elimination of carbon dioxide and produce a respectable quantity of oxygen.

Nevertheless, there is a risk of the rescuer and the sick individual being exposed to infectious material through direct mouth-to-mouth contact. This is why, if they are accessible, people may choose to use barrier devices like resuscitation masks or other suitable protective gear. The success of mouth-to-mouth ventilation relies on keeping the airway open and creating the right seal to ensure that the air is able to enter the lungs instead of exiting.

Bag-Valve-Mask Ventilation

An apparatus that delivers positive-pressure ventilation is known as a bag-valve-mask (BVM), and it is operated by hand. When someone is unable to breathe properly on their own, it is very helpful

in healthcare and emergency situations. The gadget enables the rescuer to avoid direct mouth-to-mouth contact while administering regulated breaths using a face mask.

A self-inflating ventilation bag, a face mask, a one-way valve, and, in cases where supplemental oxygen is accessible, an oxygen connection make up a standard BVM system. Compressing the ventilation bag allows gas mixtures or air with oxygen added to enter the patient's airway via the mask. Release of pressure causes the bag to re-inflate, setting it up for the subsequent ventilation cycle. To ensure proper ventilation, it is crucial to position the mask correctly and keep the airway open.

For qualified medical staff, BVM ventilation is a lifesaver since it allows for positive-pressure ventilation with minimal patient-rescuer contact. Resuscitation and interim respiratory assistance during the arrangement of more sophisticated airway management or mechanical ventilation are two further possible uses.

Mechanical Ventilation

The use of a mechanical ventilator to augment or substitute natural breathing is an advanced form of respiratory support known as mechanical ventilation. When a patient's natural breathing is not present, is insufficient, or cannot sustain proper oxygenation and carbon dioxide removal, it is mostly employed in hospital settings.

Inhalation and exhalation timing, oxygen concentration, tidal volume, airway pressure, and respiratory rate are all regulated or assisted by a mechanical ventilator. Ventilators can either let the patient breathe on their own or give them full respiratory support, depending on their condition.

The mechanical process of airflow into and out of the lungs is supported by mechanical ventilation, which does more than just supply oxygen. Factors such as the patient's general physiological state, carbon dioxide levels, respiratory mechanics, oxygenation needs, and underlying disease dictate the particular ventilator technique. Maintaining adequate breathing and minimising problems typically necessitates continuous monitoring.

Indications for Artificial Ventilation

In cases where adequate spontaneous breathing is not present or is substantially hindered, artificial ventilation may be necessary. When breathing becomes ineffective, a condition known as respiratory arrest occurs, which is a crucial sign. In cases of severe respiratory depression, when breathing becomes too sluggish or inadequate to sustain proper gas exchange, it may also be required.

When breathing becomes difficult as a result of toxic substances or pharmaceuticals, artificial ventilation may be necessary, especially in cases of severe central nervous system depression. When a person's neurological function is impaired, it might decrease the muscles needed for proper

ventilation or disrupt the brain's capacity to regulate breathing. Inadequate ventilation can result from a severe airway blockage as well; however, it is necessary to treat the obstruction first, as maintaining ventilation is impossible while the airway is obstructed.

Damage to the airway, respiratory muscles, neurological system, or chest can make it difficult, if not impossible, to breathe normally after some catastrophic traumas. Consequently, in some terrifying cases, artificial breathing may be necessary as a supplementary treatment. In a similar vein, when a patient's respiratory system is unable to sustain sufficient gas exchange on its own, mechanical or assisted ventilation may be necessary.

As soon as possible, find out what's causing your breathing problems and fix them. While artificial ventilation is life-sustaining, it cannot cure the respiratory condition caused by the underlying illness, poisoning, injury, or obstruction.

- **Importance of Oxygenation**

The proper functioning of every tissue depends on sufficient oxygenation, but the brain is especially susceptible to insufficient oxygen delivery. The normal functioning of neurones is highly dependent on continuous aerobic metabolism due to their high metabolic requirements. Due to their limited energy stores, cells can quickly get damaged if their oxygen supply is interrupted for an extended period of time.

The gradual reduction of blood oxygen levels and the accumulation of carbon dioxide occur when efficient breathing is halted. An increase in carbon dioxide levels can disrupt the acid-base balance and hinder normal physiological functions, while a decrease in oxygen availability restricts aerobic energy production. Prolonged periods of insufficient breathing can lead to cellular malfunction and tissue damage.

Assisted breathing, also known as artificial respiration, keeps air flowing into the lungs and helps with the exchange of carbon dioxide and oxygen while the final treatment is planned. So, until improved respiratory management is put in place or spontaneous breathing is restored, artificial ventilation is a crucial supportive strategy in crises and serious disease. It helps retain proper gas exchange.

3.3.2 Resuscitation Methods

When respiration and circulation are no longer possible or seriously damaged, a person may need resuscitation, a set of emergency measures designed to restore or support these processes. When the regular flow of oxygen to critical organs is endangered, resuscitation is necessary. Cardiopulmonary resuscitation (CPR) is the gold standard for emergency resuscitation procedures performed in cases of abrupt cardiac arrest. Cardiopulmonary resuscitation (CPR) is just one part of resuscitation; other

procedures may involve managing the airway, providing aided breathing, administering medication by qualified healthcare providers, and identifying and treating reversible causes. Achieving and maintaining sufficient oxygen delivery and blood flow to critical organs, particularly the heart and brain, is the overarching goal until breathing and effective spontaneous circulation are back to normal.

Cardiopulmonary Resuscitation

The goal of cardiopulmonary resuscitation (CPR) in the event of a cardiac arrest is to restore blood flow and respiration by performing a series of chest compressions and, if necessary, ventilations. The brain and other critical organs do not receive enough oxygenated blood when the heart stops pumping effectively. While breathing helps remove carbon dioxide and oxygen from the blood, chest compressions stimulate the cardiovascular system to pump blood more artificially. While cardiopulmonary resuscitation (CPR) cannot, on its own, bring the heart rate back to normal, it can keep blood flowing until either the patient's own circulation can be restored or more sophisticated treatments like defibrillation are accessible.

Physiological Basis of CPR

When the heart stops pumping blood effectively, it causes a severe decrease in blood supply to vital organs like the brain and heart during cardiac arrest. Cellular function can be quickly impaired due to a shortage of oxygen and nutrients if this situation is not addressed. As a stopgap measure, chest compressions can stimulate the heart to pump blood forward. Changes in intra-thoracic pressure, brought about by chest compression, aid in the pumping of blood via the heart and main arteries.

Upon relief of pressure, the chest reverts to its resting position, enabling the heart and its surrounding structures to restock. Rhythmic pumping effect, thus, is produced by repeated compression and release, which helps maintain circulation to some extent during cardiac arrest. The quality of the compressions has a significant impact on how effective this technique is. Proper hand positioning, sufficient compression depth, suitable compression rate, full chest recoil, and minimal interruptions are important criteria. Performing compressions quickly or continuously without technique is less crucial than providing high-quality CPR.

Basic Adult CPR Sequence

Quick resuscitation is required in the event of an adult who is unresponsive and not breathing regularly. Before doing anything more, make sure the rescuer and the victim are both secure at the spot. After making sure the person is still alive, the rescuer should call for help from the local EMTs. Obtain an automated external defibrillator (AED) if one is available without delay. Without further ado, the patient should begin chest compressions, and qualified rescuers should administer rescue

breaths as needed. It is important to keep performing cardiopulmonary resuscitation (CPR) until the person demonstrates clear indications of life, trained emergency workers arrive, or it becomes unsafe to continue.

- ***Recognition of Cardiac Arrest***

Prompt beginning of cardiopulmonary resuscitation (CPR) can assist preserve circulation until definitive therapy is available, therefore early diagnosis of cardiac arrest is vital. In the event of a cardiac arrest, the victim is usually unresponsive and has irregular breathing. The occasional irregular gasping that occurs with normal breathing is called agonal breathing. Agonal gasps are not the same as regular efficient breathing and might happen during cardiac arrest.

By rapidly identifying the patient, help can be summoned and cardiopulmonary resuscitation can be initiated without delay. Prolonged cessation of circulation and reduced chances of effective resuscitation can occur from delays in recognising cardiac arrest.

- ***Chest Compressions***

When administering chest compressions to an adult, the rescuer should position themselves such that they apply downward pressure most effectively across the center of the chest. The ideal rate of compression is between 100 and 120 compressions per minute, with enough depth to provide good circulation and full recoil between each compression. It is standard practice for skilled rescuers to administer 30 compressions followed by 2 breaths in traditional cardiopulmonary resuscitation (CPR).

If at all possible, the individual should be placed on a level, firm surface. By keeping their arms reasonably straight and placing their hands on the lower half of the sternum, rescuers can use their body weight to aid in compressions. It is important to let the chest return to its usual posture completely after each compression. To facilitate venous return to the heart and to prepare the cardiovascular system for the next compression, it is crucial to perform a full chest recoil.

Because the circulation generated by cardiopulmonary resuscitation (CPR) can quickly decrease when compressions are interrupted, it is important to minimise interruptions in chest compressions. Therefore, keeping blood flowing to the brain and other critical organs after cardiac arrest relies heavily on doing compressions consistently and in an appropriately technical manner.

- ***Rescue Breaths During CPR***

In order to aid in the removal of carbon dioxide, rescue breaths ventilate the lungs and deliver oxygen. Each breath administered by qualified rescuers should be just enough to raise the chest visibly without delivering excessive volumes or pressures. In order for the given air to reach the lungs, it is necessary to have an open airway that is both positioned correctly.

Because it raises intracranial pressure and blocks venous return to the heart, excessive ventilation should be avoided. The possibility of stomach inflation adds to the dangers of aspiration and regurgitation. For people experiencing sudden cardiac arrest, compression-only cardiopulmonary resuscitation (CPR) is a crucial alternative to mouth-to-mouth ventilation in the absence of or inconvenient for a rescuer who is unable to administer the treatment.

Automated External Defibrillator (AED)

A gadget called an automated external defibrillator (AED) may detect irregular heartbeats and shock the patient when necessary. In cases of cardiac arrest brought on by rhythms that can be shocked, like ventricular fibrillation or pulseless ventricular tachycardia, automated external defibrillators play a crucial role. Restoring a regular heart rhythm can be achieved with early defibrillation if it is indicated.

Function of an AED

By providing visual and/or auditory instructions, automated external defibrillators (AEDs) simplify defibrillation for rescuers. The patient's electrical heart activity can be monitored by applying adhesive electrode pads to their chest. If an appropriate defibrillation rhythm is recognised, the automated external defibrillator (AED) will activate. The device gives directions on how to administer a shock if that is what the doctor orders. The automated external defibrillator (AED) instructs the rescuer to proceed with suitable resuscitation procedures and refrains from shocking the patient if the rhythm is not deemed curable by defibrillation.

Importance of Early Defibrillation

When ventricular fibrillation or pulseless ventricular tachycardia causes cardiac arrest, early defibrillation is especially crucial. Under these circumstances, the heart's electrical activity is incorrect, rendering it unable to generate sufficient circulation. The heart may be able to return to a regular rhythm when an electrical shock stops the irregular beat.

As time goes by without adequate action, the chances of successfully defibrillating a patient often diminish. Hence, a crucial part of emergency cardiac care is performing CPR quickly and getting the patient to an AED as soon as possible. Even as an AED is being sought for and utilised as needed, cardiopulmonary resuscitation (CPR) helps keep blood flowing to a certain extent.

Chain of Survival

The "chain of survival" describes the series of interdependent steps necessary for effective cardiopulmonary resuscitation. The critical connections are prompt identification of cardiac arrest, prompt activation of emergency medical services, prompt administration of high-quality

cardiopulmonary resuscitation, prompt defibrillation if needed, and advanced resuscitation and care following cardiac arrest.

The chances of a full recovery are improved with each link that helps keep blood flowing and oxygen levels high. Quick diagnosis enables therapy to commence, and efficient cardiopulmonary resuscitation (CPR) keeps blood flowing until definite treatment is available. Advanced medical care offers additional treatment and monitoring after initial resuscitation, and rapid defibrillation can be especially crucial in shockable heart rhythms.

- ***Rescue Breathing***

Skilled rescuers can administer rescue breathing to help a person breathe if they are not breathing normally but have a pulse. Even when effective breathing has ceased, circulation may initially persist in this scenario. Subpar oxygenation and CO2 removal are hence of paramount importance.

Age, clinical status, and available equipment are some of the variables that determine the specific technique of rescue breathing. When a real emergency occurs, it is imperative that the local emergency medical system be engaged without delay and that, whenever possible, people should adhere to the directions given by professional emergency officials.

Rescue Breathing in Respiratory Arrest

In the early stages of respiratory arrest, efficient circulation may persist despite the cessation of breathing, distinguishing it from cardiac arrest. But oxygen levels fall and carbon dioxide builds up without air circulation. Therefore, maintaining gas exchange while addressing the underlying problem can be critically dependent on providing ventilation.

If proper oxygenation is not restored, cardiac arrest can develop from respiratory arrest, so the patient's status needs to be closely monitored. Rescue breathing gives way to cardiopulmonary resuscitation (CPR), which includes chest compressions and other necessary resuscitation procedures, in the event of a cardiac arrest.

- ***Special Considerations in Resuscitation***

The specifics of the emergency situation will dictate whether or not resuscitation measures are necessary. In addition to basic resuscitation, particular techniques may be necessary in cases when respiration is impaired, such as foreign-body airway obstruction, drowning, or trauma.

Foreign-Body Airway Obstruction

Respiratory arrest can occur quickly if air cannot reach the lungs due to a foreign body airway blockage. The age of the patient, the severity of the obstruction, and whether or not the patient is cognisant all play a role in determining the best course of action. Initiate emergency resuscitation

techniques in accordance with current first-aid and cardiopulmonary resuscitation guidelines if the affected individual becomes unresponsive.

When the airway is totally closed, breathing is ineffective, hence the root cause of the blockage must be removed. In order to avoid respiratory and cardiac arrest, it is crucial to identify severe airway blockage as soon as possible.

Drowning

Inadequate oxygenation and respiratory impairment are the main effects of drowning. The goal of cardiopulmonary resuscitation in these cases is to restore oxygenation and ventilation without endangering the life of the rescuer. Because problems may continue even after it seems like you're doing OK, it's crucial that you get emergency medical help right away.

Trauma

Trauma patients may require multi-modal care, including evaluation and treatment of airway, head, neck, chest, and other injuries. Injuries affecting the central nervous system can compromise respiratory control, whereas injuries to the chest can directly interfere with ventilation. In some cases, prompt evaluation and cutting-edge medical care may be necessary.

- ***Complications and Precautions***

Although CPR and artificial ventilation are lifesaving procedures, they may be associated with complications. Possible complications include rib or sternal fractures, chest-wall injury, regurgitation, aspiration, gastric inflation during ventilation, and lung injury associated with excessive ventilation.

The possibility of these complications should not normally prevent CPR when cardiac arrest is suspected because untreated cardiac arrest poses an immediate and much greater threat to life. Proper technique, appropriate compression and ventilation practices, and avoidance of unnecessary interruptions can help improve the effectiveness of resuscitation while reducing preventable complications.

- ***Post-Resuscitation Care***

Restoration of a pulse or spontaneous breathing does not necessarily mean that the emergency has completely resolved. After return of spontaneous circulation (ROSC), the individual may remain physiologically unstable and may require continued medical assessment and treatment.

Post-resuscitation care may include airway support, appropriate oxygenation and ventilation, circulatory support, continuous cardiac monitoring, assessment of neurological function, and identification and treatment of the underlying cause of cardiac arrest. Continued monitoring is

important because abnormalities in breathing, circulation, heart rhythm, and neurological function may persist after spontaneous circulation has been restored.

Post-cardiac-arrest care is therefore an essential continuation of the resuscitation process. The aim is not only to maintain circulation and breathing but also to prevent further organ injury and support recovery.

- **Clinical Significance**

Artificial respiration and resuscitation are fundamental components of emergency care because respiratory and cardiac failure can rapidly compromise the function of vital organs. The brain and heart are particularly dependent on an adequate supply of oxygenated blood, making early intervention essential when effective breathing or circulation is lost.

Successful resuscitation depends on more than performing an individual procedure. It requires early recognition of the emergency, rapid activation of emergency medical services, effective airway and ventilation support when required, high-quality chest compressions, timely defibrillation when indicated, and rapid transition to advanced medical care. Understanding the physiology of ventilation, gas exchange, oxygen transport, and circulation helps explain why maintaining both adequate oxygenation and blood flow is central to effective resuscitation.

3.4 PATHOPHYSIOLOGY OF RESPIRATORY DISORDERS

Respiratory disorders are conditions that affect one or more components of the respiratory system and interfere with the normal process of breathing. Depending on the disease, abnormalities may occur in the airways, lung tissue, pulmonary blood vessels, respiratory muscles, or mechanisms responsible for gas exchange. These changes can reduce the movement of air into and out of the lungs and impair the transfer of oxygen and carbon dioxide.

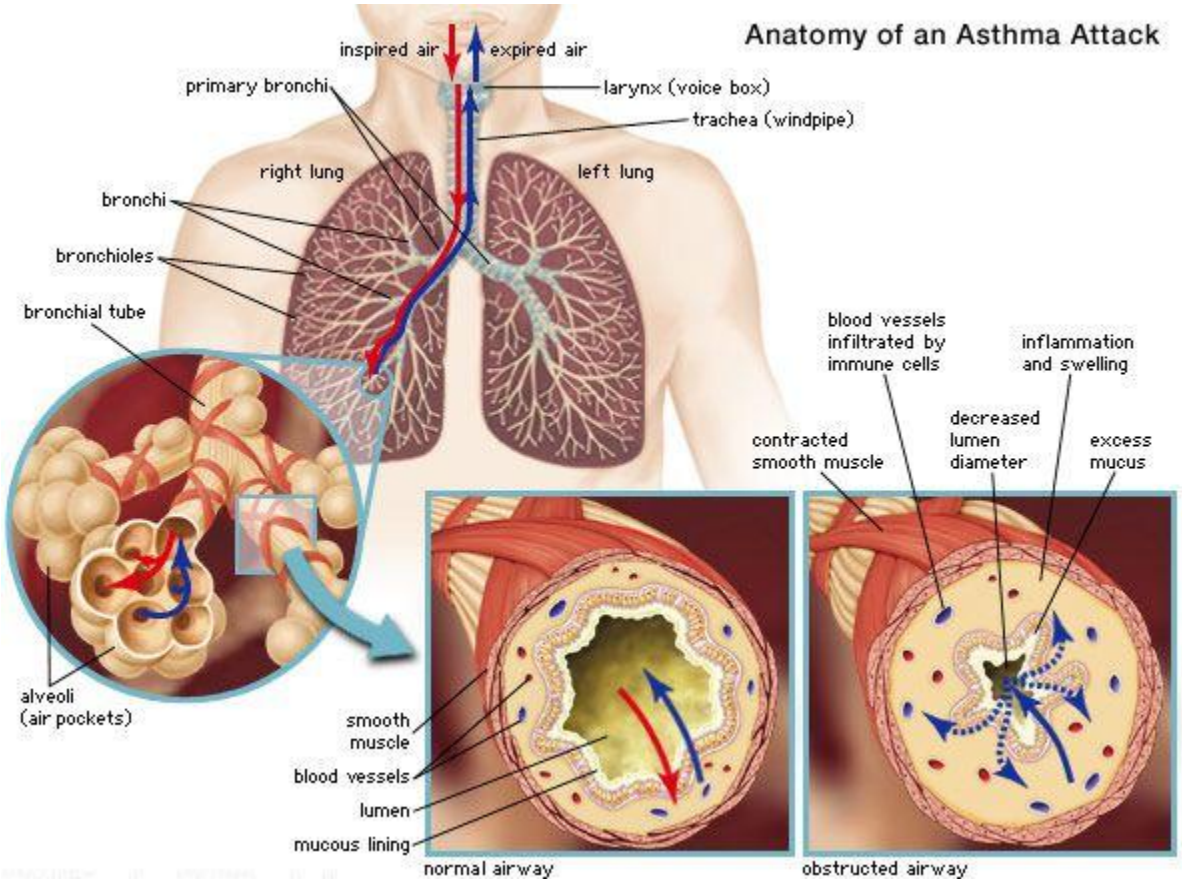


Figure 3.4: Respiratory Disease

Source: (https://www.britannica.com/science/respiratory-disease)

Respiratory disorders can interfere with:

- **Airway patency** – narrowing or obstruction of the airways can increase resistance to airflow.
- **Ventilation** – inadequate movement of air may reduce the amount of fresh air reaching the alveoli.
- **Gas exchange** – damage or inflammation of lung tissue can interfere with oxygen uptake and carbon dioxide removal.
- **Pulmonary circulation** – abnormalities in blood flow through the lungs can affect oxygenation.
- **Lung expansion** – stiffness, obstruction, or destruction of lung tissue may limit normal expansion during inspiration.
- **Oxygen delivery** – reduced oxygenation of blood can decrease the amount of oxygen available to body tissues.
- **Carbon dioxide elimination** – inadequate ventilation may result in accumulation of carbon dioxide in the blood.

The disorders included in your syllabus are:

1. **Asthma**
2. **Chronic obstructive pulmonary disease (COPD)**
3. **Tuberculosis (TB)**

3.4.1 Asthma

Asthma is a chronic inflammatory disease of the airways characterized by variable respiratory symptoms and variable expiratory airflow limitation. The degree of airway narrowing can change considerably over time, either spontaneously or in response to treatment.

Asthma involves interaction between airway inflammation, bronchial smooth muscle activity, mucus secretion, and structural changes in the airway wall. These changes increase the sensitivity of the bronchi to different environmental and physiological stimuli.

The airway abnormalities can include:

- **Bronchial hyperresponsiveness** – the airways react excessively to stimuli that may cause little or no response in healthy individuals.
- **Airway inflammation** – inflammatory cells and chemical mediators contribute to swelling and increased sensitivity of the airway lining.
- **Bronchoconstriction** – contraction of bronchial smooth muscle reduces the internal diameter of the airways.
- **Mucus production** – excessive or thick mucus can partially obstruct the bronchial passages.
- **Airway wall swelling** – inflammation increases tissue oedema and contributes further to narrowing.

Pathophysiology

When a susceptible person encounters a trigger, several inflammatory and bronchial mechanisms may occur simultaneously. The resulting airway narrowing makes expiration particularly difficult because the smaller airways tend to become compressed during forced expiration.

Common triggers include:

- **Allergens** such as pollen, house-dust mites, moulds, and animal allergens
- **Respiratory infections**, particularly viral infections
- **Exercise**, especially in susceptible individuals
- **Cold air**, which may irritate sensitive airways
- **Air pollution**
- **Tobacco smoke**

- **Occupational irritants**, including dusts, fumes, and chemicals

The combination of smooth-muscle contraction, swelling of the airway wall, and mucus accumulation produces variable obstruction. Because these changes may improve between episodes or following appropriate treatment, airflow limitation in asthma is often reversible to a substantial degree.

Symptoms

The clinical manifestations result mainly from temporary airway narrowing and increased resistance to airflow.

- **Wheezing** – a musical or whistling sound produced by airflow through narrowed airways.
- **Shortness of breath** – a sensation of difficulty or discomfort while breathing.
- **Chest tightness** – a feeling of pressure or constriction in the chest.
- **Cough** – may occur alone or together with other respiratory symptoms and can be particularly prominent at night.

Symptoms often vary over time and may become more noticeable at night or during the early morning hours. The intensity of symptoms can also vary according to exposure to triggers and the effectiveness of treatment.

Severe asthma

A severe acute asthma attack can produce substantial narrowing of the airways, resulting in marked difficulty in breathing. Increased respiratory effort may occur as the individual attempts to overcome airway resistance.

If obstruction becomes severe, ventilation may become inadequate and blood oxygenation can deteriorate. Respiratory muscle fatigue may develop when the episode is prolonged. Severe acute asthma is therefore a **medical emergency** requiring prompt assessment and appropriate treatment.

3.4.2 Chronic Obstructive Pulmonary Disease

The standard term is **chronic obstructive pulmonary disease (COPD)**.

COPD is a chronic respiratory disease characterized by persistent respiratory symptoms and airflow limitation resulting from abnormalities of the airways and/or alveoli. Unlike the episodic nature commonly seen in asthma, the structural abnormalities of COPD tend to persist and may progressively impair lung function.

COPD develops through a combination of chronic inflammatory responses and structural changes in the respiratory system. These changes can affect both the conducting airways and the gas-exchanging portions of the lungs.

Important pathological components include:

- **Chronic bronchitis**
- **Emphysema**

These components may occur together, and their relative contribution differs between individuals.

Chronic Bronchitis

Chronic bronchitis involves chronic productive cough associated with inflammation and mucus hypersecretion of the bronchi. Persistent irritation of the bronchial lining stimulates increased mucus production and contributes to airway narrowing.

There may be:

- **Increased mucus production** – excessive secretions can obstruct smaller airways.
- **Airway inflammation** – persistent inflammatory activity causes swelling and irritation of the bronchial walls.
- **Thickening of airway walls** – long-standing inflammation can produce structural changes that reduce airway calibre.
- **Airflow limitation** – narrowed airways increase resistance and make air movement, particularly expiration, more difficult.

Mucus accumulation can also interfere with normal clearance of respiratory secretions, making the airways more susceptible to infection and further inflammation.

Emphysema

Emphysema involves destruction of alveolar walls and enlargement of air spaces distal to the terminal bronchioles. The loss of alveolar architecture reduces the efficiency of the lungs as a gas-exchanging organ.

Normally, the elastic properties of lung tissue help maintain the forces required for expiration and keep smaller airways open. Destruction of alveolar structures reduces these supporting forces.

This results in:

- **Reduced elastic recoil** – the lungs lose part of their natural tendency to return to their resting size during expiration.
- **Loss of alveolar surface area** – destruction of alveolar walls reduces the available area for oxygen and carbon dioxide exchange.
- **Air trapping** – air may remain within the lungs because narrowed small airways close prematurely during expiration.

- **Reduced efficiency of gas exchange** – the loss of functioning alveolar surfaces interferes with effective transfer of respiratory gases.

Persistent air trapping may cause **hyperinflation**, increasing the work required for breathing and contributing to progressive breathlessness.

- **Major Causes and Risk Factors for COPD**

COPD generally develops following prolonged exposure to harmful substances that produce chronic irritation and inflammation of the respiratory system.

The most important risk factor is:

Long-term tobacco smoking

Tobacco smoke contains numerous substances capable of producing airway inflammation, oxidative stress, and structural damage. The risk generally increases with the duration and intensity of exposure.

Other factors include:

- **Biomass smoke exposure** – prolonged exposure to smoke from burning wood, crop residues, charcoal, or other fuels can damage the respiratory tract.
- **Occupational dust and chemicals** – repeated workplace exposure to dust, fumes, vapours, and chemical substances can contribute to chronic lung injury.
- **Air pollution** – long-term exposure to polluted air may worsen respiratory inflammation and contribute to disease progression.
- **Genetic susceptibility** – inherited factors can increase vulnerability to COPD. **Alpha-1 antitrypsin deficiency** is an important but relatively uncommon genetic cause that can predispose individuals to emphysema, particularly at a younger age.

Pathophysiology of COPD

The development of COPD can be understood as a gradual process in which repeated exposure to harmful substances produces persistent inflammation and structural changes.

The disease may initially produce mild symptoms that become more apparent during physical activity. As airflow limitation and structural damage progress, breathing requires greater effort and everyday activities may become increasingly difficult.

Clinical features

- **Chronic cough** – often persistent and may be accompanied by sputum.
- **Sputum production** – reflects increased airway secretions and impaired clearance.
- **Shortness of breath** – particularly noticeable during physical activity in earlier stages.

- **Wheezing** – may occur because of narrowed airways.
- **Reduced exercise tolerance** – limited airflow and increased work of breathing restrict physical activity.
- **Recurrent respiratory infections** – impaired mucus clearance and abnormal airway structure may increase susceptibility to infections.

Advanced disease can lead to:

- **Hypoxaemia** – abnormally low oxygen levels in arterial blood.
- **Hypercapnia** – increased carbon dioxide concentration resulting from inadequate ventilation.
- **Pulmonary hypertension** – increased pressure within the pulmonary circulation, which may develop because of chronic abnormalities in the pulmonary vessels and persistent low oxygen levels.
- **Right-sided heart strain** – increased resistance within the pulmonary circulation places additional workload on the right side of the heart.

Table 3.1: Asthma vs COPD

Feature	**Asthma**	**COPD**
Airflow limitation	Usually variable and often reversible	Persistent, although the degree of reversibility varies
Airway inflammation	Prominent	Prominent
Common triggers/risk factors	Allergens, exercise, infections, and irritants	Smoking and long-term exposure to harmful particles or gases
Onset	Can occur at any age	Usually develops in adulthood
Symptoms	Often variable in intensity and frequency	Usually persistent and progressively limiting
Major pathology	Bronchoconstriction, inflammation, and airway hyperresponsiveness	Airway disease and/or emphysematous destruction

The distinction is clinically important because asthma and COPD can both cause cough, wheezing, and breathlessness but differ in their underlying mechanisms and typical patterns of airflow limitation.

3.4.3 Tuberculosis

Tuberculosis (TB) is an infectious disease caused primarily by the bacterium Mycobacterium tuberculosis. It is an important communicable disease that can affect different organs of the body, although the lungs are the most common site of infection. Pulmonary involvement is common because the organism is usually acquired by inhalation and can reach the deeper portions of the respiratory tract. Although TB primarily affects the lungs, the infection may spread to other organs, particularly when the immune system is unable to contain the bacteria effectively. The progression of tuberculosis depends on the interaction between the organism and the host's immune response.

- ***Transmission***

Pulmonary tuberculosis is mainly transmitted through the **air**. A person with infectious pulmonary TB can release bacteria-containing respiratory particles into the surrounding air while coughing, speaking, singing, or performing other activities that generate respiratory particles. When another susceptible person inhales these particles, the organisms may enter the respiratory tract and potentially reach the alveoli.

The risk of transmission is influenced by several factors, including the infectiousness of the affected person, duration and closeness of exposure, ventilation of the environment, and susceptibility of the exposed individual. Poorly ventilated or crowded environments may facilitate the accumulation of infectious particles in the air. Not every person exposed to *M. tuberculosis* develops active disease because the immune system may successfully contain the infection.

Pathophysiology of Tuberculosis

Following inhalation, Mycobacterium tuberculosis travels through the respiratory passages and may reach the alveoli. Once the bacteria reach the alveolar regions, they interact with cells of the innate immune system, particularly **macrophages**. Macrophages attempt to engulf and destroy the organisms, but *M. tuberculosis* possesses mechanisms that enable it to survive within host cells. Consequently, the initial immune response may not completely eliminate the bacteria.

The development of tuberculosis can be summarized as:

M. tuberculosis enters the respiratory tract → Organisms reach the alveoli → Bacteria are taken up by macrophages → Cell-mediated immune response develops → Granulomatous inflammation develops → Bacteria may be contained or disease may progress

Following the initial infection, the immune system develops a stronger cell-mediated immune response. Various immune cells become involved and organize around areas containing infected macrophages and bacteria. This immune response results in the formation of granulomas, which are

organized collections of immune cells that represent an attempt by the body to restrict the spread of the infection.

In some individuals, the immune response is sufficiently effective to contain the bacteria within granulomatous lesions. The organisms may remain present in the body without producing active disease, a state referred to as latent tuberculosis infection. During latent infection, the bacteria are controlled by the immune system and the person does not have active tuberculosis disease.

If immune containment is inadequate, however, the bacteria can multiply and cause progressive tissue injury. This may result in active tuberculosis, in which the infection produces clinical manifestations and can cause damage to the affected organs. Previously contained infection may also become active again if immune protection is weakened, a process known as reactivation. Thus, the outcome of TB infection depends significantly on the ability of the immune system to maintain control over the organism.

Clinical Features of Pulmonary Tuberculosis

The clinical manifestations of pulmonary tuberculosis generally develop **gradually** rather than appearing suddenly. Symptoms may persist for several weeks and can initially be mild or nonspecific, making early recognition sometimes difficult. The disease commonly produces a combination of respiratory symptoms and general constitutional symptoms resulting from the ongoing infectious and inflammatory process.

The most common respiratory manifestation is a **persistent cough**, which may continue for an extended period. The cough develops because infection and inflammation affect the pulmonary tissues and airways. As the disease progresses, additional respiratory symptoms may develop depending on the extent and location of pulmonary involvement.

- ***Fever and Night Sweats***

Fever is a common systemic manifestation of tuberculosis and reflects the body's inflammatory response to infection. The fever may be relatively low-grade and may occur intermittently. Night sweats are another characteristic constitutional symptom and may be associated with prolonged infection and systemic inflammatory activity.

- ***Weight Loss and Loss of Appetite***

Patients with pulmonary TB may experience unintentional weight loss and loss of appetite. Prolonged infection can increase metabolic demands while simultaneously reducing appetite and nutritional intake. As a result, progressive loss of body weight and general physical weakness may occur, particularly when the disease remains untreated.

- ***Fatigue***

Fatigue is another common manifestation of tuberculosis. Persistent infection and the body's ongoing immune response can contribute to weakness, reduced energy, and decreased ability to perform normal daily activities. Fatigue may occur along with fever, poor appetite, and weight loss.

- ***Chest Pain***

Some individuals with pulmonary tuberculosis may experience chest pain, particularly when inflammation involves structures surrounding the lungs. The nature and severity of pain can vary depending on the location and extent of the disease. Chest discomfort may therefore accompany other respiratory manifestations in patients with pulmonary involvement.

- ***Haemoptysis***

Haemoptysis, or the presence of blood in sputum, may occur in pulmonary tuberculosis when the disease causes sufficient damage to pulmonary tissues or blood vessels associated with the airways. The amount of blood may vary, and its presence is clinically significant because it can indicate more extensive pulmonary involvement.

- **Complications**

Untreated or severe tuberculosis can produce progressive tissue damage and may extend beyond the lungs.

Possible complications include:

- **Extensive lung destruction** – prolonged infection and inflammation can cause substantial structural damage.
- **Respiratory impairment** – extensive pulmonary involvement can reduce effective ventilation and gas exchange.
- **Haemoptysis** – damage to pulmonary tissue and blood vessels may result in bleeding into the airways.
- **Spread to other organs** – organisms can disseminate through the bloodstream or lymphatic system.
- **Meningitis** – infection involving the meninges can cause serious neurological complications.
- **Disseminated tuberculosis** – widespread involvement of multiple organs can occur in severe disease.

- **Overall Clinical Presentation**

The combination of persistent cough, fever, night sweats, weight loss, loss of appetite, and fatigue is characteristic of the systemic and respiratory presentation of pulmonary tuberculosis. Some patients

may additionally experience chest pain or haemoptysis. Because many of these symptoms can also occur in other respiratory illnesses, their persistence, particularly in a person with relevant exposure or epidemiological risk, should raise suspicion of tuberculosis and warrant appropriate clinical evaluation.

Tuberculosis therefore represents a disease in which infection, immune response, granuloma formation, bacterial containment, and possible tissue damage are closely interconnected. The lungs are the principal site of disease, but inadequate immune control can permit progression or spread beyond the respiratory system.

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Unit IV…

URINARY SYSTEM

In keeping the internal environment and homeostasis of the body in check, the urinary system is an important network of organs. It filters the blood of excess chemicals and metabolic waste by means of urine production. The kidneys aid in maintaining stable conditions required for optimal cellular activity by regulating water balance, electrolyte concentrations, osmotic pressure, and acid-base balance.

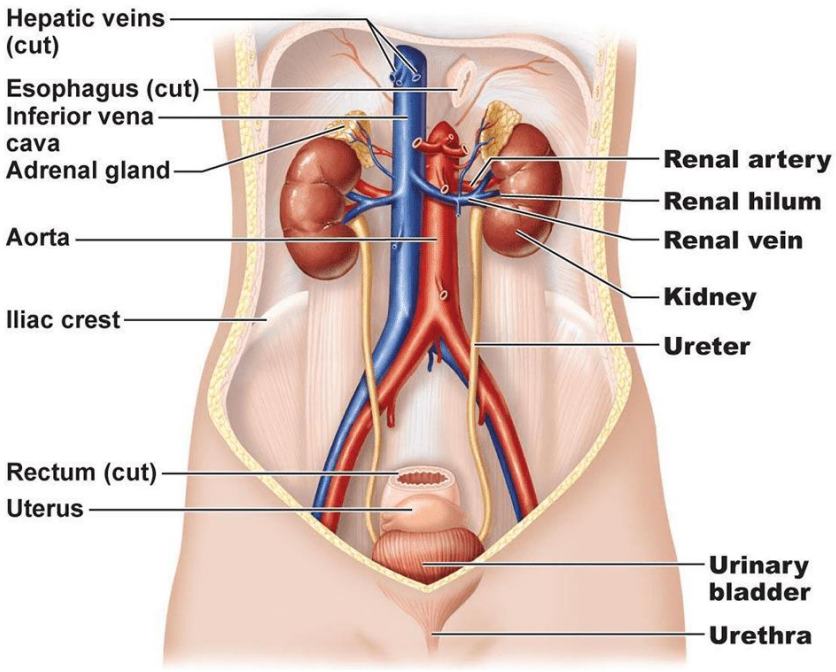


Figure 4.1: Urinary System

Source: (https://nurseslabs.com/urinary-system/)

An individual's kidneys, ureters, bladder, and urethra make up what is known as the urinary system. The kidneys filter blood, eliminate waste, and control the composition of bodily fluids; they are the principal organs responsible for these functions. The kidneys release urine into the urinary bladder via the ureters, which carry it there. Expulsion of pee from the body is facilitated by the urethra.

The kidneys process waste products, but they also play a crucial regulatory and endocrine role. All of these roles played by the urinary system contribute to the body's ability to regulate its fluid and chemical levels and to function normally physiologically.

4.1 ANATOMY OF THE URINARY SYSTEM

4.1.1 Anatomy of the Urinary Tract

From its origin in the kidneys to its final destination outside the body, urine travels down a network of tubes called the urinary tract. From anatomical perspective, it encompasses the urethra, urinary bladder, kidneys, and ureters. In the process of pee transit and expulsion, each part plays a unique function. A kidney's filtration and subsequent modification of filtrate produces urine, while the remaining structures pave the route for its transit, short-term storage, and eventual elimination.

1. Kidneys

Peripheral to the spinal column, the kidneys are a pair of bean-shaped organs located in the back of the abdomen. They are called retroperitoneal organs because of their location behind the peritoneal cavity. They are able to stay in close proximity to the urinary tract and main blood vessels while also being protected from direct external harm due to their placement.

Around the lower thoracic to higher lumbar region is where you can find the kidneys. Due to the large amount of space occupied by the liver above it, the right kidney typically lays slightly lower than the left. There is a medial and lateral border, an anterior and posterior surface, and an upper and lower pole in each kidney. The renal hilum indents the medial border, while the lateral border is convex.

An integral part of the kidney's communication with its environment is the renal hilum. This area is traversed by the ureter, lymphatic vessels, nerves, and kidneys. A collecting channel for urine produced by the kidney tissue, the renal pelvis continues into the ureter within the kidney.

The kidneys are protected by several surrounding layers and tissues, including:

- **Fibrous renal capsule** – a tough connective-tissue layer closely covering the kidney.
- **Perirenal fat** – a layer of fatty tissue surrounding the kidney and providing cushioning.
- **Renal fascia** – connective tissue that helps enclose and support the kidney and surrounding structures.
- **Pararenal fat** – fat located outside the renal fascia that provides additional protection.

Together, these coverings help reduce mechanical stress and assist in maintaining the kidneys in their anatomical position.

2. Ureters

A network of paired muscular tubes called ureters connects the kidneys to the urine bladder. The renal pelvis is the starting point for each ureter, which then descends toward the pelvis and enters the bladder through the back wall.

The average length of an adult ureter is between 25 and 30 centimetres. The smooth muscle lining its outside is responsible for the coordinated production of peristaltic waves. pee does not rely only on gravity to move toward the bladder; even when lying down, these regular contractions push pee toward the bladder.

The ureter can be divided into:

- **Abdominal part** – extends from the renal pelvis toward the pelvic brim.
- **Pelvic part** – continues through the pelvic cavity toward the bladder.
- **Intramural part** – passes obliquely through the wall of the urinary bladder.

The oblique entry of the ureter into the bladder wall contributes to a functional **anti-reflux mechanism**, helping prevent urine from flowing backward toward the kidneys when bladder pressure rises.

There are three clinically important sites where the ureter is relatively narrow:

1. **Ureteropelvic junction**
2. **Point where the ureter crosses the pelvic brim**
3. **Ureterovesical junction**

These natural narrowings are important clinically because a urinary calculus travelling from the kidney to the bladder may become lodged at one of these locations. Obstruction can interfere with urine drainage and, if significant or prolonged, may increase pressure within the urinary tract.

3. Urinary Bladder

The **urinary bladder** is a distensible, hollow muscular organ situated within the pelvic cavity. Its primary function is to **receive and temporarily store urine** until a suitable opportunity for its elimination occurs. The bladder therefore allows urine production by the kidneys to continue continuously while urination takes place intermittently.

The appearance of the bladder changes according to its degree of filling. When empty, it is relatively collapsed and lies mainly within the pelvis. As urine accumulates, its walls stretch and the organ enlarges, allowing it to accommodate increasing volumes.

The main anatomical parts of the urinary bladder include:

- **Apex** – the anterior pointed portion.
- **Body** – the largest central portion.
- **Fundus** – the posterior surface or base.
- **Neck** – the inferior region that continues toward the urethra.

The bladder wall consists mainly of:

- **Mucosa** – the inner lining that comes into direct contact with urine.
- **Submucosa** – connective tissue supporting the mucosal layer.
- **Muscular layer** – composed predominantly of smooth muscle.
- **Outer connective tissue/adventitial or serosal covering** – the exact covering varies according to the surface of the bladder.

The detrusor muscle is the name of the layer of muscles. It stays loose when the bladder is filled, letting it expand, and it contracts when the bladder is empty, creating pressure that pushes urine into the urethra.

The trigone refers to a clearly defined triangle area on the inside. It is created by the internal urethral opening on the lower side and the two ureter apertures on the upper side. The inside of the trigone is rather smooth, in contrast to most of the bladder lining.

4. Urethra

When urine is ready to be discharged from the body, it travels through the urethra, the last branch of the urinary system. It starts at the base of the bladder and goes all the way to the outside of the urethra.

Males and females have different urethral structures and lengths:

- On the outside of the female reproductive organs, near the external genitalia, is where the short urethra opens.
- The male urethra is much longer and goes through many anatomical areas before it opens externally. As a conduit for semen, it serves an additional reproductive purpose in men.

Both smooth and skeletal muscles make up the urethral wall. These structures help keep urine in the bladder by working with the bladder neck and the sphincter mechanisms that are connected to it. In order for pee to be expelled from the bladder and into the outside world, the appropriate sphincter mechanisms must relax in unison during urination.

The kidneys produce urine, the ureters carry it, the bladder stores it, and the urethra is the last conduit for its removal. This is how the urinary tract works.

In order to keep the body's fluids in proper volume, composition, and chemical balance, the kidneys—a highly specialised organ—perform continual filtration of the blood. Their operations and internal structure are highly interdependent. The kidney is able to filter plasma, change the filtrate, and finally create urine because of its cortex, medulla, collecting system, and network of blood arteries.

External Structure

Each kidney has a characteristic bean-shaped appearance with distinct surfaces, borders, and poles. The main external features include:

- **Superior pole**
- **Inferior pole**
- **Anterior surface**
- **Posterior surface**
- **Medial border**
- **Lateral border**

The lateral border is rounded and convex, while the medial border is indented. The indentation forms the renal hilum, which provides an entry and exit point for important structures associated with the kidney.

At the hilum, the renal artery, renal vein, nerves, lymphatic vessels, and renal pelvis are closely related. The renal pelvis continues inferiorly as the ureter, providing the pathway through which urine leaves the kidney.

Internal Structure

When the kidney is sectioned longitudinally, its internal tissue can be divided into two principal regions:

1. **Renal cortex**
2. **Renal medulla**

These regions have different anatomical appearances and contain different parts of the nephron and collecting system.

Renal Cortex

The **renal cortex** forms the outer portion of the kidney and extends inward between the medullary pyramids. It has a granular appearance because it contains numerous small renal structures.

The cortex contains:

- Renal corpuscles
- Proximal convoluted tubules
- Distal convoluted tubules
- Portions of collecting tubules and ducts

Because they house the glomerulus, which is responsible for the first stage of blood filtering, the renal corpuscles are of paramount importance. After that, the filtrate undergoes modifications at the tubular structures' level via secretion and reabsorption.

The renal columns connect the outside and inside of the kidney by extending the cortex between neighbouring pyramids.

Renal Medulla

The renal medulla is located deeper in the kidney and, due to its parallel arrangement of tubules and blood arteries, gives it a more striated look. Renal pyramids are the structures that organise it.

Each pyramid has a wide base that faces the cortex and a tiny tip that faces the collecting system. The renal papilla is the name given to the tip.

The medulla contains:

- **Loops of Henle**
- **Collecting ducts**
- **Blood vessels associated with the medullary circulation**

The specialized arrangement of these structures is important for establishing and maintaining the concentration gradient within the renal medulla, which contributes to the kidney's ability to regulate water conservation and urine concentration.

- ***Renal Columns***

The **renal columns** are projections of cortical tissue that extend inward between adjacent renal pyramids. Besides providing structural continuity between the cortex and medulla, they contain branches of the renal blood vessels that supply the kidney tissue.

Renal Pelvis and Calyces

The collecting system provides a progressively larger pathway through which urine moves from the kidney tissue toward the ureter. After urine reaches the collecting ducts, it passes through the renal papilla and enters the calyces.

The pathway is:

Renal papilla → Minor calyx → Major calyx → Renal pelvis → Ureter

The minor calyces are cup-shaped structures that surround the renal papillae and collect urine emerging from them. Several minor calyces unite to form larger major calyces.

The major calyces subsequently converge to form the renal pelvis. The renal pelvis is a funnel-shaped collecting region located within the renal sinus and continues directly into the ureter. It therefore forms the transition between the kidney's internal collecting system and the urinary tract.

Blood Supply of the Kidney

The kidneys receive a high volume of blood flow in relation to their size because filtration of blood is one of their primary functions. The renal circulation is arranged in a highly organized branching pattern that distributes blood throughout the kidney and establishes the specialized capillary networks required for filtration and tubular exchange.

The general sequence of renal blood flow is:

Renal artery → Segmental arteries → Interlobar arteries → Arcuate arteries → Interlobular arteries → Afferent arterioles → Glomerular capillaries → Efferent arterioles → Peritubular capillaries/vasa recta → Renal veins

The afferent arteriole delivers blood to the glomerulus, where pressure within the glomerular capillaries promotes filtration of fluid and small dissolved substances from the blood into the renal corpuscle.

The filtered blood then leaves the glomerulus through the efferent arteriole. Instead of immediately returning to the systemic venous circulation, it enters a second capillary network. The peritubular capillaries surround much of the renal tubules, whereas the vasa recta are specialized vessels associated particularly with the medullary region.

These vascular arrangements support the exchange of water and solutes between the blood and renal tubules and are essential for processes such as tubular reabsorption and secretion. Blood is ultimately collected into the renal venous system and returned through the renal veins to the general circulation.

4.1.2 Structure of the Nephrons

Every kidney begins with the nephron, its fundamental structural and functional unit. It is a tiny tube-shaped organ that has evolved to filter blood and turn the filtrate into urine. Although it might vary from person to person, the average number of nephrons in a kidney is around one million.

The kidneys' cortex and medulla include nephrons. The nephron's structure enables its many components to carry out distinct roles, including as filtering, reabsorption, secretion, and control of electrolyte and water balance.

There are primarily two parts to a nephron:

1. **Renal corpuscle**
2. **Renal tubule**

A. Renal Corpuscle

The renal corpuscle is the principal location for blood filtration and is located at the beginning of the nephron. The glomerulus, encased in Bowman's capsule, is a component of this structure in the renal

cortex. In a typical filtering procedure, the tubular fluid is kept free of blood cells and the majority of big plasma proteins while water and tiny solutes are removed from the blood.

Glomerulus

Afferent arterioles supply the glomerulus, which is a network of capillaries or a specialised tuft. Its design ensures that the cellular and protein components of blood remain in circulation while allowing for filtration. Water and tiny dissolved compounds are pushed beyond the filtration barrier by the comparatively high hydrostatic pressure within the glomerular capillaries. Once produced, the fluid is known as the first glomerular filtrate and makes its way into the nephron's tubular section.

Capillary endothelium, basement membrane, and podocyte-associated filtration slits are the specialised components that make up the glomerular filtration barrier. Which chemicals are able to enter into the filtrate is determined by their combined structure.

Bowman's Capsule

Bowman's capsule, also called the **glomerular capsule**, is a double-layered cup-like structure that surrounds the glomerulus.

It consists of:

- **Parietal layer** – forms the outer wall of the capsule.
- **Visceral layer** – closely covers the glomerular capillaries.

The visceral layer contains specialized epithelial cells called **podocytes**. These cells extend processes around the capillaries and form narrow filtration slits that contribute to the selective filtration barrier. The fluid that crosses the filtration barrier collects within **Bowman's space**, the region between the two layers. From here, the filtrate passes into the renal tubule for further processing.

B. Renal Tubule

The filtrate is received by the renal tubule, a continuous tubular system, from Bowman's capsule. The filtrate undergoes gradual chemical modification as it passes through its various stages.

What makes up the renal tubule are:

1. **Proximal convoluted tubule**
2. **Loop of Henle**
3. **Distal convoluted tubule**
4. **Connecting tubule and collecting duct system**

Different portions have different epithelial structures and transport properties, allowing the kidney to selectively retain useful substances and remove substances that are not required.

1. Proximal Convoluted Tubule

The proximal convoluted tubule (PCT) is the first major tubular segment following the renal corpuscle. It is highly specialized for bulk reabsorption, returning many filtered substances from the tubular fluid to the bloodstream.

It reabsorbs a large proportion of filtered:

- **Water**
- **Sodium**
- **Chloride**
- **Bicarbonate**
- **Glucose**
- **Amino acids**

The PCT also participates in **tubular secretion**, through which selected substances are transferred from the blood into the tubular fluid. This contributes to the removal of certain metabolic products, ions, and foreign substances.

The epithelial cells lining the PCT possess numerous **microvilli**, which form a prominent **brush border**. These microscopic projections greatly increase the luminal surface area and facilitate efficient transport of substances between the tubular fluid and surrounding capillaries.

2. Loop of Henle

The **loop of Henle** is a U-shaped portion of the nephron that extends from the renal cortex into the medulla before returning toward the cortical region. Its structure establishes different transport properties along the descending and ascending portions.

It consists broadly of:

- **Descending limb**
- **Ascending limb**

The two limbs differ in their permeability to water and solutes. These differences allow the loop to contribute to the countercurrent multiplication mechanism, which establishes an osmotic gradient within the renal medulla.

This medullary gradient is particularly important when the body needs to conserve water. It provides the osmotic conditions necessary for the later concentration of tubular fluid and formation of concentrated urine.

3. Distal Convoluted Tubule

The distal convoluted tubule (DCT) is primarily located within the renal cortex and receives fluid after it has passed through the loop of Henle.

The DCT participates in the fine regulation of electrolyte and acid–base balance, particularly involving:

- **Sodium**
- **Potassium**
- **Calcium**
- **Hydrogen ions**
- **Acid–base balance**

Unlike the proximal tubule, which performs much of the bulk reabsorption, the distal nephron makes more precise adjustments according to the body's physiological requirements.

Hormonal regulation is particularly important in this region. **Aldosterone**, for example, promotes sodium reabsorption and influences potassium secretion in the distal nephron, thereby contributing to the maintenance of electrolyte balance and extracellular fluid volume.

4. Collecting Duct System

The **collecting duct system** receives tubular fluid from several nephrons and carries it through the renal cortex and medulla toward the renal papilla. Although collecting ducts are not technically part of an individual nephron, they are an essential continuation of the renal tubular system involved in the final modification of urine.

One of their most important functions is the regulation of water reabsorption. Their permeability to water is strongly influenced by antidiuretic hormone (ADH).

When ADH levels rise, water permeability of the collecting ducts increases. More water can then move from the tubular fluid into the surrounding medullary tissue and subsequently return to the circulation. This helps conserve body water and produces a smaller volume of more concentrated urine.

- ❖ ***Juxtaglomerular Apparatus***

The juxtaglomerular apparatus (JGA) is a specialized anatomical region where the distal tubule comes into close association with the vascular pole of its renal corpuscle. It provides an important connection between the tubular composition of the filtrate and the regulation of renal blood flow and filtration.

The JGA includes:

- **Macula densa**
- **Juxtaglomerular cells**
- **Extraglomerular mesangial cells**

The macula densa consists of specialized cells in the distal tubule that detect changes in the concentration of sodium chloride in the tubular fluid. This information contributes to mechanisms that adjust renal blood flow and glomerular filtration.

The juxtaglomerular cells are modified smooth muscle cells associated with the afferent arteriole. They act as mechanosensitive cells and also function as endocrine cells by releasing renin when appropriate physiological signals are present.

The JGA therefore contributes to the regulation of:

- **Renal blood flow**
- **Glomerular filtration**
- **Sodium balance**
- **Blood pressure**

Renin and the Renin–Angiotensin–Aldosterone System

Renin is an enzyme released by juxtaglomerular cells. It initiates the renin–angiotensin–aldosterone system (RAAS), an important hormonal mechanism involved in maintaining blood pressure and extracellular fluid volume.

Activation of this system ultimately promotes mechanisms such as vasoconstriction and sodium and water retention, helping restore blood pressure and circulating volume when they fall.

Thus, the nephron is not simply a filtration structure. Its different segments work together to filter plasma, selectively reabsorb useful substances, secrete unwanted substances, regulate electrolytes and acid–base balance, control water conservation, and produce urine with an appropriate concentration.

4.2 PHYSIOLOGY OF THE URINARY SYSTEM

The **physiology of the urinary system** deals with the processes by which the kidneys and urinary tract maintain the internal environment of the body. The kidneys continuously filter blood, selectively retain substances required by the body, eliminate unwanted materials, and adjust the volume and composition of body fluids according to physiological needs.

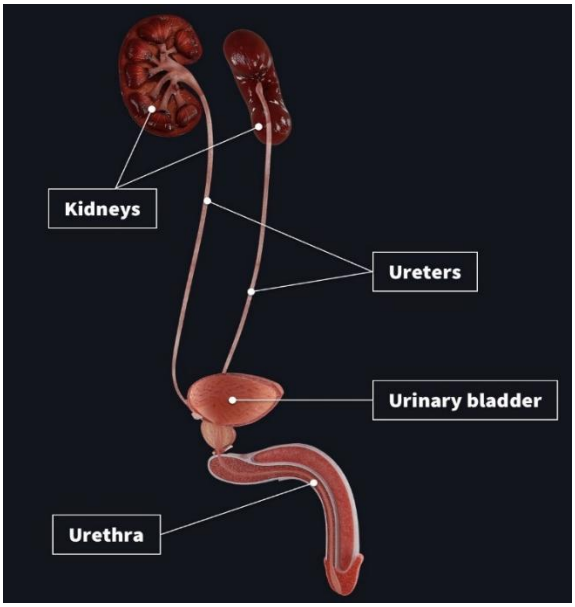


Figure 4.2: Physiology Of the Urinary System

Source: (https://3d4medical.com/blog/physiology-of-the-urinary-system)

The urinary system also works closely with the cardiovascular, endocrine, and nervous systems. Through hormonal and neural mechanisms, it contributes to regulation of blood pressure, fluid balance, electrolyte concentrations, acid–base status, and red blood cell production. The following functions explain how these processes are achieved.

4.2.1 Functions of the Kidneys

The kidneys perform several vital functions that are essential for maintaining **homeostasis**. Their role extends beyond simple removal of waste because they continuously adjust the composition of blood according to the body's requirements.

1. Excretion of Metabolic Waste

The kidneys remove metabolic end products and other substances that accumulate in the blood. Important examples include:

- **Urea** – produced mainly from the metabolism of amino acids.
- **Creatinine** – generated from normal muscle metabolism and commonly used as a marker of kidney function.
- **Uric acid** – produced during the breakdown of purine-containing compounds.
- **Metabolites of various substances** – including products generated during metabolism or processing of certain chemicals and medications.

These substances are filtered, secreted, or otherwise processed by the kidneys and ultimately eliminated primarily in urine. Efficient excretion prevents potentially harmful substances from accumulating in the body.

2. Regulation of Water Balance

The kidneys continuously adjust urinary water loss according to the body's hydration status. This is important for maintaining blood volume, blood pressure, and the concentration of dissolved substances in body fluids.

When the body is dehydrated, water conservation becomes more important. The kidneys reduce water loss and produce a relatively small amount of concentrated urine. In contrast, when water intake is greater than the body's needs, urinary water excretion increases and the urine becomes more dilute. This adjustment is strongly influenced by antidiuretic hormone (ADH) and the osmotic conditions of the renal medulla.

3. Regulation of Electrolytes

The kidneys regulate the concentrations of several electrolytes by adjusting their filtration, reabsorption, and secretion.

Important electrolytes include:

- **Sodium**
- **Potassium**
- **Calcium**
- **Phosphate**
- **Chloride**
- **Magnesium**

Electrolyte regulation is essential because these ions participate in numerous physiological processes. Sodium contributes to extracellular fluid volume and nerve function, potassium is particularly important for membrane excitability and cardiac activity, while calcium and phosphate are important for skeletal health and cellular signaling.

The amount retained or eliminated can change according to dietary intake, hormonal influences, and the body's immediate requirements.

4. Regulation of Acid–Base Balance

The kidneys provide an important long-term mechanism for maintaining the pH of body fluids. They regulate the concentration of acids and bases by controlling the handling of hydrogen ions and bicarbonate.

The major renal mechanisms include:

- **Excreting hydrogen ions**
- **Reabsorbing bicarbonate**
- **Producing new bicarbonate**
- **Excreting acid in buffered forms**

These processes allow the kidneys to compensate for changes in acid production and help maintain blood pH within a narrow physiological range.

5. Regulation of Blood Pressure

The kidneys influence blood pressure through both fluid-volume regulation and hormonal mechanisms.

They regulate:

- **Sodium and water balance**
- **Extracellular fluid volume**
- **Renin release**
- **The renin–angiotensin–aldosterone system**

Changes in sodium and water excretion alter the volume of extracellular fluid and, consequently, circulating blood volume. The kidneys also respond to changes in renal perfusion by modifying renin release, linking renal function with systemic blood pressure regulation.

6. Endocrine Functions

The kidneys function as important endocrine organs because they produce hormones and activate hormone-related substances involved in several body processes.

They participate in:

- **Blood pressure regulation**
- **Red blood cell production**
- **Calcium and bone metabolism**

The kidneys produce erythropoietin, a hormone that stimulates the bone marrow to increase the production of red blood cells. This response is particularly related to the oxygen supply available to renal tissue. The kidneys also convert vitamin D into its biologically active form, calcitriol. Calcitriol promotes appropriate calcium and phosphate handling and contributes to normal bone mineralization.

7. Gluconeogenesis

The kidneys can contribute to glucose production through **gluconeogenesis**, particularly during prolonged fasting. In this process, certain non-carbohydrate substrates are converted into glucose. Although the liver is the major organ responsible for gluconeogenesis under many conditions, renal glucose production can become physiologically significant during prolonged fasting. This contributes to maintaining an adequate blood glucose concentration when dietary carbohydrate is unavailable.

4.2.2 Functions of the Urinary Tract

The kidneys are responsible for urine formation, whereas the remaining structures of the urinary tract provide an organized system for **transporting, storing, and eliminating urine**. Their functions are coordinated with bladder sensation and nervous control.

- ***Ureters***

The ureters:

- **Transport urine from the kidneys to the bladder**
- **Use peristaltic contractions to propel urine**
- **Limit backward movement of urine through their oblique entry into the bladder**

Peristaltic activity occurs through coordinated contractions of the ureteric smooth muscle. The oblique passage through the bladder wall acts as a valve-like mechanism, particularly when pressure rises inside the bladder.

- ***Urinary Bladder***

The urinary bladder acts as a temporary reservoir for urine.

It:

- **Receives urine from the ureters**
- **Stores urine temporarily**
- **Expands as urine volume increases**
- **Contracts during micturition**

During filling, the bladder wall accommodates increasing volume without a proportionate increase in pressure. When the appropriate conditions for urination are reached, neural mechanisms coordinate contraction of the bladder wall with relaxation of the urinary outlet.

- ***Urethra***

The urethra provides the final pathway for urine to leave the body.

It:

- **Conducts urine from the bladder to the exterior**
- **Participates in controlled urinary elimination**

Its associated sphincter mechanisms allow urinary elimination to be regulated rather than occurring continuously. Thus, the urinary tract provides a coordinated pathway for **urine transport, storage, and elimination**.

4.2.3 Physiology of Urine Formation

Urine formation is a continuous process through which the kidneys transform filtered plasma into a final fluid containing substances that need to be eliminated. The composition of the final urine is very different from that of the initial filtrate because useful substances and appropriate amounts of water are returned to the circulation.

Urine formation occurs through three major processes:

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

These processes occur at different locations within the nephron and collectively determine the amount and composition of substances ultimately excreted.

1. Glomerular Filtration

Glomerular filtration is the first stage of urine formation. Blood reaching the glomerulus is subjected to filtration pressure that drives water and small dissolved molecules across the filtration barrier.

The filtrate normally contains:

- **Water**
- **Glucose**
- **Amino acids**
- **Electrolytes**
- **Urea**
- **Other small molecules**

The filtration barrier is selective. Blood cells and most plasma proteins are normally retained within the circulation because of their size and other properties. The resulting fluid enters **Bowman's capsule** and becomes the starting fluid for subsequent tubular processing. Filtration therefore

establishes the initial composition of the tubular fluid but does not itself determine the final composition of urine.

Glomerular Filtration Rate

The glomerular filtration rate (GFR) represents the volume of filtrate produced by all functioning glomeruli per unit of time. In a healthy young adult, GFR is approximately 120 mL/min, although normal values vary with factors such as age, sex, and body size.

GFR is an important indicator of overall kidney function. A sustained reduction may indicate impaired filtration capacity, while changes can also occur temporarily due to physiological factors such as blood pressure and circulating volume.

2. Tubular Reabsorption

A large quantity of water and solutes enters the nephron during filtration, but most of these substances are not intended to be lost from the body. Tubular reabsorption returns selected substances from the tubular fluid to the surrounding blood. This process occurs throughout different portions of the nephron and involves a combination of active transport, passive transport, osmosis, and facilitated transport.

Substances that are extensively reabsorbed include:

- **Water**
- **Sodium**
- **Glucose**
- **Amino acids**
- **Bicarbonate**
- **Chloride**

The extent of reabsorption differs according to the substance and nephron segment. Some substances, such as glucose and amino acids, are normally recovered almost completely under ordinary physiological conditions. Reabsorption is essential because it prevents the excessive urinary loss of substances needed for metabolism, cellular function, and maintenance of fluid balance.

3. Tubular Secretion

Tubular secretion is the transfer of selected substances from the blood surrounding the renal tubules into the tubular fluid. It provides an additional route for removing substances from the circulation after the initial filtration process.

Substances secreted include:

- **Hydrogen ions**
- **Potassium ions**
- **Ammonium**
- **Creatinine**
- **Certain drugs and metabolites**

Tubular secretion is particularly useful for maintaining **acid**–base balance and controlling concentrations of selected electrolytes. It also assists in the elimination of substances that may not be sufficiently removed through filtration alone.

4.2.4 Micturition Reflex

Micturition refers to the coordinated process by which urine is expelled from the urinary bladder. It involves interaction between the bladder wall, urinary sphincters, spinal cord, and higher centres of the nervous system. The bladder can accommodate increasing quantities of urine because its wall can stretch. As filling continues, stretch receptors within the bladder wall become increasingly activated and send sensory information to the nervous system.

Steps of the Micturition Reflex

1. Urine enters the bladder.
2. The bladder gradually expands as its volume increases.
3. Stretch receptors detect increased tension in the bladder wall.
4. Sensory impulses are transmitted to the sacral spinal cord.
5. Parasympathetic activity increases.
6. The detrusor muscle contracts.
7. The internal urethral sphincter relaxes.
8. Voluntary control permits relaxation of the external urethral sphincter.
9. Urine passes through the urethra and is expelled.

The basic reflex pathway is mediated largely by the autonomic nervous system, but higher centres of the brain can facilitate or inhibit bladder emptying. This allows adults to postpone urination until an appropriate time and place. In infants, voluntary control over the external urinary sphincter and higher neural control mechanisms are not fully developed. Consequently, bladder emptying is predominantly reflexive during early life and becomes increasingly controlled with nervous-system maturation and learning.

4.2.5 Role of the Kidneys in Acid–Base Balance

Maintaining an appropriate **acid–base balance** is essential because changes in body-fluid pH can interfere with enzyme activity, membrane function, metabolism, and other cellular processes. The kidneys provide a relatively slow but powerful mechanism for regulating acid–base status. Their actions complement the rapid buffering systems and respiratory mechanisms that also participate in pH regulation.

The kidneys contribute through three major mechanisms:

1. **Reabsorption of Bicarbonate: Bicarbonate (HCO_3^-)** is an important component of the body's buffering system. Large quantities of bicarbonate are filtered at the glomerulus, but most are normally recovered by the renal tubules. The **proximal tubule** performs much of this reabsorption. Conserving bicarbonate helps preserve the blood's capacity to neutralize excess acids.
2. **Hydrogen Ion Secretion:** Renal tubular cells actively move **hydrogen ions (H^+)** into the tubular fluid. This process allows excess acid to be removed from the body through urine. Hydrogen ions can also combine with urinary buffers, enabling greater quantities of acid to be excreted without producing an excessively low urinary pH.
3. **Excretion of Titratable Acids and Ammonium:** Hydrogen ions are buffered within tubular fluid by substances such as **phosphate**, allowing them to be eliminated as titratable acids. The kidneys also generate **ammonia (NH_3)**, particularly from glutamine metabolism. Ammonia binds hydrogen ions to form **ammonium (NH_4^+)**, which remains in the tubular fluid and is excreted. This mechanism becomes especially important when the body is producing or retaining increased amounts of acid.

4.3 PATHOPHYSIOLOGY OF URINARY DISORDERS

Urinary disorders develop when abnormalities affect the kidneys or other structures responsible for urine formation, transport, storage, and elimination. Because the kidneys play a central role in maintaining homeostasis, impairment of their function can produce changes throughout the body. The severity of these effects depends on the type, duration, and extent of the underlying disorder.

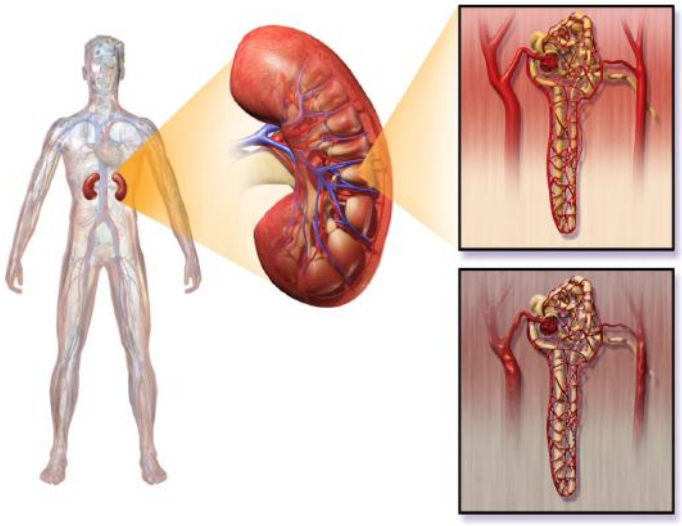


Figure 4.3: Disorders of the Urinary System

Source:(https://bio.libretexts.org/Bookshelves/Human_Biology/Human_Biology_%28Wakim_and_Grewal%29/19%3A_Urinary_System/19.5%3A_Disorders_of_the_Urinary_System)

Urinary disorders can interfere with:

- **Glomerular filtration** – reducing the ability of the kidneys to filter plasma effectively.
- **Tubular function** – disturbing reabsorption and secretion of water and solutes.
- **Urine concentration** – impairing the ability to conserve or eliminate water appropriately.
- **Fluid and electrolyte balance** – causing abnormal accumulation or loss of water and ions.
- **Acid–base regulation** – reducing the ability to remove acids and maintain bicarbonate levels.
- **Waste excretion** – allowing metabolic products to accumulate in the circulation.
- **Hormonal functions of the kidneys** – affecting erythropoietin production, vitamin D activation, and blood-pressure regulation.
- **Urine transport and elimination** – causing obstruction, impaired drainage, or difficulty in bladder emptying.

The major disorders included in this unit are:

1. Acute kidney injury (AKI)
2. Chronic kidney disease (CKD) / chronic renal failure
3. Urinary tract infections (UTIs)

4.3.1 Acute Renal Failure

The modern clinical term acute kidney injury (AKI) is commonly used for what was traditionally called acute renal failure. It refers to a rapid decline in kidney function, generally developing over hours to days.

Because the kidneys normally remove waste and regulate the composition of body fluids, a sudden reduction in their function can quickly disturb the internal environment. The severity of AKI ranges from a mild increase in blood markers of kidney dysfunction to severe kidney failure requiring temporary renal replacement therapy.

As kidney function decreases, the kidneys become less capable of:

- **Removing nitrogenous waste**
- **Maintaining fluid balance**
- **Regulating electrolytes**
- **Maintaining acid–base balance**

Consequently, substances that are normally eliminated in urine may accumulate in the blood, while water and electrolytes may become abnormally retained or distributed.

➢ **Clinical Manifestations**

The clinical presentation varies according to the severity and cause of AKI.

Patients may develop:

- **Reduced urine output** – although urine production may remain relatively normal in some cases.
- **Swelling** – resulting from retention of sodium and water.
- **Fatigue** – associated with metabolic disturbances and accumulation of waste products.
- **Nausea and vomiting**
- **Shortness of breath** – particularly when excess fluid accumulates in the lungs.
- **Confusion** – especially when severe metabolic abnormalities or uremia develop.
- **Abnormal electrolyte levels**
- **Increased blood urea and creatinine**

Some patients may have significant kidney dysfunction without a marked reduction in urine volume. Therefore, urine output alone does not reliably determine the severity of AKI.

➢ **Complications**

Possible complications include:

- **Fluid overload** – excessive accumulation of fluid can increase cardiovascular and pulmonary workload.
- **Hyperkalemia** – elevated potassium can interfere with normal cardiac electrical activity.
- **Metabolic acidosis** – impaired acid excretion causes accumulation of acid in the body.

- **Uremia** – accumulation of waste products and other metabolic abnormalities can affect multiple organs.
- **Pulmonary edema** – severe fluid retention can cause accumulation of fluid in the lungs.
- **Cardiac rhythm disturbances** – particularly associated with significant electrolyte abnormalities.
- **Neurological complications** – severe accumulation of metabolic waste may affect brain function.

Severe AKI may require **renal replacement therapy**, such as dialysis, when complications cannot be adequately controlled through conservative measures.

4.3.2 Chronic Renal Failure

The preferred modern term chronic kidney disease (CKD) refers to abnormalities of kidney structure or function that persist for at least three months. When progressive kidney disease results in severe and sustained loss of renal function, the patient may develop kidney failure, historically referred to as chronic renal failure. Unlike AKI, CKD usually develops over a prolonged period. Progressive nephron loss may eventually become irreversible, although appropriate treatment can slow progression and reduce complications.

- **Causes of Chronic Kidney Disease**

Common causes include:

- **Diabetes mellitus**
- **Hypertension**
- **Chronic glomerular diseases**
- **Polycystic kidney disease**
- **Recurrent or chronic kidney injury**
- **Obstructive urinary tract disorders**

Different diseases damage the kidney through different mechanisms. For example, prolonged hypertension can injure renal blood vessels, whereas diabetes can progressively damage the glomerular filtration apparatus.

- **Systemic Effects**

Because the kidneys influence many physiological systems, chronic renal dysfunction produces effects beyond the urinary system.

Cardiovascular Effects

Kidney disease is strongly associated with:

- **Hypertension**
- **Fluid overload**
- **Increased cardiovascular risk**

Retention of sodium and water can increase circulating volume, while hormonal and vascular changes can further contribute to elevated blood pressure.

- **Hematological Effects:** Reduced renal production of erythropoietin decreases stimulation of red blood cell production in the bone marrow. This contributes to anemia of chronic kidney disease, which can worsen tiredness and reduced exercise capacity.
- **Bone and Mineral Effects:** The kidneys normally participate in vitamin D activation and phosphate regulation. With declining kidney function, impaired phosphate excretion and reduced formation of active vitamin D can disturb calcium–phosphate homeostasis. Over time, these abnormalities contribute to chronic kidney disease–mineral and bone disorder, affecting bone strength and mineral metabolism.
- **Acid–Base Effects:** Reduced renal capacity to excrete acid and maintain bicarbonate balance can result in metabolic acidosis. Persistent acidosis may contribute to further physiological complications.

Electrolyte Effects

Advanced kidney disease may produce abnormalities such as:

- **Hyperkalemia**
- **Hyperphosphatemia**
- **Disturbances of calcium balance**

The severity of these changes depends on residual kidney function, dietary intake, medications, and other clinical factors.

4.3.3 Urinary Tract Infections

A **urinary tract infection (UTI)** is an infection involving one or more parts of the urinary system. The clinical effects depend on the site of infection and the extent to which microorganisms invade the urinary tissues.

UTIs can involve:

- **Urethra — urethritis**
- **Bladder — cystitis**

- **Ureters**
- **Kidneys — pyelonephritis**

Most uncomplicated bacterial infections affect the lower urinary tract, especially the bladder. Infection involving the upper urinary tract is generally more serious because it can directly affect renal tissue.

Causative Organisms

The most common cause of bacterial UTI is Escherichia coli (E. coli). It normally forms part of the intestinal microbial population but may reach the urinary tract and establish infection.

Other bacteria and, less commonly, other microorganisms can also cause UTIs. The organisms involved may vary according to factors such as previous antibiotic exposure, urinary instrumentation, structural abnormalities, and whether the infection is complicated.

Routes of Infection

Most UTIs develop through an **ascending route**, in which microorganisms enter through the urethral opening and move upward.

The sequence is:

Periurethral region → Urethra → Bladder → Ureters → Kidneys

The urinary system possesses several mechanisms that normally restrict microbial growth and prevent infection.

These include:

- **Regular urine flow**
- **Complete bladder emptying**
- **Ureterovesical junction mechanisms**
- **Antimicrobial properties of the urinary tract**
- **Host immune defenses**

Urine flow helps mechanically remove microorganisms, while normal bladder and ureteric function limit their persistence and movement toward the upper urinary tract.

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Unit V…

ENDOCRINE SYSTEM

The endocrine system is a major regulatory system of the human body. It consists of specialized endocrine glands and hormone-producing tissues that release chemical messengers called hormones into the blood. These hormones act on specific target cells or organs and regulate important functions such as growth, development, metabolism, reproduction, stress responses, fluid and electrolyte balance, and maintenance of internal homeostasis.

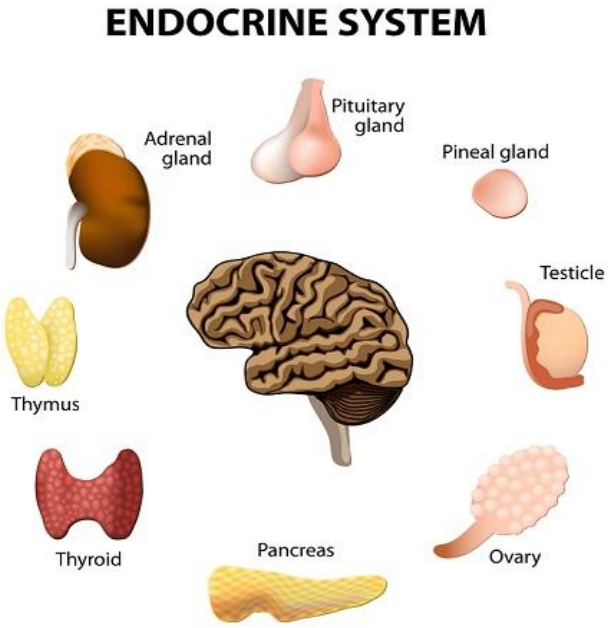


Figure 5.1: The Endocrine System

Source: (https://thyroiduk.org/the-basics/an-overview-of-your-endocrine-system/)

Unlike the nervous system, which generally produces rapid and short-lasting responses through nerve impulses, the endocrine system usually produces slower but longer-lasting effects. The endocrine and nervous systems also work together to coordinate many physiological processes.

5.1 INTRODUCTION TO HORMONES

Hormones are essential chemical regulators of the human body. They coordinate the activities of different organs and tissues and help maintain a stable internal environment. The endocrine system works closely with the nervous system to regulate processes that require coordination, adaptation, and long-term control.



Figure 5.2: Hormones

Source: (https://www.endocrine.org/patient-engagement/endocrine-library/hormones-and-endocrine-function)

Hormones are chemical messengers produced by specialized endocrine cells or glands and released into the bloodstream or surrounding tissue fluids. They are transported to specific target cells, where they bind to receptors and alter cellular activity.

Hormonal communication may occur in several ways:

- **Endocrine action:** A hormone travels through the blood to act on a distant target organ.
- **Paracrine action:** A chemical messenger acts on nearby cells within the same tissue.
- **Autocrine action:** A substance acts on the same type of cell that produced it.
- **Local or tissue action:** Some chemical messengers act close to their site of production without significant systemic circulation.

The biological effect of a hormone depends largely on the presence of a specific receptor. Therefore, although a hormone may circulate throughout the body, only cells containing the appropriate receptor respond to it.

➢ **Major Functions of Hormones**

Hormones participate in almost every major physiological process. Their important functions include:

1. **Growth and development:** Hormones regulate physical growth, tissue development, and maturation of organs.
2. **Basal and energy metabolism:** They influence how the body uses, stores, and produces energy.

3. **Blood glucose regulation:** Hormonal mechanisms maintain glucose levels within an appropriate range.
4. **Water and electrolyte balance:** Hormones help control body-fluid volume and concentrations of sodium, potassium, and other electrolytes.
5. **Calcium and phosphate metabolism:** They regulate mineral levels required for normal bones, teeth, muscles, and cellular functions.

5.1.1 Classification of Hormones

Hormones can be classified according to their chemical composition, solubility, receptor location, and mode of action. Their chemical nature strongly influences how they are synthesized, transported in blood, stored, and recognized by target cells.

A. Peptide and Protein Hormones

Peptide and protein hormones consist of amino acids linked together in chains. Their size varies considerably, from relatively small peptides to larger proteins.

Examples

- Insulin
- Glucagon
- Growth hormone
- Prolactin
- Parathyroid hormone
- Adrenocorticotropic hormone
- Thyroid-stimulating hormone
- Antidiuretic hormone

B. Steroid Hormones

Steroid hormones are chemically derived from cholesterol. They are produced mainly by the adrenal cortex and gonads, although other tissues can also produce steroid-related hormones.

Examples

- Cortisol
- Aldosterone
- Testosterone
- Oestrogen
- Progesterone

C. Amino Acid-Derived Hormones

Amino acid-derived hormones are synthesized from individual amino acids. Tyrosine and tryptophan are particularly important precursors.

Examples

- Thyroxine (T4)
- Triiodothyronine (T3)
- Adrenaline
- Noradrenaline
- Melatonin

Although these hormones belong to the same broad chemical category, their properties are not identical. Their solubility and receptor location depend on their molecular structure.

Thyroid Hormones

T3 and T4 are derived from **tyrosine** and contain iodine. They are relatively lipid-soluble and can enter cells. Their principal receptors are intracellular, where they regulate gene expression and influence metabolic activity, growth, and development.

Catecholamines

Adrenaline and noradrenaline are also derived from tyrosine, but they are **water-soluble**. They generally act through receptors located on the cell membrane and can produce rapid physiological effects, particularly during situations requiring an immediate response.

Melatonin

Melatonin is derived from tryptophan and is produced mainly by the pineal gland. It contributes to the regulation of biological timing and the sleep–wake cycle.

Thus, classification by chemical origin alone does not completely predict hormonal behaviour; molecular structure determines solubility, transport, receptor location, and mechanism of action.

D. Fatty Acid-Derived Hormones

Several important local chemical mediators are derived from polyunsaturated fatty acids, especially arachidonic acid. They are often grouped with lipid mediators rather than classical circulating endocrine hormones.

Examples

- Prostaglandins
- Thromboxanes

- Leukotrienes

These substances are generally produced near the site where they exert their effects and are rapidly metabolized. Therefore, they usually function as local signalling molecules rather than as hormones that travel long distances through the bloodstream.

Functions

They participate in several physiological and pathological processes, including:

- Regulation of blood-vessel diameter
- Inflammatory responses
- Smooth-muscle contraction
- Bronchial activity
- Regulation of platelet aggregation
- Control of vascular and tissue responses

Their local and short-lived actions allow tissues to respond rapidly to changing conditions.

5.1.2 Mechanism of Hormone Action

Hormones exert their effects by interacting with **specific receptors** present on or within target cells. The receptor determines whether a particular cell can recognize and respond to a hormone.

The basic sequence can be represented as:

Hormone secretion → Transport → Receptor binding → Intracellular signalling → Cellular response

The exact mechanism varies according to the chemical nature of the hormone. The most important distinction is between **water-soluble hormones**, which generally act through cell-surface receptors, and **lipid-soluble hormones**, which generally act through intracellular receptors.

A. Action of Water-Soluble Hormones

Water-soluble hormones, including most peptide hormones and catecholamines, generally cannot cross the lipid-rich cell membrane easily.

Therefore, they bind to receptors located on the plasma membrane. Binding activates intracellular signalling mechanisms that transmit the hormonal message from the cell surface to the interior of the cell.

The receptor may activate enzymes or signalling proteins, which subsequently alter the activity of existing proteins within the cell.

- **Major Signalling Systems**

Important intracellular signalling mechanisms include:

- **cAMP pathway:** Activation of certain receptors increases cyclic AMP, which can activate protein kinase A and modify cellular proteins.
- **IP_3/DAG pathway:** Some receptors activate phospholipase C, producing IP_3 and DAG. These molecules participate in calcium release and protein kinase activation.
- **Calcium-mediated signalling:** Changes in intracellular calcium concentration can activate enzymes and other cellular proteins.
- **Protein kinase pathways:** Signalling cascades involving protein phosphorylation can regulate metabolism, transport, growth, and other cellular activities.

B. Action of Lipid-Soluble Hormones

Lipid-soluble hormones include most steroid hormones and thyroid hormones. Their chemical properties allow them to cross cell membranes or otherwise reach intracellular receptor systems. They bind mainly to receptors located within the cytoplasm or nucleus.

After the hormone binds to its receptor, the hormone–receptor complex interacts with specific regions of DNA or with nuclear regulatory proteins. This modifies the transcription of selected genes.

The resulting changes in messenger RNA and protein production can alter the structure, metabolism, or functional activity of the target cell.

Characteristics of Intracellular Action

This mechanism generally:

- Produces changes in **gene expression**
- Requires synthesis or modification of cellular proteins
- Has a **slower onset** than many membrane-receptor responses
- Can produce effects that persist after the hormone has been removed from the circulation
- Allows hormones to produce long-term changes in cellular function

5.2 MAJOR ENDOCRINE GLANDS

The major endocrine glands are specialized organs that release hormones into the blood or surrounding tissues. Unlike exocrine glands, which release their secretions through ducts, endocrine glands are **ductless glands** and their secretions enter the circulation directly.

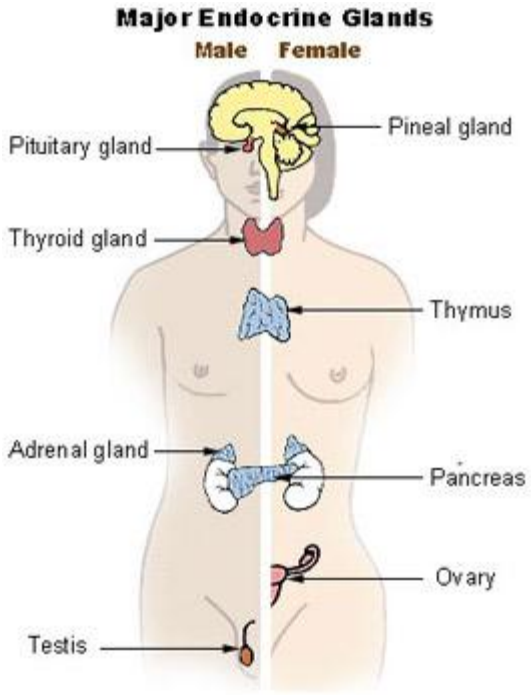


Figure 5.3: Endocrine Glands

Source: (https://training.seer.cancer.gov/anatomy/endocrine/glands/)

The major endocrine glands included in this unit are:

1. **Pituitary gland**
2. **Thyroid gland**
3. **Parathyroid glands**
4. **Adrenal glands**
5. **Pancreas**
6. **Pineal gland**
7. **Thymus**

Although these glands differ considerably in their location, microscopic organization, and hormonal products, they function as an integrated system. Their hormones influence growth, metabolism, reproduction, fluid balance, stress responses, calcium regulation, immune development, and other physiological activities.

5.2.1 Pituitary Gland

The pituitary gland, also known as the hypophysis, is a small but highly important endocrine gland situated at the base of the brain. It has a close anatomical and functional relationship with the hypothalamus, which provides major regulatory signals controlling pituitary activity.

Because the pituitary influences the function of several other endocrine glands, it is traditionally referred to as the "master gland." However, this term should be understood in context because the pituitary itself is controlled to a large extent by hypothalamic signals.

- **Structure**

The pituitary gland is housed within a bony depression of the sphenoid bone called the **sella turcica**. This protected location helps secure the gland at the base of the cranial cavity. The gland is connected with the hypothalamus by the infundibulum, or pituitary stalk. This connection provides both neural and vascular communication between the two structures and permits the hypothalamus to regulate pituitary secretion.

The pituitary is divided into two major portions:

1. Anterior Pituitary

The **anterior pituitary**, or **adenohypophysis**, is composed primarily of glandular tissue. It synthesizes and secretes several hormones that regulate growth, thyroid activity, adrenal function, reproduction, and lactation.

The major hormones produced by the anterior pituitary are:

- **Growth hormone (GH)**
- **Thyroid-stimulating hormone (TSH)**
- **Adrenocorticotropic hormone (ACTH)**
- **Follicle-stimulating hormone (FSH)**
- **Luteinizing hormone (LH)**
- **Prolactin (PRL)**

These hormones act either directly on tissues or indirectly by stimulating other endocrine glands.

2. Posterior Pituitary

The **posterior pituitary**, or **neurohypophysis**, differs from the anterior portion because it is primarily neural tissue associated with the hypothalamus.

It stores and releases:

- **Antidiuretic hormone (ADH)**
- **Oxytocin**

Importantly, these hormones are synthesized mainly by specialized neurons in the **hypothalamus**. They are transported along the nerve fibres of these neurons to the posterior pituitary, where they are stored until appropriate stimulation causes their release into the circulation.

5.2.2 Thyroid Gland

The thyroid gland is an endocrine gland situated in the anterior region of the neck. It is one of the principal regulators of the body's metabolic activity.

Its hormones have widespread effects because almost all tissues require appropriate thyroid hormone activity for normal physiological function.

- **Structure**

The thyroid gland is positioned below the larynx and surrounds the anterior and lateral surfaces of the upper portion of the trachea.

It consists mainly of:

- **Right lobe**
- **Left lobe**
- **Isthmus**, which connects the two lobes

The gland is composed microscopically of numerous thyroid follicles. These follicles are spherical structures lined by follicular cells. Their central cavity contains colloid, which contains thyroglobulin and serves as a storage reservoir involved in thyroid hormone synthesis. The thyroid also contains parafollicular cells, commonly called C cells. These cells are functionally distinct from the follicular cells and produce calcitonin.

5.2.3 Parathyroid Glands

The parathyroid glands are small endocrine structures located in association with the posterior surface of the thyroid gland. Despite their small size, they have a major role in maintaining the concentration of calcium and phosphate in body fluids.

- **Structure**

Most individuals have four parathyroid glands, although their number and exact anatomical position may vary.

They are usually situated on the posterior aspect of the thyroid gland. Microscopically, the glands contain two principal cell types:

- **Chief cells**
- **Oxyphil cells**

The chief cells are the principal secretory cells and are responsible for producing parathyroid hormone (PTH).

5.2.4 Adrenal Glands

The adrenal glands, also called the suprarenal glands, are paired endocrine glands located superior to the kidneys.

Each adrenal gland contains two anatomically and functionally different regions:

1. **Adrenal cortex**
2. **Adrenal medulla**

Although both regions belong to the same gland, they differ substantially in their cellular organization and hormonal products.

- **Structure**

Adrenal Cortex

The adrenal cortex forms the **outer portion** of the gland. It is subdivided into three zones:

1. **Zona glomerulosa**
2. **Zona fasciculata**
3. **Zona reticularis**

Each cortical zone has characteristic steroid-producing functions.

Adrenal Medulla

The adrenal medulla forms the inner portion of the gland. It contains specialized neuroendocrine cells known as chromaffin cells. These cells are responsible for producing catecholamines that participate in rapid responses to stressful situations.

5.2.5 Pancreas

The **pancreas** is a **mixed gland** because it performs both exocrine and endocrine functions.

Its exocrine component contributes to digestion, whereas its endocrine component produces hormones involved in the regulation of metabolism, particularly blood glucose control.

- **Structure**

The pancreas lies in the upper abdomen, extending from the region of the duodenum toward the spleen.

Its major anatomical parts are:

- **Head**
- **Neck**
- **Body**
- **Tail**

The endocrine portion consists of clusters of specialized cells called the **islets of Langerhans**.

Table 5.1: Important endocrine cell types include:

Cell type	Major hormone	Main function
β-cells	Insulin	Decreases blood glucose
α-cells	Glucagon	Increases blood glucose
δ-cells	Somatostatin	Regulates secretion of several hormones
PP cells	Pancreatic polypeptide	Influences pancreatic and gastrointestinal functions

5.2.6 Pineal Gland

The pineal gland is a small endocrine structure located within the brain. Although it is considerably smaller than several other endocrine organs, it has an important role in regulating biological timing.

- **Structure**

The pineal gland is situated near the roof of the third ventricle, within the region of the epithalamus. It contains specialized secretory cells known as pinealocytes. These cells produce melatonin, the principal hormone associated with the endocrine activity of the pineal gland.

5.2.7 Thymus

The thymus is primarily a lymphoid organ but also possesses important endocrine functions. It is particularly significant during childhood, when the immune system is undergoing active development.

With increasing age, especially after puberty, the thymus undergoes considerable **involution**, meaning that functional thymic tissue gradually decreases and is partly replaced by other tissue.

- **Structure**

The thymus is located in the upper anterior mediastinum, behind the sternum.

It consists of two lobes and has two principal internal regions:

- **Outer cortex**
- **Inner medulla**

The cortex contains numerous immature **T** lymphocytes, while the medulla contains more mature T cells and characteristic structures called Hassall's corpuscles.

5.3 PATHOPHYSIOLOGY OF ENDOCRINE DISORDERS

Endocrine disorders develop when the normal production, secretion, transport, recognition, or action of hormones is disturbed. Since hormones regulate numerous interconnected physiological processes, an abnormality in one component of the endocrine system can affect several organs and body functions. The disturbance may occur at the level of the endocrine gland itself, the hormone, its receptor, or the regulatory mechanisms controlling hormone secretion. Endocrine disorders may result from excessive or insufficient hormone secretion, abnormal hormone receptors, resistance to hormone action, autoimmune processes, genetic abnormalities, tumours, inflammation or destruction of endocrine tissue, nutritional deficiencies, or disorders of hypothalamic and pituitary regulation. The major endocrine disorders covered in this section are diabetes mellitus, hypothyroidism, hyperthyroidism, goitre, and polycystic ovary syndrome (PCOS).

5.3.1 Diabetes Mellitus

Diabetes mellitus is a chronic metabolic disorder characterised by persistent elevation of blood glucose, known as hyperglycaemia. It develops when insulin secretion, insulin action, or both become inadequate to maintain normal glucose regulation. Glucose is an important source of energy for many cells of the body, while insulin plays a central role in enabling the body to utilise and store glucose appropriately. When insulin is absent, insufficient, or ineffective, glucose remains in the bloodstream instead of being adequately utilised by tissues.

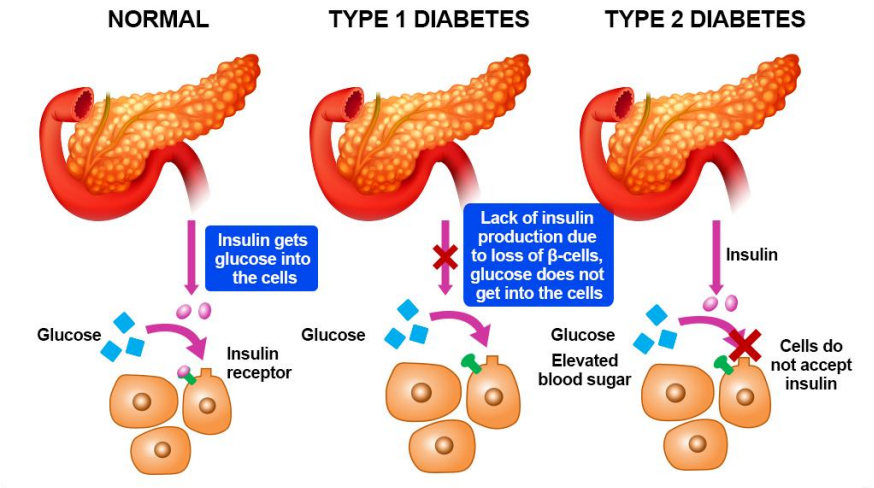


Figure 5.4: Diabetes Mellitus

Source: (https://www.rejoyhealth.com/blog/introdcution-to-diabetes-mellitus)

❖ ***Normal Glucose Regulation***

After food is consumed, carbohydrates are digested and glucose enters the bloodstream. The resulting rise in blood glucose stimulates the β-cells of the pancreas to release insulin. Insulin facilitates the

movement of glucose into appropriate tissues and promotes its storage, allowing blood glucose levels to gradually return towards the normal range. During fasting, insulin secretion decreases while glucagon secretion increases. Glucagon acts particularly on the liver and promotes the production and release of glucose, helping prevent blood glucose levels from falling excessively. Therefore, normal glucose regulation depends on a balance between hormones that promote glucose storage and utilisation and those that promote glucose availability.

❖ ***Pathophysiology of Diabetes***

Diabetes develops when the normal relationship between insulin secretion and insulin action becomes disturbed. The exact mechanism differs between the major forms of diabetes. In general, inadequate insulin availability or reduced responsiveness to insulin prevents normal glucose utilisation and results in persistent elevation of blood glucose. Over time, prolonged hyperglycaemia can affect multiple tissues and contribute to complications involving the blood vessels, kidneys, retina, peripheral nerves, and cardiovascular system.

Type 1 Diabetes Mellitus

Type 1 diabetes mellitus is characterised by autoimmune destruction of pancreatic β-cells, which are responsible for insulin production. As these cells are progressively destroyed, the body's ability to produce insulin becomes severely reduced or nearly absent. The resulting process can be represented as ↓ Insulin → ↓ glucose uptake → ↑ blood glucose → hyperglycaemia. Because adequate insulin is unavailable, glucose cannot be effectively utilised by tissues that depend on insulin-mediated uptake. The body consequently begins to rely increasingly on alternative energy sources, particularly stored fat and protein.

➢ **Increased Fat Breakdown**

When glucose cannot be adequately utilised, the body increases the breakdown of stored fat to provide an alternative energy source. This process produces ketone bodies. If ketone production becomes excessive and the body's compensatory mechanisms are overwhelmed, the blood becomes increasingly acidic, resulting in diabetic ketoacidosis (DKA). DKA is a serious metabolic complication that requires prompt medical treatment.

Type 2 Diabetes Mellitus

Type 2 diabetes mellitus is primarily associated with two interacting abnormalities: insulin resistance and progressive impairment of pancreatic β-cell insulin secretion. In insulin resistance, target tissues do not respond adequately to the available insulin, meaning that greater amounts of insulin may initially be required to produce the same physiological effect. During the early stages, pancreatic β-

cells may compensate by increasing insulin secretion, which can temporarily help maintain blood glucose within an acceptable range.

- **Progressive β-Cell Dysfunction**

With continued insulin resistance, the demand placed on pancreatic β-cells may increase. Over time, these cells may no longer compensate adequately, and their insulin-secretory capacity may gradually decline. Consequently, insulin resistance + declining β-cell function → inadequate insulin action → persistent hyperglycaemia. This explains why type 2 diabetes may develop progressively rather than appearing suddenly.

- **Major Effects of Diabetes**

Persistent hyperglycaemia can gradually damage tissues, particularly structures containing small and large blood vessels. Important organs and systems affected include the blood vessels, kidneys, retina, peripheral nerves, and cardiovascular system. Therefore, the effects of prolonged high blood glucose are not limited to glucose metabolism; they can eventually interfere with circulation, renal function, vision, nerve function, and cardiovascular health.

- **Common Manifestations**

Diabetes may produce characteristic manifestations such as increased thirst, increased urination, increased hunger, fatigue, blurred vision, unexplained weight loss, and delayed wound healing. Increased urination occurs because excess glucose in the blood can increase urinary glucose excretion and promote water loss. The resulting loss of fluid contributes to increased thirst. Weight loss may be particularly noticeable when insulin deficiency is marked because the body is unable to utilise glucose adequately and increasingly depends on stored energy sources.

5.3.2 Hypothyroidism

Hypothyroidism is a condition in which the availability or action of thyroid hormones is insufficient to meet normal physiological requirements. Thyroid hormones influence metabolic activity in many tissues; therefore, their deficiency produces a general slowing of physiological processes. Hypothyroidism may develop because of a problem within the thyroid gland itself or because of inadequate stimulation from higher regulatory centres.

- ***Pathophysiology***

Reduced thyroid hormone activity causes a general reduction in metabolic processes. The degree of impairment depends on the severity and duration of the hormone deficiency. Because thyroid hormones influence energy expenditure, cardiovascular activity, gastrointestinal function, neuromuscular activity, and other physiological processes, reduced hormone activity can produce manifestations across several body systems.

❖ ***Primary Hypothyroidism***

In primary hypothyroidism, the abnormality originates within the thyroid gland. When thyroid hormone production decreases, the normal negative-feedback effect on the pituitary is reduced. In response, the pituitary increases production of thyroid-stimulating hormone (TSH) in an attempt to stimulate the thyroid gland. The relationship can therefore be represented as ↓ Thyroid hormone → loss of negative feedback → ↑ TSH. Increased TSH in this situation represents an attempt by the regulatory system to restore thyroid hormone production.

❖ ***Secondary Hypothyroidism***

In secondary hypothyroidism, the primary problem occurs at the level of the pituitary gland. Because insufficient TSH is produced, the thyroid gland does not receive adequate stimulation to produce thyroid hormones. Thus, the thyroid gland may be structurally capable of producing hormones, but its activity becomes reduced because of inadequate upstream stimulation.

➢ **Common Causes**

Hypothyroidism may result from autoimmune thyroid disease, iodine deficiency, thyroid surgery or destruction of thyroid tissue, certain medications, and disorders involving the pituitary or hypothalamus. Identifying the underlying cause is important because it determines whether the primary abnormality is located within the thyroid gland or within the regulatory centres controlling thyroid function.

➢ **Effects of Hypothyroidism**

Reduced thyroid hormone activity can produce reduced metabolic rate, fatigue, weight gain, cold intolerance, dry skin, constipation, slow heart rate, reduced concentration, muscle weakness, and menstrual disturbances. These manifestations reflect the widespread influence of thyroid hormones on energy expenditure, cardiovascular function, gastrointestinal activity, neuromuscular function, and reproductive physiology.

5.3.3 Hyperthyroidism

Hyperthyroidism occurs when the thyroid gland produces excessive amounts of thyroid hormones. Increased thyroid hormone activity accelerates many metabolic and physiological processes throughout the body. This produces a characteristic pattern of increased metabolic activity along with cardiovascular and nervous-system manifestations.

<u>Pathophysiology</u>

Excess thyroid hormone increases the body's metabolic activity and makes tissues more responsive to catecholamines, such as adrenaline and noradrenaline. This increased metabolic activity, together

with enhanced catecholamine responsiveness, explains many of the cardiovascular and nervous-system manifestations associated with hyperthyroidism.

❖ ***Graves' Disease***

One common cause of hyperthyroidism is Graves disease, an autoimmune disorder. In Graves disease, antibodies stimulate the TSH receptor on thyroid cells. As a result, the thyroid gland receives a continuous stimulatory signal even though normal pituitary regulation would otherwise reduce TSH secretion. The mechanism can be summarised as TSH-receptor stimulation → ↑ T3/T4 production → ↓ pituitary TSH through negative feedback. The important abnormality is therefore stimulation of the thyroid receptor by TSH-receptor antibodies, rather than simply excessive production of TSH.

Effects of Hyperthyroidism

Increased thyroid hormone activity can result in increased metabolic rate, weight loss despite increased appetite, heat intolerance, excessive sweating, increased heart rate, palpitations, nervousness, tremors, increased bowel movements, muscle weakness, and sleep disturbances. The combination of increased metabolic activity and enhanced sensitivity to catecholamines accounts for many of these cardiovascular and nervous-system manifestations.

- **Eye Manifestations:** Individuals with Graves disease may develop characteristic **eye manifestations** because the autoimmune process can involve tissues surrounding the eyes. These changes are an important clinical feature that may accompany the thyroid disorder.
- **Thyroid Storm:** Severe untreated hyperthyroidism can progress to **thyroid storm**, which is a medical emergency characterised by extreme systemic manifestations. It represents an acute and potentially life-threatening exaggeration of the physiological effects associated with excessive thyroid hormone activity.

5.3.4 Goitre

A goitre is an abnormal enlargement of the thyroid gland. It is important to understand that goitre describes a structural enlargement rather than one specific hormonal disorder. A person with a goitre may have normal thyroid function, reduced thyroid hormone production, or excessive hormone production, depending on the underlying cause.

Pathophysiology

One important mechanism responsible for goitre involves prolonged stimulation of thyroid tissue. For example, when iodine availability is insufficient, thyroid hormone synthesis may decrease. Reduced thyroid hormone production weakens the normal negative feedback on the pituitary, resulting in increased TSH stimulation. The sequence can be represented as Iodine deficiency → ↓ thyroid hormone synthesis → ↓ negative feedback → ↑ TSH → thyroid stimulation → thyroid

enlargement. Continued stimulation promotes growth of thyroid tissue and can eventually produce visible enlargement. Goitre may also occur because of autoimmune thyroid disease, multinodular thyroid disease, thyroid nodules, certain medications, excessive or insufficient iodine intake, and other thyroid disorders. Therefore, thyroid enlargement does not necessarily indicate iodine deficiency or a particular thyroid functional state.

Types of Goitre

- **Diffuse Goitre:** In a **diffuse goitre**, the thyroid gland becomes enlarged relatively uniformly without distinct dominant nodules. The enlargement involves the gland more generally rather than being concentrated in one or more specific areas.
- **Nodular Goitre:** A **nodular goitre** develops when one or more localised nodules form within the thyroid gland. These nodules may contribute to an uneven appearance or enlargement of the gland.
- **Multinodular Goitre:** A **multinodular goitre** contains multiple nodules that contribute to enlargement of the thyroid gland. The number and size of nodules can vary between individuals.

Goitres can also be classified according to thyroid functional status. A euthyroid goitre occurs when thyroid hormone production remains within the normal range, a hypothyroid goitre is associated with reduced thyroid hormone production, and a hyperthyroid **goitre** is associated with excessive thyroid hormone production.

- **Clinical Effects**

A small goitre may not produce noticeable symptoms and may be discovered during routine examination. As the thyroid gland becomes larger, however, it may exert mechanical pressure on structures within the neck. This can result in visible swelling in the neck, difficulty swallowing, difficulty breathing, hoarseness, and a sensation of pressure in the neck. Because thyroid function can vary among individuals with goitre, identifying the underlying cause and hormonal status is essential for proper evaluation.

5.3.5 Polycystic Ovary Syndrome

Polycystic ovary syndrome (PCOS) is a common endocrine and metabolic disorder associated with reproductive dysfunction, abnormal androgen activity, and metabolic disturbances. It involves several interacting physiological systems rather than a single hormonal abnormality.

Pathophysiology

PCOS involves complex interactions between ovarian function, hypothalamic–pituitary signalling, androgen production, insulin action, and metabolic factors. A common feature is hyperandrogenism,

meaning excessive androgen activity. Insulin resistance may also occur in many individuals with PCOS. Increased insulin levels can interact with ovarian hormone regulation and contribute to increased androgen production.

❖ ***General Mechanism***

The general mechanism can be summarised as Insulin resistance → compensatory increase in insulin → increased ovarian androgen production and altered hormone regulation → impaired follicular development → ovulatory dysfunction. This interaction can interfere with normal maturation of ovarian follicles and the regular occurrence of ovulation. The ovaries may contain numerous small follicles that have not progressed normally through development. However, the presence of multiple follicles on ultrasound is **not essential for diagnosis**, and the term "polycystic" does not mean that every affected individual necessarily has ovarian cysts.

Major Features

PCOS may present through several overlapping reproductive, hormonal, and metabolic features. The clinical presentation can vary considerably between individuals because not every person experiences the same combination or severity of manifestations.

1. **Ovulatory Dysfunction:** Abnormal or absent ovulation can interfere with the normal menstrual cycle. It may result in irregular menstrual cycles, infrequent menstruation, difficulty with ovulation, and reduced fertility. The irregularity occurs because normal cyclic ovarian activity is disrupted, affecting the predictable sequence of follicular development and ovulation.
2. **Hyperandrogenism:** Increased androgen activity may produce physical manifestations such as excess facial or body hair, acne, and androgen-related hair thinning. The severity and combination of these manifestations can vary considerably between individuals.
3. **Metabolic Abnormalities:** PCOS may also be associated with metabolic changes, particularly abnormalities in insulin action. Some individuals may develop insulin resistance, impaired glucose regulation, dyslipidaemia, and an increased long-term risk of metabolic disease. These features demonstrate that PCOS is not limited to the reproductive system and may also affect glucose and lipid metabolism.
4. **Ovarian Changes:** Ultrasound examination may show multiple small ovarian follicles in some individuals. These follicles may reflect altered follicular development rather than true pathological cysts. Importantly, ovarian appearance can vary, and the presence of multiple follicles alone is not sufficient to establish PCOS.

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Unit VI…

REPRODUCTIVE SYSTEM AND CANCER

The **reproductive system** is a group of organs responsible for reproduction, production of sex cells, secretion of reproductive hormones, and development of offspring. The male reproductive system mainly produces sperm and delivers them to the female reproductive tract, whereas the female reproductive system produces ova, provides the site for fertilization, supports implantation and pregnancy, and participates in childbirth. Reproductive functions are regulated by hormones produced by the hypothalamus, pituitary gland, testes, and ovaries.

This unit also includes sexually transmitted diseases (STDs) and cancer. Sexually transmitted diseases are infections that are commonly spread through sexual contact and may affect the reproductive organs as well as other body systems. Cancer is a group of diseases characterized by abnormal, uncontrolled cell growth, which can invade surrounding tissues and, in some cases, spread to distant parts of the body.

6.1 MALE REPRODUCTIVE SYSTEM

The male reproductive system is a specialized organ system responsible for reproductive functions in males. It includes a combination of external and internal reproductive organs, ducts, accessory glands, and supporting tissues that work together in a coordinated manner. The system is involved in the formation of male gametes, hormonal regulation of reproductive activity, maturation of sperm, movement of sperm through the reproductive ducts, and their eventual deposition into the female reproductive tract.

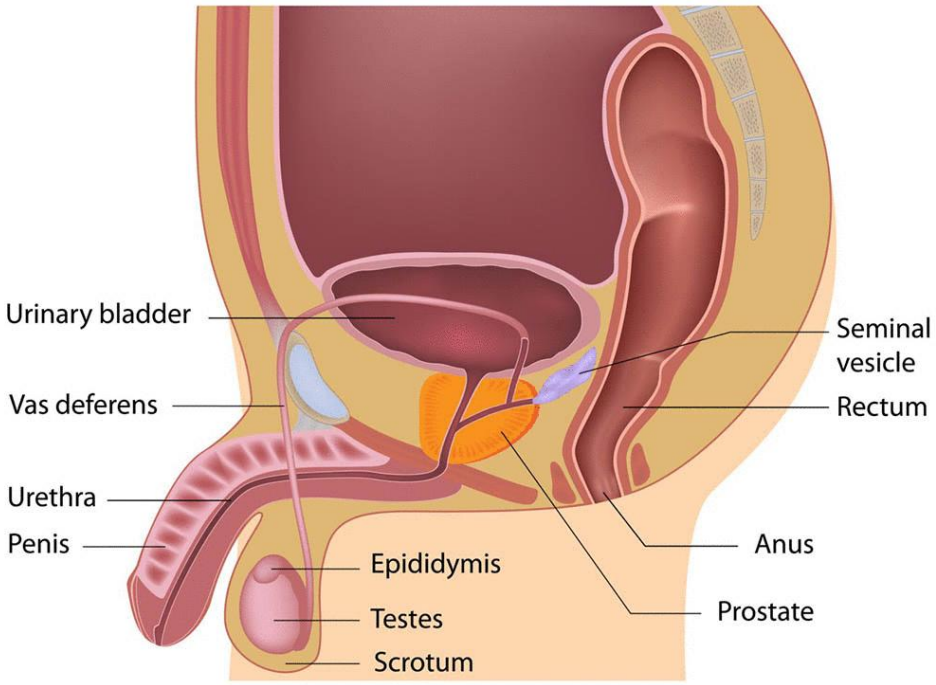


Figure 6.1: Male Reproductive System

Source: (https://www.healthdirect.gov.au/male-reproductive-system)

The reproductive functions of the male system are closely controlled by hormones, particularly testosterone, as well as hormones released from the hypothalamus and pituitary gland. The different organs have distinct roles, but their activities are integrated to ensure the continuous production and functional development of sperm after puberty.

6.1.1 Anatomy of the Male Reproductive System

The major organs of the male reproductive system include the testes, epididymis, vas deferens, ejaculatory ducts, urethra, penis, scrotum, seminal vesicles, prostate gland, and bulbourethral glands. These structures can be broadly classified into reproductive organs that produce or transport sperm and accessory glands that contribute secretions to semen.

The testes are responsible primarily for sperm production and hormone secretion, while the ducts provide a pathway through which sperm can travel. The accessory glands add fluids containing nutrients, protective substances, and other components that support sperm function.

- ***Testes***

The **testes** are the primary male reproductive organs and are present as a pair of oval-shaped structures within the scrotum. Their location outside the main body cavity is important because sperm formation requires a temperature slightly lower than the normal internal body temperature.

Each testis is surrounded by a tough protective connective-tissue covering. Internally, connective tissue partitions divide it into numerous lobules. These lobules contain tightly coiled seminiferous tubules, which form the principal site of sperm production.

The seminiferous tubules contain developing germ cells arranged at different stages of development. As these cells mature, they gradually move toward the lumen of the tubules. Sertoli cells are present among the developing germ cells and provide structural and nutritional support. They also help create a controlled microenvironment required for the development of sperm cells.

Located in the connective tissue between the seminiferous tubules are Leydig cells. These endocrine cells synthesize testosterone in response to stimulation by luteinizing hormone. Thus, the testes have both an exocrine role, through sperm production, and an **endocrine role**, through hormone secretion.

- ***Scrotum***

The **scrotum** is an external pouch that houses the testes and their associated structures. It is composed of skin, connective tissue, and muscular components that contribute to temperature regulation.

Sperm formation is sensitive to temperature changes. The muscles associated with the scrotum respond to changes in environmental conditions. In colder conditions, the testes are drawn closer to the body, whereas in warmer conditions they are positioned farther away. This mechanism helps maintain a relatively appropriate temperature for spermatogenesis. The scrotum therefore acts not simply as a protective covering but also as an important **temperature-regulating structure** for the testes.

- ***Epididymis***

The **epididymis** is a long, narrow and highly coiled duct situated along the posterior aspect of each testis. Although it appears relatively small externally, its extensive coiling provides a considerable surface and length through which sperm can pass.

Sperm entering the epididymis from the testis are not yet fully functionally mature. During their passage through this duct, they undergo biochemical and structural modifications that allow them to develop the ability to move progressively and participate effectively in fertilization. The epididymis also provides a suitable environment for **temporary storage of sperm**. Contractions of its muscular wall later assist in moving sperm toward the vas deferens.

- ***Vas Deferens***

The **vas deferens**, or ductus deferens, is a thick-walled muscular tube that continues from the epididymis. It travels from the scrotal region into the pelvic cavity and forms an important part of the sperm-transport pathway.

Its muscular wall is particularly important during ejaculation. Coordinated contractions generate waves that propel sperm forward through the duct. The vas deferens therefore provides both a transport route and a mechanism for rapid movement of sperm during reproductive activity.

- ***Ejaculatory Ducts***

The ejaculatory ducts are short ducts formed through the union of the terminal portion of the vas deferens with the ducts associated with the seminal vesicles. They pass through the prostate and open into the urethra.

Their position allows sperm arriving through the vas deferens to mix with secretions contributed by the seminal vesicles before entering the urethral passage. They consequently form an important connection between the sperm-transport system and the final common pathway.

- ***Urethra***

The urethra extends from the urinary bladder and passes through the male reproductive tract before opening externally through the penis. It has a dual role in the male body because it is involved in both the urinary and reproductive systems.

During reproduction, semen passes through the urethra toward the exterior. During urination, urine follows the same general passage. Specialized mechanisms associated with the bladder neck and reproductive tract help prevent the simultaneous movement of urine and semen through the urethra.

- ***Penis***

The penis is the external organ involved in sexual intercourse and the delivery of semen. Its internal structure contains specialized erectile tissues composed of vascular spaces. During sexual stimulation, increased blood flow into these tissues causes them to become firm, producing an erection. This enables the organ to perform its reproductive function during intercourse.

The distal end of the penis contains the glans, while the external opening of the urethra allows semen and urine to leave the body. During ejaculation, muscular contractions help propel semen through the urethra and outside the body.

- ***Seminal Vesicles***

The seminal vesicles are paired accessory glands situated posterior to the urinary bladder. Their secretions make up a substantial portion of the fluid component of semen. The fluid produced by these glands contains fructose, which can serve as an energy substrate for sperm. It also contains other substances that contribute to the chemical environment surrounding sperm after ejaculation.

The secretion helps provide an appropriate medium for sperm survival and movement and therefore contributes significantly to the functional properties of semen.

- ***Prostate Gland***

The prostate gland is a single accessory gland positioned inferior to the urinary bladder. It surrounds the upper portion of the urethra and is closely associated with the ejaculatory ducts.

The prostate contributes a specialized fluid to semen. This secretion contains substances that help maintain conditions favorable for sperm function and contributes to the characteristic composition of seminal fluid. Because the urethra passes through the prostate, changes in the size or structure of this gland can also influence urinary flow.

- ***Bulbourethral Glands***

The bulbourethral glands, also known as Cowper's glands, are small paired accessory glands located below the prostate. Their ducts open into the urethra. These glands produce a clear lubricating secretion that is released into the urethral passage. The secretion contributes to lubrication of the reproductive tract and forms part of the fluid associated with semen.

6.1.2 Functions of the Male Reproductive System

The male reproductive system performs several interconnected functions that support reproduction and hormonal regulation.

1. **Production of Sperm:** The testes generate male gametes through the process of **spermatogenesis**. This process transforms specialized germ cells into spermatozoa capable of participating in fertilization.
2. **Secretion of Male Sex Hormones:** The testes function as endocrine organs and produce **testosterone and other androgens**. These hormones regulate reproductive development and influence several tissues throughout the body.
3. **Sperm Maturation:** Sperm produced in the seminiferous tubules require additional functional development before they can effectively participate in fertilization. Much of this maturation occurs as sperm pass through the **epididymis**.
4. **Transport of Sperm:** A series of ducts provides a continuous pathway for sperm movement from the testes toward the exterior. Muscular activity within these ducts is particularly important during ejaculation.
5. **Formation of Semen:** Semen is formed when sperm combine with secretions from the **seminal vesicles, prostate gland, and bulbourethral glands**. These fluids provide nutrients, lubrication, and a suitable environment for sperm.
6. **Delivery of Sperm:** The penis provides the final route for introducing semen into the female reproductive tract during sexual intercourse. This brings sperm into proximity with the site where fertilization may occur.

7. **Maintenance of Male Reproductive Characteristics:** Androgens, particularly testosterone, influence the development and maintenance of reproductive structures and male secondary sexual characteristics. They also contribute to changes in body composition, sexual behavior, and other physiological processes associated with male reproductive function.

6.1.3 Male Sex Hormones

Male reproductive activity is controlled by a group of hormones that regulate sexual development, sperm production, and the activity of reproductive organs. Although **testosterone** is the principal androgen, its actions occur as part of a larger hormonal network involving the hypothalamus, pituitary gland, testes, and other tissues.

Testosterone

Testosterone is the principal male sex hormone and is produced mainly by the **Leydig cells of the testes**. Its production begins to increase substantially during puberty and remains important throughout adult life. Testosterone enters the circulation and acts on numerous tissues. Some of its effects occur directly, while others result after its conversion into more active androgenic or estrogenic metabolites.

Testosterone contributes to:

- Development and maturation of male reproductive organs
- Maintenance of reproductive tissues
- Development of male secondary sexual characteristics
- Support of normal spermatogenesis
- Maintenance of muscle and bone tissues
- Sexual desire and reproductive behavior
- Various metabolic and blood-forming effects

During puberty, increasing testosterone levels contribute to the enlargement and functional maturation of reproductive organs. They also participate in the development of features such as increased facial and body hair, voice changes, and changes in muscle mass.

Dihydrotestosterone

Some testosterone is converted by the enzyme 5-alpha-reductase into dihydrotestosterone (DHT). DHT has greater androgenic activity than testosterone in certain tissues. It is particularly important during development of the external male genitalia and contributes to the growth and function of the prostate and development of certain androgen-dependent secondary sexual characteristics.

Regulation of Male Sex Hormones

The production of testosterone and the regulation of sperm formation are controlled through the hypothalamic–pituitary–gonadal axis. The process begins in the hypothalamus, which releases gonadotropin-releasing hormone (GnRH) in a pulsatile manner. GnRH acts on the anterior pituitary gland and stimulates the secretion of the gonadotropins:

- **Luteinizing hormone (LH)**
- **Follicle-stimulating hormone (FSH)**

Role of LH

LH acts primarily on the Leydig cells of the testes. Its stimulation promotes testosterone synthesis and secretion. The testosterone produced then acts on reproductive tissues and also participates in maintaining the hormonal environment required for sperm production.

Role of FSH

FSH acts mainly on the **Sertoli cells** within the seminiferous tubules. It supports the cellular processes involved in spermatogenesis and helps maintain the specialized environment required for developing germ cells.

6.1.4 Spermatogenesis

Spermatogenesis is the biological process through which immature male germ cells develop into mature **spermatozoa**. It occurs within the **seminiferous tubules of the testes** and becomes established at puberty. The process involves coordinated cellular division, differentiation, and structural remodeling. It converts diploid precursor cells into highly specialized haploid sperm cells. Sertoli cells provide essential support throughout this process, while testosterone and FSH contribute to its hormonal regulation. Spermatogenesis can be understood through several sequential stages.

Multiplication of Spermatogonia

Spermatogonia are diploid germ cells positioned close to the basement membrane of the seminiferous tubules. They serve as the starting population for sperm production. Through repeated **mitotic divisions**, these cells maintain an adequate supply of germ cells. Some daughter cells remain within the renewing germ-cell population, while others become committed to further differentiation. This arrangement allows sperm production to continue over an extended period after puberty.

Formation of Primary Spermatocytes

Selected spermatogonia differentiate into primary spermatocytes. These cells enlarge and prepare for meiosis. Before entering meiosis, their DNA is replicated. They then undergo meiosis I, a specialized

form of cell division that reduces the chromosome number and introduces genetic variation through processes such as chromosome assortment and recombination.

Formation of Secondary Spermatocytes

Following meiosis I, each primary spermatocyte gives rise to two secondary spermatocytes. These cells are haploid with respect to chromosome number, although each chromosome still consists of two sister chromatids. Secondary spermatocytes have a relatively short existence because they proceed rapidly into the next meiotic division.

Formation of Spermatids

Secondary spermatocytes undergo meiosis II, producing spermatids. The resulting spermatids are haploid cells containing a single set of chromosomes. At this stage, however, they have a relatively simple and immature structure and are not yet capable of performing the functions of mature spermatozoa.

Spermiogenesis

Spermiogenesis is the differentiation stage in which spermatids are transformed into structurally specialized sperm cells without further cell division. Several important changes occur during this stage. The nucleus becomes highly condensed, reducing the volume of the sperm head. The acrosome develops over the anterior portion of the nucleus and contains enzymes important during fertilization.

Mitochondria become concentrated in the middle region, where they are positioned to support the energy requirements of movement. A long **flagellum** develops, producing the characteristic tail of the sperm. The excess cytoplasm is removed as the developing cell becomes streamlined. These modifications allow the final spermatozoon to be small, mobile, and specialized for delivering its genetic material to the female gamete.

Release of Spermatozoa

At the end of spermiogenesis, the mature spermatozoa are released from their association with the Sertoli cells into the lumen of the seminiferous tubules. This process is called **spermiation**.

From there, sperm move through the intratesticular ducts and enter the epididymis. Although structurally mature, sperm undergo additional functional changes during epididymal passage before acquiring full progressive motility and fertilizing capacity.

- **Structure of a Sperm**

A mature spermatozoon is a highly specialized cell designed primarily for movement and delivery of the paternal genetic material. Its streamlined structure minimizes unnecessary cytoplasm and concentrates specialized components in particular regions.

- **Head:** The **head** contains the highly condensed haploid nucleus, which carries the paternal genetic material. Covering much of the anterior portion is the **acrosome**, a specialized cap containing enzymes that participate in interactions with the coverings of the ovum during fertilization.
- **Neck:** The **neck** forms the short connecting region between the head and the middle piece. It contains structural components that establish the connection between the nucleus-containing head and the sperm's locomotory apparatus.
- **Middle Piece:** The middle piece contains numerous mitochondria arranged around the proximal portion of the flagellum. These mitochondria generate ATP required to support the energy demands associated with sperm movement.
- **Tail:** The **tail**, or flagellum, is responsible for sperm motility. Its rhythmic movements propel the sperm through the male reproductive tract and, after ejaculation, through the female reproductive tract.

The coordinated structure of the head, neck, middle piece, and tail allows sperm to perform their principal reproductive function: transporting paternal genetic material toward the ovum for potential fertilization.

6.2 FEMALE REPRODUCTIVE SYSTEM

The female reproductive system is a specialized organ system involved in **gamete production,** hormonal regulation, fertilization, pregnancy, and childbirth. It consists of internal reproductive organs located mainly within the pelvic cavity and external genital structures that protect the openings of the reproductive tract.

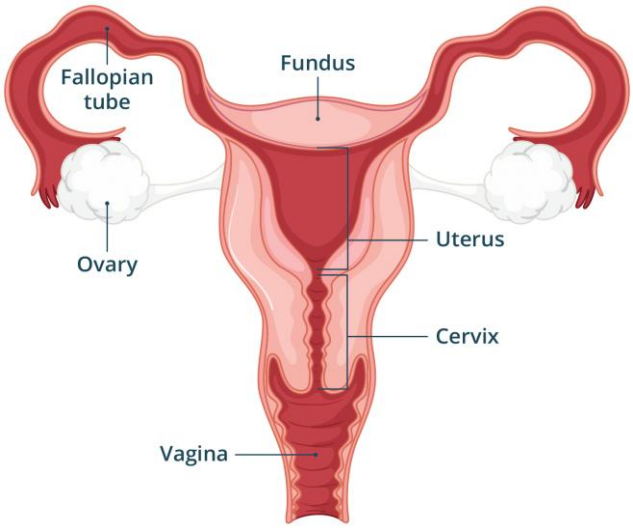


Figure 6.2: Female Reproductive System

Source: (https://www.healthdirect.gov.au/female-reproductive-system)

Unlike the male reproductive system, the female reproductive system is also adapted to support the developing conceptus after fertilization. The reproductive organs undergo regular structural and functional changes under hormonal influence, particularly during the menstrual cycle. These changes prepare the reproductive tract for the possibility of fertilization and the uterus for implantation and pregnancy.

6.2.1 Anatomy of the Female Reproductive System

The principal female reproductive organs include the ovaries, uterine tubes, uterus, cervix, vagina, and external genitalia. These structures form a continuous reproductive pathway and work together to produce and transport the female gamete, facilitate fertilization, and support pregnancy and childbirth.

- **Ovaries**

The **ovaries** are paired female gonads situated within the pelvic cavity. They are small, oval-shaped organs that are supported by ligaments and associated with the surrounding pelvic structures. The ovaries have both reproductive and endocrine functions. Their reproductive role involves the development and release of female gametes, while their endocrine role involves the production of hormones that regulate reproductive tissues and the menstrual cycle.

The outer region of the ovary contains numerous ovarian follicles. Each follicle contains an immature oocyte surrounded by supporting follicular cells. Follicles progress through different stages as they develop, although most undergo degeneration during the reproductive years. As a follicle matures, the oocyte within it also undergoes important developmental changes. Following ovulation, the remaining follicular tissue is transformed into the corpus luteum, an endocrine structure that contributes to hormone production during the latter part of the menstrual cycle.

- **Uterine Tubes**

The uterine tubes, also known as fallopian tubes or oviducts, are paired structures extending from the region of each ovary toward the uterus. They provide a pathway through which the oocyte can travel after ovulation. The uterine tube is not directly attached to the surface of the ovary. Instead, its expanded end lies close to the ovary and helps capture the released oocyte.

The tube is commonly divided into four regions:

- **Infundibulum:** The infundibulum is the funnel-shaped lateral end of the uterine tube. Its margin contains finger-like projections called fimbriae. These projections help guide the ovulated oocyte toward the opening of the tube.
- **Ampulla:** The ampulla is the widest and longest portion of the uterine tube. It is the region in which fertilization most commonly occurs. The relatively large diameter of this region

provides an appropriate environment for the interaction between sperm and the secondary oocyte.

- **Isthmus:** The isthmus is a narrower, more muscular segment situated between the ampulla and the uterine portion. It helps regulate movement of reproductive material toward the uterus.
- **Uterine Part:** The uterine part is the portion that passes through the muscular wall of the uterus and opens into the uterine cavity.

Movement through the uterine tube is assisted by ciliary activity and muscular contractions. Together, these mechanisms help transport the oocyte or, following fertilization, the early developing embryo toward the uterus.

❖ **Uterus**

The **uterus** is a hollow, muscular, pear-shaped organ located within the pelvis between the urinary bladder and rectum. It is highly adaptable and undergoes substantial changes during the menstrual cycle and pregnancy. The uterus is divided anatomically into regions including the **fundus, body, and cervix**. The main body of the uterus provides the environment in which implantation occurs and where the embryo and fetus develop. The uterine wall consists of three major layers:

- **Perimetrium:** The **perimetrium** is the outermost covering of the uterus. It is largely formed by a layer of visceral peritoneum and provides an external protective surface.
- **Myometrium:** The **myometrium** is the thick middle layer composed primarily of smooth muscle. Its muscle fibres enlarge considerably during pregnancy to accommodate the growing fetus. During childbirth, coordinated contractions of the myometrium generate the force necessary to push the fetus through the birth canal. After delivery, continued contraction also assists in reducing bleeding from the placental attachment site.
- **Endometrium:** The **endometrium** is the inner mucosal lining of the uterus. It is highly responsive to ovarian hormones and changes throughout the menstrual cycle. It contains glands and blood vessels that undergo cyclical modifications. During the reproductive cycle, the endometrium becomes progressively prepared for possible implantation. If implantation does not occur, the superficial functional portion is shed during menstruation.

❖ **Cervix**

The **cervix** is the lower, narrower portion of the uterus that extends into the upper part of the vagina. It contains a central canal through which the uterine cavity communicates with the vaginal passage.

The cervix produces **cervical mucus**, whose thickness and composition vary according to hormonal changes during the menstrual cycle. Around ovulation, the mucus generally becomes thinner and

more favorable for sperm passage. At other stages, it becomes relatively thicker and provides a greater barrier to microorganisms and sperm movement.

The cervix also has an important role during pregnancy and childbirth. During pregnancy, it remains relatively closed to help maintain the uterine contents, while during labour it gradually dilates to permit passage of the fetus.

- ❖ **Vagina**

The **vagina** is a fibromuscular canal extending from the cervix to the exterior. Its walls contain elastic and muscular tissues that allow it to accommodate changes in diameter. It serves several reproductive and physiological functions. It provides the passage through which menstrual material leaves the body and receives the penis during sexual intercourse.

During childbirth, the vagina forms the lower portion of the **birth canal**. Its considerable elasticity allows expansion as the fetus passes through. The vaginal environment also contains microorganisms that contribute to its normal physiological conditions and help protect against colonization by certain pathogens.

- ❖ **External Female Genitalia**

The external female genitalia are collectively known as the **vulva**. They surround and protect the external openings of the reproductive and urinary systems. Important structures include the mons pubis, labia majora, labia minora, clitoris, and vestibular structures.

The mons pubis is a fatty prominence located over the pubic region. The labia majora are larger external folds that provide protection, while the labia minora are smaller folds located medially. The clitoris is a highly sensitive erectile structure associated primarily with sexual sensation. The vestibule contains the openings of the urethra and vagina as well as the openings of certain associated glands. Together, these structures provide mechanical protection and contribute to sexual function.

6.2.2 Functions of the Female Reproductive System

The female reproductive system performs multiple functions extending from gamete production to the maintenance of pregnancy.

- o **Production and Maturation of Ova:** The ovaries contain developing oocytes within ovarian follicles. Through follicular development, an oocyte undergoes the changes necessary for potential fertilization.
- o **Secretion of Estrogen and Progesterone:** The ovaries produce hormones that regulate the menstrual cycle and influence reproductive tissues. These hormones also contribute to changes occurring in the uterus, breasts, bones, and other tissues.

- **Reception of Sperm:** During sexual intercourse, the vagina receives semen and provides the initial environment through which sperm enter the female reproductive tract.
- **Transport of the Ovum:** After ovulation, the released oocyte is directed into the uterine tube. Ciliary movements and muscular activity within the tube contribute to its transportation.
- **Provision of the Usual Site for Fertilization:** The uterine tube, particularly its ampullary region, provides the usual location where sperm and the secondary oocyte meet. Fertilization results in the formation of a **zygote**.
- **Preparation of the Uterus for Implantation:** Hormonal changes following ovulation modify the endometrium, increasing its vascularity and secretory activity. These changes create conditions suitable for implantation if fertilization and subsequent embryo development occur.
- **Support of Embryonic and Fetal Development:** Once implantation occurs, the uterus provides physical and nutritional support for the developing conceptus. The uterine environment changes progressively throughout pregnancy to accommodate the increasing size and requirements of the fetus.
- **Formation of the Maternal Part of the Placenta:** During pregnancy, the maternal endometrium undergoes specialized changes and contributes to the maternal component of the **placenta**. The placenta establishes an important interface between maternal and fetal circulations for exchange of gases, nutrients, and metabolic products.
- **Participation in Childbirth:** At the end of pregnancy, coordinated hormonal and mechanical events initiate labour. Contractions of the uterine myometrium and progressive cervical dilation allow the fetus to pass through the birth canal.
- **Provision of the Pathway for Menstrual Discharge:** When pregnancy does not occur, the functional portion of the endometrium is shed. Blood, tissue fragments, and uterine secretions pass through the cervix and vagina to the exterior as menstrual discharge.

6.2.3 Female Sex Hormones

Female reproductive physiology is regulated by several hormones produced by the ovaries, hypothalamus, pituitary gland, and placenta during pregnancy. The principal ovarian sex hormones are **estrogens and progesterone**. Their concentrations vary during the menstrual cycle, producing corresponding changes in the ovaries and reproductive tract.

- **Estrogen**

Estrogens are a group of steroid hormones, with **estradiol** being the predominant estrogen during the reproductive years. They are produced mainly by developing ovarian follicles, although other tissues can contribute smaller amounts.

Estrogen has widespread effects on the female reproductive system and other body tissues.

It contributes to:

- Development and maturation of female reproductive organs
- Development of female secondary sexual characteristics
- Proliferation of the endometrial lining
- Regulation of ovarian and menstrual-cycle events
- Maintenance of reproductive tissues
- Preservation of bone strength

During the follicular phase, increasing estrogen levels stimulate proliferation of the endometrium after menstruation. Estrogen also participates in the hormonal feedback mechanisms that regulate secretion of FSH and LH. Near the middle of the cycle, sufficiently high estrogen concentrations can switch from predominantly negative to **positive feedback** on the hypothalamic–pituitary system. This contributes to the LH surge responsible for ovulation.

❖ **Progesterone**

Progesterone is another major ovarian steroid hormone. Following ovulation, it is produced mainly by the corpus luteum. During pregnancy, progesterone production becomes increasingly associated with the placenta. Progesterone produces important changes in the reproductive tract.

It:

- Converts the proliferative endometrium into a secretory state suitable for implantation
- Supports the uterine lining during pregnancy
- Helps maintain reduced uterine excitability during pregnancy
- Contributes to development and preparation of mammary tissue
- Participates in cyclical regulation of the reproductive system

Progesterone also contributes to the rise in **basal body temperature** that can be observed after ovulation. If pregnancy does not occur, degeneration of the corpus luteum results in a decline in progesterone secretion, contributing to the hormonal changes that precede menstruation.

6.2.4 Physiology of Menstruation

Menstruation is the periodic shedding of the functional layer of the uterine endometrium when pregnancy has not occurred. It represents one component of the larger menstrual cycle, during which coordinated changes occur in the ovaries, uterus, cervix, and reproductive hormones. The cycle is regulated through interactions among the hypothalamus, anterior pituitary gland, and ovaries.

Although a 28-day cycle is commonly used as a reference model, actual cycle length and the duration of individual phases can vary considerably between individuals and from one cycle to another. The cycle can be described through ovarian and uterine phases.

Menstrual Phase

The menstrual phase marks the beginning of the cycle and is counted as day 1. When fertilization and implantation do not occur, the corpus luteum eventually degenerates. As a result, estrogen and progesterone concentrations decrease. The withdrawal of these hormones causes changes in the blood vessels supplying the functional endometrium. Reduced blood flow and tissue breakdown lead to the shedding of the superficial endometrial layer. The resulting blood and tissue are expelled through the cervix and vagina as menstrual flow.

Follicular or Proliferative Phase

During the follicular phase, a group of ovarian follicles begins to develop under the influence of FSH. As follicular development progresses, one follicle usually becomes dominant. The developing follicle produces increasing levels of estrogen. At the uterine level, this corresponds to the proliferative phase. Estrogen stimulates regeneration of the endometrium following menstruation. Endometrial cells multiply, glands develop, and the lining gradually becomes thicker. The increasing estrogen concentration also participates in feedback regulation of pituitary gonadotropins.

Ovulation

Ovulation is the release of a secondary oocyte from a mature ovarian follicle. As the dominant follicle produces increasingly high estrogen levels, the hormonal feedback relationship changes. Sustained high estrogen stimulation produces positive feedback on the hypothalamic–pituitary system. This results in a rapid increase in LH secretion, known as the LH surge. The LH surge causes structural and biochemical changes in the mature follicle, ultimately leading to its rupture and release of the secondary oocyte. The released oocyte is then captured by the fimbriae of the uterine tube and begins its passage through the reproductive tract.

Luteal or Secretory Phase

Following ovulation, the ruptured follicle is transformed into the **corpus luteum**. This temporary endocrine structure produces substantial amounts of progesterone as well as estrogen. The corresponding uterine stage is called the **secretory phase**. Under progesterone influence, the endometrial glands become more active and the tissue becomes increasingly suitable for possible implantation. The endometrial blood supply also becomes more developed, supporting the metabolic requirements of a potential early embryo. If fertilization and implantation do not occur, the corpus luteum eventually loses its functional activity. Estrogen and progesterone concentrations

subsequently decline, causing the endometrium to lose hormonal support. This initiates another cycle of tissue breakdown and leads to the onset of menstruation.

6.2.5 Oogenesis

Oogenesis is the process through which female germ cells develop into mature female gametes. It differs significantly from spermatogenesis in its timing, pattern of cell division, and number of functional gametes produced. Oogenesis begins before birth. During fetal development, primordial germ cells differentiate into oogonia, which multiply through mitotic divisions.

Many oogonia subsequently enter meiosis and become primary oocytes. These primary oocytes begin meiosis I but do not complete it immediately. Instead, they remain arrested in a prolonged stage of meiotic development. At birth, the ovaries therefore contain a finite population of primary oocytes. During childhood, these cells remain largely inactive, while many undergo natural degeneration.

- ***Follicular Development After Puberty***

With the onset of puberty, cyclic reproductive activity begins. During each menstrual cycle, FSH promotes the growth and development of a group of ovarian follicles. As follicles develop, the associated primary oocytes continue their maturation. Usually, one dominant follicle completes the necessary changes to become capable of ovulation.

Just before ovulation, the primary oocyte completes meiosis I, producing a large secondary oocyte and a much smaller first polar body. The unequal distribution of cytoplasm ensures that most of the cellular resources remain within the developing female gamete.

- ***Ovulation***

The secondary oocyte is released from the ovary during ovulation. At this point, it has begun **meiosis II**, but the division does not normally reach completion unless fertilization occurs. The secondary oocyte enters the uterine tube, where it may encounter sperm.

6.3 HUMAN REPRODUCTION

Human reproduction is a coordinated physiological process involving the formation of male and female gametes, their union during fertilization, and the subsequent development of the new individual. It includes several sequential stages such as fertilization, implantation, embryonic and fetal development, pregnancy, and childbirth. These events are regulated by complex interactions between the reproductive organs, hormones, and developing conceptus.

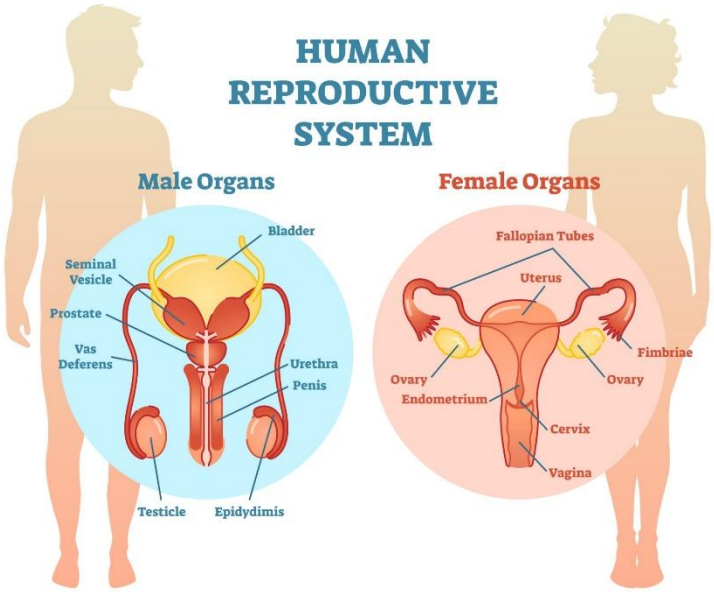


Figure 6.3: Human Reproduction

Source: (https://www.biologyonline.com/tutorials/human-reproduction)

6.3.1 Fertilization

Fertilization is the process in which a sperm fuses with a secondary oocyte to form a zygote, and it usually takes place in the ampulla of the uterine tube. Following ejaculation, sperm travel through the female reproductive tract, although only a small number ultimately reach the uterine tube. Before they can fertilize the oocyte, sperm undergo capacitation, a series of physiological changes that increase their motility and prepare them for interaction with the oocyte. The sperm then passes through the protective coverings surrounding the oocyte with the assistance of enzymes released from its acrosome. Fusion of the sperm and oocyte membranes permits entry of the paternal genetic material. At the same time, changes occur in the oocyte membrane and surrounding structures that prevent penetration by additional sperm. The genetic material from both gametes subsequently combines, restoring the diploid chromosome number and producing the zygote. The zygote begins rapid mitotic divisions known as **cleavage**, progressing through stages that ultimately produce a blastocyst capable of implantation.

6.3.2 Pregnancy

Pregnancy is the period during which the developing embryo and fetus grow within the uterus. It lasts approximately 40 weeks when calculated from the first day of the last menstrual period. Following fertilization, the early conceptus travels through the uterine tube and reaches the uterus, where the blastocyst attaches to and becomes embedded within the endometrium in a process called implantation. During the embryonic period, the basic structures and major organ systems develop,

making this stage particularly sensitive to harmful environmental factors. From approximately the ninth week after fertilization, the developing organism is generally called a fetus, and the remainder of pregnancy is characterized mainly by growth, maturation, and functional development of organs. The placenta develops between maternal and fetal tissues and serves as an important exchange and endocrine organ. It permits the transfer of oxygen and nutrients to the fetus and facilitates removal of carbon dioxide and metabolic wastes. It also produces hormones including hCG, progesterone, estrogens, and human placental lactogen, which help maintain pregnancy and support maternal physiological adaptations.

6.3.3 Parturition

Parturition refers to the physiological process of childbirth, in which coordinated uterine contractions lead to cervical dilation and delivery of the fetus, followed by expulsion of the placenta. It occurs in three major stages. The first stage begins with regular uterine contractions and ends when the cervix is fully dilated; during this stage, the cervix gradually becomes thinner and wider. The second stage begins after complete dilation and involves movement of the fetus through the birth canal until the baby is delivered. The third stage follows delivery of the baby and involves separation and expulsion of the placenta and fetal membranes. Labour is regulated by hormonal and mechanical mechanisms.

6.4 SEXUALLY TRANSMITTED DISEASES

Sexually transmitted diseases (STDs), also known as sexually transmitted infections (STIs), are infections that are primarily transmitted through sexual contact with an infected person. They may be caused by bacteria, viruses, parasites, or other microorganisms and can affect the reproductive and urinary systems as well as other parts of the body. Some infections produce noticeable symptoms such as discharge, ulcers, pain, or rashes, while others may remain asymptomatic, allowing transmission without the infected person being aware of it. Prevention includes safer sexual practices, appropriate vaccination, regular testing, early diagnosis and treatment, and communication with sexual partners.

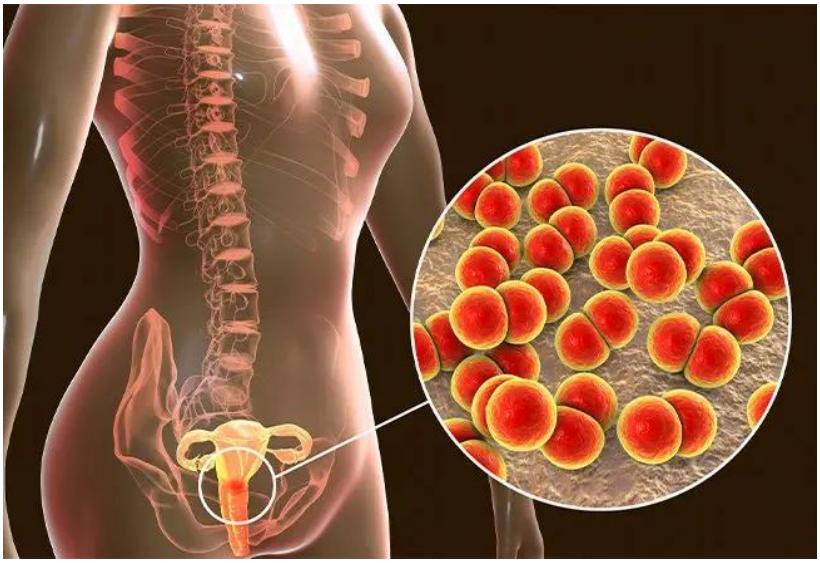


Figure 6.4: Sexually Transmitted Diseases (STDs)

Source:(https://www.medicinenet.com/sexually_transmitted_diseases_stds_in_women/article.htm)

6.4.1 AIDS

Acquired Immunodeficiency Syndrome (AIDS) is the advanced stage of infection caused by the human immunodeficiency virus (HIV). HIV primarily attacks CD4 T lymphocytes, which are important components of the immune system. As the infection progresses without effective treatment, destruction and dysfunction of these cells weaken immune defences and increase susceptibility to opportunistic infections and certain cancers. HIV may initially cause a flu-like illness or produce no symptoms, while advanced infection may be associated with persistent fever, unexplained weight loss, chronic diarrhoea, enlarged lymph nodes, and recurrent or unusual infections. HIV is transmitted mainly through unprotected sexual exposure, infected blood, contaminated needles or injection equipment, and from mother to child during pregnancy, childbirth, or breastfeeding. It is not transmitted through ordinary casual contact such as hugging, handshaking, sharing food, or being near an infected person. Prevention includes safer sexual practices, screening of blood, avoiding shared injection equipment, and appropriate preventive measures. Antiretroviral therapy (ART) suppresses viral replication, protects immune function, and enables many people with HIV to live long and healthy lives.

6.4.2 Syphilis

Syphilis is a bacterial sexually transmitted infection caused by Treponema pallidum. It is mainly transmitted through direct contact with an infectious lesion during sexual activity and can also pass from a pregnant person to the fetus, causing congenital syphilis. The infection progresses through characteristic stages. Primary syphilis commonly produces a painless ulcer called a chancre at the site of infection, which may disappear without treatment even though the infection remains.

Secondary syphilis may cause a widespread rash, including the palms and soles, together with fever and enlarged lymph nodes. The infection can then enter a latent stage, during which symptoms are absent. If untreated for a long period, some individuals may develop tertiary syphilis, which can damage the cardiovascular system, nervous system, and other organs. Diagnosis involves clinical evaluation and laboratory testing, and syphilis can be effectively treated with appropriate antibiotics.

6.4.3 Gonorrhea

Gonorrhea is a bacterial STI caused by Neisseria gonorrhoeae. It commonly affects the mucous membranes of the reproductive and urinary tracts but may also involve the rectum, throat, and eyes. Transmission primarily occurs through sexual contact, and an infected mother can transmit the infection to a newborn during childbirth. Many infected individuals may have few or no symptoms; when present, manifestations can include painful urination, genital discharge, pelvic discomfort, abnormal bleeding, or rectal symptoms. Untreated infection can spread into the upper reproductive tract and cause pelvic inflammatory disease, potentially resulting in infertility or ectopic pregnancy. In males, infection may cause inflammation of reproductive structures, while spread through the bloodstream can produce disseminated gonococcal infection. Prevention involves safer sexual practices, appropriate testing, and treatment of infected individuals and their partners. Gonorrhea is treated with appropriate antibiotics, although antimicrobial resistance has become an important challenge in its management.

6.5 CANCER

Cancer is a group of diseases in which abnormal cells lose the normal mechanisms that regulate their growth, division, differentiation, and survival. These cells may continue multiplying despite signals that normally stop cell division or cause damaged cells to undergo programmed cell death. Cancer can arise in almost any tissue and may be classified according to its tissue of origin, including **carcinomas, sarcomas, leukemias, lymphomas, and melanomas**. Malignant cells can invade nearby tissues and, in advanced disease, spread to distant organs through the blood or lymphatic system.

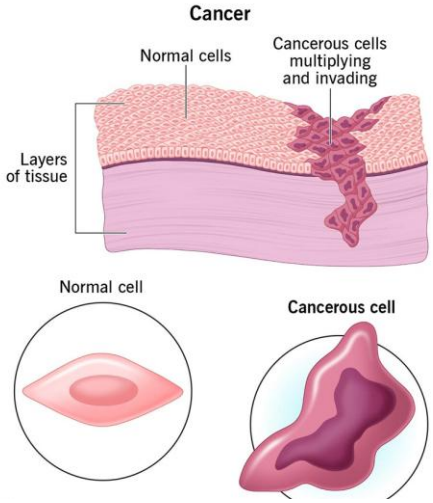


Figure 6.5: Cancer

Source: (https://my.clevelandclinic.org/health/diseases/12194-cancer)

6.6.1 Etiology of Cancer

The etiology of cancer involves multiple interacting factors rather than one specific cause. Genetic abnormalities affecting oncogenes, tumour-suppressor genes, and DNA-repair genes can disturb normal cellular regulation, while inherited mutations may increase susceptibility to particular cancers. Important environmental and lifestyle factors include tobacco use, excessive alcohol consumption, exposure to ionizing or ultraviolet radiation, certain chemical carcinogens, unhealthy dietary patterns, and obesity. Some infections can also contribute to cancer development, including HPV, hepatitis B and C viruses, Epstein–Barr virus, and Helicobacter pylori. Hormonal influences, increasing age, and impaired immune function can further modify cancer risk. These factors may cause or promote DNA damage and other cellular changes that gradually increase the likelihood of malignant transformation.

6.6.2 Pathogenesis of Cancer

The development of cancer, known as carcinogenesis, is a multistep process involving progressive genetic and epigenetic alterations. During initiation, cellular DNA becomes damaged and the abnormal change may persist if it is not adequately repaired. During promotion, initiated cells are stimulated to survive and multiply, while progression involves the accumulation of additional abnormalities that make the tumour increasingly aggressive. Cancer cells may acquire the ability to proliferate continuously, resist programmed cell death, evade immune responses, and stimulate angiogenesis, allowing the tumour to obtain oxygen and nutrients. As the tumour progresses, malignant cells can break through surrounding tissues and enter blood or lymphatic vessels. Through metastasis, they may travel to distant organs and establish secondary tumours.

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